# Structure-Function Studies of a Purple Acid Phytase

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## Abstract

The enzymatic cleavage of phosphate monoesters of *myo*-inositol hexakisphosphate (InsP<sub>6</sub>) or phytate is the property of a group of enzymes collectively known as phytases. These enzymes adopt a variety of protein folds and utilise a number of different reaction mechanisms and may be classified accordingly. Among these, the purple acid phytases (PAPhy), a subclass of the purple acid phosphatases (PAP), are the least well characterised. The aim of this thesis is a biochemical and structural characterisation of cereal PAPhy with the additional purpose of the identification of structural features that distinguish PAPhy from PAP.

In this project, the partial enzymatic deglycosylation of a recombinant PAPhy from wheat yielded high quality crystals that allowed the solution of the high-resolution X-ray crystallographic structure of the first PAPhy, with inorganic phosphate bound in different poses and in complex with the inhibitor myo-inositol hexakissulfate. Molecular dynamics simulations of the enzyme-substrate complex allowed the identification of key protein-substrate interactions, leading to the proposal of six phytate specificity pockets for the wheat PAPhy isoform b2 (TaPAPhy\_b2). A characterisation of TaPAPhy\_b2 allowed the estimation of its kinetic parameters, revealed optimum phytase activity at pH 5.5 and 37°C, with denaturation and subsequent inactivation over 50°C, and the determination of the D-4/6-phosphate as preferred initiation site of InsP<sub>6</sub> hydrolysis. A conservation of the pathway of phytate hydrolysis identified in TaPAPhy\_b2 was observed in other cereal PAPhy, while the soybean PAPhy displayed higher positional promiscuity. Structure-function relationships of TaPAPhy\_b2 were elucidated by site-directed mutagenesis and mutant characterisation alongside the wild type enzyme. Two amino acid residues critical for phytase activity were identified, His229 and Lys410, while a third, Lys348, was shown to influence substrate affinity more subtly.

The work described in this thesis provides novel insights into the structure and phytase activity of the purple acid phytases.

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# Abbreviations

μ-ОН	μ-Hydroxo bridge EC		Enzyme Commission			
2D	Two-dimensional ED		Ethylenediaminetetraacetic acid			
3D	Three-dimensional	Endo H/F	<b>1</b> End	Endoglycosidase H/F1		
6xHis	Poly-histidine tag ER		Endoplasmic Reticulum			
ADP	Adenosine diphosphate	GAP	Glyceraldehyde-3-phosphate			
AMP	Adenosine monophosphate		dehydrogenase			
ΑΟΧ	Alcohol oxidase	Gen		Gentamycin		
АТВ	Automated Topology Builder	GF	Gel Filtration			
ΑΤΡ	Adenosine triphosphate	GMP	Gua	nosine monophosphate		
B factor	Temperature factor	GmPAPhy	/_b	Soybean ( <i>Glycine max</i> ) PAPhy isoform b		
В-В	DSC buffer-buffer run	GST	Glut	tathione S-Transferase tag		
BLAST	Basic Local Alignment Search Tool	GTP	Gua	Guanosine triphosphate		
BLASTP	Protein BLAST	НАР	Hist	idine Acid Phosphatase		
B-P	DSC buffer-protein run	HAPhy	Hist	idine Acid Phytase		
BPP	β-Propeller Phosphatase	HEPES	4-(2-hydroxyethyl)-1- piperazineethanesulfonic acid			
BPPhy	β-Propeller Phytase	HMW	Higł	n Molecular Weight (PAPs)		
CAI	Codon Adaptation Index	HPLC	Higł	n Performance Liquid		
Cam	Chloramphenicol		Chro	omatography		
CC <sub>1/2</sub>	Correlation coefficient of random half-dataset	HvPAPhy_	_a	Barley ( <i>Hordeum vulgare</i> ) PAPhy isoform a		
cDNA	Complementary DNA	1	Inte	nsity of reflections		
СР	Cysteine Phosphatase	I/σ(I)	Sign	nal-to-noise ratio		
Ср	Molar heat capacity	IbPAP1		eet potato ( <i>Ipomoea</i>		
CPhy	Cysteine Phytase			atas) PAP1 phosphatase		
cv	Column Volumes	InsP		sitol phosphate		
DLS	Diamond Light Source	InsP <sub>1</sub>		p-Inositol monophosphate		
DMSO	Dimethyl sulfoxide	InsP <sub>2</sub>	,	p-Inositol bisphosphate		
DNA	Deoxyribonucleic acid	InsP <sub>3</sub>				
DSC	Differential Scanning Calorimetry	InsP₄ InsP₅	<i>myo</i> -Inositol tetrakisphosphate <i>myo</i> -Inositol pentakisphosphate			
DTT	Dithiothreitol	InsP <sub>6</sub>		p-Inositol hexakisphosphate		

InsP <sub>7</sub>	nsP <sub>7</sub> Diphosphoinositol pentakisphosphate		Nicotinamide adenine dinucleotide phosphate				
InsP <sub>8</sub>	Bis-diphosphoinositol NA		N-a	N-acetylglucosamine			
InsS <sub>6</sub>	myo-Inositol hexakissulfate	NCBI	National Center for Biotechnology Information				
IPTG	Isopropyl	Ni-NTA	Nic	kel-nitrilotriacetic acid			
IUBMB	β-D-1-thiogalactopyranoside	NMWL	Nominal Molecular Weight Limit				
IOBIVIB	International Union of Biochemistry and Molecular	np	Not	provided			
	Biology	<b>OD</b> <sub>600</sub>		ical density measured at 600 nm			
IUPAC	International Union of Pure and Applied Chemistry	ORF		A = 600 nm Open Reading Frame			
Kan	Kanamycin	OsPAPhy_		Rice ( <i>Oryza sativa</i> ) PAPhy			
<b>k</b> <sub>cat</sub>	Enzymatic turnover number		-	isoform b			
K <sub>m</sub>	Michaelis constant	Ρ	Pho	sphorus			
LB	Lysogeny Broth	P1-P6		sphate groups in carbons of InsP <sub>6</sub>			
LIC	Ligation-Independent Cloning	ΡΑΡ		ple Acid Phosphatase			
LMW	Low Molecular Weight (PAPs)	PAPhy		Purple Acid Phytase			
MD	Molecular Dynamics	, PCR	Polymerase Chain Reaction				
MES	2-(N-Morpholino) ethanesulfonic acid	PD		ton Donor			
MGPA	Mature Grain Phytase Activity	PDB	Pro	tein Data Bank			
МІ	Binding site for Fe <sup>3+</sup> in PAPs	PEG	Poly	yethylene glycol			
МІІ	Binding site for Fe <sup>2+</sup> , Zn <sup>2+</sup> or	Pi	Ino	rganic phosphate			
	Mn <sup>2+</sup> in PAPs	PNGase F	Рер	tide N-glycosidase F			
MINPP	Multiple Inositol Polyphosphate Phosphatase	pNP	•	<i>a</i> -Nitrophenyl			
MPE	Calcineurin-like	pNPP	•	a-Nitrophenyl phosphate			
	Metallophosphoesterase	pNPS	•	a-Nitrophenyl sulfate			
mRNA	Messenger RNA	PP		osphate Pocket			
MSA	Multiple Sequence Alignment	PP-InsP		sitol pyrophosphates or nosphoinositol			
MUSCLE	MUltiple Sequence Comparison by Log-Expectation algorithm		•	yphosphates			
MW	Molecular Weight	РТР	Pro	tein Tyrosine Phosphatase			
MWCO	Molecular Weight Cut-Off	PTPhy	Pro	tein Tyrosine Phytase			
n/a	Not applicable	PvPAP1		l kidney bean ( <i>Phaseolus</i> garis) PAP1 phosphatase			

	<b>R</b> <sub>free</sub>	Free	e residual factor	TRAPs	Tart	rate-Resistant Acid
	R <sub>merge</sub>	Resi	dual factor on data		Pho	sphatases
	-	redu	uction	TRX	Thio	redoxin fusion protein
	RMSD	Roo	t Mean Square Deviation	U	Unit	S
	RMSF	Roo	t Mean Square Fluctuations	UV	Ultra	aviolet
	RNA	Ribo	onucleic acid	V <sub>max</sub>	Max	imum rate of catalysis
	ROS	Read	ctive Oxygen Species	wт	Wilc	і Туре
	Rt	Rete	ention time	YPD		st extract Peptone Dextrose
	R <sub>work</sub>	Resi	dual factor			lium
	S1-S6		ate groups in carbons 1-6 of	Zeo	Zeo	
		InsS		ZmPAPhy	_b	Maize ( <i>Zea mays</i> ) PAPhy isoform b
	SAD		le-wavelength Anomalous action			
	S <sub>A</sub> -S <sub>F</sub>		APhy_b2 substrate :ificity pockets			
	pol		um dodecyl sulfate acrylamide gel trophoresis			
			er Optimal broth with bolite repression			
	SP	Sign	al Peptide			
	SPC	Simp	ole Point Charge			
	Spec	Spec	ctinomycin			
	SSS	Subs	strate Specificity Site			
	Str	Stre	ptomycin			
	т	Tem	perature			
	TaPAPhy_a1		Wheat ( <i>Triticum aestivum</i> ) PAPhy isoform a1			
TaPAPhy_b1		b1	Wheat ( <i>Triticum aestivum</i> ) PAPhy isoform b1			
	TaPAPhy_b		Wheat ( <i>Triticum aestivum</i> ) PAPhy isoform b2			
	TaPAPhy_	b2d	Partially deglycosylated TaPAPhy_b2			
	Tet	Tetr	acycline			
	T <sub>m</sub>	Mel	ting temperature			

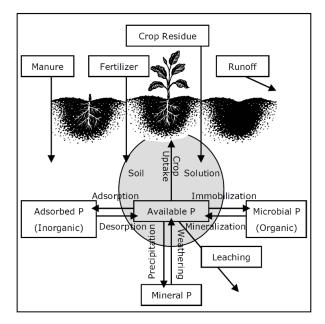
## Chapter 1. Introduction

### **1.1.** The phosphorus problem

Phosphorus is one of the essential elements required for the growth of all living organisms. It is a key component of biomolecules such as ATP and both DNA and RNA, therefore responsible for cell energy transfer and storage of genetic material, respectively. It is also present in cell membranes as phospholipids, as well as critical in bone and teeth formation and maintenance in vertebrate animals (Ruttenberg, 2014).

Autotrophs are the base of the food chain. Crops are mainly grown for direct human consumption and to produce feed for livestock. As autotroph organisms, plants need to obtain phosphorus and other nutrients from the soil to use in their metabolism. Plant phosphorus uptake depends on phosphorus being present in the soil in a form that the plants can use. Phosphorus in soil is present mainly in four forms: inorganic P, organic P, adsorbed P and primary mineral P. Of these forms, only inorganic P is available to plants. There are three general processes that transform soil phosphorus from one form to the other, described in Figure 1. The processes that increase plant available phosphorus are weathering, mineralization and desorption, whereas precipitation, immobilization and adsorption make phosphorus unavailable to plants (Hyland *et al.*, 2005).

Fertilizers containing phosphorus are applied to crops to ensure plants have a source of this mineral available. However, fertilizers are often applied in excess, leading to a waste of phosphorus and other nutrients that end up getting carried over to aquatic ecosystems (Runoff in Figure 1), affecting the quality of the water. Phosphorus is also lost in unrecycled crop, animal and human waste, increasing the problem of eutrophication of natural waters (Childers *et al.*, 2011). Eutrophication occurs when the oxygen is depleted in water bodies as a result of an algal bloom triggered by the increase of nutrients in the water. When the algae die, bacteria use all the oxygen in the water to decompose them (Hyland *et al.*, 2005).



#### Figure 1. Phosphorus cycle

Weathering is the process by which P-rich minerals present in the soil are eroded and very slowly become available to plants. Precipitation consists of the non-reversible reaction of inorganic phosphorus with other elements dissolved in the soil (such as iron or calcium) forming phosphate minerals and making phosphorus unavailable to plants. Mineralization is the transformation of organic P to orthophosphates ( $H_2PO_4^-$  or  $HPO_4^{2-}$ , available forms of phosphorus) by microbial organisms in the soil. Immobilization is the process by which microorganisms turn orthophosphates into organic P, making them unavailable to plants again until the death of those microorganisms. Adsorption occurs when available phosphorus chemically binds soil particles and desorption is the slow release of this bound phosphorus back to solution in the soil. Runoff is the water flow over the soil that carries over the phosphorus (adsorbed to the soil or dissolved in the manure and fertilizers applied) to water bodies. Leaching is a vertical water flow that also makes phosphorus unavailable to plants (Hyland *et al.*, 2005).

Phosphorus is therefore indispensable to produce food, but it is a limited resource. Phosphorus is obtained from mining rocks with high content in phosphate minerals (rock-phosphate) and exploiting aquatic sediments. The demand of phosphorus has increased so much that these sources are effectively non-renewable: the phosphate cycle is too slow (time scales of thousand to millions of years) compared with its accelerated extraction. Sustainable strategies to close the human P cycle are needed to avoid phosphorus depletion, seeming the most effective those that seek the reduction of phosphorus loses and the recycling of agricultural, farming and human waste (Childers *et al.*, 2011).

## **1.2.** Inositol phosphates

Inositols are cyclohexanes with an alcohol group in each carbon. There are nine possible stereoisomers (Figure 2), all of them known to occur in nature apart from

*cis*-inositol. Inositol phosphates are esters of inositol with various phosphorylation states. They are organic phosphorus compounds present extensively in the natural environment, with *myo*-inositol phosphate being the most common isomer. The *myo* isomer is characterised for having the substituent group attached to carbon two in axial position, while all the others are equatorial (Turner *et al.*, 2002; Thomas, Mills and Potter, 2016).

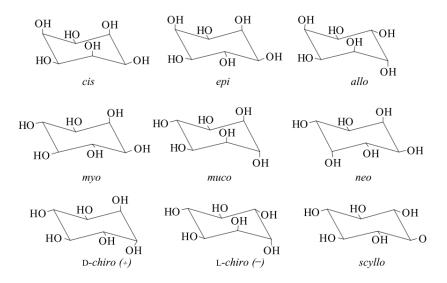


Figure 2. Stereoisomers of unsubstituted inositols

Chair representation of the nine possible inositol stereoisomers. All the stereoisomers except *cis*-inositol can be found in nature (Turner *et al.*, 2002).

Inositol phosphates are named with the prefixes mono, bis, tris, tetrakis, pentakis and hexakis depending on how many alcohol groups of the inositol ring are substituted with phosphate. They are synthesised by plants and they accumulate in the soil, from where they can potentially run off to aquatic ecosystems and contribute to eutrophication (Turner *et al.*, 2002).

#### 1.2.1. myo-Inositol hexakisphosphate

The most common inositol phosphate by far is *myo*-inositol hexakisphosphate (InsP<sub>6</sub>), also known as phytic acid (in its free acid form) and phytate (for the salts of phytic acid). The chemical structure of *myo*-inositol hexakisphosphate is shown in Figure 3. Phytate is the principal form of phosphorus and inositol storage in plant seeds, constituting the 60–90% of the total phosphorus content in plants (Rao *et al.*, 2009). InsP<sub>6</sub> is a strong chelator of cations. It binds metal ions, such as Ca<sup>2+</sup>, Mg<sup>2+</sup>, Zn<sup>2+</sup>, Mn<sup>2+</sup>,

Cu<sup>2+</sup> or Fe<sup>2+</sup>, and forms complexes with positively charged proteins. During seed germination, free phosphates and the chelated metal ions are released from phytate through enzymatic hydrolysis by phytase enzymes (Rao *et al.*, 2009; Yao *et al.*, 2012). As well as storage functions, phytate is believed to play a role in the cellular response to abscisic acid in plants and *myo*-inositol is a cell wall precursor (Irvine and Schell, 2001). InsP<sub>6</sub> is also ubiquitous in animal cells (Irvine and Schell, 2001). Various functions have been reported for InsP<sub>6</sub> through the activation or inhibition of intracellular proteins: it seems to act as a co-factor in DNA repair (Hanakahi *et al.*, 2000; Hanakahi, 2011), it is involved in mRNA export from the nucleus to the cytosol (York *et al.*, 1999), and has a role in secretion or vesicular recycling (Irvine and Schell, 2001). Aside its physiological roles, phytate is known to be an antinutrient due to its strong binding affinity to important minerals (Schlemmer *et al.*, 2009). Medical properties as antioxidant (Graf, Empson and Eaton, 1987) and anticancer (Shamsuddin, 1995; Bizzarri *et al.*, 2016) agents have also been reported for InsP<sub>6</sub>.

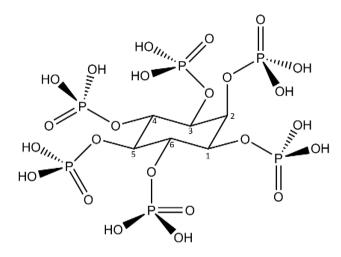


Figure 3. Chemical structure of myo-inositol hexakisphosphate

The structure of *myo*-inositol hexakisphosphate is shown in the pentaequatorial (1a5e) conformation. A conformational change to a pentaaxial (5a1e) state has been observed for *myo*-inositol hexakisphosphate under certain circumstances. However, it is unclear at which pH values each of the two possible conformations appear (Turner *et al.*, 2002; Veiga *et al.*, 2014). Image created with ChemDraw Prime version 15.0 (PerkinElmer Informatics).

#### **1.2.2.** Other inositol phosphates

Inositol-1,4,5-trisphosphate was the first inositol phosphate identified as second messenger in eukaryotic cells. It controls  $Ca^{2+}$  signalling through the ion channel of the Ins(1,4,5)P<sub>3</sub> receptor, regulating several essential cellular processes (Streb *et al.*, 1983).

Ins(1,2,6)P<sub>3</sub> is a non-naturally occurring inositol triphosphate resulting from the partial degradation of  $InsP_6$  by phytases. It is produced commercially for its analgesic and antiinflammatory properties (Bell and McDermott, 1998).

A number of inositol tetrakisphosphates have also been reported to participate in cell signalling.  $Ins(1,3,4,5)P_4$  is a product of the metabolism of  $Ins(1,4,5)P_3$  and they participate together in the modulation of cellular calcium ion levels (Irvine *et al.*, 1984; Batty, Nahorski and Irvine, 1985).  $Ins(3,4,5,6)P_4$  seems to be an inhibitor of calciumactivated chloride channels in epithelial cells (Kachintorn *et al.*, 1993).  $Ins(1,4,5,6)P_4$  is a coregulator of histone deacetylases, thus it is involved in chromatin organization and gene expression (Watson *et al.*, 2012; Millard *et al.*, 2013).

The second most abundant inositol phosphate in mammalian cells after  $InsP_6$  is  $Ins(1,3,4,5,6)P_5$ . This inositol pentakisphosphate is believed to be involved in the modulation of haemoglobin interactions in some erythrocytes (Coates, 1975) and it has also been attributed anticancer properties (Piccolo *et al.*, 2004).

Inositol pentakis and hexakisphosphates can be phosphorylated further to form inositol pyrophosphates or diphosphoinositol polyphosphates (PP-InsP). InsP<sub>7</sub> and InsP<sub>8</sub> have been related to vesicular trafficking, apoptosis, DNA repair, telomere length, stress responses, neurological function, and immune responses (Thomas, Mills and Potter, 2016).

All the inositol phosphates described above are *myo* isomers. Inositol stereoisomers other than *myo* are far less studied and their suggested roles are very diverse, with no wide conclusions. Different isomers seem to have different effects in different systems (Thomas, Mills and Potter, 2016).

### 1.3. Phytases

Phosphatases are enzymes that catalyse the hydrolysis of a phosphoric acid monoester into a free phosphate ion and an alcohol. Phosphatases have varying substrate specificity. While some only act on a particular substrate, others can cleave phosphate groups from a wide range of organic phosphates. Phytases or *myo*-inositol hexakisphosphate phosphohydrolases are phosphatases that can initiate the sequential dephosphorylation of phytate or *myo*-inositol hexakisphosphate, releasing inorganic phosphates and lower *myo*-inositol phosphates (Mullaney and Ullah, 2003). The reaction intermediates of phytate hydrolysis vary with different phytases and they serve as substrates for further hydrolysis (Konietzny and Greiner, 2002; Li *et al.*, 2010). Phytases can also liberate phosphate groups from various other phosphorylated compounds, with only a few phytases described as highly specific for phytate. In addition to phytate, phytases are usually able to hydrolyse substrates such as adenosine mono-, di- and triphosphate (AMP, ADP and ATP, respectively), guanosine mono- and triphosphate (GMP and GTP, respectively), nicotinamide adenine dinucleotide phosphate (NADP), *para*-nitrophenyl phosphate (pNPP), phenyl phosphate, naphthyl phosphates, fructose 1,6-diphosphate, fructose and glucose 6-phosphate, glucose 1-phosphate, galactose 1-phosphate (Konietzny and Greiner, 2002).

Phytases have been isolated from diverse sources, as well as expressed in a wide range of hosts and purified through a variety of biochemical methods. The biophysical and biochemical properties of phytases are dependent on the source from which they are extracted and/or the expression system in which they are produced (Rao *et al.*, 2009). The molecular weight of phytase enzymes is highly variable, ranging from approximately 35 to 700 kDa (Li *et al.*, 2010). Eukaryotic phytases have a higher molecular weight than bacterial ones due to glycosylation (Rao *et al.*, 2009). Phytases are usually active in the pH range of 4.5-6.0 and at temperatures of 45-60°C, with microbial enzymes often being more stable to pH and temperature changes than plant phytases (Konietzny and Greiner, 2002; Li *et al.*, 2010).

The activity of most phytases is affected by the presence of metal ions. However, it is not clear if the inhibitory effect of specific metal ions in some phytases is caused by binding of the metal to the enzyme or the decrease in substrate solubility when certain metal ion-phytate complexes are formed. Fluoride has been found to be a strong competitive inhibitor of phytases (Konietzny and Greiner, 2002). The phytate hydrolysis product orthophosphate has also been reported as a competitive inhibitor of phytase enzymes. Other suggested inhibitors of these phytases include molybdate, tungstate

18

and vanadate, which form complexes that resemble the geometry of the transition state in the catalytic mechanism of these enzymes (Zhang *et al.*, 1997).

#### **1.3.1.** Phytase sources and physiological roles

Phytases were first discovered in fungi and they have been reported in a large variety of microorganisms, plants and animals (Dvořáková, 1998; Konietzny and Greiner, 2002; Vohra and Satyanarayana, 2003). The wide spread of these enzymes in all kingdoms of life is not surprising due to phytate having such an important presence in nature, as described in **section 1.2.1.** (Mullaney and Ullah, 2007).

Microbial phytases have been isolated from fungi, yeast, bacteria and protozoa (Lei *et al.*, 2007). Most microorganisms produce only intracellular phytases. Production of extracellular phytases has been observed in filamentous fungi, yeast and some bacteria. (Konietzny and Greiner, 2002). Most microbial phytases are synthesised in the stationary growth phase under nutrient limited conditions. This way, phytases provide microorganisms with the ability to use phytate as a source of carbon and phosphate (Konietzny and Greiner, 2004).

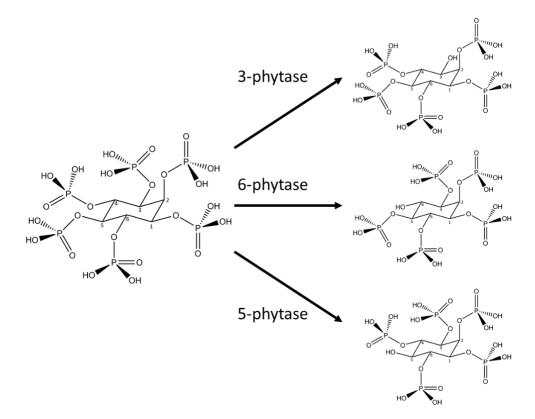
Plant phytases occur mostly in grains, seeds and pollen of higher plants. They are responsible for phytate degradation during seed germination to liberate phosphate, minerals and *myo*-inositol for plant growth and development. Low phytase activity has also been observed in roots. The presence of phytase in plant root has been associated with increasing the phosphate availability in the soil for plant uptake, although soil microorganisms producing extracellular phytases are more significant in this role. Cereals exhibit a higher phytase activity than legumes and oilseeds (Konietzny and Greiner, 2002). Other functions of phytases in plants are believed to be the production of antioxidants and secondary messengers (Shears, 1998).

Animal phytases were first detected in calf blood and liver. Following this, they have been observed in blood of several vertebrates, and secreted by the mucosa of the small intestine of some mammals. The investigation of animal phytases is more limited than in plants or microorganisms. They are believed to maintain the supply of InsP<sub>6</sub> and lower InsP derivatives critical in cell signalling pathways. Animal phytases do not seem

to have a significant role in phytate digestion. Phytate digestion in animals is mainly attributed to the microbial flora of the intestine and dietary phytases (Konietzny and Greiner, 2002; Vohra and Satyanarayana, 2003).

#### **1.3.2.** Classification of phytases based on initiation site of hydrolysis

Phytase enzymes can be classified according to different criteria. The IUPAC-IUBMB (International Union of Pure and Applied Chemistry and the International Union of Biochemistry and Molecular Biology) divides phytases in three groups based on the initial dephosphorylation site of the  $InsP_6$  inositol ring (Figure 4): (1) 3-phytases (EC 3.1.3.8), which initiate hydrolysis at the D-3-phosphate (anticlockwise nomenclature) or the L-1-phosphate (clockwise nomenclature); (2) 6-phytases (EC 3.1.3.26, 4-phytases under current naming convention), which start with phosphate in position D-4 or L-6; and (3) 5-phytases (EC 3.1.3.72), which first hydrolyse the phosphate group in carbon five (Brinch-Pedersen, Sørensen and Holm, 2002; Bohn, Meyer and Rasmussen, 2008).



#### Figure 4. Classes of phytases based on initiation site of phytate hydrolysis

The product of 3-phytases is L-1-OH InsP<sub>5</sub> or D-3-OH InsP<sub>5</sub>; the product of 6-phytases is D-4-OH InsP<sub>5</sub> or L-6-OH InsP<sub>5</sub>; and 5-phytases produce 5-OH InsP<sub>5</sub>. Image created with ChemDraw Prime version 15.0 (PerkinElmer Informatics).

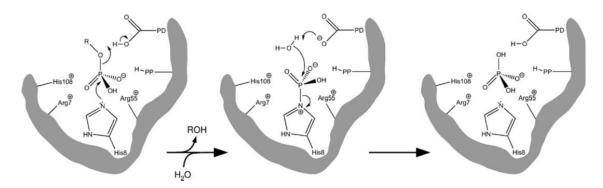
Subsequent attacks to the InsP<sub>5</sub> are not random, they occur adjacent to the free hydroxyl group resulting from the first dephosphorylation of phytate. Therefore, the site at which phytases initiate the hydrolysis of phytate determines the sequence of further hydrolysis (Brinch-Pedersen, Sørensen and Holm, 2002). In general, microorganisms were considered to produce 3-phytases and rarely 5-phytases, whereas 6-phytases were found in plants. However, this classification seems to be inaccurate as several exceptions have been reported. For example, bacteria such as *E. coli* have been found to produce 6-phytases (Greiner, Konietzny and Jany, 1993) and a phytase from lily pollen is a 5-phytase (Barrientos, Scott and Murthy, 1994).

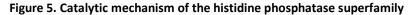
# 1.3.3. Classification of phytases based on structure and catalytic mechanism

Not all phytase enzymes are structurally similar or employ the same catalytic mechanism to hydrolyse phosphate. A second phytase classification criterion is based on the different catalytic mechanisms (and, therefore, three-dimensional structures) that have evolved in nature to accomplish the phosphate hydrolysis of phytate. Four classes of phosphatase enzymes have been reported to have representatives with phytase activity so far, dividing phytases into four groups: (1) histidine acid phytases, (2)  $\beta$ -propeller phytases, (3) protein tyrosine phytases or cysteine phytases and (4) purple acid phytases. The existence of different catalytic mechanisms to develop the same activity has the potential to make phytase enzymes versatile for industrial applications (Mullaney and Ullah, 2003, 2007, Lei *et al.*, 2007, 2013).

#### **1.3.3.1.** Histidine acid phytases

The histidine acid phytases (HAPhy) were the first discovered and the most broadly investigated group of phytases (Lei *et al.*, 2013). They belong to the histidine phosphatase superfamily, a large group of proteins with very diverse functions, although most of them are phosphatases. All proteins belonging to the histidine phosphatase superfamily are characterised for having the catalytic core conserved with four invariant residues: two histidines and two arginines (Arg7, His8, Arg55 and His108 in the *E. coli* SixA enzyme, as shown in Figure 5). These four conserved residues, together with additional non-conserved neutral or positive residues (PP in Figure 5), form the 'phosphate pocket' of the enzyme. The catalytic mechanism initiates with the transfer of a phosphate group from the substrate to the enzyme. This occurs through the phosphorylation of one of the conserved histidine residues, mediated by electrostatic interactions and hydrogen bonding of the phosphate with the other residues in the phosphate pocket. The histidine acts as a nucleophile that attacks the phosphate group of the substrate. A proton donor residue (PD in Figure 5) donates a proton to the substrate's leaving group while the phosphate group gets transferred to the catalytic histidine. Aspartate and glutamate residues have been reported as proton donors. The phosphate is finally removed from the histidine through hydrolysis. The negatively charged proton donor attacks a water molecule followed by the attack of this water molecule to the phosphate group, generating free phosphate and a regenerated enzyme (Vincent, Crowder and Averill, 1992; Rigden, 2008).





The two-step catalytic mechanism of the enzymes belonging to the histidine phosphatase superfamily, with the catalytic core residues numbered as in the *E. coli* SixA phosphatase representative. His8 is the catalytic histidine and forms the 'phosphate pocket' together with Arg7, Arg55, His108 and other variable residues (PP). PD represents the proton donor residue (Rigden, 2008).

Proteins of the histidine phosphatase superfamily can be divided in two branches with low sequence similarity. The first branch groups mostly intracellular bacterial proteins with a wide variety of functions, which only present an RH[G/N] active site motif conserved. The second branch contains predominantly extracellular eukaryotic proteins with two conserved motifs: an N-terminal RH[G/N]xRx[P/A/S] catalytic motif and a C-terminal HD/HAE proton donor motif, which are positioned together in the 3D structure to form the active site of these enzymes. Well known members of this branch

are histidine acid phosphatases with no known phytase activity (HAP) and histidine acid phytases (HAPhy) (van Etten *et al.*, 1991; Rigden, 2008; Lei *et al.*, 2013).

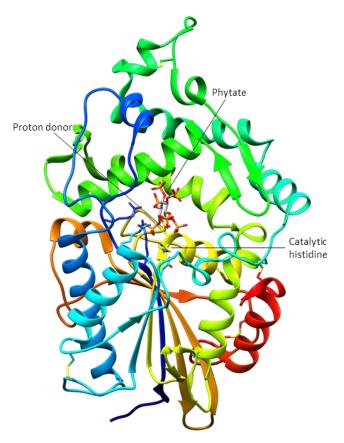


Figure 6. Crystal structure of the HAPhy representative AppA E. coli phytase in complex with phytate

Polypeptide chain coloured following the rainbow spectrum from blue (N-terminus) to red (C-terminus). Side chains of residues involved in the binding of phytate are displayed as sticks and coloured by heteroatom: Arg16, Arg20, Asp88, Arg92, His303 (catalytic histidine) and Asp304 (PD). Disulfide bridges are displayed as sticks and coloured by heteroatom. Phytate is shown as sticks and coloured by element. Structure extracted from the Protein Data Bank (PDB; Berman *et al.*, 2000), accession 1DKQ (Lim *et al.*, 2000). Image created with the UCSF Chimera package (Pettersen *et al.*, 2004).

HAPhy is the term used to designate the histidine acid phosphatases that can accommodate the negatively charged phytate as substrate. They carry out their activity at acidic pH, which makes their active site positively charged and facilitates the binding of phytate. Several crystal structures of HAPhy are available, all comprising an  $\alpha$ -helix-only domain and an  $\alpha/\beta$  domain with two helices on each side of the sevenstranded sheet. They are also characterised by the presence of several disulfide bridges that maintain their 3D structure. The amino acid residues encircling the active site are known as substrate specificity site (SSS) due to their role in determining substrate affinity and pH profile of these enzymes. HAPhy can be divided in two classes correlated with the composition of the SSS: broad substrate specificity and low specific activity against phytate or narrow substrate specificity and high specific activity against phytate (Mullaney and Ullah, 2003; Lei *et al.*, 2007).

Several prokaryotic and eukaryotic HAPhy have been reported. The *Escherichia coli* AppA phytase is the best characterised prokaryotic HAPhy and its crystal structure is shown in Figure 6. The fungal phytase PhyA from *Aspergillus niger* and *A. fumigatus* is a well-studied representative eukaryotic HAPhy with crystal structures also available (Kostrewa *et al.*, 1997; Liu *et al.*, 2004).

More recently, another group of enzymes presenting phytase activity has also been reported as members of the histidine phosphatase branch two. They are multiple inositol polyphosphate phosphatases (MINPP) first described in animals (Caffrey *et al.*, 1999; Chi *et al.*, 1999), and later in plants (Mehta *et al.*, 2006; Dionisio, Holm and Brinch-Pedersen, 2007) and bacteria (Stentz *et al.*, 2014).

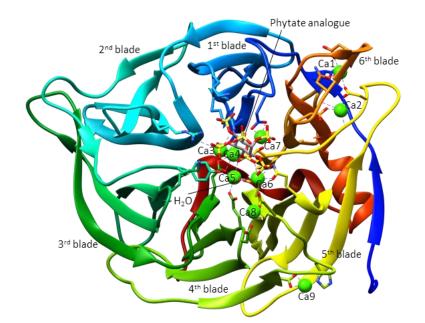
#### **1.3.3.2.** β-Propeller phytases

β-Propeller phytases (BPPhy) were first discovered in *Bacillus* species, presenting high sequence identity with each other, but no obvious homology to previously reported phytases or any known phosphatase class of enzymes (Kerovuo *et al.*, 1998; Kim *et al.*, 1998; Lei *et al.*, 2007). Further genome sequence analysis revealed that BPPhy-like sequences are widely distributed in the genomes of a number of microbes. To date, β-propeller phytases have been characterised from different groups of microorganisms, including archaea, bacteria, fungi and cyanobacteria (Kumar *et al.*, 2017). All BPPhy are active at neutral to alkaline pH (ranging from pH 6 to 8 in most cases), characteristic that has earned them to be also known as alkaline phytases. As most aquatic and terrestrial environments have a neutral pH, the optimum pH range of BPPhy suggests they may be the major phytate hydrolysing enzyme in nature with a key role in phytate-phosphorus cycling (Kumar *et al.*, 2017). Some plant phytases have also been reported as alkaline phytases and they share some characteristics with BPPhy, but their molecular structures have not yet been determined (Mullaney and Ullah, 2007).

Most BPPhy have molecular masses in the range of 35 to 68 kDa and optimum temperature between 30 and 70°C, presenting higher thermostability than other

phytases (Kumar et al., 2017). The 3D structure of the phytases from this family has been determined (Ha et al., 2000; Zeng et al., 2011). They have the shape of a propeller with six blades, corresponding to five four-stranded and one five-stranded antiparallel  $\beta$ -sheets (Figure 7). All BPPhy contain Ca<sup>2+</sup> ions in their structure, which are required for the activity of the enzymes and their thermostability. Although most of the residues involved in calcium binding are conserved, variable numbers of Ca<sup>2+</sup> ions have been reported in different BPPhy distributed in two classes of Ca<sup>2+</sup> binding sites. At least three Ca<sup>2+</sup> ions are present in the active site of these phytases and involved in catalysis and at least two contribute to their thermostability and maintain their 3D structure. The active site of BPPhy lays on top of the  $\beta$ -propeller and contains two phosphate binding sites: a 'cleavage site', in which the hydrolysis of a phosphate from the substrate occurs, and an adjacent 'affinity site', which increases the binding affinity for substrates that feature neighbouring phosphate groups. These particular active site characteristics allow BPPhy to be highly specific for the substrate phytate, showing no activity on other phosphate esters. The calcium ions in the active site facilitate the binding of the substrate by creating a favourable electrostatic environment (Kumar et al., 2017).

The proposed catalytic mechanisms for BPPhy consists on the nucleophile attack of a water molecule, coordinated by two of the Ca<sup>2+</sup> ions, to a phosphate of the substrate in the cleavage site, while a second phosphate group binds in the affinity site (Hamelryck, 2003). An aspartate residue in the conserved C-terminal motif DG has been suggested to act as a proton donor to the oxygen atom of the scissile phosphomonoester bond. Only substrates that fill both phosphate binding sites simultaneously can be hydrolysed by BPPhy, which explains their substrate preference for phytate and results in these enzymes only being able to remove three phosphates from it. Most of the BPPhy characterised to date have a common phytate degradation pathway via  $lns(1,2,4,5,6)P_5$ and  $lns(2,4,5,6)P_4$  to produce  $lns(2,4,6,)P_3$  as final product (Kumar *et al.*, 2017).



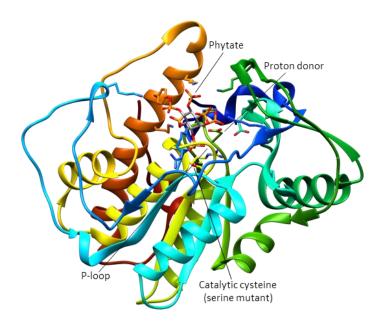
# Figure 7. Crystal structure of representative BPPhy from *Bacillus subtilis* in complex with *myo*-inositol hexakissulfate

The representative *Bacillus subtilis* alkaline phytase structure in complex with the phytate analogue *myo*-inositol hexakissulfate contains five  $Ca^{2+}$  ions involved in catalysis (Ca4-Ca8), while the rest are involved in thermostability (Ca1-Ca3 and Ca9) or crystal packing (Ca10 and Ca11, not displayed in the figure). All the sulfates of the substrate analogue except the first one have direct or indirect interactions with amino acid residues in the enzyme active site. The 4- and 5-sulfates occupy the 'cleavage site' and the 'affinity site', respectively. Polypeptide chain coloured following the rainbow spectrum from blue (N-terminus) to red (C-terminus). Side chains of residues involved in the binding of substrate analogue and  $Ca^{2+}$  ions are displayed as sticks and coloured by heteroatom. *myo*-Inositol hexakissulfate is shown as sticks and coloured by element. The nucleophilic water molecule is displayed as a red sphere. Structure extracted from the PDB (Berman *et al.*, 2000), accession 3AMR (Zeng *et al.*, 2011). Image created with the UCSF Chimera package (Pettersen *et al.*, 2004).

#### 1.3.3.3. Protein tyrosine phytases or cysteine phytases

Another class of phytases was discovered upon investigation of microbial phytase activity in the rumen of animals with complex digestive tracts (ruminants). A phytase from the anaerobic bacteria *Selenomonas ruminantium* was isolated, characterised, and its crystal structure solved. It consisted of a monomer approximately 46 kDa in size with an optimal acidic pH in the range of 4.0-5.5 and optimal temperature of 50-55°C (Yanke, Selinger and Cheng, 1999; Chu *et al.*, 2004). Similar phytases have been identified since then in other anaerobic gut bacteria, plant and mammalian pathogens and a predatory bacterium (Gruninger *et al.*, 2014). The 3D structure and proposed catalytic mechanism of these enzymes suggest they are members of the cysteine phosphatase (CP) superfamily, which gave them the name of cysteine phytases (PTP), a member of

the CP superfamily, making them also known as protein tyrosine phytases (PTPhy). PTPs contain the signature sequence  $Cx_5R[S/T]$  in their active site, a conserved motif also known as P-loop that serves as substrate binding pocket. The depth of the P-loop in PTPs seems to determine substrate specificity. PTPhy present a wider and deeper pocket than the non-phytase PTPs which, together with the presence of a favourable electropositive environment, allows them to accommodate phytate as substrate (Lei *et al.*, 2007; Gruninger *et al.*, 2012). The invariant cysteine residue is the nucleophile that attacks a phosphate group from the substrate to form a phosphocysteine intermediate. Main chain amines and a conserved arginine coordinate the scissile phosphate in the active site and stabilise the negative charge of phytate, while a conserved aspartate acts as a general acid and donates a proton to the leaving group (Puhl *et al.*, 2007; Weber *et al.*, 2014).



# Figure 8. Crystal structure of PTPhy representative from *Selenomonas ruminantium* in complex with phytate

The structure of the *Selenomonas ruminantium* PTPhy displayed corresponds to an inactive mutant with the catalytic cysteine mutated to a serine residue. The overall fold consists of a 'sandwich' domain mostly surrounded by  $\alpha$ -helices. Polypeptide chain coloured following the rainbow spectrum from blue (N-terminus) to red (C-terminus). Side chains of residues involved in the binding of phytate are displayed as sticks and coloured by heteroatom. Phytate is shown as sticks and coloured by element. Structure extracted from the PDB (Berman *et al.*, 2000), accession 3MMJ (Gruninger *et al.*, 2012). Image created with the UCSF Chimera package (Pettersen *et al.*, 2004).

The first crystal structure reported for the representative *S. ruminantium* PTPhy in complex with the substrate analogue *myo*-inositol hexakissulfate suggested proteins of this class might be 5-phytases (Chu *et al.*, 2004). However, a more recent structure of

an inactive mutant of the *S. ruminantium* PTPhy in complex with phytate (Figure 8) proposed a preference for hydrolysis of the 3-phosphate, which also agreed with the kinetic studies carried out with this enzyme (Gruninger *et al.*, 2012). The structures solved by Gruninger *et al.* also indicated that inositol phosphates may have multiple, overlapping binding sites within the binding pocket of the PTPhy. Structural and binding studies of PTPhy are in accordance with a two-step binding mechanism: a rapid initial binding step in which the substrate binds the electropositive binding pocket in one of several possible conformations, followed by a slower step in which the substrate reorients to adopt a catalytically competent conformation (Puhl *et al.*, 2007; Gruninger *et al.*, 2012). PTPhy have been reported to sequentially hydrolyse phytate to the end product inositol 2-monophosphate (Chu *et al.*, 2004).

#### **1.3.3.4.** Purple acid phytases

The class of purple acid phytases (PAPhy) was first reported upon the discovery of a phytase in the cotyledons of germinating soybean (*Glycine max*) seedlings that contained the purple acid phosphatase (PAP) sequence pattern (Hegeman and Grabau, 2001). The PAP class of proteins belong to the calcineurin-like metallophosphoesterase (MPE) superfamily (Matange, Podobnik and Visweswariah, 2015). PAPhy contain two metal ions involved in catalysis and creation of a favourable electrostatic potential for the binding of phytate (Lei *et al.*, 2013). Since PAPhy are the subject of this thesis, the literature concerning this class of phytases will be reviewed in detail.

#### 1.3.3.4.1. The metallophosphoesterase superfamily

The calcineurin-like metallophosphoesterase (MPE) superfamily is a large superfamily of enzymes that contain two closely spaced metal ions forming a binuclear metal centre. They depend on these metals to hydrolyse phosphomono-, phosphodi- or phosphotri-esters. Members of the MPE superfamily include nucleases, phosphoprotein phosphatases, cyclic nucleotide phosphodiesterases, pyrophosphatases, nucleotidases and purple acid phosphatases. Although the members of this superfamily are functionally diverse and have low overall sequence similarity, both the core MPE fold and the architecture of the active site are conserved (Matange, Podobnik and Visweswariah, 2015).

The three-dimensional fold of the MPE domain is called calcineurin-like fold in honour of one of the best characterised members of the family (i.e. calcineurin phosphatase). In general, it consists of two parallel  $\beta$ -sheets forming a  $\beta$ -sandwich decorated by  $\alpha$ -helices, arranged in a  $\beta\alpha\beta\alpha\beta$  architecture, although the number of secondary structure elements can vary among different MPEs. The active site of MPEs is located at the top of the  $\beta$ -sandwich and consists of two metal ions (MI and MII) usually octahedrally coordinated by seven conserved amino acids. These metal-coordinating residues are contained in five sequence motifs that constitute the sequence pattern characteristic of the MPE superfamily. Small variations of this sequence pattern can be observed in different members of the MPE superfamily (Matange, Podobnik and Visweswariah, 2015). The two metal ions in the active site are separated by distances ranging 3.1-3.5 Å and are linked by bridging groups, which are generally hydroxides derived from the solvent, side chains of amino acid residues, or a combination of both (Mitić et al., 2006; Schenk et al., 2012; Matange, Podobnik and Visweswariah, 2015). Different MPEs can use a very diverse range of metals and they can have heteronuclear or homonuclear metal centres. The two metal binding sites also have differences in affinity for cations. Different metals can occupy the binding sites of most MPEs, but not all of them support catalytic activity in an equal manner. It is believed that, in vivo, cells regulate the local concentrations of metals so that they can control the metal occupancy of these enzymes (Matange, Podobnik and Visweswariah, 2015).

Sequence signatures related to substrate binding and recognition have not been clearly identified for the different MPEs, and several members of this enzyme superfamily can utilize multiple substrates. MPEs have variable tertiary structures ranging from monomers to hexamers, although the individual subunits of the oligomeric MPEs are self-sufficient in forming the active site and coordinating the two catalytic metals (Matange, Podobnik and Visweswariah, 2015).

#### 1.3.3.4.2. Purple acid phosphatases

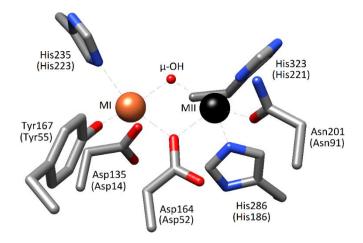
Purple acid phosphatases (PAPs) are members of the MPE superfamily with optimum activity at acidic pH. Unlike other phosphatases, PAPs are resistant towards inhibition by L-tartrate, characteristic that makes them also known as tartrate-resistant acid phosphatases (TRAPs) (Schenk *et al.*, 2013). They are known to require an heterovalent metal centre (MI<sup>3+</sup>-MII<sup>2+</sup>) for their catalytic activity. Furthermore, in PAPs MI is always a ferric ion (Fe<sup>3+</sup>), with a metal centre of the type Fe<sup>3+</sup>-M<sup>2+</sup> where the identity of M has been reported to be either Fe<sup>2+</sup>, Zn<sup>2+</sup> or Mn<sup>2+</sup> depending on the protein. In most PAPs, the MI metal binding site has a higher affinity for cations than MII (Schenk *et al.*, 2013; Matange, Podobnik and Visweswariah, 2015). A schematic representation of the sequence pattern with the five conserved motifs characteristic of PAPs is shown in Figure 9. While most of the other members of the MPE superfamily contain a histidine residue in motif I of the MPE domain, all PAPs have a glycine in this position. They also have a conserved tyrosine residue in motif II that coordinates the Fe<sup>3+</sup>, interaction from which results a charge transfer transition responsible for the characteristic purple colour that names these enzymes. A conserved valine residue in motif III has also been reported (Matange, Podobnik and Visweswariah, 2015).



Figure 9. Schematic representation of the PAP sequence pattern

The general architecture of the PAPs active site can be observed in Figure 10, with residue numbers corresponding to the red kidney bean (*Phaseolus vulgaris*) and pig (*Sus scrofa*) PAP representatives, two of the most studied enzymes of this group (Klabunde *et al.*, 1996; Guddat *et al.*, 1999). The ferric ion is coordinated by the side chains of a histidine (PAP motif V), a tyrosine (PAP motif II) and an aspartate residue (PAP motif I), while the divalent metal is coordinated by two histidine residues (PAP motif IV and V, respectively) and an asparagine residue (PAP motif III). In addition, a solvent derived hydroxide and one aspartate residue (known as the bridging aspartate, PAP motif II) coordinate both metal ions (Mitić *et al.*, 2006; Schenk *et al.*, 2012; Matange, Podobnik and Visweswariah, 2015).

The PAP sequence pattern consists of five conserved motifs containing seven invariant metal ligands that coordinate the two metals in the active site. 'x' represents any amino acid. Residues coordinating the Fe<sup>3+</sup> (MI) are coloured in brown. Residues coordinating the MII are represented in bold. The aspartate residue that coordinates both metal ions is coloured in grey. Residues marked with '\*' are variations of the MPE active site characteristic of PAPs.



#### Figure 10. Active site of PAPs

In PAPs, MI is always an Fe<sup>3+</sup> ion (brown) coordinated by a tyrosine, a histidine and two aspartate residues. MII (black) can be Fe<sup>2+</sup>, Zn<sup>2+</sup> or Mn<sup>2+</sup> and it is coordinated by two histidines, an asparagine and an aspartate residue. A bridging solvent molecule ( $\mu$ -OH, in red) coordinates the two metal ions. The numbering of the metal ligand residues is according to the red kidney bean PAP and the pig PAP (in brackets). Image created with the UCSF Chimera package (Pettersen *et al.*, 2004).

There are characterised PAP representatives in various plants, mammals, and some fungi. PAPs have also been identified in a limited number of bacteria, but none have been characterised yet (Ullah and Cummins, 1988; Klabunde and Krebs, 1997; Schenk et al., 1999, 2000). PAPs are often grouped into two distinct categories according to their molecular weight. The first category contains PAPs 55-60 kDa in size sometimes known as high molecular weight (HMW) PAPs. They are mostly large plant and invertebrate enzymes with an N-terminal regulatory domain in addition to the MPE domain. HMW PAPs are usually homodimers linked by a disulfide bridge formed by a conserved cysteine and contain a heteronuclear metal centre with Zn<sup>2+</sup> or Mn<sup>2+</sup> in the MII site (Olczak, Morawiecka and Watorek, 2003; Schenk et al., 2013; Matange, Podobnik and Visweswariah, 2015). Representatives of this category with published crystal structures are the red kidney bean (Phaseolus vulgaris) PAP, with an Fe<sup>3+</sup>-Zn<sup>2+</sup> metal centre (Klabunde et al., 1996; Schenk et al., 2008), and the sweet potato (Ipomoea batatas) PAP, with an Fe<sup>3+</sup>-Mn<sup>2+</sup> metal centre (Schenk et al., 2005). The overall crystal structure of the two subunits of the red kidney bean PAP is shown in Figure 11A. The second category is formed by smaller mammalian and mammalian-like PAPs (from plant and invertebrate genomes) which contain only the MPE domain. They are monomers approximately 35 kDa in size usually referred to as low molecular weight (LMW) PAPs. They all present a Fe<sup>3+</sup>-Fe<sup>2+</sup> homonuclear metal centre (Olczak, Morawiecka and Watorek, 2003; Schenk *et al.*, 2013; Matange, Podobnik and Visweswariah, 2015). Representatives of this category with published crystal structures are pig (*Sus scrofa*) (Guddat *et al.*, 1999; Selleck *et al.*, 2017), rat (*Rattus norvegicus*) (Lindqvist *et al.*, 1999; Uppenberg *et al.*, 1999) and human (*Homo sapiens*) (Sträter *et al.*, 2005) PAPs. The crystal structure of the pig PAP can be observed in Figure 11B.

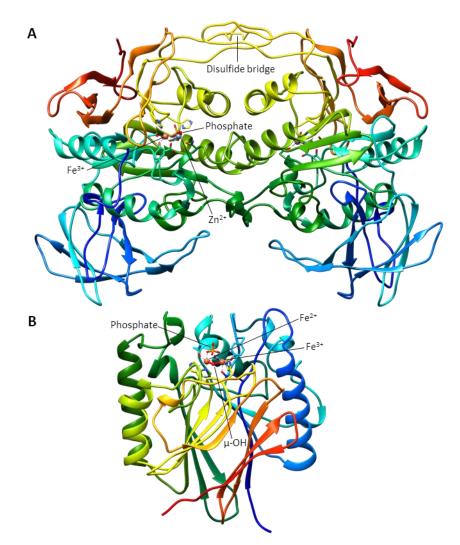


Figure 11. Crystal structures of two PAP representatives in complex with phosphate

(A) The red kidney bean (*Phaseolus vulgaris*) PAP is a homodimer with the two subunits linked by a disulfide bridge which is conserved in most HMW plant PAPs. It contains a dinuclear  $Fe^{3+}-Zn^{2+}$  active site. (B) The pig (*Sus scrofa*) PAP is a representative of the small mammalian PAPs. It is a monomer with an  $Fe^{3+}-Fe^{2+}$  metal centre. Polypeptide chains coloured following the rainbow spectrum from blue (N-terminus) to red (C-terminus). Side chains of residues involved in coordination of the metal ions are displayed as sticks and coloured by heteroatom. The  $\mu$ -OH in the pig PAP is shown in red as ball and stick. Phosphate is shown as sticks and coloured by element. Structures extracted from the PDB (Berman *et al.*, 2000). Red kidney bean PAP accession 4KBP (Klabunde *et al.*, 1996). Pig PAP accession 1UTE (Guddat *et al.*, 1999). Images created with the UCSF Chimera package (Pettersen *et al.*, 2004).

However, the classification of PAPs in these two categories is not exhaustive. Mono- and heterodimeric plant PAPs have been reported (Bozzo, Raghothama and Plaxton, 2002, 2004), as well as the homohexameric yellow lupin (*Lupinus luteus*) PAP (Antonyuk *et al.*, 2014).

The physiological substrates of most PAPs are not known (Matange, Podobnik and Visweswariah, 2015). Mammalian PAPs can be reversibly oxidized to the inactive diferric form due to the low redox potential of the divalent iron. This oxidation of the heterovalent diiron centre is accompanied by a change in colour from pink to purple (Mitić *et al.*, 2006). Although they act predominantly as hydrolases, the reversible oxidation/reduction of the active site of mammalian PAPs provides them with the ability to carry out peroxidations. Mammalian PAPs are therefore equipped with a mechanism that allows them to regulate their activity *in vivo*. The suggested roles for mammalian PAPs include iron transport, the generation of reactive oxygen species (ROS) as an immune response, energy metabolism, and bone resorption (Schenk *et al.*, 2013). Due to the metal ion composition of plant PAPs, their activity cannot be regulated by reversible oxidation/reduction. The main biological function of PAPs in plants seems to be organophosphate degradation, but assigning them specific functions has proved difficult due to the presence of multiple isoforms (Mitić *et al.*, 2006; Schenk *et al.*, 2013).

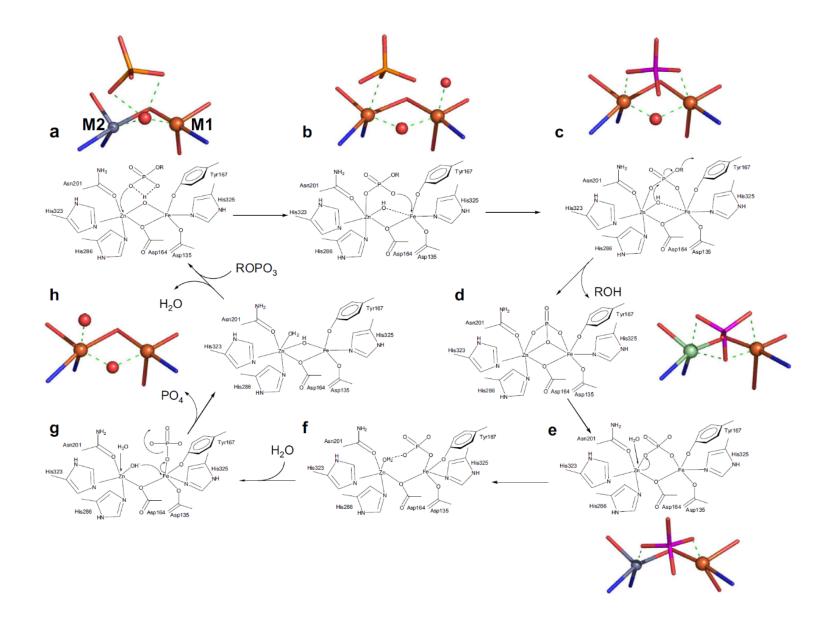
The active site metals are key in the catalytic mechanism of PAPs, and MPEs in general (Matange, Podobnik and Visweswariah, 2015). The currently accepted catalytic mechanism employed by PAPs is represented in Figure 12 and consist of eight steps, six of which are supported by crystal structures of representative PAPs (Schenk *et al.*, 2008, 2012). In the initial step, the substrate binds the active site in a precatalytic complex not directly coordinated to the metal ions. This state is stabilised by hydrogen bonds involving the  $\mu$ -hydroxide and residues in the second coordination sphere (Figure 12a). This initial step is followed by a rearrangement of the substrate to coordinate first with the divalent metal ion in MII (Figure 12b) and second with the ferric ion in MI. The coordination of the metals with the substrate forms a  $\mu$ -1,3 catalytic complex that facilitates the nucleophilic attack (Figure 12c). The identity of the attacking nucleophile that initiates hydrolysis of the phosphorylated substrate has been subject of an extensive debate, and it may be dependent on the type of substrate and metal ion composition of the active site. A solvent derived hydroxide coordinated to one or both metal ions in the active site has been proposed as the most likely candidate, although a

second coordination sphere hydroxide has also been reported in some cases. The leaving group is then protonated by an active site amino acid residue, allowing its release from the protein but leaving behind the phosphate. The nucleophilic attack by the hydroxide and the esterolysis of the substrate leaves the phosphate bound to the active site in a tripodal geometry (Figure 12d). The release of the bound phosphate that allows the regeneration of the enzyme is the least understood step of the catalytic cycle. It is believed to consist on the addition of at least two water molecules. A plausible sequence involves a rotation of the bound phosphate to rearrange from tripodal to  $\mu$ -1,3 coordination with the metal ions (Figure 12e). A water molecule is believed to replace the phosphate in MII, leaving it only coordinated to MI. A hydrogen bond likely forms between the water molecule and the phosphate (Figure 12f), leaving it deprotonated and facilitating its coordination with MI, which would regenerate the  $\mu$ -hydroxide and weaken the MI-phosphate bond. A second water molecule also binds MII (Figure 12g), which together with the release of the phosphate group enables the regeneration of the resting state of the enzyme (Figure 12h) (Schenk et al., 2008, 2012, 2013; Matange, Podobnik and Visweswariah, 2015).

PAPs differ from other MPEs in the residue responsible for the protonation of the leaving group. Glutamate has been observed in sweet potato PAP and aspartate in human PAP, instead of the usual histidine in MPEs. This is consistent with the PAPs acidic pH optimum, while other MPEs work best at slightly alkaline pH (Matange, Podobnik and Visweswariah, 2015)

#### Figure 12. Representation of the eight-step catalytic mechanism proposed for PAPs (on following page)

(a) Pre-catalytic complex in the red kidney bean PAP-sulfate complex (2QFR). (b) Monodentate coordination of the substrate to MII in rat PAP-sulfate complex (1QHW), the water bound to MI is believed to be an artefact of crystallisation. (c) Substrate complex with bidentate coordination, before the nucleophilic attack by the  $\mu$ -OH, in pig PAP-phosphate complex (1UTE). (d) Tripodal complex of the product, after the release of the leaving group, in sweet potato PAP-phosphate complex (1XZW). (e) Product-bound state with bidentate coordination in red kidney bean PAP-phosphate complex (4KBP). (f) Monodentate coordination of the product to MI. (g) Regeneration of the  $\mu$ -OH bridge, before the release of the phosphate group. (h) Resting state in red kidney bean PAP (1KBP), the  $\mu$ -OH bridge and the water molecule bound to MII have been modelled (Schenk *et al.*, 2008).



#### 1.3.3.4.3. Purple acid phosphatases with phytase activity or PAPhy

As happens in HAPs and PTPs, not all PAPs can effectively utilise phytate as substrate. Purple acid phosphatases that can hydrolyse phytate are known as PAPhy. Although they are active against phytate, PAPhy in general exhibit broad affinity for various phosphorylated compounds. PAPhy have only been found in plants and no structural information has been published so far (Brinch-Pedersen *et al.*, 2014). However, a number of PAPhy have been purified and biochemically characterised.

The first phytase containing a PAP sequence pattern was discovered in cotyledons of germinating soybean seedlings (Hegeman and Grabau, 2001). However, phytases from rice (Hayakawa, Toma and Igaue, 1989), rye (Greiner, Konietzny and Jany, 1997), wheat (Nakano et al., 1999) and barley (Greiner, Jany and Larsson Alminger, 2000) discovered and characterised earlier are also believed to belong to this class of phytases (Dionisio et al., 2011; Brinch-Pedersen et al., 2014). Among these, the two monomeric acid phosphatases with phytase activity and violet colour purified from rice bran (F1 and F2) may represent different glycosylation states of the same enzyme (Brinch-Pedersen et al., 2014). Among the 29 PAP-like proteins identified in Arabidopsis thaliana (Li et al., 2002), only AtPAP15 has been confirmed to have phytase activity (Zhang et al., 2008; Kuang et al., 2009; Wang et al., 2009). Purified recombinant AtPAP23 was reported to have a weak activity towards phytate (Zhu et al., 2005). PAPhy from Medicago truncatula (Xiao, Harrison and Wang, 2005; Xiao et al., 2006), tobacco (Lung et al., 2008), maize (Dionisio et al., 2011), white lupin (Maruyama et al., 2012) and orange (Shu, Wang and Xia, 2015) have also been characterised. In addition, phytase genes from einkorn, goatgrass and rye have been isolated from genomic libraries or by PCR (Madsen et al., 2013). Potential phytases have also been identified in mungbean (Wongkaew, Srinives and Nakasathien, 2013), red kidney bean (Lazali et al., 2013, 2014) and the microalgal Chlamydomonas reinhardtii (Rivera-Solís et al., 2014). Table 1 summarises the PAPhy that have been reported in the literature and some of their characteristics.

## Table 1. Reported PAPhy in the literature

Data not provided is labelled 'np'.

Organism	Protein	Source	Length (Aa) /MW (kDa)	pH/T (°C) optimum	Oligomeric state	Phytase activity	Reference
Rice ( <i>Oryza sativa</i> )	F1	Rice bran	np/66	4.4/40	Monomer	K <sub>m</sub> = 170 μM	(Hayakawa, Toma and Igaue, 1989)
Rice ( <i>Oryza sativa</i> )	F2	Rice bran	np/68	4.6/40	Monomer	K <sub>m</sub> = 90 μM	(Hayakawa, Toma and Igaue, 1989)
Rye (Secale cereale)	np	Germinating seeds	np/67	6.0/45	Monomer	$K_m$ = 300 $\mu M$ , $K_{cat}$ = 358 s $^{\text{-1}}$	(Greiner, Konietzny and Jany, 1997)
Wheat (Triticum aestivum)	РНҮІ	Mature grains	np/66	np	np	np	(Nakano <i>et al.,</i> 1999)
Wheat (Triticum aestivum)	РНҮП	Mature grains	np/68	np	np	np	(Nakano <i>et al.,</i> 1999)
Barley ( <i>Hordeum vulgare</i> )	P1	Germinating seeds	np/66	5.0/45	Monomer	$K_m$ = 72 $\mu$ M, $k_{cat}$ = 136 s <sup>-1</sup>	(Greiner, Jany and Larsson Alminger, 2000)
Barley (Hordeum vulgare)	P2	Mature seeds	np/66	6.0/55	Monomer	$K_m$ = 190 $\mu$ M, $k_{cat}$ = 43 s <sup>-1</sup>	(Greiner, Jany and Larsson Alminger, 2000)
Soybean ( <i>Glycine max</i> )	GmPhy	Germinating seeds	547/62.3	4.5-5/58	np	K <sub>m</sub> = 61 μM	(Hegeman and Grabau, 2001; Singh et al., 2013)
Barrel medic ( <i>Medicago truncatula</i> )	MtPHY1	Roots and leaves, recombinant	543/np	np	np	Effective phytate hydrolysis	(Xiao, Harrison and Wang, 2005; Xiao <i>et al.</i> , 2006)
Arabidopsis thaliana	AtPAP23	Recombinant	np/77.7	np	np	Weak activity	(Zhu <i>et al.,</i> 2005)
Tobacco (Nicotiana tabacum)	NtPAP	Roots	551/56	np	Monomer	$K_m = 14.7 \ \mu M$ , $k_{cat} = 908 \ s^{-1}$	(Lung <i>et al.,</i> 2008)
Arabidopsis thaliana	AtPAP15	Recombinant	532/60	4.5/23-37	Monomer	Specific activity = 10 U mg <sup>-1</sup> , K <sub>m</sub> = 278 $\mu$ M, V <sub>max</sub> = 13.44 U mg <sup>-1</sup>	(Zhang et al., 2008; Kuang et al., 2009; Wang et al., 2009)
Wheat (Triticum aestivum)	TaPAPhy_a1	Mature grain, recombinant	550/58	5.5/55	Monomer	$K_m$ = 35 μM, V <sub>max</sub> = 223 μmol min <sup>-1</sup> mg <sup>-1</sup> , $k_{cat}$ = 279 s <sup>-1</sup> , $k_{cat}/K_m$ = 796 x10 <sup>4</sup> s <sup>-1</sup> M <sup>-1</sup>	(Dionisio <i>et al.,</i> 2011)
Wheat (Triticum aestivum)	TaPAPhy_a2	Mature grain, recombinant	549/58.6	np	Monomer	np	(Dionisio <i>et al.,</i> 2011)
Wheat (Triticum aestivum)	TaPAPhy_b1	Germinating seeds, recombinant	538/57.4	5.0/50	Monomer	$K_m$ = 45 μM, V <sub>max</sub> = 216 μmol min <sup>-1</sup> mg <sup>-1</sup> , $k_{cat}$ = 270 s <sup>-1</sup> , $k_{cat}/K_m$ = 600 x10 <sup>4</sup> s <sup>-1</sup> M <sup>-1</sup>	(Dionisio <i>et al.,</i> 2011)
Wheat (Triticum aestivum)	TaPAPhy_b2	Germinating seeds, recombinant	537/57.4	np	Monomer	np	(Dionisio <i>et al.,</i> 2011, 2012)
Barley (Hordeum vulgare)	HvPAPhy_a	Mature grain, recombinant	544/57.8	np	Monomer	$K_m$ = 36 μM, $V_{max}$ = 208 μmol min <sup>-1</sup> mg <sup>-1</sup> , $k_{cat}$ = 260 s <sup>-1</sup> , $k_{cat}/K_m$ = 722 x10 <sup>4</sup> s <sup>-1</sup> M <sup>-1</sup>	(Dionisio <i>et al.,</i> 2011)
Barley (Hordeum vulgare)	HvPAPhy_b1	Germinating seeds, recombinant	536/57.2	np	Monomer	np	(Dionisio <i>et al.,</i> 2011, 2012)
Barley (Hordeum vulgare)	HvPAPhy_b2	Germinating seeds, recombinant	537/57.2	np	Monomer	$K_m = 46 \ \mu$ M, $V_{max} = 202 \ \mu$ mol min <sup>-1</sup> mg <sup>-1</sup> , $k_{cat} = 253 \ s^{-1}$ , $k_{cat}/K_m = 550 \ x10^4 \ s^{-1} \ M^{-1}$	(Dionisio <i>et al.,</i> 2011)

Organism	Protein	Source	Length (Aa) /MW (kDa)	pH/T (°C) optimum	Oligomeric state	Phytase activity	Reference
Maize ( <i>Zea mays</i> )	ZmPAPhy_b	Germinating seeds, recombinant	544/57.4	np	Monomer	$K_m$ = 48 μM, V <sub>max</sub> = 198 μmol min <sup>-1</sup> mg <sup>-1</sup> , k <sub>cat</sub> = 248 s <sup>-1</sup> , k <sub>cat</sub> /K <sub>m</sub> = 517 x10 <sup>4</sup> s <sup>-1</sup> M <sup>-1</sup>	(Dionisio <i>et al.,</i> 2011)
Rice ( <i>Oryza sativa</i> )	OsPAPhy_b	Germinating seeds, recombinant	539/57.5	np	Monomer	$K_m = 54 \ \mu$ M, $V_{max} = 185 \ \mu$ mol min <sup>-1</sup> mg <sup>-1</sup> , $k_{cat} = 231 \ s^{-1}$ , $k_{cat}/K_m = 428 \ x10^4 \ s^{-1} \ M^{-1}$	(Dionisio <i>et al.,</i> 2011)
Mungbean ( <i>Vigna radiata</i> )	VrPAP1	Germinating seeds	547/62	np	np	Contains five PAP motifs and partial homology with four PAPhy motifs	(Wongkaew, Srinives and Nakasathien, 2013)
White lupin ( <i>Lupinus albus</i> )	LASAP3	Germinating seeds, recombinant	543/np	5.5/np	np	K <sub>m</sub> = 83.1 μM	(Maruyama <i>et al.,</i> 2012)
Wheat (Triticum aestivum)	TaPAPhy_a3	Mature grain	539/np	np	np	Gene isolated	(Madsen <i>et al.,</i> 2013)
Wheat (Triticum aestivum)	TaPAPhy_b3	Germinating seeds	536/np	np	np	Gene isolated	(Madsen <i>et al.,</i> 2013)
Einkorn (Triticum monococcum)	TmPAPhy_a1	Mature grain	np	np	np	Gene isolated	(Madsen <i>et al.,</i> 2013)
Einkorn (Triticum monococcum)	TmPAPhy_b1	Germinating seeds	np	np	np	Gene isolated	(Madsen <i>et al.,</i> 2013)
Goatgrass (Aegilops tauschii)	AtaPAPhy_a1	Mature grain	np	np	np	Gene isolated	(Madsen <i>et al.,</i> 2013)
Goatgrass (Aegilops tauschii)	AtaPAPhy_b1	Germinating seeds	np	np	np	Gene isolated	(Madsen <i>et al.,</i> 2013)
Rye (Secale cereale)	ScPAPhy_a1	Mature grain	np	np	np	Gene isolated	(Madsen <i>et al.,</i> 2013)
Rye (Secale cereale)	ScPAPhy_a2	Mature grain	np	np	np	Gene isolated	(Madsen <i>et al.,</i> 2013)
Rye (Secale cereale)	ScPAPhy_b1	Germinating seeds	np	np	np	Gene isolated	(Madsen <i>et al.,</i> 2013)
Red kidney bean (Phaseolus vulgaris)	np	Root nodules	np	np	np	Expression levels of transcript correlate with phytase activity	(Lazali <i>et al.,</i> 2013, 2014)
Soybean (Glycine max)	GmPAP4	Roots and recombinant	442/50.3	np	np	0.15 μΜ Pi h <sup>-1</sup> U <sup>-1</sup> (control = 0.06 μΜ Pi h <sup>-1</sup> U <sup>-1</sup> )	(Kong <i>et al.,</i> 2014)
Chlamydomonas reinhardtii	CrPAP1	np	np	np	np	Gene expression induced by addition of phytate	(Rivera-Solís <i>et al.,</i> 2014)
Chlamydomonas reinhardtii	CrPAP5	np	np	np	np	Gene expression induced by addition of phytate	(Rivera-Solís <i>et al.</i> , 2014)
Trifoliate orange (Poncirus trifoliata)	PtPAP3	Germinating seeds, recombinant	np/66	5.5/37	Monomer	$K_m = 46.2 \ \mu M$ , $V_{max} = 214 \ \mu mol \ min^{-1} \ mg^{-1}$ , $k_{cat} = 243 \ s^{-1}$ , $k_{cat}/K_m = 5.49 \ s^{-1} \ \mu mol^{-1}$	(Shu, Wang and Xia, 2015)

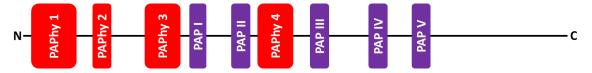
When studying plant purple acid phytases, it is worth highlighting the research carried out by Professor Henrik Brinch-Pedersen's group (Flakkebjerg Research Centre, Aarhus University, Denmark), which is focussed on improving the quality of the cereal plant and seed. As phytate is the major phosphorus reserve in plant seeds, phytate degradation for phosphorus mobilization during seed germination becomes particularly important. Differences in the strategies to accomplish this purpose can be observed across different plant species. Among cereals, the members of the Triticeae tribe wheat (Triticum aestivum), barley (Hordeum vulgare), rye (Secale cereale), einkorn (Triticum monococcum) and goatgrass (Aegilops tauschii) have been reported to possess significant levels of phytase activity in mature grains (mature grain phytase activity or MGPA). These cereals synthesise and accumulate phytases during grain development (preformed phytase) as well as during germination. On the contrary, non-Triticeae cereals such as maize (Zea mays), rice (Oryza sativa), oat (Avena sativa) and purple false brome (Brachypodium distachyon) showed little or no MGPA, depending fully on de novo phytase synthesis during germination. MINPP phytases and PAPhy constitute the cereal phytase complement and recent studies have underlined the importance of PAPhy at least in the Triticeae. Based on the presence or absence of phytase activity in the mature grain, PAPhy can be divided in two groups with very similar sequence but distinguished by the C-terminal. PAPhy\_a isoforms are predominantly expressed during grain development and present in the mature grains, whereas PAPhy b isoforms are predominantly expressed during germination (Dionisio et al., 2011; Madsen et al., 2013; Brinch-Pedersen et al., 2014).

A series of cereal PAP cDNAs were cloned from wheat, barley, maize and rice, and the derived recombinant proteins showed to be efficient phytases when expressed in *Pichia pastoris*. Two isogenes with two variants each were cloned from wheat (TaPAPhy\_a1, TaPAPhy\_a2, TaPAPhy\_b1 and TaPAPhy\_b2); three cDNAs where cloned from barley (HvPAPhy\_a, HvPAPhy\_b1 and HvPAPhy\_b2); and one PAP gene was cloned from each maize (ZmPAPhy\_b) and rice (OsPAPhy\_b). All open reading frames (ORF) encoded monomeric proteins 538-551 amino acids long, with predicted N-terminal signal peptides and molecular masses of 57.2-59 kDa. With phytate as substrate, the K<sub>m</sub> values of the recombinant PAPhy ranged from 35-54  $\mu$ M. The pH and temperature

optima were 5.0-5.5 and 50-55°C, respectively, for the wheat isozymes (Dionisio *et al.*, 2011). Traditionally, mammalian PAPs have been reported to have iron in two different oxidation states in their active sites, whereas plant PAPs seem to contain Zn<sup>2+</sup> or Mn<sup>2+</sup> in the MII site (Olczak, Morawiecka and Watorek, 2003; Schenk *et al.*, 2013; Matange, Podobnik and Visweswariah, 2015). However, Dionisio *et al.* (2011) have reported a preference for Fe<sup>2+</sup> as divalent metal in several of the cereal PAPhy they have studied, in particular the ones belonging to the isoform b group, while the isoform a group have a preference for Mn<sup>2+</sup>. Through a sequence analysis including a collection of plant PAPhy reported in the literature and PAPs without known phytase activity, Dionisio *et al.* (2011) have also revealed four conserved regions in PAPhy sequences and suggested them as PAPhy-specific consensus motifs:

- (1) RG[H/V/Q/N]A[V/I]D[L/I]P[D/E]TDP[R/L]VQR[R/N/T];
- (2) S[V/I]V[R/Q][Y/F]G;
- (3) AMSxx[H/Y][A/Y/H]F[R/K]TMP; and
- (4) DCYSC[S/A]FxxxTPIH

Some of these motifs are insertions not present in non-phytase PAPs, making the phytases larger than most plant HMW PAPs (Dionisio *et al.*, 2011). A schematic representation of the distribution of the PAPhy and PAP motifs can be seen in Figure 13.



# Figure 13. Schematic representation of the distribution of PAPhy motifs and PAP motifs in the amino acid sequence

Sequence motifs conserved in PAPs are represented in purple boxes and numbered I to V. PAP I, GDxG; PAP II, GDx<sub>2</sub>Y; PAP III, GNHE/D; PAP IV, Vx<sub>2</sub>H; and PAP V, GHxH. Additional motifs conserved in sequences of PAPs that display phytase activity are represented in red boxes and numbered 1 to 4. PAPhy 1, RG[H/V/Q/N]A[V/I]D[L/I]P[D/E]TDP[R/L]VQR[R/N/T]; PAPhy 2, S[V/I]V[R/Q][Y/F]G; PAPhy 3, AMSxx[H/Y][A/Y/H]F[R/K]TMP; and PAPhy 4, DCYSC[S/A]FxxxTPIH.

In summary, PAPhy enzymes exhibit broad affinity for various phosphorylated compounds. These proteins have only been identified in plants so far and there are no crystal structures available. All the characterised plant PAPhy to date seem to be HMW, bigger than most of the non-phytase HMW PAPs, and monomeric instead of homodimeric. They are usually discovered by assaying phytase activity of plant extracts followed by the classification of the enzyme into the PAP family due to its characteristics, or by overall sequence homology with other plant PAPhy.

#### **1.3.4.** Phytases in the animal feed industry

The main application of phytases is a as animal feed supplement to improve phosphorus bioavailability.

#### 1.3.4.1. Nutritional, economic and environmental perspectives

Phytate is the principal form of phosphorus storage in the cereals grains and legume seeds used in commercial animal feeds (Yao et al., 2012). From the end of the twentieth century, the use of plant-based feeds has been established for being cheaper and safer than animal-based protein sources (Lei et al., 2013; Brinch-Pedersen et al., 2014). Whereas ruminant animals, like cows or sheep, possess intrinsic phytases in their complex digestive tract mainly produced by their gut microbiota, non-ruminants or monogastric animals such as pigs, poultry and fish (as well as humans, cats and dogs), have very limited phytase activity in their digestive system. In addition, many plant feed components have no phytase activity in the mature seed or phytases get inactivated during the feed production (Vohra and Satyanarayana, 2003; Brinch-Pedersen et al., 2014). For these reasons, phytate-phosphorus in plant feeds is not readily available for monogastric animals, making inorganic phosphorus supplementation of the feed required to satisfy their dietary phosphorus needs and with the consequent elevation of the costs of raising these animals. The supplementation of animal feed with inorganic phosphorus does not compensate for the loss of other nutrients phytate is capable of chelating and, therefore, their assimilation by the animals is still reduced. Moreover, phosphorus is a limited resource which price has raised in the new millennium. As well as its antinutrient effects in non-ruminants, phytate passes undigested through the digestive tract of these animals resulting in high concentrations of phosphorus in their excreta, which have the potential to trigger adverse environmental consequences like the eutrophication of aquatic ecosystems if runoff occurs (Lei et al., 2013; Brinch-Pedersen et al., 2014).

The above described scenario has provoked the exponential growth of phytase research in the last few decades. The addition of exogenous phytases to animal feed constitutes a cost-effective measure to reduce the concentration of phosphorus in animal excreta as well as to improve nutrient bioavailability in monogastric species (Lei *et al.*, 2013).

#### **1.3.4.2.** Commercial phytases

Organisms do not naturally produce phytase activity sufficiently high to be commercially viable. The first commercial phytase to be added to animal feedstock launched in 1991 under the name of Natuphos<sup>®</sup> (BASF animal nutrition). It was produced from the overexpression of *Aspergillus niger* PhyA thanks to the development of the recombinant DNA technology in the 1980s (van Hartingsveldt *et al.*, 1993). Other fungal phytases have been commercialised since, such as Allzyme<sup>®</sup> SSF (Alltech), Finase<sup>®</sup> P/L (AB Vista) or Ronozyme<sup>®</sup> P (Novozyme and DSM). Fifteen years later *Escherichia coli* AppA and AppA2 phytases were proved to be more effective than the previous fungal phytases (Rodriguez *et al.*, 1999; Rodriguez, Han and Lei, 1999). Further research on bacterial phytases led to the development of a new generation of commercial phytases superior to the first generation of fungal phytases (Lei *et al.*, 2013). AppA2 is commercialised under the name of OptiPhos<sup>®</sup> (Enzyvia, JBS United), while an engineered version of AppA has been named Quatum<sup>®</sup> Blue (AB Vista).

All phytases commercialised to date belong to the HAPhy class. The global phytase market has been estimated to represent more than 60% of the total feed enzyme market and to be worth \$350 million per year (Lei *et al.*, 2013).

The principal characteristics that commercial phytases are desired to fulfil are: (1) catalytic efficiency or specific activity towards phytate; (2) an appropriate pH-activity profile as well as protease and acid resistance, so that the enzymes have the ability to effectively hydrolyse phytate-phosphorus in the upper digestive tract of the animal; (3) thermostability to allow them to resist the high temperatures reached during the feed pelleting (80-90°C), a step of the feed processing; and (4) cheap production costs. Commercial phytases need to be effective in the stomach (pH 2-5) and inactivated in the lower gut (pH 6.5-7.5). In this way, phytases are not destroyed during stomach digestion and can hydrolyse phytate there, so that phosphorus can be absorbed in the small intestine of the animal. The phytases then become inactive before excretion, avoiding contribution to the increase of inorganic phosphorus in the environment (Lei and Stahl, 2001; Lei *et al.*, 2013; Brinch-Pedersen *et al.*, 2014).

Although all phytases commercialised as feed additives so far are HAPhy, BPPhy may be a good alternative due to having better thermostability, proteolytic resistance and absolute substrate specificity. The unique properties of these class of phytases makes them perfect feed additives for the aquaculture industry, although they present lower activity compared to HAPhy and optimum activity at alkaline pH (Kumar *et al.*, 2017).

#### 1.3.4.3. Alternative strategies to the use of phytases as feed additives

Despite supplementing animal feed with phytases seeming to be the most convenient and feasible solution, other alternative strategies have been proposed to solve the problems associated with feed phytate-phosphorus in animal production (Lei *et al.*, 2013). The development of transgenic plants with increased phytase production (Lucca, Hurrell and Potrykus, 2002; Chan, Lung and Lim, 2006; Holme *et al.*, 2017) or transgenic animals overexpressing phytase (Golovan *et al.*, 2001) are limited by the public concern regarding the safety of genetically modified organisms. Low phytate biosynthesis mutants have also been reported, but it is accompanied by deleterious effects for the plants (Raboy, 2009). The possibility of chemically degrading feed phytate before feeding was also contemplated, but it turned out to affect feed quality (Pandey *et al.*, 2001). Another strategy consists of inoculating phytase-producing microorganisms into the digestive system of monogastric animals, but this may destabilise their natural microbiota and contaminate the environment through their faeces (Pagano, Roneker and Lei, 2007).

#### **1.3.4.4.** Future prospects for phytases in the animal feed industry

The need for further decreasing the amount of phosphate present in the environment in areas of intensive farming and agriculture have resulted in the issue of special laws to incorporate phytase into animal diets in many countries. This together with the accelerated depletion of phosphorus reserves in the next 50 years is likely to make the phytase market to expand to greater values than the current \$350 million per year.

The identification of novel wild type phytases or engineering desired characteristics of the already known ones through random mutagenesis, rational design or a combination of both, are the two paths that can be followed in the search for phytases suitable for applications in the animal feed industry. Because an ideal phytase for all applications might be too ambitious, a next generation of phytases tailored for specific species of animals and diets has been suggested, as well combining the use of different phytases or other enzymes (Lei *et al.*, 2013).

## **1.3.5.** Other applications of phytases

The antinutrient effect of phytate due to its ability to chelate important minerals makes phytases also relevant in the human food industry. However, the use of phytases in human nutrition is not as widespread as in animals due to the consumer reluctantly to include recombinant proteins in their diet, the potential availability of low-phytate crops and the beneficial roles of phytate as an antioxidant (Lei *et al.*, 2013).

Novel applications of phytases in human health and medicine have also been suggested, such as potential candidates in osteoporosis treatment (Pagano *et al.*, 2007) or in the large scale production of inositol phosphates associated with health benefits (Quan, Fan and Ohta, 2003). Phytases may also have applications in the biofuel and brewing industries (Fujita *et al.*, 2001; Hubenova and Mitov, 2010). In addition, thermostable phytases in conjunction with xylanases are powerful additives in the pulp and paper industry (Uma Maheswari and Chandra, 2000; Nampoothiri *et al.*, 2004).

# 1.4. Aims and objectives of the project

This project aims to study the structure-function relationships of purple acid phytases (PAPhy), members of the purple acid phosphatase (PAP) class and the calcineurin-like metallophosphoesterase (MPE) superfamily of proteins. PAPhy are the least studied enzymes among the four structural classes of phytases, with no structural information available and no members employed as commercial feed additives. The project focuses on the identification of the specific features of PAPhy that make them able to use phytate as substrate through the study of their amino acid sequence and 3D structure. The main objectives of the project can be outlined in three points: (1) analysis of PAP sequences with and without phytase activity for the selection of targets for structural and enzymatic studies; (2) preparation of recombinant PAPhy samples for X-ray crystallography experiments with the aim to obtain the first crystal structure of a PAPhy enzyme; and (3) rational mutagenesis, biochemical and biophysical characterisation of PAPhy to stablish structure-function relationships of these enzymes in order to determine the PAPhy substrate specificity pockets.

# Chapter 2. Bioinformatic analysis of PAP sequences

In this chapter, the amino acid sequences of known PAPhy are analysed and compared with those of PAPs not demonstrated to show phytase activity. The aim of the analysis is to identify the key differences between PAPs with and without phytase activity, using sequence and structure information. Only a limited number of PAPhy have been characterised so far. Others have been predicted by sequence homology with previously characterised PAPhy. However, even taking predicted proteins into account, not many PAPhy have been identified considering that PAPs constitute a large class of enzymes. This analysis could provide bioinformatic tools to help in the identification of novel PAPhy candidates among known PAPs through database searches.

Multiple sequence alignments allow the assessment of sequence conservation of protein domains, tertiary and secondary structures, as well as evolutionary relationships. No structure information is available for PAPhy yet, but various crystal structures of HMW plant and LMW animal PAPs have been solved (Klabunde *et al.*, 1996; Guddat *et al.*, 1999; Lindqvist *et al.*, 1999; Uppenberg *et al.*, 1999; Schenk *et al.*, 2005, 2008; Sträter *et al.*, 2005; Feder *et al.*, 2012; Antonyuk *et al.*, 2014; Selleck *et al.*, 2017). The identification of homologues of PAPhy with crystal structures deposited in the PDB would allow the generation of a PAPhy 3D homology model as a first step towards obtaining a crystal structure by molecular replacement.

All PAPs with phytase activity identified so far have been found in plants. They are usually purified from the source or expressed in eukaryotic expression systems to allow for the post-translational modification essential for the protein function, such as N-linked glycosylation. Abundant and homogeneous protein samples are required to determine a structure through X-ray crystallography, hence simple, robust bacterial expression systems would be desirable. Finding PAPhy homologues in simpler organisms than higher plants, such as bacteria, would be advantageous to potentially simplify the process of protein expression and purification for crystallographic purposes.

# 2.1. Materials and methods

#### 2.1.1. Collection of PAP sequences

Amino acid sequences from all the PAPhy and several PAPs found in the literature review (see **Chapter 1**) were collected from the UniProt database (Bateman et al., 2017). Twenty-eight PAPhy, forty-four HMW plant PAP, fifteen LMW plant PAP, ten HMW animal PAP, ten LMW animal PAP and two fungal PAP sequences were included in the analysis. Six bacterial PAP sequences out of the fifty-eight prokaryotic sequences analysed by Yeung et al. were found in the UniProt database and added to the collection (Yeung et al., 2009). Twelve PAP sequences from microscopic algae, reported by Rivera-Solís et al. but not present in the UniProt database, were also included, as the gene expression of two of them had been correlated with phytase activity. The microalgal sequences were retrieved from Phytozome version 8.0 (Goodstein et al., 2012) or Protein BLAST (BLASTP; Altschul and Gish, 1996) searches following the methods in the article Rivera-Solís et al. (2014). A total of 127 sequences were collected. Sequence groups were created to facilitate the analysis, taking into account (1) reported phytase activity of the protein, (2) kingdom of life of the source organism, and (3) estimated molecular weight of the protein. Inside the PAPhy group, distinctions were made for characterised proteins, those predicted by sequence homology with characterised PAPhy, or sequence outliers compared to the rest of the PAPhy enzymes. A specific group was created for the microalgal PAPs, as they shared insufficient sequence conservation with the higher plant enzymes. The sequences collected are shown in **Appendix 1**, Table A1.

## **2.1.2.** Analysis of PAP sequences through multiple sequence alignments

Multiple sequence alignments (MSA) of the PAP sequences were performed and analysed with Jalview (Waterhouse *et al.*, 2009). The MUltiple Sequence Comparison by Log-Expectation (MUSCLE) algorithm (Edgar, 2004) with default parameters was used for all the MSAs. A phylogenetic analysis of the PAP sequences was performed with the MEGA7 software (Kumar, Stecher and Tamura, 2016), and a phylogenetic tree constructed using the Maximum Likelihood method with default parameters. Four MSAs were performed: (1) including all PAP sequences; (2) a comparison of PAPhy sequences with plant and animal HMW PAPs; (3) a comparison of PAPhy sequences with plant and animal LMW PAPs; and (4) a comparison of PAPhy sequences with microalgal, fungal and bacterial PAPs (i.e. microbial PAPs). The comparison of PAPhy with LMW PAPs had to be manually modified in order to force the alignment of the PAP motifs in all sequences, due to the difference in length between the PAPhy and the LMW PAPs. The alignment containing all the PAP sequences was used to generate the phylogenetic tree. Upon examination of the tree, the sequences in the MSAs were manually sorted within each group according to the tree to help in the identification of conserved and non-conserved regions.

The conservation of the five PAP consensus motifs was examined in all sequences, paying special attention to the metal ligands. The conservation of the PAPhy motifs was also studied, both inside the PAPhy groups and in comparison with other PAPs lacking phytase activity.

#### 2.1.3. Protein homology modelling of a PAP phytase

Crystal structures of PAP enzymes were obtained from the PDB (Berman *et al.*, 2000). The sequences of two HMW plant PAPs with published structures, the red kidney bean (*Phaseolus vulgaris*) PvPAP1 and the sweet potato (*Ipomoea batatas*) IbPAP1, were aligned to the sequence of the wheat (*Triticum aestivum*) isoform b2 purple acid phytase (TaPAPhy\_b2) using the T-Coffee server (Notredame, Higgins and Heringa, 2000) with default parameters. The alignment of the three proteins with secondary structure information was displayed with ESPript 3.0 (Robert and Gouet, 2014). Optimal global sequence alignments of TaPAPhy\_b2 with each of the two HMW plant PAPs were generated with EMBOSS Needle (Rice, Longden and Bleasby, 2000) using the Needleman-Wunsch algorithm (Needleman and Wunsch, 1970). The pairwise sequence alignments were used as input to generate 3D homology models of TaPAPhy\_b2 based on the HMW plant PAP structures. The 3D models were produced using the SWISS-MODEL automated protein structure homology-modelling server employed in alignment mode (Biasini *et al.*, 2014).

#### 2.1.4. Identification of novel PAPhy through database searches

A PAPhy consensus sequence was obtained from the alignment of all characterised and predicted PAPhy, excluding two PAPhy outliers. Signal peptides and endoplasmic reticulum (ER) retention sequences were excluded from the consensus sequence. The PAPhy consensus was used as query sequence in the NCBI BLASTP server (Altschul *et al.*, 1990) to perform searches using default parameters against the non-redundant protein sequences database. Searches were performed (1) without organism restriction in the output results; (2) excluding plant sequences; and (3) including only prokaryotic sequences.

# 2.2. Results and discussion

#### **2.2.1.** Analysis of PAP sequences through multiple sequence alignments

The three MSAs comparing PAPhy with other PAP groups are shown in **Appendix 1**, Figure A2, Figure A3 and Figure A4. These were analysed in conjunction with the phylogenetic tree (shown in Figure 14) to determine the correct allocation of each PAP sequence into a group.

Three of the initial sequences were excluded from the analysis at different stages. AtPAP13 contained only three out of seven of the PAP metal ligands, and so was removed from the initial alignment of all the sequences before generation of the phylogenetic tree. LIPPD3 was similarly removed from the alignment of LMW PAPs against PAPhy for reason of its much shorter amino acid sequence than the rest of the PAPs. ZmPAP was excluded at the same stage for lacking PAP motifs I and II. In addition to these rejections, some sequences were reassigned to a different group than the one initially deduced from the literature after analysis of the MSAs and the phylogenetic tree. AtPAP23 and GmPAP4 seemed more related to some HMW plant PAPs than to the rest of PAPhy in size, sequence homology and phylogenetic relationships, so they were treated as PAPhy outliers and counted as HMW plant PAPs in the PAP motif analysis. On the other hand, the characteristics of three HMW plant PAPs (RcPAP1, VvPAP and AlPAP15) were more similar to the predicted PAPhy group. The results of this sequence

analysis are then based on 124 sequences (100%): twenty-nine PAPhy (23.4%), of which fourteen are characterised and fifteen predicted; forty-two HMW plant PAPs (33.9%), with two of them being PAPhy outliers; thirteen LMW plant PAPs (10.5%); ten HMW animal PAPs (8.1%); ten LMW animal PAPs (8.1%); twelve microalgal PAPs (9.7%); two fungal PAPs (1.6%); and six bacterial PAPs (4.8%).

The PAPhy sequences range from 442 to 566 amino acids, with only the two PAPhy outliers being shorter than 532 residues. HMW Plant PAP sequences are 396 to 638 amino acids long, with the majority of the proteins in this group being shorter than 500 amino acids. HMW animal PAPs are between 378 and 463 amino acids long. LMW plant PAPs range from 312 to 366 residues, while LMW animal PAPs are between 325 and 340 amino acids long. The microalgal PAPs are the most diverse in this respect, with sequences from 264 to 691 residues. The two fungal PAPs are 614 and 618 amino acids long, and bacterial enzymes range from 434 to 561 residues.

#### 2.2.1.1. Phylogenetic relationships

The first branching event of the tree appears to differentiate LMW from HMW PAP sequences. As expected, PAPhy are found in the HMW PAP branch with the LMW PAPs being their most distant relatives. Most of the PAPs within the groups chosen for this analysis are observed to be phylogenetically related in the tree, with a few exceptions. Microalgal PAPs are the group most dispersed across the tree. All LMW plant PAPs except LIPPD3 are in the same clade and share a common ancestor with the LMW animal PAPs, which also form a common clade. However, although CePAP1 was initially classified as a HMW animal PAP, it appears to be more related to LMW animal PAPs, as it appears within their clade. Its size and sequence conservation does not match very well with any of the two groups, so it was still treated as HMW for the sequence analysis. Two microalgal PAPs, CrPAP6 and MpPAP3, occupy an outgroup in the LMW PAPs clade. Most of the HMW plant PAPs, including PAPhy, form a clade. An outgroup of this clade containing the HMW animal PAP CePAP3 and the LIPPD HMW plant PAPs is observed. The remaining HMW animal PAPs form a separate clade, more related to microbial PAPs than to the HMW plant PAPs. Microalgal MpPAP4 is an outgroup of this clade. Five microalgal PAPs (i.e. MpPAP1, OIPAP2, CrPAP1, CrPAP2 and CrPAP3) are contained in

the HMW plant PAP branch, but not within the PAPhy clade. The six bacterial PAPs group all together and seem to be related to HMW animal PAPs and two microalgal PAPs, OIPAP1 and MpPAP2. Fungal PAPs form a clade with the microalgal PAPs CrPAP4, CrPAP5 and MpPAP4, in between HMW plant and animal PAPs.

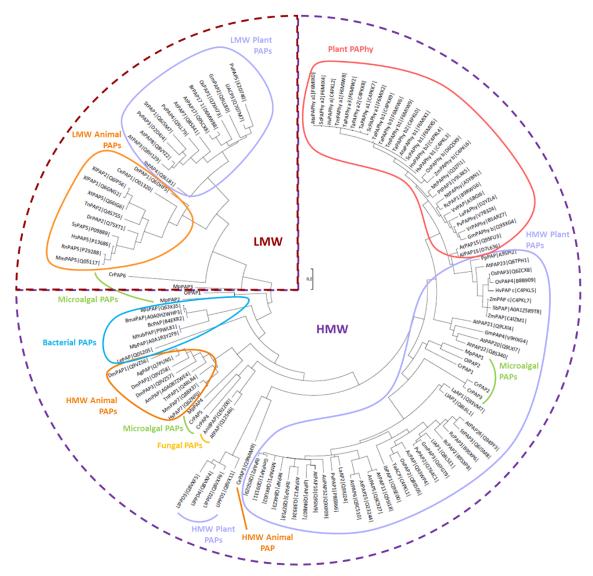


Figure 14. Molecular Phylogenetic analysis of PAP sequences by Maximum Likelihood method

The evolutionary history was inferred by using the Maximum Likelihood method based on the JTT matrixbased model (Jones, Taylor and Thornton, 1992). The tree with the highest log likelihood (-5950.08) is shown. Initial tree(s) for the heuristic search were obtained automatically by applying Neighbour-Join and BioNJ algorithms to a matrix of pairwise distances estimated using a JTT model, and then selecting the topology with superior log likelihood value. The tree is drawn to scale, with branch lengths measured in the number of substitutions per site. The analysis involved 126 amino acid sequences. All positions containing gaps and missing data were eliminated. There was a total of 59 positions in the final dataset. Evolutionary analyses were conducted in MEGA7 (Kumar, Stecher and Tamura, 2016).

Neither of the two microalgal PAPs, CrPAP1 or CrPAP5, for which expression had been correlated with phytate response, is found in the PAPhy clade. The PAPhy outlier

AtPAP23 appears in a clade of non-phytase HMW plant PAPs, but these are the closest non-phytase relatives to PAPhy. GmPAP4 belongs to a more distant clade of the HMW plant PAP group. Of the three newly-identified predicted PAPhy, RcPAP1 and VvPAP are in the main PAPhy clade, while AlPAP15 forms a separate one with the characterised PAPhy AtPAP15, immediately adjacent to the main one.

#### 2.2.1.2. PAP motif conservation

Tables showing details of the conservation of the PAP motifs can be seen in **Appendix 1** (Table A2, Table A3, Table A4, Table A5 and Table A6 for motif PAP I, II, III, IV and V, respectively). For the PAP motif analysis, both characterised and predicted PAPhy were considered as a single group, while PAPhy outliers were counted among the HMW plant PAPs. After the initial exclusions, all but one of the sequences included in the analysis contained all five PAP motifs. The HMW animal PAP, TnPAP1, lacked PAP I motif, but it was retained in the analysis as it contained the remaining four PAP motifs with the expected invariant metal ligands. Five exceptions among the PAP sequences were identified that deviate from one of the usual PAP metal ligands, as shown in Table 2.

Protein	Group	PAP motif	Expected	Observed
PtPAP3	PAPhy	П	xDxxY	xGxxY
OsPAP1	LMW Plant PAP	П	xDxxY	xDxxL
LIPPD2	HMW Plant PAP	Ш	xNxx	xSxx
MpPAP3	Microalgal PAP	Ш	xNxx	xDxx
TaPAPhy_b1	PAPhy	IV	xxxH	xxxY

Table 2. PAP invariant metal ligands exceptions

According to the literature (Schenk *et al.*, 2013), the PAP sequence pattern shared by proteins of this class is comprised of the following five conserved motifs:  $GDxG-x_n-GDx_2Y-x_n-GNH[E/D]-x_n-Vx_2H-x_n-GHxH$ . However, the results of the present sequence analysis suggest a wider variability of some of the amino acids comprising these motifs.

The GDxG PAP I motif reported in the literature was shared by the 87.1% of the sequences analysed, with 7.3% of the sequences bearing a different amino acid in the first position of the motif (alanine, asparagine, serine or cysteine instead of glycine),

while 4% of the sequences had a different amino acid in the fourth position (alanine, serine or cysteine instead of glycine). Only one sequence (0.8%), the microalgal CrPAP1, had variant amino acids in both first and fourth positions. The amino acid observed in the third position of the GDxG PAP I motif varied between leucine, tryptophan, methionine, threonine, valine and isoleucine. The identity of this third amino acid was conserved for some of the PAP groups. 90.1% of HMW plant PAPs, including the PAPhy, showed a PAP I motif of the form GDLG. Two bacterial PAPs, MbPAP and MtubPAP, contained a similar motif, but interrupted by a four-residue insertion (**GD**QSTPA**LG**). All the LMW plant and animal PAPs showed a PAP I motif of the form GDLG. Two bacterial of the form GDWD. The microalgal MpPAP3 and CrPAP6 also showed this motif.

Little variation was observed for the GDx<sub>2</sub>Y PAP II motif described in the literature, with 98.4% of the sequences analysed agreeing with it. Only two exceptions were observed in sequences presenting a different amino acid in the first or second position of the motif. As indicated in Table 2, the characterised PAPhy PtPAP3 presented a PAP II motif of the form GGVTY, with an unusual metal ligand. The HMW animal PAP TnPAP1, which also lacked the PAP I motif, contained a PAP II motif of the form RDFAY. The PAP II motif was GDVSY in 51.7% of the PAPhy; GDLSY in 73.8% of the HMW plant and 100% of the fungal PAPs; GDFAY in 70% of the HMW animal PAPs; GDNFY in 100% of the LMW plant and animal PAPs; and GDLCY in 83.3% of the bacterial PAPs analysed.

The reported GNH[E/D] PAP III motif was conserved in 96% of the sequences included in this analysis. This motif was ANHE in the two microalgal PAPs CrPAP2 and CrPAP3; GNYE in the HMW plant PAP AtPAP11; GSHE in the HMW plant PAP LIPPD2; and GDHD in the microalgal PAP MpPAP3. The PAP III motif was GNHE in 93.8% of the HMW plant and animal PAPs, 50% of the microalgal PAPs, 100% of the fungal PAPs and 83.3% of the bacterial PAPs. Only 3.7% of the HMW plant and animal PAPs showed GNHD, in contrast with 100% of the LMW plant and animal, 25% of the microalgal and 16.7% of the bacterial PAPs.

Only 57.3% of the sequences included in this analysis presented a PAP IV motif of the form  $Vx_2H$ . Valine in the first amino acid position of the motif was replaced by alanine in 31.5% of the sequences, by threonine in 5.6%, by phenylalanine in 3.2%, by leucine in 1.6% and by isoleucine in 0.8%. As already indicated in Table 2, TaPAPhy\_b1 constitutes a metal ligand exception with the sequence AGWY in the PAP IV motif, meaning the metal in the MII site (predicted to be iron for this enzyme) is coordinated by asparagine, histidine and tyrosine residues rather than asparagine and two histidine residues as in the rest of PAPs (Dionisio *et al.*, 2011; Schenk *et al.*, 2013). The motif was not conserved within any group analysed, but 58.6% of the PAPhy had a motif of the form AGWH, while 47.6% of the HMW plant PAPs contained VLMH.

The GHxH PAP V motif reported in the literature was shared by 93.5% of the sequences analysed, with 6.5% of the sequences, all in the HMW animal PAP group, replacing glycine with alanine. The PAP V motif was GHVH in 98.6% of the HMW plant PAPs, including the PAPhy, and 50% of the microalgal PAPs. GHDH was observed in 86.7% of the LMW plant and animal PAPs, and in 66.7% of the bacterial PAPs. The fungal PAPs had a PAP IV motif of the form GHIH, while 80% of the HMW animal PAPs contained AHEH.

In summary, a higher variability has been observed in this sequence analysis for motifs PAP I, IV and V than previously reported in the literature (Schenk *et al.*, 2013). Some exceptions have also been observed for motifs PAP II and III, but these were minor compared to the other motifs. Therefore, a modified PAP sequence pattern is proposed based on the results of this analysis, being xDx<sub>2</sub>-x<sub>n</sub>-GDx<sub>2</sub>Y-x<sub>n</sub>-GNH[E/D]-x<sub>n</sub>-x<sub>3</sub>H-x<sub>n</sub>-[G/A]HxH.

#### 2.2.1.3. PAPhy motif conservation

Tables showing the conservation of the PAPhy motifs can be seen in **Appendix 1** (Table A7, Table A8, Table A9 and Table A10 for motif PAPhy 1, 2, 3 and 4, respectively). For the purposes of PAPhy motif analysis, characterised, predicted and PAPhy outliers were considered separately (with fourteen, fifteen and two sequences, respectively, and thirty-one sequences in total). HMW plant and animal PAPs (forty and ten sequences, respectively), as well as the three microbial PAP groups (twelve microalgal, two fungal and six bacterial sequences) were examined for PAPhy motif conservation with the aim to identify new targets. The LMW plant and animal PAPs were excluded from this part

of the analysis due to their low sequence similarity with PAPhy. Therefore, a total of 101 sequences were analysed for PAPhy motif conservation.

64.5% of the PAPhy sequences matched the PAPhy 1 motif RG[H/V/Q/N]A[V/I]D[L/I]P[D/E]TDP[R/L]VQR[R/N/T] described by Dionisio *et al.* (2011). These included ten of fourteen characterised PAPhy and ten of fifteen predicted PAPhy, with no other sequences in the analysis showing this exact motif. The PAPhy 1 motif was not conserved in the PAPhy outlier GmPAP4. The PAPhy outlier AtPAP23, the six HMW plant PAPs that appear as the closest relatives to PAPhy in the phylogenetic tree (i.e. PpPAP, OsPAP3, OsPAP4, HvPAP c, ZmPAP c and SbPAP) and the microalgal CrPAP5 showed partial to low conservation in PAPhy 1. Accepting one substitution, the PAPhy 1 motif would give the RGx[A/T][V/I]D[L/I]P[D/E][T/S]DP[R/L]V[Q/R]R[R/N/T] consensus, including all the characterised PAPhy except LaPAPhy and eleven out of fifteen predicted PAPhy. This motif would agree with 77.4% of the PAPhy and would still not be present in any non-phytase PAPs. Allowing two to four substitutions to PAPhy 1 would result in [R/P][G/T]x[A/T/S][V/I]D[L/I]P[D/E/P][T/S]DP[R/L]V[Q/R]R[R/N/T] and would include 90.3% of the PAPhy sequences. This motif would only rule out the predicted VrPAPhy and the outlier AtPAP23 and it still would not include the outlier GmPAP4 or any non-phytase PAP. The inclusion of VrPAPhy and AtPAP23 would require nine and ten substitutions, respectively. However, if such a number of substitutions were accepted, five of the six non-phytase HMW plant PAPs mentioned above would also show conservation of the motif.

Of the 83.9% PAPhy sequences with a conserved PAPhy 2 motif S[V/I]V[R/Q][Y/F]G, thirteen of the fourteen characterised PAPhy and thirteen of the fifteen predicted PAPhy were included. A modification of the motif to S[V/I]V[R/Q/H][Y/F]G would also include LaPAPhy and, therefore, all the characterised PAPhy, all the predicted PAPhy except VrPAPhy and RcPAP1, and not the PAPhy outliers. The inclusion of one to two substitutions would give the motif SxVx[Y/F]G and would include 100% of the PAPhy, including the two sequence outliers. However, conservation of this last motif could also be observed in 32% of non-phytase HMW plant and animal PAPs. Two microalgal sequences, MpPAP4 and CrPAP1, showed only a single substitution from the original PAPhy 2 motif, while the three fungal PAPs showed three

substitutions. Therefore, the present analysis of PAPhy 2 motif suggested that it may not be exclusive of PAPhy enzymes.

The published PAPhy 3 AMSxx[H/Y][A/Y/H]F[R/K]TMP motif was conserved in 77.4% of the PAPhy sequences. These include all the characterised PAPhy and ten of fifteen predicted ones. The motif was not conserved in the PAPhy outlier GmPAP4, and four substitutions would be necessary to include PAPhy outlier AtPAP23, the same as for the predicted VrPAPhy. Five to six substitutions in the motif would include 15.7% of non-phytase PAPs from HMW plant, HMW animal and microalgal PAP groups. A single substitution would include all the characterised and predicted PAPhy except VrPAPhy, and would result in a motif with the sequence [A/T][M/T]Sx[V/I/T][H/Y]xF[R/K]TMP.

The PAPhy 4 DCYSC[S/A]FxxxTPIH motif described in the literature was conserved in 80.7% of the PAPhy sequences, including thirteen of fourteen characterised PAPhy and twelve of fifteen of the predicted ones. One to two substitutions would result in DCY[S/K]C[S/A]Fxx[S/-][T/S]PIH and would include all the characterised PAPhy and all the predicted PAPhy except VrPAPhy. The PAPhy 4 motif was not conserved in the outlier GmPAP4 and four substitutions would be needed to include AtPAP23. However, four to five substitutions would also result in conservation of the PAPhy 4 motif in 15% of non-phytase HMW plant PAPs, the six closest relatives to PAPhy. Two microalgal PAPs, CrPAP2 and CrPAP3, showed a very low conserved motif with nine substitutions.

Therefore, to properly account for the diversity of all the characterised and predicted PAPhy studied in this analysis, the four published PAPhy motifs would need to be subject to modification. The PAPhy outliers AtPAP23 and GmPAP4 only had PAPhy 2 motif conserved. The sequence of LaPAPhy was the worst fit to the currently published PAPhy motifs, but the modifications to the motifs proposed in this analysis would accommodate it and still discriminate non-phytase PAPs. However, the degree of conservation of the PAPhy motifs in the predicted VrPAPhy was similar to that of AtPAP23, suggesting that, even if phytase activity was confirmed for this protein, it would also lie in the PAPhy outliers group. The possibility of PAPhy 2 motif not being exclusive to PAPs with phytase activity was also noted. In addition to the four PAPhy motifs described by Dionisio *et al.* (2011), another conserved region was observed in the MSAs for all the characterised and predicted PAPhy. The region was partially conserved in the six HMW plant PAPs with a close phylogenetic relationship to the PAPhy group, and was missing in the remaining non-phytase PAPs and PAPhy outliers. It consisted of a long sequence near the C-terminus and it could be considered an extra PAPhy motif. The proposed PAPhy 5 consensus sequence is displayed in Figure 15.

#### PAPhy 5 motif in PAP phytases

REKMA[T/I/V]x[H/F/Y]AD[E/D/A][P/A][G/R]xCP[D/E/K]Pxx[T/K][P/S][D/N]xx[M/I/L][G/A/R] [G/R][-/G][-/K][F/L]C[A/G]xNF[T/I][S/F/P][G/D/S]xx[A/V/-][G/S/D]x[F/Y]CWD[R/H/Q]

PAPhy 5 motif in non-phytase PAP

IE[K/E][I/V][D/G]x**[D/A]HADD**[P/S]**G[K/L/S]CP**[G/S]**P[G/S]D**N[H/Q/V]PE**[F/Y]**-G G--[V/L]C[H/R]**[L/S]NFT[S/F]GPA**[K/V]**GKFCW**[D/E][R/K/Q]

#### Figure 15. Proposed PAPhy 5 motif

Motif conservation in PAPs with phytase activity (top) compared with relatives lacking phytase activity (bottom, with conserved residues in bold).

The distribution of the PAP and PAPhy motifs, including the proposed PAPhy 5 motif, is shown in Figure 16.

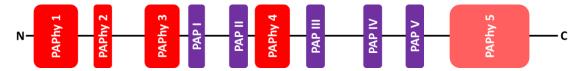


Figure 16. Schematic representation of the distribution of PAPhy motifs and PAP motifs in the amino acid sequence, including a potential new PAPhy motif

Sequence motifs conserved in PAPs are represented in purple boxes. The PAPhy motifs conserved in sequences of PAPs that display phytase activity identified by Dionisio *et al.* (2011) are represented in red boxes. The new PAPhy 5 phytase motif proposed in this analysis is represented in a light red box.

#### 2.2.2. Protein homology modelling of a PAP phytase

Sequence information can be used to generate 3D models of PAPhy enzymes from the crystal structures of PAP homologues. TaPAPhy\_b2 was selected as target to generate a 3D homology model, as it is one of the best characterised enzymes of this class of phytase. The closest homologues to PAPhy enzymes with published crystal structures are HMW plant PAPs. Several structures for the red kidney bean PvPAP1 are available in the PDB (accessions 1KBP, 4KBP, 3KBP, 2QFR, 2QFP, 4DT2, 4DSY, 4DHL and 4KKZ), as well as a structure for the sweet potato IbPAP1 (PDB accession 1XZW) and the yellow lupin LIPPD1 (PDB accession 3ZK4). LIPPD1 was discarded as a candidate template, as it is an exception among the HMW plant PAPs. While most HMW plant PAPs are homodimers of approximately 55 kDa subunits, LIPPD1 presents a homohexameric organisation of 75 kDa subunits (Antonyuk *et al.*, 2014). Among the red kidney bean PAP structures published, SWISS-MODEL identified the PvPAP1:SO<sub>4</sub> complex structure (PDB accession 2QFR) as the best template match to generate the TaPAPhy\_b2 model.

The alignment between TaPAPhy\_b2, the red kidney bean and the sweet potato PAPs revealed the conservation of most of the secondary structure elements (Figure 17), but not the cysteine residue involved in the formation of the disulfide bridge that links the two PAP subunits. This result agreed with the fact that cereal PAPhy have been previously purified as monomers (Dionisio *et al.*, 2011, 2012).

The quality of a protein structure model can be evaluated with the QMEAN4 scoring function. QMEAN4 gives a score for the whole model indicating its reliability. It allows comparison between alternative models of a target (Benkert, Tosatto and Schomburg, 2008). The TaPAPhy\_b2 model generated with SWISS-MODEL using the red kidney bean PAP as template had a QMEAN4 of -8.65 and 43.54% sequence identity. The model generated using the sweet potato PAP as template had a QMEAN4 of -9.36 and the sequence identity was 42.29%. Both models were fairly similar and in both cases TaPAPhy\_b2 was modelled as a homodimer following the quaternary structure of the template proteins, but only one subunit was analysed. Based on the QMEAN4 score, the model from the red kidney bean PAP was chosen as it had better quality than the sweet potato one, as well as higher sequence identity with the target.

The TaPAPhy\_b2 model resulting from the red kidney bean PAP template is shown in Figure 18. As predicted in the alignment, the overall structure was well conserved, with only a few loops poorly modelled. The PAP motifs with the residues coordinating the metal ligands in the active site were conserved. An overlay of the TaPAPhy\_b2 model and the red kidney bean PAP template locating the PAPhy motifs in the phytase is shown in Figure 19.

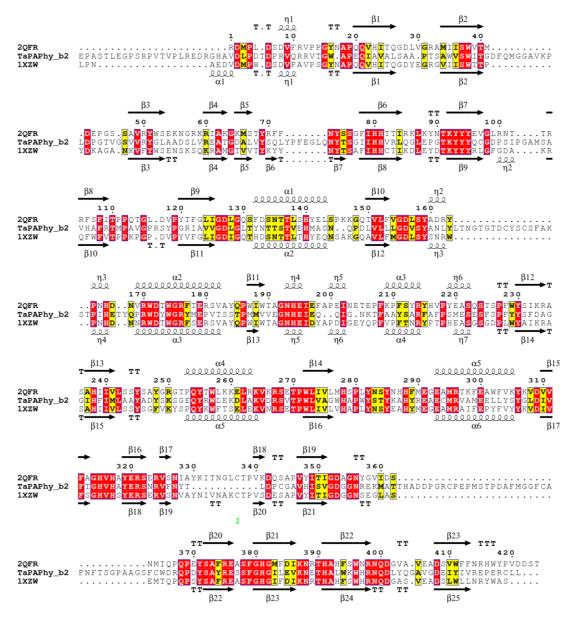


Figure 17. Alignment of TaPAPhy\_b2 and two HMW plant PAP homologues with solved structures

The top sequence corresponds to one subunit of a structure of the red kidney bean PAP (PvPAP1; PDB accession 2QFR), along with its secondary structure. The middle sequence corresponds to the wheat phytase TaPAPhy\_b2 without its signal peptide and ER-retention signal. The bottom sequence corresponds to one subunit of the structure of the sweet potato PAP (IbPAP1; PDB accession 1XZW), along with its secondary structure. The  $\eta$  symbol represents 3<sub>10</sub>-helices.  $\alpha$ -Helices, 3<sub>10</sub>-helices and  $\pi$ -helices are displayed as medium, small and large squiggles, respectively.  $\beta$ -Strands are rendered as arrows, strict  $\beta$ -turns as **TT** letters and strict  $\alpha$ -turns as **TT**. The green digit (1) at the bottom of the sixth line of the alignment shows the disulphide bridge that links the two subunits of HMW plant PAPs. Red boxes show regions with strict identity. Yellow boxes show regions with similarity. The alignment was generated with T-Coffee (Notredame, Higgins and Heringa, 2000) and displayed with ESPript (Robert and Gouet, 2014).

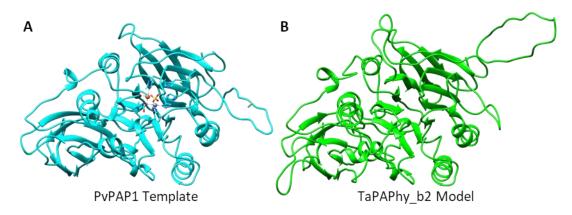


Figure 18. TaPAPhy\_b2 homology model and PvPAP1 template

One subunit of the red kidney bean PvPAP1 (PDB accession 2QFR), displayed in cyan (**A**), was used as template to generate a 3D homology model of TaPAPhy\_b2, in green (**B**). Cartoon representations of the proteins are displayed, created with the UCSF Chimera package (Pettersen *et al.*, 2004). Fe<sup>3+</sup>, brown sphere;  $Zn^{2+}$ , purple sphere; sulfate ion coloured by element and displayed as sticks.

The structure of the PAPhy motifs 2 and 3 was conserved and partially conserved, respectively, in the red kidney bean phosphatase. These motifs appear to be located away from the active site in the 3D organization of the enzymes (Figure 19A). The PAPhy 1 motif was modelled as the N-terminus of the wheat phytase due to its proximity to the beginning of the protein and its absence in the kidney bean PAP template structure. PAPhy 4 corresponded to an insertion in the model with respect to the kidney bean enzyme, so it was modelled as a loop. The long insertion identified as a potential PAPhy 5 motif during the sequence analysis is observed as a loop not present in the PAP enzyme. Motifs PAPhy 1, 4 and 5 were modelled as loops located in the proximity of the catalytic centre of TaPAPhy\_b2 (Figure 19B). The predicted structural arrangement of these motifs possibly allows them to fold over the active site, making them potential good 'phytase signature sequences' for the identification of novel PAPhy enzymes.

Examination of the model in Figure 19B, the alignment in Figure 17 and the MSAs in **Appendix 1** Figure A2, Figure A3 and Figure A4, reveals the PAPhy 4 motif is located in an insertion absent in non-phytase PAPs a few amino acids longer than the currently defined motif (Dionisio *et al.*, 2011), suggesting that the PAPhy 4 motif could be extended to L[T/S]NGT[G/S][T/A/S]DCY[S/K]C[S/A]Fxx[S/-][T/S]PIH.

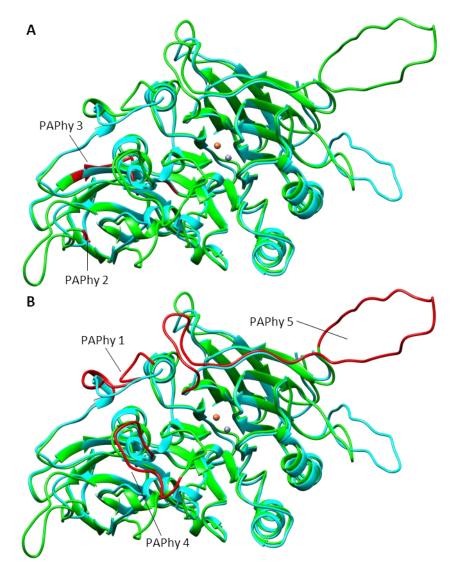


Figure 19. Localisation of PAPhy motifs in TaPAPhy\_b2 model overlay with red kidney bean PAP

TaPAPhy\_b2 model is displayed in green overlaid with the red kidney bean PvPAP1 (PDB accession 2QFR), displayed in cyan. The brown sphere depicts the Fe<sup>3+</sup> metal ion from PvPAP1, while the Zn<sup>2+</sup> is represented as a purple sphere. PAPhy motifs are coloured red in TaPAPhy\_b2. (**A**) PAPhy motifs 2 and 3. (**B**) PAPhy motifs 1, 4 and 5. Cartoon representations of the proteins are displayed, created with the UCSF Chimera package (Pettersen *et al.*, 2004).

# 2.2.3. Identification of novel PAPhy through database searches

The PAPhy consensus sequence used as query for the BLASTP searches is shown in Figure 20. Tables with the results of the three BLASTP searches carried out with the PAPhy consensus against the non-redundant protein sequences database can be found in **Appendix 1** Table A11, Table A12 and Table A13. 100 hits were retrieved per search. >PAPhy consensus/1-541 Percentage Identity Consensus

EPASTLEGPSRPVTVPLREDLRGHAVDLPDTDPRVQRRVTGWAPEQIAVALSAAPTSAWVSWITGEFQMGGAVKPLD PGTVGSVVRYGLAADSLVREATGDALVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTKYYYQCGDPAIPGAMSAVHAFR TMPAVGPRSYPGRIAVVGDLGLTYNTTSTVDHMASNRPDLVLLVGDVSYANLYLTNGGTGTDCYSCSFAKSTPIHETYQ PRWDYWGRYMEPVTSSTPMMVVEGNHEIEEQIGNKTFAAYSSRFAFPSKESGSFSPFYYSFDAGGIHFIMLGAYADYS KSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYSTYKAHYREAECMRVAMEELLYSYGLDIVFTGHVHAYERSNRV FNYTLDPCGAVHISVGDGGNREKMATTHADEPGHCPDPLSTPDAFMGGGGFCAFNFTSGPAAGRFCWDRQPDYSA YRESSFGHGILEVKNETHALWRWHRNQDLYQGSVAGDEIYIVREPERCL

#### Figure 20. PAPhy consensus sequence for BLASTP searches

The PAPhy consensus sequence was obtained from the alignment of all the characterised and predicted PAPhy, excluding the two PAPhy outliers GmPAP4 and AtPAP23, after the removal of signal peptides and potential ER-retention signals.

The sequences resulting from the three BLASTP searches performed were analysed for conservation of the three PAPhy motifs identified as PAP phytase signature sequences. Figure 21 shows the consensus sequences of the three motifs, deducted from the MSA analysis, that were used to discriminate PAPhy from non-phytase PAPs among the BLAST hits.

#### PAPhy 1 motif

[R/P][G/T]x[A/T/S][V/I]D[L/I]P[D/E/P][T/S]DP[R/L]V[Q/R]R[R/N/T]

PAPhy 4 motif DCY[S/K]C[S/A]Fxx[S/-][T/S]PIH

#### PAPhy 5 motif

REKMA[T/I/V]x[H/F/Y]AD[E/D/A][P/A][G/R]xCP[D/E/K]Pxx[T/K][P/S] [D/N]xx[M/I/L][G/A/R][G/R][-/G][-/K][F/L]C[A/G]xNF[T/I][S/F/P] [G/D/S]xx[A/V/-][G/S/D]x[F/Y]CWD[R/H/Q]

#### Figure 21. PAPhy motifs used to identify new PAPhy in the BLASTP results

Consensus amino acid sequences of the PAPhy signature sequences PAPhy 1, 4 and 5 motifs. The sequences were obtained from the MSA analysis carried out in **section 2.2.1.3**. Among the different consensus sequence options presented for each motif, those that included the maximum number of PAPhy enzymes without comprising any non-phytase PAPs were selected.

The BLASTP search with no organism restrictions resulted in a collection of plant

PAP protein sequences, ranging from cereals, grasses and legumes to flowering plants, trees and shrubs. 34% of the sequences corresponded to already characterised or predicted PAPhy and were ignored in the analysis. 21% of the sequences were not directly identified as PAPhy in the search results, although they belonged to plants that already have known characterised or predicted PAPhy, while the remaining 45% corresponded to plants with no PAPhy enzymes reported so far. 25% of the sequences had the three PAPhy signature motifs conserved, 27% had two motifs conserved and

one partially conserved, and 11% of the sequences had one motif conserved and two partially conserved. All the sequences with partially conserved motifs showed only one to two substitutions compared to the motifs in Figure 21. Only 3% of the sequences presented either an absent PAPhy 1 motif or a low conserved PAPhy 4 motif. Therefore, twenty-five sequences resulting from this BLAST search could be considered new predicted PAPhy. Among them, *Oryza brachyantha* (XP\_015690330.1), *Corchorus capsularis* (OMO71036.1), *Citrus trifoliata* (AFY06666.1), *Hevea brasiliensis* (XP\_021641480.1 and XP\_021641479.1), *Solanum lycopersicum* (XP\_004247857.1), *Solanum pennellii* (XP\_015086742.1 and XP\_015086743.1) and *Cicer arietinum* (XP\_004502218.1) were plants with no previously reported PAPhy enzymes. Another thirty-eight plant PAP sequences could also be considered new predicted PAPhy if a little more flexibility was allowed in the PAPhy signature motifs, but they would need to be examined more closely and tested for phytase activity before making a decision.

However, none of these newly identify PAPhy sequences would, in principle, present an advantage as targets for crystallographic structure determination over those already known. A BLASTP search excluding plant proteins from the results was carried out in order to try to expand the range of predicted PAPhy to other organisms. The sequences retrieved from this search belonged to a wider variety of organisms, including animals, protists and archaea. The first eight hits corresponded to synthetic constructs of already known plant PAPhy. A single sequence belonged to a bat species, while six others were from anemones and corals. There were five amoeba proteins among the results, forty-eight sequences corresponded to proteins from microscopic algae, and twenty-five were proteins from fungus-like moulds. Only five of the sequences obtained were non-eukaryotic proteins, belonging to organisms classified inside the archaea domain. All the sequences in the search results had the PAP motifs conserved. However, none of them showed conservation for the PAPhy motifs. PAPhy 1, 4 and 5 motifs were deletions in 53% of the sequences (Figure 22A). Another 12% of the sequences did not present deletions for one or two of the PAPhy signature motifs, but they were not conserved. 18% and 8% of the sequences presented very low conservation in one or two of the PAPhy motifs, respectively, and only one microalgal sequence showed very low conservation of the three motifs (Figure 22B). Three of the five archaea sequences

retrieved showed deletions in place of PAPhy 1 and 4 motifs, and no conserved or very low conserved PAPhy 5 motifs. Hence, it was not possible to discern from these results the presence of novel PAPhy.

A final BLASTP search was performed restricting the results to proteins from prokaryotic organisms only. The 100 resulting sequences were comprised of bacterial proteins with the PAP consensus motifs conserved. 55% of the sequences belonged to bacteria from the *Streptomyces* genus. The bacterial protein sequences resulting from the search were significantly shorter than the PAPhy consensus sequence, meaning that only PAPhy 4 conservation could be assessed due to the absence of PAPhy 1 and PAPhy 5 in all the sequences. The PAPhy 4 motif was a complete deletion in 47% of the bacterial proteins (Figure 23A), while another 44% showed a non-conserved sequence aligned to half of the motif (Figure 23B). 1% of the sequences showed non-conservation of PAPhy 4, while 8% presented very low conservation (Figure 23C). As for the previous BLAST search, it was not possible to determine if novel PAPhy were found among the sequences identified. А

#### Iron(III)-zinc(II) purple acid phosphatase [Phytophthora megakarya] Sequence ID: <u>OWZ23938.1</u> Length: 462 Number of Matches: 1

Score		Expect	Method		Identities	Positives	Gaps
227 bi	its(578	<li>6e-65</li>	Compositio	nal matrix adjust.	152/466(33%)	225/466(48%)	88/466(18%)
Query	43	APEQIAVAL		SWITGEFQMGG		RYGLAADSLV 95 RYGL+ D L	
Sbjct	43			AIRTSNTEELELRLGM			2
Query	96	REATGDAL	VSQLYPFEGL	QNYTSGIIHHVRLQG-	-LEPGTKYYYQCGDP	AIPGAMSAVH 15	3
Sbjct	103	SVQLAEEPO		+YTS +HHV + G CSYTSPWLHHVTIPGD			5
Query	154			GDLGLTYNTTSTVDH			1
Sbjct	156	+F+T VC		GDLG T + TV H GDLGQTEYSRQTVRH			.0
Query	212	NGGTGTDC	SCSFAKSTPI	HE TYOPRWDYWGRYME			9
Sbjct	211			+ Q RWD WG+ ME SEQYRWDRWGKLME	P+ + P M+ GNH PLIARMPWMIAPGNH		9
Query	270			FSPFYYSFDAGGIH			.7
Sbjct	250		RF P + RFRMPYERENR	LORRNLYYGFRVGFVH	FILTPYVDSTSTSL		9
Query	328			STYKAHYREAECMR			5
Sbjct	310	+VDRS+TPM RVDRSITPM		++ AH M+ NSNTAHQGMEPHMGMK	ME++LY +D++ KNMEDILYRNKVDVI		9
Query	386			GDGGNREKMATTHADE	PGHCPDPLSTPDAFM	IGGGGFCAFNF 44	5
Sbjct	370	S+ V+ + SHPVYEEK		GD GNRE +A T+ GDAGNREGLAPTY		40	1
Query	446	TSGPAAGRE		YRESSEGHGILEVKNE		1	
Sbict	402			+R++ +G +L V N FROADYGFSMLNVINR		7	

В

Purple acid phosphatase 15 [Auxenochlorella protothecoides] Sequence ID: XP\_011400105.1 Length: 551 Number of Matches: 1 > See 1 more title(s)

Score		Expect	Method		Identities	Positives	Gaps
374 bi	ts(961	1) 8e-121	Compositio	nal matrix adjust.	213/499(43%)	298/499(599	6) 32/499(6%)
Query	27	DLPDTDPRV D+P +DPR+		IAVALSAAPTSAWVSM	ITGEFOMG-GAVKP	DPGTVGSVV 8	5
Sbjct	60			VSVTY-YGPTSVRFG			16
Query	86			SQLY-PFEGLQNYTSG			44
Sbjct	117	+ GL+ + QLGLSPSAY		Q+Y F NYTS DQIYYGFSNALNYTSP	+H V ++ L P T		75
Query	145			SYPERIAVEDLELTY			04
Sbjct	176			SYPLRFGLVADVGQTD			33
Query	205			AKSTPIHE	TYOPRWDYWGRY		54
Sbjct	234	YA+ Y NG YADNYEANG		S P + NISYPGEDIWIPFDVE	T+QPRWD W R YGTFQPRWDKWARL		89
Query	255			YSSRFAFPSKESGSFS			14
Sbjct	290	+ GNHE+		YNARYPSNYEASGSSN	+YS + G H	+ +YADY + ITSYADYDQ 3	49
Query	315			PWLVAGWHAPWYSTYK			74
Sbjct	350			PWL+ G+HAPWY++Y+ PWLIVGFHAPWYTSYR			09
Query	375			DPCGAVHISVGDGGI			33
Sbjct	410	V GHVHAY VLNGHVHAY	ER+ V+NYTL ERTFPVYNYTL	+ CG VH+++GDGGN NDCGPVHLTLGDGGNI	EK+A AD PG+C		69
Query	434	FMGGGGFCA		FCWDROPDYSAYRESS			93
Sbjct	470	QPEVCNQLL	++ G YDGE	FC OP++SA+RE S FCSTSOPEWSAFREPS	FGH +L++ N+THA FGHSVLDILNDTHA	+ W+RNQD FAWYRNQDA 5	22
Query	494		IYIVREPERC	512			
Sbict	523		+ +VR PE C VILVRNPEEC	539			

# Figure 22. Two BLASTP hits with PAPhy consensus as query against the non-redundant protein sequences database excluding plant proteins

(A) Hit 40, a slime mould PAP showing deletions in place of the three PAPhy signature motifs. (B) Hit 11, a microalgal PAP with very low conservation of the three PAPhy signature motifs. Purple frames, PAP motifs. Red frames, PAPhy 1,4 and 5 motifs (when present).

А

#### hypothetical protein [Armatimonadetes bacterium GXS] Sequence ID: <u>WP\_073995362.1</u> Length: 372 Number of Matches: 1

Score		Expect	Method		Identities	Positives	Gaps
116 bi	its(29	0) 6e-25	Composition	al matrix adjust	. 99/346(29%)	) 147/346(42%	b) 66/346(19%)
uery	44			ITGEFQMGGAVKPL KP+	DPGTVGSVVRYGLA + VV YG		102
bjct	5	P Q+ +A PTQLRIAY			ESPVVEYGTT	+R + PQLGMRVSAT	50
uery	103	LVYSQLYP			YYQCGDPAIPGAMS		162
bjct	51				YY+ G ++ G+ S YYRVGSVQGSFS		94
uery	163				DLVLLVGDVSYANL +VGD+SYAN	YLTNGGTGTDCY	220
bjct	95	PR P PRREPHDF		+ ++ P FSQRNTRNVLAHNP	TFHFINGDLSYAN-		141
uery	221	SCSFAKST			MVVEGNHETEEQIG		280
bjct	142		QP WDGRQPIWDV		MV GNHE E++G MVCLGNHE-NERVG		188
uery	281				SGEQYRWLEKDLAK		339
bjct	189	FP G FPMPNDGK	+YY F G YYYHFAIGN/	F+ ++ AFFVAFNSNEPD	EQ RWLE+ L DTEQRRWLERTLQD	R+ W +A	243
uery	340			RVAMEELLYSYGLD		385	
bjct	244	H P YS FMHHPPYS		LL YG+D IQTFVPLLERYGVD		288	

#### B hypothetical protein [Nocardioides szechwanensis] sequence ID: <u>WP\_091025310.1</u> Length: 447 Number of Matches: 1 See 1 more title(s)

Score			Method			tities	Positives	Gaps
117 bi	ts(29	2) 8e-25	Composition	nal matrix adjus	t. 94/2	279(34%)	129/279(46%	6) 32/279(11%)
Query	121		SLEPGTKYYYQC LEP T Y Y+	GDPAIPGAMSAVHA		VGPRSYPGR PR++ P		180
Sbjct	88	VYHHARLAN	HLEPDTTYRYRY	SHAGSAPAEG	FRTAPA	R-PRAFF	FAAFGDMGINA	141
Query	181			GDVSYANLYLTNG		YSCSFAKST + FA	PIHETYQPRWD WD	239
Sbjct	142	AAAAHVAL		GDLCYADSSG				187
Query	240	YWGRYMEP				AFPSKESGS A P +	FSPFYYSFDAG SP YSF G	299
Sbjct	188			INHE HEAGNGELGY				246
Query	300			GEQYRWLEK				350
Sbjct	247		3 A Y + SNDASYEIARNA	Q RWL + DYLGAAQDRWLVRF				306
Query	351	AHYREAECI		GLDIVFTGHVHAYE		389		
Sbjct	307	VHGSDG-GI		GVDLVVNGHNHCY		344		

# C hypothetical protein [Agarilytica rhodophyticola]

Sequence ID: WP\_086934137.1 Length: 976 Number of Matches: 1

Range	1: 78	to 327 GenPept Graphics		Vext Ma	itch 🔺 Previous Matc
Score		Expect Method	Identities	Positives	Gaps
105 bi	its(26	2) 2e-20 Compositional matrix adjust.	90/280(32%)	131/280(46%	) 46/280(16%)
Query	123	HHVRLQGLEPGTKYYYQCGDPAIPGAMSAVHAFI H VR+ L P TKYYY G I G ++ + F		IAVVGDLGLTY	180
Sbjct	78	HEVRITNLSPLTKYYYSVGSTTETIAGGNTS-YRF			135
Query	181	NTTSTVDHMASNRPDLVLLVGDVSYANLYL		AKSTPIHETYQ	235
Sbjct	136	RNSAAVYNAYLNYRGSSDTDLWVMLGDNAY			188
Query	236	PRWDYWGRYMEPVTSSTPMMVVEGNHELEEQIGNK	TFAAYSSRFAFPSK Y + F P	-ESGSFSP E+G S +	291
Sbjct	189	PVWPTLGNHDGRSADSSS			231
Query	292	FYYSFDAGGIHFIMLGAY-ADYSKSGEQYRWLEKD YYSFD G IHFI L +Y D S++G WL+ D		GWHAPWYSTYK WH P Y T	350
Sbjct	232	AYYSFDYGDIHFICLDSYETDRSRNGAMMTWLKND			287
Query	351	AHYREAECMRVAMEELLYSYGLDIVFTGHVH +H + E + M + ++ SYG+D+VF+GH H			
Sbjct	288	SHNSDTERALIEMRONALPIIESYGVDLVFSGHSH			

# Figure 23. Three BLASTP hits with PAPhy consensus as query against the non-redundant protein sequences database, results restricted to prokaryotic proteins

(A) Hit 2, a hypothetical PAP showing a deletion in place of PAPhy 4. (B) Hit 3, a hypothetical PAP showing a partial deletion in place of PAPhy 4. (C) Hit 76, a hypothetical PAP showing a poorly conserved PAPhy 4 motif. Purple frames, PAP motifs. Red frames, PAPhy 4.

## 2.3. Conclusions

The analysis of purple acid phosphatase sequences performed in this chapter suggests that proteins of this class seem to be even more widespread across all kingdoms of life than the current literature suggests. More flexibility in the sequence pattern characteristic of PAPs currently described would also be necessary to account for the diversity of all the proteins already classified as PAPs.

Key differences in the five PAP consensus motifs have not been identified between PAPs which have or do not have the ability to hydrolyse phytate. Further PAP motif conservation beyond the consensus seems to be more related to kingdom or complexity of the organism producing the enzyme than to the enzyme's substrate preference, data that is absent for the majority of the sequences identified. However, sequence information has shown potential to be sufficient to discern between phytase and non-phytase PAPs in particular cases. Two out of the four PAPhy consensus motifs, together with the fifth PAPhy motif proposed in this chapter, could be used to predict phytase activity in PAPs from plants with sufficient sequence similarity to the currently characterised PAPhy. Despite PAPs being present across all kinds of organisms, it has not been possible to predict phytase activity in organisms other than plants based on sequence information alone, as the PAPhy motifs have not shown conservation in PAPs from other organisms.

All the phytases from the PAP class identified to date, except two exceptions considered outliers, have strong phylogenetic relationships. A group of non-phytase HMW plant PAPs has been identified as close phylogenetic neighbours of the PAPhy, with the PAPhy 2 motif conserved and low conservation of the other PAPhy motifs observed, as well as being of similar size. The sequence conservation between the PAPhy and the proteins of this group has been used to update the PAPhy motifs so that they represent the maximum number of PAPs with proven phytase activity, without including those that are known to lack it. The PAPhy outlier AtPAP23 shares both phylogenetic relationships and sequence conservation with the PAPhy-related, non-phytase HMW plant PAPs, rather than with the PAPhy. The fact that only a weak phytase activity has been reported for this protein could explain the differences in sequence with the

remaining PAPhy. Based on this hypothesis, the predicted VrPAPhy would also be expected to show weak phytase activity due to its sequence similarity with AtPAP23. As for GmPAP4, the other PAPhy outlier, the sequence similarity with other PAPhy is lower, and not even very close to AtPAP23 and the PAPhy-related PAP group. Although a weak activity is not specifically described for this enzyme, that explanation could also apply in this case. The two microalgal PAPs whose gene expression had been correlated with phytase activity, CrPAP1 and CrPAP5, do not share enough sequence homology with the currently characterised plant PAPhy to assure or discard their ability to use phytate as substrate.

In light of these results, the most reasonable way to proceed the work of this thesis seemed to be to attempt the determination of the three-dimensional structure of a PAPhy enzyme that has already been characterised, rather than to pursue the identification of new targets in simpler organisms.

# Chapter 3. Generation of recombinant plant PAPhy samples for X-ray crystallography

In the previous chapter, the identification of PAPhy in organisms other than plants proved unsuccessful. Attempts to produce protein samples of known plant PAPhy suitable for X-ray crystallography are detailed in this chapter. Two different expression systems are described.

There are six different PAPs with known structures in the PDB. The three HMW plant PAP structures (i.e. red kidney bean, sweet potato and yellow lupin PPD1 PAPs), as well as the pig PAP structures, were obtained by crystallising native protein samples purified from the source organisms. Only the structures of two PAPs have been generated using recombinant protein. The rat PAP structure was obtained with protein generated with a baculovirus-insect cell expression system, while human PAP structures were obtained from protein samples produced in *Escherichia coli* and *Pichia pastoris*. The purification of native proteins from the source organism and especially from plants, however, can be an expensive, complicated and long process. The heterologous expression of recombinant proteins allows the production of proteins in simpler organisms than the natural source, making large-scale production and purification for the study of biochemical and biophysical properties easier (Yesilirmak and Sayers, 2009). Several PAPhy have been successfully expressed in heterologous expression systems, as summarised in Table 3.

#### Table 3. Heterologous expression of recombinant PAPhy summary

N- = N-terminal; C- = C-terminal; HIS = 6x histidine tag; GST = glutathione S-transferase fusion protein; TRX = thioredoxin fusion protein;  $\Delta$ SP.= N-terminal signal peptide sequence excluded from the expression construct;  $\Delta$ C-term = C-terminal ER-retention signal sequence excluded from the expression construct.

Source	Protein	Host	Strain	Vector	Tag	Purification/Results	Reference
Soybean	GmPhy	E. coli	BL21 (DE3)	pET-28a	N-HIS	62kDa ΔSP pET-GmPhy band in non-purified cell-free extracts.	(Singh <i>et al.,</i> 2013)
	GmPAP4	E. coli	Transetta	pET-32a (+)	C-HIS	61.2kDa ΔSP GmPAP4-His electrophoretic band from His-bind Purification Kit.	(Kong <i>et al.,</i> 2014)
Arabidopsis	AtPAP15	E. coli	BL21	pGEX-4T-3	N-GST	GST affinity column purification.	(Zhang <i>et al.,</i> 2008)
		S. cerevisiae	INVSc1 MATα hishis3∆1 leu2 trp1-289 ura3-52	pYES2/CT	C-HIS	Metal affinity column purification.	(Zhang <i>et al.,</i> 2008)
	ATPAP23	E. coli	XA90	pGEX-KG	N-GST	77.7kDa GST-AtPAP23 band from affinity chromatography and GF.	(Zhu <i>et al.,</i> 2005)
White lupin	LASAP3	E. coli	Origami (DE3) pLysS	pET-32b (+)	N-TRX	Non-purified cell lysate.	(Maruyama <i>et al.,</i> 2012)
Wheat	TaPAPhy_a1	P. pastoris	KM71H	pPICZαA (Ndel)	C-HIS	2.5 mg L $^{\rm -1}$ of secreted $\Delta SP$ $\Delta C$ -term protein purified from soluble fraction.	(Dionisio <i>et al.,</i> 2011)
	TaPAPhy_b1	E. coli	Rosetta B pRARE 2 (DE3) pLysS	pET15m	N-HIS	Insoluble protein used for antibody production.	(Dionisio <i>et al.,</i> 2011)
		P. pastoris	КМ71Н	pPICZαA (Ndel)	C-HIS	12-20 mg $L^1$ of secreted $\Delta SP$ $\Delta C$ -term protein purified from soluble fraction.	(Dionisio <i>et al.,</i> 2011)
	TaPAPhy_b2	P. pastoris	KM71H	pPICZαA	C-HIS	30 mg $L^1$ of secreted $\Delta SP$ $\Delta C$ -term protein purified from soluble fraction.	(Dionisio <i>et al.,</i> 2012)
Barley	HvPAPhy_a	P. pastoris	KM71H	pPICZαA (NdeI)	C-HIS	1.5 mg L <sup>-1</sup> of secreted $\Delta$ SP $\Delta$ C-term protein purified from soluble fraction.	(Dionisio <i>et al.,</i> 2011)
	HvPAPhy_b1	P. pastoris	KM71H	pPICZαA	C-HIS	2.4 mg L $^{-1}$ of secreted $\Delta SP$ $\Delta C$ -term protein purified from soluble fraction.	(Dionisio <i>et al.,</i> 2012)
	HvPAPhy_b2	P. pastoris	KM71H	pPICZαA	C-HIS	2.5 mg L $^{-1}$ of secreted $\Delta SP$ $\Delta C$ -term protein purified from soluble fraction.	(Dionisio <i>et al.,</i> 2011)
Maize	ZmPAPhy_b	P. pastoris	KM71H	pPICZαA	C-HIS	3.5 mg L <sup>-1</sup> of secreted $\Delta$ SP $\Delta$ C-term protein purified from soluble fraction.	(Dionisio <i>et al.,</i> 2011)
Rice	OsPAPhy_b	P. pastoris	KM71H	pPICZαA	C-HIS	3.5 mg L <sup>-1</sup> of secreted $\Delta$ SP $\Delta$ C-term protein purified from soluble fraction.	(Dionisio <i>et al.,</i> 2011)

A wide variety of protein expression systems with different expression vectors is available. Among them, Escherichia coli is the most popular host choice due to its rapid growth rate, ease of culture and rapid expression with high production levels at a relatively low cost. PAPhy from soybean, Arabidopsis and white lupin have been successfully expressed in *E. coli*, with soluble protein obtained and purified in some cases (see Table 3). One of the main objectives of this project was to determine the crystal structure of a PAPhy. The engineering of phytases with improved characteristics is a common step towards their potential application as feed additives. Due to the nature of the project, the advantages of succeeding in *E. coli* expression justified it being the first choice for expression trials of PAPhy enzymes. As depicted in Table 3, yeast hosts, in particular Pichia pastoris, are the organism of choice for the heterologous expression of most PAPhy. The main advantages of eukaryotic expression systems over bacterial ones are their ability to produce posttranslational modifications, such as glycosylation and disulfide bonds, representative of the native eukaryotic protein. Yeast systems are easier and less expensive to work with than insect or mammalian cells, and P. pastoris usually gives better protein yields (Demain and Vaishnav, 2009; Yesilirmak and Sayers, 2009).

A subset of plant PAPhy constructs were obtained and subjected to extensive expression trials in various *E. coli* strains under different conditions. One target was taken forward to the *Pichia pastoris* expression system to obtain samples for crystallographic and enzymological studies.

# 3.1. Materials and methods

#### **3.1.1.** Expression of recombinant plant PAPhy in *Escherichia coli*

Plasmids containing the coding region of several plant PAPhy genes were obtained from two different sources. Seven constructs for expression of cereal PAPhy in *Pichia pastoris* were kindly donated through a collaboration with Professor Henrik Brinch-Pedersen's group (Flakkebjerg Research Centre, Aarhus University, Denmark). The constructs contained the coding region of PAPhy genes from wheat (TaPAPhy\_a1, TaPAPhy\_b1 and TaPAPhy\_b2), barley (HvPAPhy\_a), rice (OsPAPhy\_b) and maize (ZmPAPhy\_b), with C-terminal 6xHis tags and without signal peptides and ER-retention signals. A synthetic construct for the expression of the soybean PAPhy (GmPAPhy\_b, also known as GmPhy) in *E. coli* was also acquired (GenScript).

#### 3.1.1.1. The Escherichia coli expression system

Escherichia coli is one of the most widely used hosts for the production of heterologous proteins. The main advantages of using E. coli as host for protein production are (1) fast growth kinetics; (2) easy achievement of cultures with high cell density; (3) inexpensive, rich and complex growth media; and (4) fast and easy transformation with exogenous DNA. These advantages make *E. coli* the least expensive, easiest and quickest expression system, with the potential for facile production of high yields of protein in a short period of time. On the down side, E. coli is unable to perform posttranslational modifications (like protein glycosylation), which are often required for the correct folding and function of proteins, and cannot produce very large proteins. In addition, proteins rich in disulfide bridges also present problems for E. coli expression and they often end up degraded by proteases or misfolded in inclusion bodies. Some eukaryotic proteins are still active in a non-glycosylated form, and protocols to solubilise and refold proteins from inclusion bodies are available. The production of proteins that are stabilised by disulfide bonds can also be targeted to the periplasm, where a reducing environment and the presence of specific enzymes allows their formation. Despite E. coli not seeming the most suitable candidate to produce eukaryotic proteins, a wide variety of engineered strains have been developed to reduce some of the problems that can arise (Yesilirmak and Sayers, 2009; Rosano and Ceccarelli, 2014).

A selection of *E. coli* expression strains relevant to this project is displayed in Table 4. All the strains used for the *E. coli* expression of PAPhy in this project contained chromosomal copies of the T7 RNA polymerase gene under the *lacUV5* promoter, allowing expression of recombinant proteins driven by the T7 promoter (i.e. DE3 or T7 strains). Expression of the T7 RNA polymerase and, therefore, the recombinant protein, is induced in the presence of the non-hydrolysable lactose analogue isopropyl  $\beta$ -D-1-thiogalactopyranoside (IPTG). Despite the expression of the T7 RNA polymerase being inducible in this system, basal expression can occur, and it leads to leaky expression of the recombinant protein. Some strains (i.e. pLysS strains) contain an additional plasmid that expresses the T7 lysozyme, an inhibitor of the T7 RNA polymerase, providing an effective control measure for leaky expression of recombinant proteins (Rosano and Ceccarelli, 2014). Auto-induction of the *lacUV5* promoter is also possible in culture media containing glucose, lactose and glycerol. The preferred carbon source of *E. coli* is glucose and it will be consumed first, preventing the uptake of lactose. Once the glucose is depleted, usually in mid to late log phase, the bacteria starts consuming the glycerol and lactose, with the second also inducing recombinant protein expression. The auto-induction method eliminates the need of biomass monitoring for addition of the inducer and allows the production of higher yields of recombinant protein.

#### Table 4. Description of some Escherichia coli expression strains

Tet, tetracycline. Str, streptomycin. Cam, chloramphenicol. Spec, spectinomycin. Gen, gentamycin. *ompT*, outer membrane protease gene. *trxB*, thioredoxin reductase gene. *gor*, glutathione reductase gene. DSbC, periplasmic chaperone and disulfide bond isomerase. Cpn10 and Cpn60, cold-adapted chaperonins from the psychrophilic bacterium *Oleispira antarctica*.

Strain	Origin	Resistance	Characteristics	Applications	
BL21	B line derivative	None	<i>lon</i> and <i>ompT</i> protease deficient, preventing degradation of foreign and extracellular proteins.	Most popular host for first expression screens.	
Origami 2	K-12 derivative	Tet + Str	<i>trxB</i> and <i>gor</i> mutations, enhancing disulfide bond formation in the cytoplasm.	Cytoplasmic expression of proteins containing disulfide bridges.	
Rosetta	BL21 derivative	Cam	pRARE plasmid expressing six rare tRNAs.	Expression of eukaryotic proteins that contain codons rarely used in <i>E. coli.</i>	
Rosetta 2	BL21 derivative	Cam	pRARE2 plasmid expressing seven rare tRNAs.	Expression of eukaryotic proteins that contain codons rarely used in <i>E. coli.</i>	
Rosetta-gami 2	Origami 2 derivative	Tet + Str + Cam	<i>trxB/gor</i> mutations and pRARE2 plasmid.	Expression of eukaryotic proteins that contain disulfide bridges and codons rarely used in <i>E. coli.</i>	
SHuffle	K-12 derivative	Spec + Str	<i>trxB/gor</i> mutations. Constitutive expression of DsbC in cytoplasm, allowing correction of mis-oxidised disulfide bonds.	Cytoplasmic expression of proteins containing multiple disulfide bridges.	
SHuffle Express	B line derivative	Spec	<i>lon</i> and <i>ompT</i> protease deficient. <i>trxB/gor</i> mutations. Constitutive expression of DsbC in cytoplasm, allowing correction of mis-oxidised disulfide bonds.	Cytoplasmic expression of proteins containing multiple disulfide bridges.	
ArcticExpress	BL21 derivative	Gen	Hte phenotype, increasing transformation efficiency. <i>endA</i> deficient, preventing plasmid DNA degradation. Constitutive expression of Cpn10 and Cpn60.	Expression of proteins at low temperatures for improved protein folding and solubility.	
ArcticExpress RIL	BL21 derivative	Gen + Str	Same as ArcticExpress. Plasmid expressing four rare tRNAs.	Expression of heterologous proteins from organisms with AT-rich genomes at low temperatures.	
ArcticExpress RP	BL21 derivative	Gen + Str	Same as ArcticExpress. Plasmid expressing three rare tRNAs.	Expression of heterologous proteins from organisms with GC-rich genomes at low temperatures.	

Vectors of the pET and pOPIN series were used for the *E. coli* expression of plant PAPhy. The pET vectors (Novagen) provide a powerful method for expression of recombinant proteins in *E. coli* driven by the T7 promoter, with a wide variety of fusion tags to choose from. The pOPIN vector suite is a versatile system designed for the high-throughput screening of recombinant protein expression across different hosts, with one-step cloning and minimal unwanted amino acids added to the final protein. It relies on a ligation-independent cloning (LIC) method carried out by the commercial In-Fusion<sup>™</sup> enzyme (Clontech-Takara Bio Europe), and a range of fusion tags are also available (Berrow *et al.*, 2007). The In-Fusion<sup>™</sup> enzyme is able to fuse a PCR amplified gene insert and a previously linearized plasmid with specific restriction enzymes when a 15 bp overlap is present at their ends.

One of the most useful characteristics of the heterologous expression of recombinant proteins is that it allows for the addition of fusion tags to the protein, extra amino acid sequences that help in its purification, solubility or detection. Vectors that include poly-histidine (6xHis) and glutathione-S-transferase (GST) tags, two of the most frequently used fusion partners, were tested for expression of plant PAPhy in *E. coli*. Although useful for the protein purification, fusion tags may interfere with subsequent steps such as crystallisation, hence mainly vectors that codify for cleavable fusion tags were used in the project.

## 3.1.1.2. GmPAPhy\_b construct design for *E. coli* expression

A synthetic construct for the expression of the soybean PAPhy (GmPAPhy\_b) in *E. coli* was designed and ordered from GenScript. The GmPAPhy\_b protein sequence was obtained from the UniProt database (Bateman *et al.*, 2017). The signal peptide of GmPAPhy\_b was predicted with the SignalP 4.1 server (Petersen *et al.*, 2011) with default parameters for eukaryotes and excluded from the construct (GmPAPhy\_b-SP). Disordered regions of the protein sequence without the signal peptide were predicted with the PrDOS server (Ishida and Kinoshita, 2007). The GmPAPhy\_b-SP sequence was aligned to the red kidney bean (PvPAP1) and sweet potato (IbPAP1) PAP homologue sequences using the T-Coffee server (Notredame, Higgins and Heringa, 2000) with

default parameters. The sequence alignment with secondary structure information was displayed with ESPript 3.0 (Robert and Gouet, 2014).

A truncated GmPAPhy\_b sequence was designed for synthesis with codon optimisation for expression in *E. coli*. The designed sequence was obtained in a pET15b vector, which allows recombinant protein expression from the T7 promoter with a cleavable N-terminal 6xHis tag and carries an ampicillin resistance selection marker. The *E. coli* preferred stop codon TAA was added at the 3' end of the truncated GmPAPhy\_b coding sequence. Cleavage sites for two restriction enzymes compatible with cloning into pOPIN vectors (although not exploited for cloning in this work), NdeI (CA<sup>V</sup>TATG, 5' end) and BamHI (G<sup>V</sup>GATCC, 3' end), were also included in the GmPAPhy\_b-pET15b construct.

## 3.1.1.3. Cloning of PAPhy into pOPIN vectors

The seven plant PAPhy available for the project were subjected to the In-Fusion™ LIC procedure into the vector pOPINB, a 5642 bp long vector for the recombinant expression of proteins in *E. coli* with an N-terminal cleavable 6xHis tag. The pPICZ $\alpha A$ constructs and GmPAPhy b-pET15b were used as templates. Specific primers to amplify the coding region of each plant PAPhy with 15 bp 5' extensions to allow cloning into the pOPINB vector were designed according to manufacturer's instructions. An ATG start codon is already included in the pOPINB vector sequence, before the N-terminal 6xHis tag and a 3C protease cleavage site. A stop codon is introduced with the reverse primer 5' extension, immediately after the 3' gene specific region of the primer. Primer properties were assessed using the Eurofins Genomics Oligo Analysis Tool (https://www.eurofinsgenomics.eu/en/ecom/tools/oligo-analysis.aspx). GC content and melting temperatures (T<sub>m</sub>) of the primers were kept between 40-60% and 58-65°C, respectively, and whenever possible. They were calculated for the 3' gene specific region of each primer, excluding the 5' extensions. The T<sub>m</sub> difference between forward and reverse primers was always below 4°C. All 3' gene specific regions were designed to be between 18 and 25 bp long.

In preparation for the cloning, the pOPINB vector was linearized by digestion with the restriction enzymes HindIII and KpnI (NEB). The reactions were set up on ice as

detailed in Table 5. The digestion was carried out by incubating the reactions at 37°C for 1 h, then at 80°C for 20 min in order to inactivate the restriction enzymes. Gene specific PCR experiments were carried out to amplify each PAPhy gene with the appropriate primers. The reactions were set up on ice as detailed in Table 6. The PCR protocol on Table 7 was used for the amplification, varying the annealing temperature for each set of primers. 20  $\mu$ L digestion and PCR trial reactions were set up to check for complete digestion of the vector and amplification of the correct PCR product. 50  $\mu$ L reactions were set up for the actual cloning. Negative control reactions were always included, using water instead of plasmid DNA. Results of the digestion and PCR reactions were assessed on 1% (w/v) agarose gels containing ethidium bromide. Once the desired results were confirmed, the 50  $\mu$ L reactions were loaded on fresh 1% (w/v) agarose gels containing ethidium bromide. DNA was extracted and purified from the agarose bands using the NucleoSpin® Gel and PCR Clean-up kit (Macherey-Nagel). The recovered DNA was assessed on 1% (w/v) agarose gels containing ethidium bromide.

Reagent	[Stock]	[rxn]	V for 1x 20 μL rxn (μL)	V for 1x 50 μL rxn (μL)
Water	n/a	n/a	Variable*	Variable*
CutSmart buffer	10x	1x	2	5
pOPINB/K	Variable*	20 ng $\mu$ L <sup>-1</sup>	Variable*	Variable*
HindIII	20 U μL <sup>-1</sup>	$0.2 \text{ U} \mu \text{L}^{-1}$	0.2	0.5
Kpnl	20 U μL <sup>-1</sup>	$0.2 \text{ U} \mu \text{L}^{-1}$	0.2	0.5
TOTAL			20	50

Table 5. Reaction set up for the digestion of pOPIN vectors

(\*) Depending on the concentration of the pOPINB (40-60 ng  $\mu$ L<sup>-1</sup>) or pOPINK (101 ng  $\mu$ L<sup>-1</sup>) plasmid stock used for each digestion.

In-Fusion<sup>TM</sup> cloning reactions were set up on ice with 2.5 µL of linearized and purified pOPINB, 1.5 µL of the appropriate purified PCR product and 1 µL of 5x In-Fusion<sup>TM</sup> HD Enzyme Premix (Clontech-Takara). The reactions were incubated at 50°C for 15 min. The total volume of each reaction (5 µL) was transformed into 50 µL of Stellar competent cells (Clontech-Takara). The reactions were added to the competent cells and left to mix by diffusion for 30 min on ice, before 'heat-shocking' at 42°C for 45 s. After the heat-shock, the transformations were put back on ice for 1-2 min before adding 350 µL of Super Optimal broth with Catabolite repression (SOC) medium. The transformations were then incubated at 37°C for 1 h with agitation. Blue/white colony screening was carried out by plating the whole volume of each transformation (400 µL) in Lysogeny Broth (LB) agar plates with kanamycin (50 µg mL<sup>-1</sup>, pOPINB resistance), IPTG (1 mM) and X-Gal (40 µg mL<sup>-1</sup>), incubated at 37°C overnight. Negative controls for the In-Fusion<sup>™</sup> reactions and the transformation were set up with water instead of plasmid DNA or reaction.

#### Table 6. Reaction set up for PCR with Phusion polymerase

All the plasmid templates were diluted to a working concentration of 2 ng  $\mu$ L<sup>-1</sup>. Primer mixes were prepared in water from 100  $\mu$ M stocks.

Reagent	[Stock]	[rxn]	V for 1x 20 μL rxn (μL)	V for 1x 50 μL rxn (μL)
Water	n/a	n/a	13.4	33.5
Phusion HF buffer	5x	1x	4	10
dNTP mix	10 mM each	0.2 mM each	0.4	1
Primer mix	$10\mu\text{M}$ each	0.5 µM each	1	2.5
Plasmid template	2 ng $\mu$ L <sup>-1</sup>	0.1 ng μL <sup>-1</sup>	1	2.5
Phusion polymerase	2 U μL <sup>-1</sup>	0.02 U μL <sup>-1</sup>	0.2	0.5
TOTAL			20	50

#### Table 7. PCR protocol for amplification with Phusion polymerase

(\*) Annealing temperatures were calculated for each set of primers, using a temperature 3°C higher than the temperature of the primer with the lowest T<sub>m</sub>. TaPAPhyA1-F1 and TaPAPhyA1-R1, 66.1°C; TaPAPhyB-F1 and TaPAPhyB-R1, 62.8°C; HvPAPhyA-F1 and HvPAPhyA-R1, 66.7°C; OsPAPhyB-F1 and OsPAPhyB-R1, 63.3°C; ZmPAPhyB-F1 and ZmPAPhyB-R1, 68.3; GmPAPhyT-F1 and GmPAPhyT-R1, 67.6.

Step	Cycles	Time	т (°С)	
Initial denaturation	1	3 min	98	
Denaturation		15 s	98	
Annealing	30	30 s	Variable*	
Extension		45 s	72	
Final Extension	1	10 min	72	
Hold	1	8	4	

White colonies were picked from the plates and each was grown in 10 mL of LB liquid culture at 37°C and 180 rpm overnight. The overnight cultures were used to purify the plasmids using the QIAprep® Spin Miniprep Kit (Qiagen). The concentration of the plasmids after their isolation was calculated by absorbance measurement at  $\lambda = 260$  nm with a NanoDrop<sup>TM</sup> Spectrophotometer (Thermo Scientific). Plasmids isolated from several colonies per cloned construct were screened for the presence of the correct gene insert by PCR. The same protocol used to amplify the PAPhy genes in preparation for the cloning was followed, using the plasmid templates of this initial PCR experiment as positive controls for the colony screening. The plasmid isolated from one colony per

construct showing the expected PCR product was also sequenced with the T7 promoter and terminator standard primers to further confirm the success of the cloning into pOPINB. Stocks of the positive transformants of PAPhy-pOPINB constructs in *E. coli* Stellar competent cells in 30% (v/v) glycerol were prepared, snap-frozen in liquid nitrogen, and stored at -80°C.

TaPAPhy\_b2 was additionally cloned into pOPINK to produce recombinant protein with an N-terminal cleavable GST tag. As pOPINK shares the same 5' extensions as pOPINB, the same PCR product previously obtained to clone the second was used for the first. The protocol described above was followed for the cloning.

## 3.1.1.4. Transformation of *E. coli* constructs into expression strains

The PAPhy *E. coli* work was initiated with the GmPAPhy\_b-pET15b synthetic construct. GmPAPhy\_b-pET15b was transformed into Rosetta 2 (DE3) pLysS, BL21 (DE3) pLysS, Rosetta-gami 2 (DE3) and SHuffle T7. The five PAPhy successfully cloned into pOPINB (GmPAPhy\_b, TaPAPhy\_b2, HvPAPhy\_a, OsPAPhy\_b and ZmPAPhy\_b) were all transformed into SHuffle T7 and SHuffle T7 Express. In addition, HvPAPhy\_a-pOPINB and OsPAPhy\_b-pOPINB were transformed into ArcticExpress (DE3) RP. The construct TaPAPhy\_b2-pOPINK was transformed into SHuffle T7, SHuffle T7 Express and BL21 (DE3). Empty pOPINB and pOPINK vectors were also transformed into the expression strains to serve as negative controls for the expression trials.

Transformations were carried out with 1  $\mu$ L of each construct into 50  $\mu$ L of the corresponding competent cells, following protocol detailed in **section 3.1.1.3.** Negative controls were set up, by transforming the competent cells with water instead of plasmid DNA. Colonies were selected in LB agar plates with ampicillin (100  $\mu$ g mL<sup>-1</sup>, pET15b construct) or kanamycin (50  $\mu$ g mL<sup>-1</sup>, pOPIN constructs) and the appropriate antibiotics for each *E. coli* strain. Selected colonies were inoculated into 10 mL LB with the same antibiotics and grown at 37°C and 180 rpm overnight. The overnight cultures were used to prepare 30% (v/v) glycerol stocks of the positive transformants and to initiate expression trials.

## 3.1.1.5. Expression trials of PAPhy in *E. coli*

Several small-scale expression trials of PAPhy enzymes were carried out in various expression hosts under different conditions. The IPTG induction expression trials were set up by inoculating 100-200  $\mu$ L of a suitable overnight culture from **section 3.1.1.4.** into 10 mL of LB media with ampicillin (100  $\mu$ g mL<sup>-1</sup>, pET15b construct) or kanamycin (50  $\mu$ g mL<sup>-1</sup>, pOPIN constructs) in 30 mL universal flasks. The cells were left to grow at 37°C and 180 rpm to an OD<sub>600</sub> of 0.5-0.8 before addition, or not (control), of up to 1 mM IPTG. For each IPTG concentration, cultures were left to express for 4 h, overnight or three days and/or at various temperatures, depending on each particular experiment.

The auto-induction expression trials were set up by inoculation 50  $\mu$ L of a suitable overnight culture from **section 3.1.1.4.** into 5 mL of auto-induction media with kanamycin (100  $\mu$ g mL<sup>-1</sup>) in 100 mL conical flasks. The ZYP-5052 (without trace metals) auto-induction media described by Studier (2005) was used for these trials, consisting of 1% (w/v) N-Z-amine, 0.5% (w/v) yeast extract, 50 mM Na<sub>2</sub>HPO<sub>4</sub>, 50 mM KH<sub>2</sub>PO<sub>4</sub>, 25 mM (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, 2 mM MgSO<sub>4</sub>, 0.5% (w/v) glycerol, 0.05% (w/v) glucose and 0.2% (w/v) lactose. The cultures were incubated overnight or for periods up to six days and/or at various temperatures, depending on the experiment. Protein expression levels were assessed by SDS-PAGE of denatured total cell protein samples normalised with the OD<sub>600</sub> of the cultures. The gels were stained with InstantBlue<sup>TM</sup> (Expedeon), a ready-to-use single step Coomassie stain. In addition, most gels were also stained with InVision<sup>TM</sup> (Life Technologies). InVision<sup>TM</sup> is a ready-to-use in-gel stain for the detection of recombinant proteins with 6xHis tags. It consists of a fluorescent dye conjugated to a nickel-nitrilotriacetic acid (Ni-NTA) complex that binds the His tag, allowing the detection of recombinant proteins under UV light.

Samples from cultures in conditions for which expression of recombinant protein was detected were taken to perform a solubility test, normalised with the OD<sub>600</sub> of the cultures. The cells were harvested from liquid culture by centrifugation. Cell pellets were snap-frozen in liquid nitrogen and stored at -80°C to aid with cell disruption. BugBuster<sup>®</sup> 10x Protein Extraction Reagent (Novagen), consisting of a mixture of detergents, was used to lyse the cells and release the proteins. The cell pellets were resuspended in 500  $\mu$ L of 1x BugBuster<sup>®</sup> diluted in lysis buffer (50 mM Tris/HCl pH 7.5, 100 mM NaCl, 1 mM EDTA, 50  $\mu$ g mL<sup>-1</sup> DNase), and incubated in gentle agitation for 20 min at room temperature. The lysed cells were centrifuged at 16000 x g for 20 min at 4°C in order to separate the soluble and insoluble phases. Insoluble fractions were resuspended in 500  $\mu$ L of the lysis buffer. The presence of recombinant protein in the soluble or insoluble fractions was checked through SDS-PAGE, staining the gels with InstantBlue<sup>TM</sup> and InVision<sup>TM</sup>.

Soluble fraction samples were further subjected to a preliminary phytase activity assay in some expression trials. The assay consists on the quantification of inorganic phosphate (Pi) released by the phytase enzymes from InsP<sub>6</sub> over a period of time at a certain pH. The detection of phosphate in the assay is based on the molybdenum blue reaction (Nagul et al., 2015), a reaction of orthophosphate ions with ammonium molybdate in acidic solution to form phosphomolybdic acid. The complex formed is reduced with sulfuric acid, acquiring an intense blue colour. The absorbance of the coloured solution can be measured at  $\lambda$  = 700 nm, and it is directly proportional to the concentration of phosphate in the solution. The phosphate release assay was carried out in 0.1 M acetate buffer pH 5 in the presence and absence of 1 mM potassium phytate ( $\geq$ 95% purity, Sigma), carrying out 100 µL reactions for 20 min at room temperature. 10 µL of soluble fraction were used per reaction. The total protein absorbance at  $\lambda$  = 280 nm was measured in the soluble fraction samples used for the assay in order to normalise the results. A standard curve was prepared with monopotassium phosphate. Buffer background and positive control reactions with 800 nM of E. Coli AppA HAP phytase were also set up. The reactions were stopped with 100  $\mu$ L of a colour reagent that reacts with the free phosphate, containing four volumes of 1.5% (w/v) ammonium molybdate in a 5.5% (v/v) sulfuric acid solution and one volume of a 10.8% (w/v) iron(II) sulfate solution. The stopped reactions were left to develop colour for 30 min before measuring the absorbance at  $\lambda$  = 700 nm in a microplate reader (Hidex Sense).

## **3.1.2.** Expression of recombinant plant PAPhy in *Pichia pastoris*

The enzyme TaPAPhy\_b2 was selected as the preferred target among the PAPhy available to generate protein samples for crystallography in *Pichia pastoris*. Selection was made on the basis that this isoform gave highest yield previously (Dionisio *et al.*, 2011, 2012), as can be seen in Table 3.

## 3.1.2.1. The *Pichia pastoris* expression system

Despite the popularity and convenience of the E. coli expression system, producing eukaryotic proteins in prokaryotic hosts often results in the formation of inclusion bodies and/or low yields of recombinant protein. Yeasts are single cell eukaryotic microbes with molecular, genetic and biochemical characteristics similar to higher eukaryotes. Pichia pastoris and Saccharomyces cerevisiae are the most commonly used yeast hosts. Unlike E. coli, yeasts have the ability to perform posttranslational modifications, can handle proteins rich in disulfide bridges and can assist protein folding. In addition, the wealth of molecular and genetic resources available for yeast, together with cost effective cultures, rapid growth and production of high yields of recombinant protein, provide substantial advantages over mammalian or insect cell hosts (Bill, 2014). Although quicker than other eukaryotic systems, yeast recombinant expression takes longer than E. coli. Other disadvantages of yeast expression systems are the lack of chaperonins, proteins required for the proper protein folding of some proteins, differences in glycosylation patterns, and hyperglycosylation of N-linked sites of recombinant proteins compared to higher eukaryotes. However, hyperglycosylation is less extensive in *P. pastoris* (up to 20 residues) than in *S. cerevisiae* (50-150 residues). Tightly regulated promoters, higher biomass, simpler transformation process and the ability to generate more posttranslational modifications, constitute other advantages over S. cerevisiae that make P. pastoris the preferred yeast host (Demain and Vaishnav, 2009; Yesilirmak and Sayers, 2009).

As a methylotrophic yeast, *P. pastoris* is able to use methanol as sole carbon source. The first step in methanol metabolism is catalysed by the enzyme alcohol oxidase (AOX). Although AOX is encoded by two genes *AOX1* and *AOX2*, most of the enzyme activity comes from *AOX1*, which has a stronger promoter. The *AOX1* promoter

is induced by methanol but repressed in the presence of excess glycerol or glucose. Several *Pichia* expression vectors, such as the pPICZ vectors, use the *AOX1* promoter for the high-level expression of recombinant proteins. Alternatively, constitutive expression of the recombinant protein can be achieved with the glyceraldehyde-3-phosphate dehydrogenase *GAP* promoter, available in the pGAPZ vectors. Both expression constructs codify for the Zeocin<sup>TM</sup> resistance selectable marker, which can also be used in *E. coli* during the cloning and vector propagation process, and integrate into the *P. pastoris* genome through recombination at the *AOX1* (pPICZ vectors) or the *GAP* (pGAPZ vectors) locus. The *P. pastoris* expression system allows for the production of proteins in the cytoplasm or secreted to the culture media, using the efficient *S. cerevisiae*  $\alpha$ -mating factor pre-pro-peptide as a secretion signal. The level of native proteins secreted by *P. pastoris* is very low, greatly simplifying the purification process of secreted recombinant proteins.

#### 3.1.2.1.1. KM71H OCH1 knock-out engineered strain

An engineered version of the KM71H *Pichia pastoris* strain was provided for this project by Professor Henrik Brinch-Pedersen's group (Flakkebjerg Research Centre, Aarhus University, Denmark). KM71H is a mutant *P. pastoris* strain compatible with Zeocin<sup>™</sup> resistant expression vectors, in which the *AOX1* gene has been deleted and replaced with the *S. cerevisiae ARG4* gene. As a result, KM71H relies on the production of alcohol oxidase from the *AOX2* gene and growth in methanol is slower than the wild type strains due to its weaker promoter.

Most secreted eukaryotic proteins are glycosylated, but different glycosylation patterns are observed depending on the organism. The cereal PAPhy enzymes appear to be heavily glycosylated secreted proteins, containing from seven to nine potential N-linked glycosylation sites (Dionisio *et al.*, 2011). Glycosylation is one of the most common and complex posttranslational modifications performed by *P. pastoris*. N-glycosylation takes place in the lumen of the ER as a protein is being translated. The oligosaccharide Glc<sub>3</sub>Man<sub>9</sub>GlcNAc<sub>2</sub> (consisting of three glucoses, nine mannoses and two N-acetylglucosamine sugars) is assembled on the cytoplasmic side of the ER and anchored to the membrane through dolichol pyrophosphate. The preassembled Glc<sub>3</sub>Man<sub>9</sub>GlcNAc<sub>2</sub> unit is translocated to the lumen of the ER and transferred from dolichol pyrophosphate to the amide nitrogen of appropriate asparagine residues from the nascent protein. The consensus sequence for N-glycosylation in *P. pastoris* is Asn-X-Thr/Ser. The three glucoses are then removed by glucosidases I and II along the secretory pathway, together with the  $\alpha$ -1,2-linked mannose by  $\alpha$ -1,2-mannosidases. The resulting glycoprotein contains the Man<sub>8</sub>GlcNAc<sub>2</sub> core structure and is transported to the Golgi for further processing. The mechanism up to this stage is highly conserved between plants, mammals and yeast, but the processing that takes place in the Golgi results in different types of N-linked glycans according to the organism (Figure 24B). Complex type oligosaccharides are found in higher eukaryotes, while in yeast only high mannose type N-linked glycans have been observed (Bretthauer and Castellino, 1999; Macauley-Patrick *et al.*, 2005). In yeast, the Man<sub>8</sub>GlcNAc<sub>2</sub> core structure is modified by the addition of an  $\alpha$ -1,6-mannose residue to the  $\alpha$ -1,3-mannose of the trimannosyl core. This reaction is catalysed by an  $\alpha$ -1,6-mannosyltransferase encoded by the OCH1 gene, and the mannose residue added is known as the branching point from which a variable number of mannose residues are added by further mannosyltransferases. Even within the same cell, different molecules of the same protein can be glycosylated with N-glycans containing heterogeneous numbers of mannoses, resulting in structural heterogeneity of the glycoprotein population (Daly and Hearn, 2005; Rich and Withers, 2009). Thus, the OCH1 gene is responsible for hyperglycosylation in yeasts, although this phenomenon is not as prominent in P. pastoris as in S. cerevisiae (average of Man<sub>8-14</sub>GlcNAc<sub>2</sub> against Man<sub>>30</sub>GlcNAc<sub>2</sub> sizes) (Bretthauer and Castellino, 1999; Ahmad et al., 2014). A schematic representation of the N-glycosylation pathway in *P. pastoris* is shown in Figure 24C.

Variations in the glycosylation pattern of recombinant proteins, e.g. produced by the pharmaceutical industry, can trigger allergic reactions in humans. For this reason, strategies have been developed to engineer the glycosylation machinery of *P. pastoris*, and commercial strains that can reproduce humanised N-glycosylation patterns are available (Ahmad *et al.*, 2014). Although immunological reactions are not relevant for this project, the heterogeneity that the *P. pastoris* expression system can introduce in recombinant proteins could reduce the ability of the obtained protein samples to form crystals. In order to reduce hyperglycosylation and, therefore, heterogeneity of recombinant proteins, a glycoengineered derivative of the KM71H *P. pastoris* strain was used for the expression of plant PAPhy. In this KM71H (*OCH1::G418R*) strain, the *OCH1* gene has been replaced with *G418R*, which confers geneticin resistance.

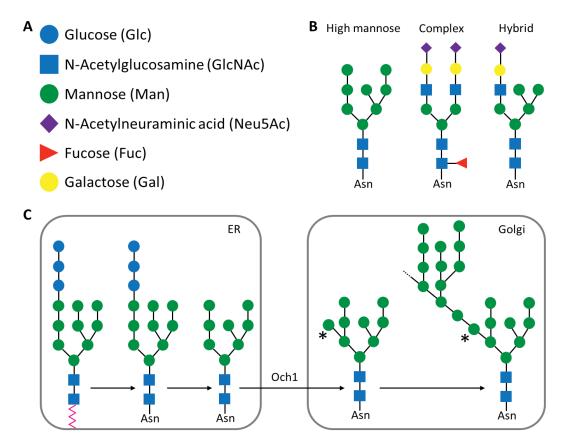


Figure 24. N-glycosylation in Pichia pastoris

(A) Symbols for monosaccharides according to the nomenclature from the Consortium for Functional Glycomics. (B) Representative structures of the three principal classes of N-gycans. (C) Schematic representation of the N-glycosylation pathway in *P. pastoris*. (\*) Branching point for hyperglycosylation.

## 3.1.2.2. Transformation of *Pichia pastoris* through electroporation

Construct TaPAPhy\_b2-pGAPZ $\alpha$ A was chosen over the equivalent pPICZ $\alpha$ A construct for the production of TaPAPhy\_b2 protein samples for crystallography, after being advised a higher yield of recombinant protein was expected from the *GAP* promoter and to avoid methanol induction. The vector pGAPZ $\alpha$ A uses the *GAP* promoter to drive the constitutive production of extracellular proteins in *Pichia pastoris*, in fusion with an N-terminal peptide encoding the *Saccharomyces cerevisiae*  $\alpha$ -factor secretion signal. A twenty-amino acid signal peptide and a C-terminal seven-amino acid

ER-retention signal was excluded from the construct, while a C-terminal 6xHis-tag was included.

20

pending on the concentration of the plasmid stock used for each digestion.							
	Reagent [Stock] [rxn] V for 1x 20 μL r						
	Water	n/a	n/a	Variable*			
	CutSmart buffer	10x	1x	2			
	pGAPZa construct	Variable*	500 ng $\mu$ L <sup>-1</sup>	Variable*			
	Avrii	5 U μL <sup>-1</sup>	0.25 U μL <sup>-1</sup>	1			

Table 8. Reaction set up for the digestion of pGAPZa vector with AvrII

TOTAL

(\*) De

Electroporation is the recommended method for the transformation of P. pastoris. In preparation for transformation, competent cells of the desired strain were prepared, and plasmid DNA was linearized with the appropriate restriction enzyme for the vector used in order to stimulate recombination and integration in the genome. P. pastoris cells can be stored for months at 4°C in 1 M sorbitol stocks. To perform the transformation, 10 µL of a KM71H (OCH1::G418R) strain 1M sorbitol stock were mixed with 190 µL of 1 M sorbitol and plated on a yeast extract peptone dextrose solid medium (YPD agar) plate containing kanamycin (100 µg mL<sup>-1</sup>). The plate was incubated for three days at room temperature to allow for the yeast to grow, before inoculating one full loop of cells into 50 mL of YPD liquid medium containing kanamycin (100  $\mu$ g mL<sup>-1</sup>). The culture was incubated at 30°C and 200 rpm overnight. 10  $\mu$ g of the TaPAPhy b2-pGAPZαA construct were linearized with AvrII (NEB) at 37°C overnight to ensure complete digestion. Reaction set up for AvrII digestion is detailed in Table 8.

Complete construct digestion before transformation was checked on a 1% (w/v) agarose gel containing ethidium bromide. The preparation of Pichia KM71H (OCH1::G418R) competent cells was initiated by harvesting cells from the 50 mL overnight culture by centrifugation. Sterile conditions were kept during the preparation of P. pastoris competent cells and all the centrifugation steps were performed in 50 mL conical centrifuge tubes for 5 min at 4000 x g and 4°C. The culture media was discarded, and the cells washed by resuspension in 50 mL of water. The cells were pelleted again by centrifugation, the water discarded and the cells resuspended in 25 mL of SED solution (50 mM Tris/HCl pH 7.5, 20 mM DTT, 25 mM EDTA pH 8.0, 1M sorbitol). The cells were incubated with the SED solution for 15 min at room temperature to allow for the disruption of the cell wall glycoproteins, which facilitates the incorporation of DNA. After the incubation, the cells were pelleted and washed by resuspension in 50 mL of 1 M sorbitol. A final centrifugation step was performed and the cells were resuspended in a final volume of 3 mL of 1 M sorbitol. The competent cells were stored on ice up to 30 min before electroporation. 10 µg of linearized TaPAPhy\_b2-pGAPZaA construct (20 µL digestion reaction) were mixed with 390 µL of KM71H (*OCH1::G418R*) competent cells in a 0.2 cm gap cuvette (BIO-RAD), and incubated on ice for 5 min. The cuvette was dried before carrying out transformation through electroporation (1.8 kV, 25 µF, 200  $\Omega$ ). After electroporation, the cuvette was returned to ice before transferring the transformed cells to 15 mL conical centrifuge tubes mixed with 1 mL of 1 M sorbitol. The cells were left to recover in agitation at 28°C overnight before plating different volumes on YPD agar plates with Zeocin<sup>TM</sup> (400 µg mL<sup>-1</sup>). After four days of incubation at 28°C, eight of the biggest colonies were picked and restreaked on a fresh YPD agar plate with Zeocin<sup>TM</sup> (400 µg mL<sup>-1</sup>) and incubated for a further two days at 28°C.

## 3.1.2.3. Trial expression of TaPAPhy\_b2 P. pastoris transformants

A small volume expression trial was set up in a 48-well plate to test the selected colonies for the production of secreted recombinant protein. Buffered minimal glucose medium (1.34% (w/v) yeast nitrogen base, 2% (w/v) casamino acids, 2% (w/v) glucose, 100 mM phosphate buffer pH 5.0, 100  $\mu$ g mL<sup>-1</sup> kanamycin, 100  $\mu$ M iron(II) sulfate, 100  $\mu$ M iron(III) citrate) was prepared for the expression and distributed in the plate, 1 mL per well. Cultures for the eight selected transformants were set up by inoculating a small amount of cells into the medium with a sterile loop. A negative control culture with the untransformed KM71H (*OCH1::G418R*) strain was also set up. Cultures were incubated for five days at 26°C and 200 rpm. The expression of recombinant TaPAPhy\_b2 was checked every day by monitoring phosphatase activity in the culture media. A 10 mM solution in 0.1 M acetate buffer pH 4.5 of the chromogenic substrate *para*-nitrophenyl phosphate (pNPP, Sigma) was used for the phosphatase activity assay. Phosphatases catalyse the hydrolysis of pNPP to *para*-nitrophenyl (pNP), a yellow compound in alkaline conditions. 10  $\mu$ L of culture media per well were taken every day, mixed with 190  $\mu$ L of substrate and incubated at 37°C for 10 min. After the incubation,

50  $\mu$ L of 1 M NaOH were added to each reaction and the absorbance at  $\lambda$  = 405 nm measured in 96-well plates in a microplate reader (Hidex Sense). The production of yellow pNP and, therefore, the absorbance at  $\lambda$  = 405 nm is proportional to the production of recombinant TaPAPhy\_b2. Cultures were also topped up daily with 100  $\mu$ M iron(II) sulfate and 100  $\mu$ M iron(III) citrate, as well as more buffered minimal glucose medium to compensate for loss by evaporation (approximately 100  $\mu$ L per day) and the samples taken to check for activity.

After five days of constitutive expression, the highest expressing KM71H (OCH1::G418R) transformant was selected for further protein expression. A 1 M sorbitol stock, for storage at 4°C, and a 10% (v/v) glycerol stock, for storage at -20°C, of the KM71H (OCH1::G418R) highest expressing transformant were prepared.

# 3.1.2.4. Expression scale-up for the generation of TaPAPhy\_b2 samples for crystallography

A fresh YPD agar plate with Zeocin<sup>M</sup> (400 µg mL<sup>-1</sup>) was prepared from the 1 M sorbitol stock of the selected *P. pastoris* KM71H (*OCH1::G418R*) transformant and incubated for at least two days at room temperature before each expression experiment in order to have inoculum.

A medium scale expression test was performed growing the selected *P. pastoris* KM71H (*OCH1::G418R*) transformant with TaPAPhy\_b2-pGAPZ $\alpha$ A in 150 mL of buffered minimal glucose medium, distributed in 250 mL conical flasks with 50 mL per flaks, for five days under continuous shaking (200 rpm) at 26°C, adding 100  $\mu$ M iron(II) sulfate and 100  $\mu$ M iron(III) citrate daily. An untransformed KM71H (*OCH1::G418R*) control culture was grown alongside. Recombinant TaPAPhy\_b2 for crystallography was obtained from 800 mL of buffered minimal glucose medium, distributed in 2 L conical flaks with 400 mL each, following the same protocol. On the third day, cultures were topped up with 200  $\mu$ M iron(II) sulfate and 200  $\mu$ M iron(III) citrate, as well as 2% (w/v) glucose and 0.5% (w/v) casamino acids. Nothing else was added to the cultures until harvesting on the fifth day.

After five days of expression, the cultures were centrifuged in order to separate the cells from the culture media containing the recombinant protein. Medium scale cultures were distributed in 50 mL conical centrifuge tubes and centrifuged for 5 min at 4000 x g and 4°C in a bench top centrifuge. Large scale cultures were distributed in 500 mL centrifuge pots and centrifuged at 11900 x g for 20 min at 4°C in a standing high-speed centrifuge. A phosphatase activity assay with pNPP as substrate was carried out in samples of the culture media to check for expression of recombinant protein as described in **section 3.1.2.3**.

## 3.1.2.5. Purification of recombinant TaPAPhy\_b2

Samples of recombinant TaPAPhy\_b2 suitable for X-ray crystallography were generated following a two-step purification procedure. All the purification steps were carried out at 4°C. Nickel-affinity chromatography was performed as first purification step using the C-terminal 6xHis tag fused to the recombinant protein. Before the nickelaffinity chromatography, the pH of the culture media was adjusted with 10 M NaOH from pH 5.0 to the recommended pH 8.0. The shifting of pH causes salts in the culture media to precipitate. Clear culture media at pH 8.0 was obtained by incubation at 4°C in gentle agitation for 15-20 min before centrifugation to separate the precipitate. The centrifugation was carried out as indicated in section 3.1.2.4., according to the expression scale. Recombinant TaPAPhy\_b2 in the medium scale expression test was purified by nickel-affinity chromatography directly from the clear culture media with pH adjusted to 8.0. Culture media volumes larger than 100-150 mL were subjected to concentration and dialysis prior to nickel-affinity chromatography. The pH-adjusted culture media was concentrated below 50 mL using a stirred cell (Amicon) with a regenerated cellulose ultrafiltration membrane (10 kDa NMWL; Merck). Dialysis against binding buffer for nickel-affinity chromatography (50 mM Tris/HCl pH 8.0, 500 mM NaCl, 20 mM imidazole) was carried out in gentle agitation at 4°C overnight using 3.5 kDa MWCO Spectra/Por dialysis tubing (Spectrum Labs). The concentrated and dialysed culture media was centrifuged once more and forced through a 0.22 µm filter to eliminate residual salt precipitate prior loading onto the nickel-affinity chromatography column.

A 5 mL Ni-NTA Superflow cartridge (Qiagen) was used to perform nickel-affinity chromatography in an ÄKTA Pure chromatography system (GE Healthcare) at a flow rate of 3 mL min<sup>-1</sup>. The culture media was loaded onto the Ni-NTA cartridge, pre-equilibrated with 10 column volumes (CV) of binding buffer (50 mM Tris/HCl pH 8.0, 500 mM NaCl, 20 mM imidazole). The culture media was recirculated twice to allow all the recombinant protein to bind the Ni-NTA resin. The cartridge was then washed with binding buffer until a stable UV signal was registered by the ÄKTA. The recombinant protein was eluted with a 50 mL imidazole gradient (20 mM-500 mM), resulting from the gradual mixing of binding buffer and elution buffer (50 mM Tris/HCl pH 8.0, 500 mM NaCl, 500 mM imidazole), and a 20 mL step with elution buffer. 2 mL fractions were collected during the elution. The success of the nickel-affinity chromatography purification was assessed by running denatured samples of the peak fractions on SDS-PAGE. The 5 mL Ni-NTA Superflow cartridge was regenerated by stripping and recharging according to the manufacturer's instructions after each TaPAPhy\_b2 batch and subsequently stored in 20% (v/v) ethanol at 4°C.

Fractions containing the TaPAPhy\_b2 recombinant protein were concentrated below 1 mL using a 10 kDa MWCO centrifugal filter (Merck). In order to reduce the imidazole concentration before the second purification step, the protein was diluted in 20 mM Tris/HCl pH 8.0 up to 15 mL (maximum capacity of the centrifugal filter) and concentrated again below 1 mL. The concentration of recombinant TaPAPhy\_b2 was calculated by absorbance measurement at  $\lambda = 280$  nm with a NanoDrop<sup>TM</sup>. Predictions of TaPAPhy\_b2 extinction coefficient and molecular weight (taking into account only the amino acid sequence) were calculated with the ExPASy ProtParam tool (Gasteiger *et al.*, 2005) and are displayed in **Appendix 2**, Table A15.

The second step of TaPAPhy\_b2 purification was realised at 4°C by gel filtration on a HiLoad 16/600 Superdex 75 pg column (GE Healthcare) pre-equilibrated and eluted at a flow rate of 0.4 mL min<sup>-1</sup> with 20 mM Tris/HCl pH 8.0 and 250 mM NaCl. Fractions (2 mL, or 200  $\mu$ L upon detection of peaks) were collected. The results of the gel filtration were assessed by SDS-PAGE. Fractions containing TaPAPhy\_b2 with the most homogeneous glycosylation degree possible were selected for crystallography. Selected fractions were concentrated and dialysed as described above for the first purification step, measuring the protein concentration in the same way.

## 3.1.2.5.1. Enzymatic deglycosylation of TaPAPhy\_b2

Trials for the enzymatic deglycosylation of recombinant TaPAPhy\_b2 produced in *P. pastoris* were initiated with two different commercial glycosidases, incubating 10 $\mu$ L reactions at 4°C and using 5  $\mu$ g of TaPAPhy\_b2 per reaction. As a starting point, time courses were performed with 100 U of commercial PNGase F (NEB) or 500 U of commercial Endo H (NEB) per reaction, with reactions set up for 1 h, 2 h, 3 h, 4 h and overnight. An overnight reaction reducing the amount of commercial Endo H to 50 U was also performed.

In addition to the commercial glycosidases tested, constructs for the 'in-house' expression of two recombinant glycosidases with GST fusion tags, GST-PNGase F and GST-Endo F1, were kindly donated by Dr Yoav Peleg (The Israel Structural Proteomics Center, The Weizmann Institute of Science, Rehovot, Israel). The expression and purification of GST-recombinant glycosidases is detailed in **Appendix 3**. In order to compare the activities of the recombinant glycosidases with respect to the commercial ones, the concentration of the former in ng  $\mu$ L<sup>-1</sup> was approximated by measuring the absorbance at  $\lambda = 280$  nm with a NanoDrop<sup>TM</sup>, employing extinction coefficients and molecular weights predicted for the wild type version of the enzymes (PNGase F from *Flavobacterium meningosepticum*, MW = 34.84 kDa and  $\varepsilon = 73340$  M<sup>-1</sup> cm<sup>-1</sup>; Endo H from *Streptomyces plicatus*, MW = 33 kDa and  $\varepsilon = 34840$  M<sup>-1</sup> cm<sup>-1</sup>). A trial for the deglycosylation of TaPAPhy\_b2 with GST-recombinant glycosidases was carried out with 0.5x, 1x, and 2x the concentration of the commercial enzymes, setting up 10  $\mu$ L overnight reactions at 4°C with 5  $\mu$ g of TaPAPhy\_b2. A second trial was performed with 10x and 50x the commercial enzymes.

All the PNGase F reactions were performed in 1x GlycoBuffer 2 (50 mM sodium phosphate pH 7.5, NEB) with 1% NP-40 (NEB), while 1x GlycoBuffer 3 (50 mM sodium acetate pH 6.0; NEB) was used for Endo H and GST-Endo F1. The results of the deglycosylation trials were assessed by running 9  $\mu$ L denatured samples of each reaction

on SDS-PAGE and performing a phosphatase activity assays using pNPP as substrate with the remaining 1  $\mu$ L, following protocol described in **section 3.1.2.3.** 

Partially deglycosylated samples of recombinant TaPAPhy\_b2 (TaPAPhy\_b2d) for crystallography were generated with either commercial Endo H or recombinant GST-Endo F1. The glycosidase treatments were performed on TaPAPhy\_b2 after nickelaffinity chromatography at a concentration of 1 mg mL<sup>-1</sup>. For Endo H deglycosylation, 10 U (approximately 16.8 ng) of glycosidase per µg of TaPAPhy\_b2 were incubated at 4°C overnight in 1x GlycoBuffer 3 (50 mM sodium acetate pH 6.0; NEB). For GST-Endo F1 deglycosylation, 168 ng (approximately 100 U) of glycosidase per µg of TaPAPhy\_b2 reactions were set up in the same conditions. Partially deglycosylated TaPAPhy\_b2d resulting from Endo H treatment was concentrated and gel filtered as described in **section 3.1.2.5.** An extra purification step was performed before gel filtration for protein deglycosylated with GST-Endo F1, using a 1 mL GSTrap 4B cartridge (GE Healthcare) and elution with a gradient of 0–10 mM of reduced glutathione (see **Appendix 3, section A3.1.3.** for method). TaPAPhy\_b2d was obtained in the flow through, while GST-Endo F1 was eluted from the column with the reduced glutathione gradient.

# 3.2. Results and discussion

## 3.2.1. Expression of recombinant plant PAPhy in *Escherichia coli*

## 3.2.1.1. GmPAPhy\_b construct design for *E. coli* expression

An N-terminal signal peptide consisting of the first 28 residues of the protein sequence was predicted for GmPAPhy\_b, with cleavage site at FGHC<sup>V</sup>HIPS (Figure 25). As signal peptides get cleaved *in vivo* when the protein is secreted, it was omitted in the final construct.

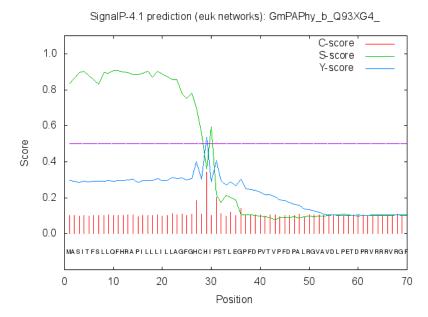


Figure 25. GmPAPhy\_b signal peptide prediction with SignalP 4.1

A peak in the C-score (red lines) indicates the potential cleavage site. A high S-score (green line) indicates the presence of a signal peptide, while low S-scores correspond to the mature protein. A combination of the two scores is represented by the Y-score (blue line).

A disorder prediction study of GmPAPhy\_b-SP was undertaken to identify potential disordered regions in the protein that could decrease its propensity to crystallise (Figure 26). The PrDOS server predicted a segment of ten amino acids in the N-terminus after the signal peptide (His29 to Phe38) and another segment of ten amino acids in the C-terminus (Arg520 to Ile527) to be disordered. GmPAPhy\_b was aligned to the sequences of two plant PAP homologues with structure information available, the red kidney bean PvPAP1 and the sweet potato IbPAP1, to check for the presence of conserved secondary structure elements in those segments.

## PrDOS disorder profile plot

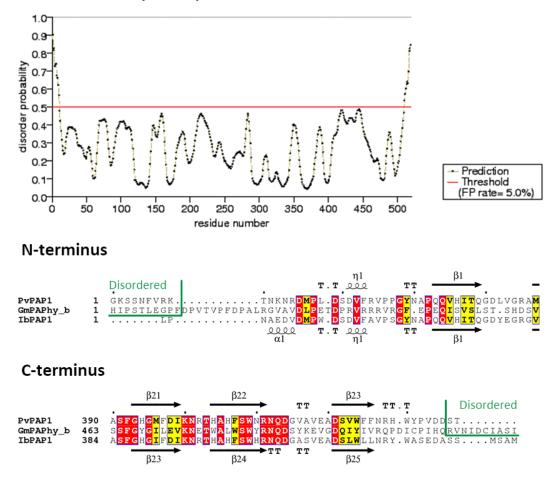
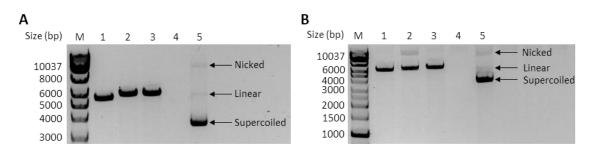


Figure 26. GmPAPhy\_b disorder prediction study

The PrDOS server output plot is shown at the top. Two segments of disordered residues above the red threshold line were predicted with a prediction false positive rate of 5%. N- and C-terminal sequences of GmPAPhy\_b are shown below, aligned to the red kidney bean PAP (PvPAP1; PDB accession 2QFR) at the top, along with its secondary structure, and the sweet potato PAP (IbPAP1; PDB accession 1XZW) at the bottom, along with its secondary structure. The alignment was generated with T-Coffee (Notredame, Higgins and Heringa, 2000) and displayed with ESPript (Robert and Gouet, 2014). PrDOS predicted disordered segments are marked in green in the alignment.

Based on the results of the disorder prediction study, N- and C-terminal truncations were introduced in the GmPAPhy\_b construct. The ten disordered residues at the N-terminus (HIPSTLEGPF) were excluded from the final construct as they are not conserved in the HMW plant PAPs. The last eight of the C-terminal disordered residues (NIDCIASI) were also omitted for the same reason. The predicted protein sequence from the codon optimised for *E. coli* expression GmPAPhy\_b-pET15b construct is displayed in **Appendix 2**, Table A15.

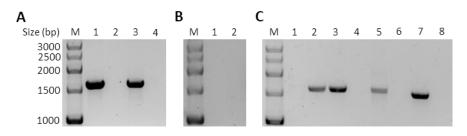
## 3.2.1.2. Cloning of PAPhy into pOPIN vectors



## Figure 27. Trial digestions of pOPINB and pOPINK with HindIII and KpnI

Results of the 20  $\mu$ L trial digestions of (**A**) pOPINB and (**B**) pOPINK in 1% (w/v) agarose gels. 5  $\mu$ L samples mixed with 6x Purple Loading Dye (NEB) were loaded. Lane M, HyperLadder 1kb DNA standards (Bioline); lane 1, HindIII and Kpn1 double digestions (5309 bp pOPINB, 5966 bp pOPINK); lane 2, HindIII digestions (5642 bp pOPINB, 6299 bp pOPINK); lane 3, KpnI digestions (5642 bp pOPINB, 6299 bp pOPINK); lane 4, digestions negative control; lane 5, circular plasmids (bands for nicked, linear and supercoiled DNA can be observed).

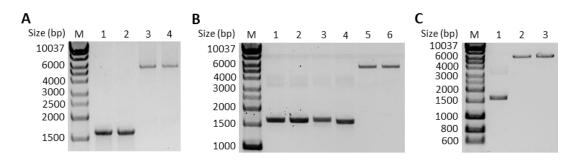
Complete double digestion of pOPINB and pOPINK with HindIII and KpnI was achieved, as displayed in Figure 27. The primers designed for the cloning of PAPhy genes into pOPIN vectors for *E. coli* expression are listed in **Appendix 2** Table A14, with expected PCR product sizes for each set of primers. Successful amplification with the designed primers was obtained for TaPAPhy\_b1, TaPAPhy\_b2, HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b, as shown in Figure 28. No amplification was obtained for TaPAPhy\_a1.



#### Figure 28. Trial PCR amplification of PAPhy coding sequences

Results of the 20  $\mu$ L gene specific PCR experiments in 1% (w/v) agarose gels, carried out to amplify the coding sequences of PAPhy for cloning into pOPIN vectors. 5  $\mu$ L samples mixed with 6x Purple Loading Dye (NEB) were loaded. Lane M, HyperLadder 1kb DNA standards (Bioline). (**A**) Lane 1, HvPAPhy\_a PCR product (1556 bp); lane 2, HvPAPhyA-F1/R1 primers negative control; lane 3, OsPAPhy\_b PCR product (1565 bp); lane 4, OsPAPhyB-F1/R1 primers negative control. (**B**) Lane 1, TaPAPhy\_a1 PCR product (1559 bp); lane 2, TaPAPhyB-F1/R1 primers negative control. (**C**) Lane 1, empty; lane 2, TaPAPhy\_b1 PCR product (1556 bp); lane 3, TaPAPhy\_b2 PCR product (1556 bp); lane 5, ZmPAPhy\_b PCR product (1565 bp); lane 6, ZmPAPhyB-F1/R1 primers negative control; lane 7, GmPAPhy\_b PCR product (1541 bp); lane 8, GmPAPhyT-F1/R1 primers negative control.

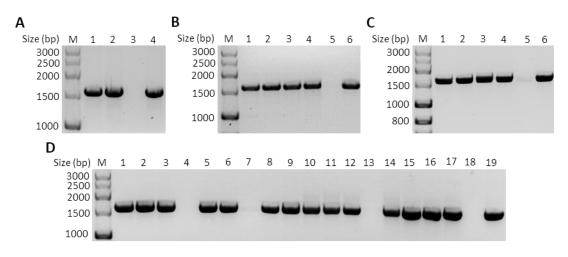
The concentration of the purified digestion and PCR products obtained after extraction from agarose gels could not be measured accurately with a NanoDrop<sup>TM</sup>, due to carry over of chaotropic salts from the gel extraction kit that interfere with DNA absorbance at  $\lambda = 260$  nm. Alternatively, the purified digestion and PCR products were assessed visually by agarose gel electrophoresis (Figure 29) prior to setting up the In-Fusion<sup>TM</sup> reactions. Bands of the purified PCR products were always more intense than those of the linearized pOPIN vectors. The use of equal amounts of PCR product and linearized vector is recommended by the In-Fusion<sup>TM</sup> manufacturer (for products from 0.5 to 10 kb and vectors shorter than 10 kb). In order to approximate this recommendation, a ratio of 1.66:1 of linearized vector over PCR product was used in the reactions.





Visual quantification of gel extracted and purified PCR and digestion products in 1% (w/v) agarose gels before setting up In-Fusion<sup>™</sup> reactions. 2.5 µL samples mixed with 6x Purple Loading Dye (NEB) were loaded. Lane M, HyperLadder 1kb DNA standards (Bioline). (**A**) Lane 1, HvPAPhy\_a PCR product; lane 2, OsPAPhy\_b PCR product; lanes 3 and 4, linearized pOPINB. (**B**) Lane 1, TaPAPhy\_b1 PCR product; lane 2, TaPAPhy\_b2 PCR product; lane 3, ZmPAPhy\_b PCR product; lane 4, GmPAPhy\_b PCR product; lanes 5 and 6, linearized pOPINB. (**C**) Lane 1, TaPAPhy\_b2 PCR product; lanes 2 and 3, linearized pOPINK.

Several white colonies and a few blue colonies were observed in the plates from transformations carried out with positive In-Fusion<sup>™</sup> reactions, and no colonies in the negative controls. All but one plasmid extracted from the white colonies picked from the plates for each of the PAPhy cloning experiments displayed bands of the expected size for the PAPhy genes in the colony screening PCR (Figure 30). Sequencing confirmed the correct gene insert and, therefore, successful cloning into pOPIN vectors of TaPAPhy\_b2 (both into pOPINB and pOPINK), HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b. Although the cloning procedure also worked for TaPAPhy\_b1-pOPINB construct turned out to be the same as TaPAPhy\_b2-pOPINB, so it was not used for expression.



#### Figure 30. Colony screening of PAPhy clones

1% (w/v) agarose gels showing the PCR screening of plasmids extracted from 2 to 4 colonies for the correct gene insert in each cloning experiment. 5 µL samples mixed with 6x Purple Loading Dye (NEB) were loaded. Lane M, HyperLadder 1kb DNA standards (Bioline). (A) Lane 1, OsPAPhy b-pOPINB colony 1; lane 2, OsPAPhy\_b-pOPINB colony 2; lane 3, OsPAPhyB-F1/R1 primers negative control; lane 4, OsPAPhy b-pPICZ $\alpha$ A positive control. (B) Lane 1, HvPAPhy a-pOPINB colony 1; lane 2, HvPAPhy\_a-pOPINB colony 2; lane 3, HvPAPhy\_a-pOPINB colony 3; lane 4, HvPAPhy\_a-pOPINB colony 4; lane 5, HvPAPhyA-F1/R1 primers negative control; lane 6, HvPAPhy\_a-pPICZαA positive control. (C) Lane 1, TaPAPhy b2-pOPINK colony 1; lane 2, TaPAPhy b2-pOPINK colony 2; lane 3, TaPAPhy b2-pOPINK colony 3; lane 4, TaPAPhy b2-pOPINK colony 4; lane 5, TaPAPhyB-F1/R1 primers negative control; lane 6, TaPAPhy b2-pPICZ $\alpha$ A positive control. (D) Lane 1, TaPAPhy b1-pOPINB colony 1; lane 2, TaPAPhy b1-pOPINB colony 2; lane 3, TaPAPhy b1-pOPINB colony 3; lane 4, TaPAPhy b2-pOPINB colony 1; lane 5, TaPAPhy b2-pOPINB colony 2; lane 6, TaPAPhy b2-pOPINB colony 3; lane 7, TaPAPhyB-F1/R1 primers negative control; lane 8, TaPAPhy\_b1-pPICZ $\alpha$ A positive control; lane 9, TaPAPhy b2-pPICZ $\alpha$ A positive control; lane 10, ZmPAPhy b-pOPINB colony 1; lane 11, ZmPAPhy\_b-pOPINB colony 2; lane 12, ZmPAPhy\_b-pOPINB colony 3; lane 13, ZmPAPhyB-F1/R1 primers negative control; lane 14, ZmPAPhy\_b-pPICZαA positive control; lane 15, GmPAPhy\_b-pOPINB colony 1; lane 16, GmPAPhy b-pOPINB colony 2; lane 17, GmPAPhy b-pOPINB colony 3; lane 18, GmPAPhyT-F1/R1 primers negative control; lane 19, GmPAPhy\_b-pET15b positive control.

The cloning results are summarised in Table 9. One PAPhy per plant species was cloned successfully into pOPINB, and the wheat PAPhy b2 isoform was also cloned into pOPINK. Including the original GmPAPhy-pET15b, a total of seven constructs were available to perform *E. coli* expression trials (sequences and parameters in **Appendix 2**, Table A16).

#### Table 9. Plant PAPhy constructs for heterologous expression

TaPAPhy\_b2, HvPAPhy\_a, OsPAPhy\_b and ZmPAPhy\_b were successfully cloned from the original pPICZ $\alpha$ A *P. pastoris* vector into the *E. coli* pOPINB vector. TaPAPhy\_b2 was also cloned into pOPINK. Primers deigned to amplify the coding region of TaPAPhy\_a1 failed in the conditions tested. The cloning procedure to clone TaPAPhy\_b1 worked, but the resulting construct was had the same sequence as TaPAPhy\_b2-pOPINB. GmPAPhy\_b was also cloned from the original pET15b vector into pOPINB.

Original construct	Organism	Original host	Origin	New construct	Cloning result
TaPAPhy_a1-pPICZαA	Wheat	Pichia pastoris	Aarhus University, Denmark	TaPAPhy_a1-pOPINB	-
TaPAPhy_b1-pPICZαA	Wheat	Pichia pastoris	Aarhus University, Denmark	TaPAPhy_b1-pOPINB	-
TaPAPhy_b2-pPICZαA	Wheat	Pichia pastoris	Aarhus University, Denmark	TaPAPhy_b2-pOPINB/K	+/+
TaPAPhy_b2-pGAPZαA	Wheat	Pichia pastoris	Aarhus University, Denmark	n/a	n/a
HvPAPhy_a-pPICZαA	Barley	Pichia pastoris	Aarhus University, Denmark	HvPAPhy_a-pOPINB	+
OsPAPhy_b-pPICZaA	Rice	Pichia pastoris	Aarhus University, Denmark	OsPAPhy_b-pOPINB	+
ZmPAPhy_b-pPICZαA	Maize	Pichia pastoris	Aarhus University, Denmark	ZmPAPhy_b-pOPINB	+
GmPAPhy_b-pET-15b	Soybean	Escherichia coli	GenScript USA Inc.	GmPAPhy_b-pOPINB	+

## 3.2.1.3. Transformation of *E. coli* constructs into expression strains

All transformations performed into the different *E. coli* expression hosts with the PAPhy constructs were successful. No colonies were observed in negative control plates in any transformation.

## 3.2.1.4. Expression trials of PAPhy in *E. coli*

Small-scale expression trials of PAPhy enzymes in *Escherichia coli* were initiated with the codon optimised GmPAPhy\_b-pET15b construct using the IPTG induction method. The heterologous expression of the soybean PAPhy with an N-terminal 6xHis tag had previously been described in BL21 (DE3) cells induced with 1 mM IPTG at 37°C for 5 h (Singh *et al.*, 2013). For this reason, a similar expression trial was carried out with GmPAPhy\_b-pET15b in BL21 (DE3) pLysS, but no recombinant expression was detected. Expression trials in Rosetta 2 (DE3) pLysS were also performed for this construct with the same results. Low levels of recombinant protein expression from the GmPAPhy\_b-pET15b construct were only observed in a Rosetta-gami 2 (DE3) expression trial. However, upon performance of solubility tests, it was concluded that all or most of the recombinant protein produced remained in the insoluble fraction.

The wheat TaPAPhy\_b2 enzyme contains nine cysteine residues, of which eight have been predicted to form disulfide bridges (Dionisio *et al.*, 2012). The cysteines in the wheat enzyme are also conserved in GmPAPhy\_b, HvPAPhy\_a, OsPAPhy\_b and

ZmPAPhy\_b, indicating that PAPhy enzymes may contain four disulfide bonds. Therefore, the SHuffle strains, engineered for the cytoplasmic expression of proteins containing multiple disulfide bridges, were the *E. coli* host of choice for further expression trials.

The construct GmPAPhy\_b-pET15b again expressed no recombinant protein from the SHuffle T7 strain. Further expression trials using the IPTG induction method were performed with constructs HvPAPhy\_a-pOPINB and OsPAPhy\_b-pOPINB. Protein expression was tested in the strains SHuffle T7, SHuffle T7 Express and ArcticExpress (DE3) RP. Although it does not address the disulfide bridge problem, the ArcticExpress strain was used to attempt to improve protein solubility by expressing at low temperature. High expression levels of recombinant PAPhy were detected in all the trials. However, the solubility tests revealed that all the protein produced was insoluble.

From this point, the expression trials were switched to the auto-induction method. Since there is no need to monitor the OD<sub>600</sub> of the cultures for induction or to try different inducer concentrations, auto-induction allows the screening of different constructs, strains and conditions in parallel for expression and solubility in a more efficient way. In addition, the yields of recombinant protein produced are expected to be higher than with conventional IPTG induction. The same expression trials carried out induction were repeated with auto-induction for with IPTG constructs HvPAPhy a-pOPINB and OsPAPhy b-pOPINB. High levels of expression, but corresponding to insoluble protein, were also obtained. Auto-induction expression trials of GmPAPhy\_b-pET15b in SHuffle T7 together with GmPAPhy\_b-pOPINB, ZmPAPhy b-pOPINB and TaPAPhy b2-pOPINB in SHuffle T7 and SHuffle T7 Express were also performed. GmPAPhy b-pET15b in SHuffle T7 produced again no target protein. No clear levels of recombinant protein expression were observed from the GmPAPhy b-pOPINB and ZmPAPhy b-pOPINB expression trials either, while TaPAPhy b2-pOPINB showed expression of high levels of insoluble protein.

Phytase activity was tested in samples of the soluble fractions resulting from several expression trials. However, no significant difference in activity was observed

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between expression trial samples from strains containing PAPhy constructs and the equivalent empty vector controls.

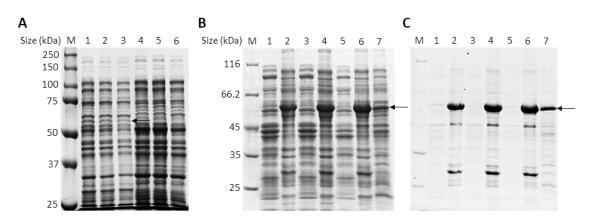


Figure 31. SDS-PAGE results of a representative expression trial of a PAPhy in E. coli

Samples run on 10% (v/v) acrylamide gels from an autoinduction expression trial with the construct OsPAPhy\_b-pOPINB in SHuffle T7. Black arrows point to the bands corresponding to recombinant OsPAPhy\_b. (A) Total cell protein gel stained with InstantBlue<sup>M</sup>. Lane M, dual colour protein standards (BIO-RAD); lane 1, 25°C expression; lane 2, 30°C expression; lane 3, 37°C expression; lane 4, 25°C empty vector control; lane 5, 30°C empty vector control; lane 6, 37°C empty vector control. (B) Solubility test gel stained with InstantBlue<sup>M</sup> and (C) InVision<sup>M</sup>. Lane M, unstained protein standards (Thermo Scientific); lane 1, 25°C soluble fraction; lane 2, 25°C insoluble fraction; lane 3, 30°C soluble fraction; lane 4, 30°C insoluble fraction; lane 5, 37°C soluble fraction; lane 6, 37°C insoluble fraction; lane 7, total cell protein control from OsPAPhy\_b 37°C expression. Bands of the target protein could only be observed in total cell protein and insoluble fraction samples.

To conclude, the TaPAPhy\_b2-pOPINK construct was used for the expression of a recombinant PAPhy with a different fusion tag other than 6xHis. An N-terminal GST tag was chosen with the hope of improving solubility. Auto-induction expression trials in SHuffle T7 and SHuffle T7 Express were carried out, as well as in BL21 (DE3). Expression of recombinant protein was observed in all the trials, with especially high levels in BL21 (DE3). However, once more all the protein obtained was insoluble.

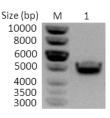
The results of the *E. coli* expression trials are summarised in **Appendix 2**, Table A17.

# 3.2.2. Expression of recombinant plant PAPhy in Pichia pastoris

## 3.2.2.1. Transformation of *Pichia pastoris* through electroporation

Complete linearization of the construct TaPAPhy\_b2-pGAPZαA was achieved by digestion with AvrII (Figure 32). The linearized construct was successfully transformed

into freshly prepared KM71H (*OCH1::G418R*) *Pichia* competent cells by electroporation. Single colonies were observed in all the transformation plates after four days of incubation. A higher concentration than the standard to select Zeocin<sup>™</sup> resistant *Pichia* transformants was used for the transformation of TaPAPhy\_b2-pGAPZαA (400 µg mL<sup>-1</sup>, rather than 100 µg mL<sup>-1</sup>), as advised by our collaborators, in order to isolate multi-copy clones. After the four days of incubation, the biggest colonies on the transformation plates presented the highest Zeocin<sup>™</sup> resistance and, therefore, were likely to contain multiple copies of the construct encoding for TaPAPhy\_b2 expression. Eight of these colonies (named A to H) were selected and transferred to fresh YPD agar plates, showing optimal growth levels to initiate expression trials after two days of incubation.



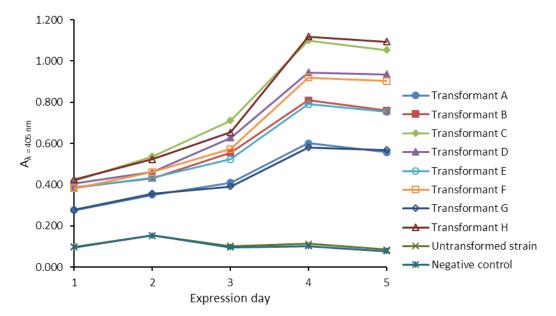
#### Figure 32. Digestion of TaPAPhy\_b2-pGAPZαA with AvrII

1% (w/v) agarose gel showing complete linearization of construct TaPAPhy\_b2-pGAPZαA by digestion with AvrII in preparation for *Pichia pastoris* transformation. Lane M, O'GeneRuler 1kb DNA standards (Thermo Scientific); lane 1, linearized TaPAPhy\_b2-pGAPZαA (4623 bp).

## 3.2.2.2. Trial expression of TaPAPhy\_b2 P. pastoris transformants

As a purple acid phosphatase, TaPAPhy\_b2 requires Fe<sup>3+</sup> for its activity. In addition, a preference for Fe<sup>2+</sup> in the MII site has been reported for the PAPhy\_b isoforms of these enzymes (Dionisio *et al.*, 2011, 2012). In order to provide the enzyme with sources of these two metal ions, the culture media for the constitutive expression of recombinant TaPAPhy\_b2 was supplemented with iron(II) sulfate and iron(III) citrate.

The levels of expression of recombinant protein can vary for different *P. pastoris* transformants. Occasionally, the recombination that takes place to integrate the expression construct into the *Pichia* genome can occur in a way that the selection marker for Zeocin<sup>M</sup> resistance gets inserted, but not the gene of interest. Screening of several transformants is thus recommended for the *P. pastoris* expression system.



**Figure 33. Results of TaPAPhy\_b2-pGAPZaA expression trial in KM71H (***OCH1::G418R***)** The expression of recombinant TaPAPhy\_b2 was monitored for five days by measuring the absorbance at  $\lambda = 405$  nm resulting from the hydrolysis of pNPP assayed in samples taken from the cultures. Transformant H was the highest expressing transformant at the end of the experiment.

The results of the trial expression of eight KM71H (OCH1::G418R) colonies resulting from the transformation with TaPAPhy b2-pGAPZ $\alpha$ A are displayed in Figure 33. The production of recombinant TaPAPhy b2 was monitored by the presence of phosphatase activity against pNPP in the culture media. As the activity assay was carried out for colony screening and no with quantification purposes, no pNP standard curve was included and the results were analysed in absorbance units. Maximum expression levels of recombinant TaPAPhy\_b2 were detected after four days of constitutive expression and remained stable on the fifth day. All transformants tested were positive for the production of recombinant protein. Transformant H showed the highest phosphatase activity and, therefore, the highest expression levels on the fifth day, followed closely by transformant C. The untransformed KM71H (OCH1::G418R) strain showed the same levels of phosphatase activity as the assay negative control (with water rather than culture media), indicating Pichia pastoris does not secrete its own phosphatases to the culture media in the expression conditions (culture media containing a high concentration of phosphate). Transformant H was selected for further expression experiments.

## 3.2.2.3. Expression scale-up and purification of samples for crystallography

## 3.2.2.3.1. Medium scale expression test

The expression scale of TaPAPhy\_b2-pGAPZαA construct in the engineered strain KM71H (*OCH1::G418R*) was first increased from 1 mL to 50 mL cultures in 250 mL conical flasks. After five days of constitutive expression, phosphatase activity was detected in the culture media of the TaPAPhy\_b2 transformant cultures and not in the untransformed strain control. The 150 mL of culture media were subjected to nickel-affinity chromatography purification to check for the yield and purity of recombinant protein generated.

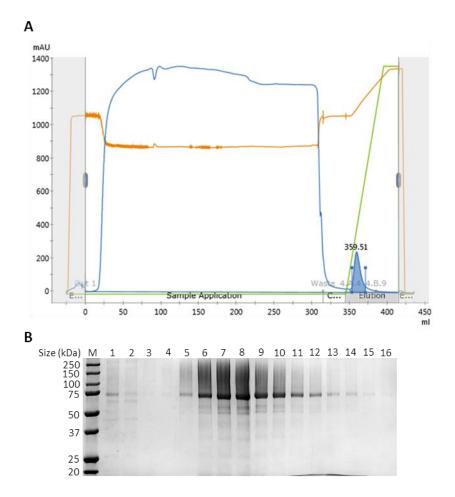


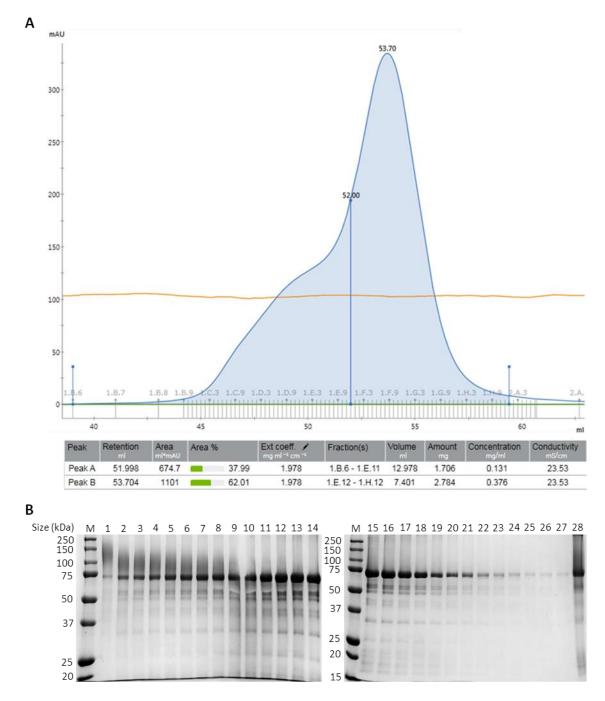
Figure 34. Results of the Ni-NTA purification of recombinant TaPAPhy\_b2 from P. pastoris culture media

(A) Chromatogram generated by the ÄKTA Pure chromatography system (GE Healthcare). Blue line, UV trace; orange line, conductivity trace; green line, concentration of elution buffer. A single peak of 18 mL volume corresponding to TaPAPhy\_b2 appears at a retention volume of 9.5 mL into the elution imidazole gradient. (B) 10% (v/v) acrylamide gel with peak fractions. Lane M, dual colour protein standards (BIO-RAD); lane 1, *P. pastoris* culture media before Ni-NTA purification; lane 2, Ni-NTA purification flow-through; lane 3, Ni-NTA purification wash; lanes 4 to 16, Ni-NTA purification elution fractions 4.A4 to 4.B4.

The results of the purification by nickel-affinity chromatography of recombinant TaPAPhy\_b2 from the culture media of KM71H (*OCH1::G418R*) *P. pastoris* strain are shown in Figure 34. Recombinant TaPAPhy\_b2 was secreted to the culture media with already a high degree of purity, and all the bands observed in the elution fraction samples run on SDS-PAGE are expected to correspond to TaPAPhy\_b2 with different levels of N-glycosylation. TaPAPhy\_b2 SDS-PAGE bands ranged from 57.49 kDa, the predicted molecular weight of the deglycosylated protein, to 75 kDa. Despite using a glycoengineered strain, a smear above 75 kDa and up to 250 kDa was observed on the SDS-PAGE, corresponding to heterogeneous hyperglycosylation of the recombinant protein. Pooling and concentrating the peak fractions yielded approximately 30 mg of recombinant TaPAPhy\_b2 recovered directly per litre of *P. pastoris* culture media by nickel-affinity chromatography.

## 3.2.2.3.2. Generation of glycosylated TaPAPhy\_b2 samples for crystallography

In order to generate enough recombinant TaPAPhy\_b2 to carry out crystallisation screenings, the expression scale was further increased to 400 mL cultures in 2 L conical flasks. Phosphatase activity of the recombinant protein was detected in the culture media after five days of expression. Purification of recombinant TaPAPhy b2 from a total of 800 mL of culture media was attempted directly as for the medium scale expression experiment. However, the recirculation of such a volume of culture media caused the stripping of the nickel particles from the Ni-NTA cartridge, resulting in the protein ending back in the culture media. Certain components of the buffered minimal glucose medium, such as iron not incorporated in the metalloprotein, could be interfering with the binding of 6xHis tags of the recombinant protein to the Ni-NTA matrix. Although adjustment of the pH of the culture media to 8.0 was an effective measure for volumes up to 150 mL, larger amounts of culture media needed further pre-processing before carrying out nickel-affinity chromatography. The culture media was successfully concentrated below 50 mL and dialysed against Ni-NTA binding buffer maintaining recombinant TaPAPhy\_b2 in solution. The addition of these steps resulted in the successful purification of TaPAPhy b2 by nickel-affinity chromatography with the expected yield of 30 mg  $L^{-1}$ .



## Figure 35. Gel filtration purification of recombinant TaPAPhy\_b2 produced in KM71H (OCH1::G418R) P. pastoris strain

(A) Amplified region of the chromatogram generated by the ÄKTA Pure chromatography system (GE Healthcare). Blue line, UV trace; orange line, conductivity trace. A single peak of 20 mL volume corresponding to TaPAPhy\_b2 begins to elute at a retention volume of 44 mL. The peak can be split into main peak fractions (62%) and higher molecular weight shoulder fractions (38%), the latter corresponding to hyperglycosylated recombinant protein. (B) 10% (v/v) acrylamide gel with peak fractions. Lane M, dual colour protein standards (BIO-RAD); lane 1, shoulder maximum (1.D8); lanes 2 to 8, interface between shoulder and main peak (1.E5 to 1.E11); lanes 9 to 27, main peak (even fractions from 1.E12 to 1.H12); lane 28, Ni-NTA purified TaPAPhy\_b2.

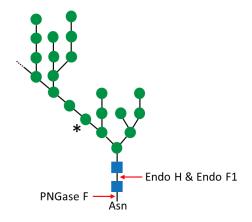
Different degrees of glycosylation are reflected in differences in molecular weight of the recombinant protein, as observed in the Ni-NTA purification SDS-PAGE (Figure 34). As gel filtration (GF) chromatography separates proteins based on size, it was chosen as second purification step to generate TaPAPhy\_b2 samples for crystallography.

The results of the purification by gel filtration of recombinant TaPAPhy\_b2 produced in KM71H (*OCH1::G418R*) *P. pastoris* strain are shown in Figure 35. A higher molecular weight shoulder corresponding to hyperglycosylated protein can be observed on the side of the main peak, indicating that partial separation of differentially glycosylated TaPAPhy\_b2 was achieved through gel filtration. A smaller hyperglycosylated protein shoulder was obtained with KM71H (*OCH1::G418R*) compared to published results of the purification of PAPhy expressed in the non-engineered strain (Dionisio *et al.*, 2011, 2012). From 6.2 mg of Ni-NTA purified TaPAPhy\_b2 injected onto the gel filtration column, 2 mg of TaPAPhy\_b2 with a lower N-glycosylation degree were recovered by pooling and concentration of the main peak fractions. In other words, two thirds of the recombinant protein obtained were not used for crystallography due to N-glycosylation heterogeneity. Two samples of glycosylated TaPAPhy\_b2 batch 02 and batch 03).

## 3.2.2.3.3. Enzymatic deglycosylation of TaPAPhy\_b2

Despite use of a glycoengineered strain for the expression of recombinant TaPAPhy\_b2 in *Pichia pastoris*, samples with certain degree of heterogeneity were still observed after two purification steps. The enzymatic deglycosylation of recombinant proteins is a common approach in the preparation of samples for X-ray crystallography. When deglycosylated proteins are generated for crystallography, a balance between homogeneity and solubility of the protein needs to be achieved, and this often requires testing the effect of different glycosidases under various conditions. Recombinant TaPAPhy\_b2 is predicted to have seven N-glycosylation sites (Dionisio *et al.*, 2011, 2012), which are susceptible to contain N-glycans of the high mannose type when *P. pastoris* is the expression host. Three glycosidases able to cleave N-linked glycans of the high

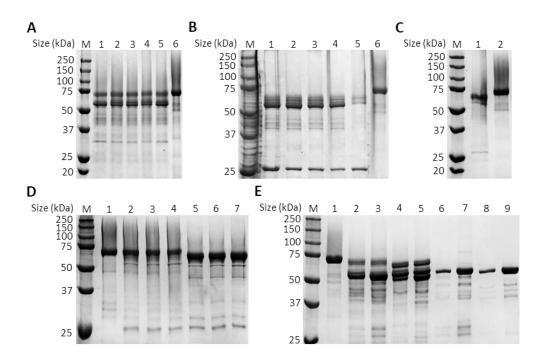
mannose type were tested for deglycosylation of TaPAPhy\_b2. A representation of the cleavage site of these enzymes is shown in Figure 36. Peptide N-glycosidase F (PNGase F) is an amidase that cleaves between the innermost N-acetylglucosamine and asparagine residues of high mannose, hybrid and complex N-glycans, removing the whole N-linked glycan. Both endoglycosidases H and F1 (Endo H and Endo F1, respectively) are able to cleave between the two N-acetylglucosamine residues of high mannose and most hybrid N-glycans, leaving one N-acetylglucosamine residue attached to the asparagine.



**Figure 36. Schematic representation of the cleavage site of glycosidases PNGase F and Endo H/Endo F1** The monosaccharides are represented with symbols according to the nomenclature from the Consortium for Functional Glycomics. Green circles, mannose; blue squares, N-acetylglucosamine. (\*) Branching point for hyperglycosylation.

The results of the TaPAPhy\_b2 deglycosylation trials are shown in Figure 37. Initially, the two commercial glycosidases PNGase F and Endo H were tested. The duration of the commercial PNGase F treatment did not seem to have an effect in the degree of TaPAPhy\_b2 deglycosylation obtained. Treatment of 5 µg TaPAPhy\_b2 samples with 100 U of commercial PNGase F resulted in the elimination of most of the hyperglycosylation smear, the reduction of the 75 kDa band and the increase of the double band above 50 kDa (Figure 37A). Treatment of recombinant proteins for X-ray crystallography with PNGase F has the advantage of the complete elimination of the protein flexibility conferred by the N-glycans, and, therefore, a higher degree of conformational homogeneity than treatment with endoglycosidases. However, being PNGase F the enzyme that cuts deepest on the N-glycan, the inaccessibility of certain cleavage sites can result in the incomplete deglycosylation of the target protein, as observed for TaPAPhy\_b2. Treating 5 µg TaPAPhy\_b2 samples with 500 U of commercial Endo H resulted in more efficient deglycosylation, with no significant differences

observed in treatments from 1 to 4 h. Complete elimination of the hyperglycosylation smear and the 75 kDa band was observed, with the strongest TaPAPhy\_b2 band running above 50 kDa accompanied by multiple, less intense bigger bands (Figure 37B). Degradation of recombinant TaPAPhy\_b2 seemed to occur in the overnight reaction. Optimisation of Endo H treatment was attempted with the aim to reduce the ratio glycosidase-target protein in the reaction and to increase the homogeneity of the resulting target protein. Treatment of 5  $\mu$ g TaPAPhy\_b2 samples with 50 U of commercial Endo H at 4°C overnight resulted in partially deglycosylated TaPAPhy\_b2 with a homogeneity deemed appropriate to allow crystallisation screenings (Figure 37C).





All the trials were carried out at 4°C with 5µg of Ni-NTA purified TaPAPhy b2 per reaction. Reactions were incubated overnight, except in the time courses (gels A and B). All the gels are 10% (v/v) acrylamide with dual colour protein standards (BIO-RAD, lanes M). (A) Commercial PNGase F time course with 100 U per reaction. Lane 1, 1 h reaction; lane 2, 2 h reaction; lane 3, 3 h reaction; lane 4, 4 h reaction; lane 5, overnight reaction; lane 6, TaPAPhy\_b2 untreated control. Bands corresponding to PNGase F can be observed at 36 kDa in lanes 1 to 5. (B) Commercial Endo H time course with 500 U per reaction. Lane 1, 1 h reaction; lane 2, 2 h reaction; lane 3, 3 h reaction; lane 4, 4 h reaction; lane 5, overnight reaction; lane 6, TaPAPhy\_b2 untreated control. Bands corresponding to Endo H can be seen at 29 kDa in lanes 1 to 5. (C) Optimisation of Endo H treatment with 50 U per reaction incubated overnight. Lane 1, deglycosylation reaction of TaPAPhy b2 with commercial Endo H (29 kDa band); lane 2, TaPAPhy b2 untreated control. (D) Recombinant glycosidases trial. Lane 1, TaPAPhy b2 untreated control; lane 2, 0.5x GST-PNGase F reaction; lane 3, 1x GST-PNGase F reaction; lane 4, 2x GST-PNGase F reaction; lane 5, 0.5x GST-Endo F1 reaction; lane 6, 1x GST-Endo F1 reaction; lane 7, 2x GST-Endo F1 reaction. (E) Optimisation of treatment with recombinant glycosidases. Lane 1, TaPAPhy b2 untreated control; lane 2, 10x GST-PNGase F reaction; lane 3, 50x GST-PNGase F reaction; lane 4, 10x GST-Endo F1 reaction; lane 5, 50x GST-Endo F1 reaction; lane 6, 10x GST-PNGase F control (61.76 kDa); lane 7, 50x GST-PNGase F control (61.76 kDa); lane 8, 10x GST-Endo F1 control (58.66 kDa); lane 9, 50x GST-Endo F1 control (58.66 kDa).

Constructs encoding recombinant glycosidases with GST fusion tags were acquired later in the project. After successful expression and purification, stocks of GST-PNGase F and GST-Endo F1 at 1 mg mL<sup>-1</sup> were prepared. The concentration of the commercial enzymes is expressed in units (U), where one unit is defined as the amount of enzyme required to remove over 95% of the N-glycan from 10 µg of denatured RNase B in 1 h at 37°C with 10 µL reactions (NEB). The ratio of commercial glycosidase per µg of TaPAPhy\_b2 (originally in U µg<sup>-1</sup>) was approximated in ng µg<sup>-1</sup> in order to compare their activity with that of the recombinant enzymes in deglycosylation trials with the same reaction conditions (Table 10). Ratios of recombinant glycosidases up to double those used for the commercial enzymes achieved less TaPAPhy\_b2 deglycosylation, indicating a lower activity of the recombinant glycosidases with respect to the commercial enzymes (Figure 37D). Nevertheless, a closer partial deglycosylation degree of TaPAPhy\_b2 was achieved with both recombinant glycosidases when using 10 to 50 times as much as the equivalent commercial enzyme, with no significant differences between these two ratios (Figure 37E).

Table 10. Comparison of commercial and recombinant glycosidases for TaPAPhy\_b2 deglycosylation

'E', commercial glycosidase enzyme; 'S', TaPAPhy\_b2 substrate; 'E/S' units or ng of commercial glycosidase used per  $\mu$ g of TaPAPhy\_b2. The activity of the recombinant glycosidases was tested at ratios half, equal, double, ten times and fifty times of the ratios used for the commercial enzymes.

E	[Ε] (U μl⁻¹)	[E] (ng μl <sup>-1</sup> )	E/S (U μg <sup>-1</sup> )	E/S (ng µg⁻¹)	0.5x (ng µg⁻¹)	1x (ng μg <sup>-1</sup> )	2x (ng μg⁻¹)	10х (ng µg <sup>-1</sup> )	50x (ng μg <sup>-1</sup> )
PNGase F	500	405	20	16.2	8.1	16.2	32.4	162	810
Endo H	500	840	10	16.8	8.4	16.8	33.6	168	840

No major losses in TaPAPhy\_b2 phosphatase activity were observed after deglycosylation with any of the glycosidases tested, as deglycosylated samples retained at least 95% of the activity with respect to the untreated controls. Carrying out deglycosylation at 4°C overnight, it was concluded that treatment with 10 U of the commercial Endo H per  $\mu$ g of TaPAPhy\_b2 yielded the best results, followed by treatment with 168 ng of the 'in-house' recombinant Endo F1 per  $\mu$ g of TaPAPhy\_b2.

## 3.2.2.3.4. Generation of partially deglycosylated TaPAPhy\_b2d samples for crystallography

Four partially deglycosylated TaPAPhy\_b2d samples were generated for X-ray crystallography by endoglycosidase treatment. Two batches (TaPAPhy\_b2d batch 01 and batch 03) were generated by treatment with commercial Endo H at 4°C overnight with a ratio of 10 U per µg of recombinant protein, deglycosylating 5 mg of TaPAPhy\_b2 per batch (Figure 38A). The loss of phosphatase activity was between 10 and 15% when compared to the phosphatase activity of untreated TaPAPhy\_b2. Another two batches (TaPAPhy\_b2d batch 04 and batch 07) were generated by treatment with recombinant gST-Endo F1 at 4°C overnight with a ratio of 100 U per µg of recombinant protein, deglycosylating 10 mg of TaPAPhy\_b2 per batch (Figure 38B). Here, the loss of phosphatase activity of untreated TaPAPhy\_b2.

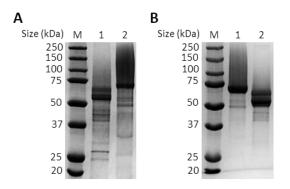


Figure 38. Partial deglycosylation of TaPAPhy\_b2 samples for crystallography with Endo H and Endo F1 SDS-PAGE (10% (v/v) acrylamide) gels with dual colour protein standards (BIO-RAD, lanes M). (A) Deglycosylation of TaPAPhy\_b2d batch 01 with commercial Endo H at 4°C overnight. Lane 1, TaPAPhy\_b2 with Endo H (29 kDa band) reaction at 10 U  $\mu$ g<sup>-1</sup> ratio; lane 2, TaPAPhy\_b2 untreated control. (B) Deglycosylation of TaPAPhy\_b2d batch 07 with recombinant GST-Endo F1 at 4°C overnight. Lane 1, TaPAPhy\_b2 untreated control; lane 2, TaPAPhy\_b2 with GST-Endo F1 (58.66k kDa) reaction at 100 U  $\mu$ g<sup>-1</sup> ratio.

Representative results of the purification of recombinant TaPAPhy\_b2d, produced in KM71H (*OCH1::G418R*) *P. pastoris* strain, after commercial Endo H treatment are shown in Figure 39. A higher molecular weight shoulder corresponding to hyperglycosylated protein was still observed on the side of the main peak even after Endo H treatment. From 5 mg of Ni-NTA purified TaPAPhy\_b2 injected onto the gel filtration column, 1.4 mg of partially deglycosylated TaPAPhy\_b2d batch 01 were recovered by pooling and concentrating the main peak fractions. For batch 03, 3.2 mg

were recovered. Complete separation of TaPAPhy\_b2 and Endo H was achieved by gel filtration. The commercial glycosidase could be recovered from the gel filtration fractions and reused in further deglycosylation reactions.

Although samples of TaPAPhy\_b2 similar to those obtained with commercial Endo H treatment could be achieved with recombinant GST-Endo F1 treatment by increasing the amount of enzyme used, the recombinant enzyme with its GST fusion tag has a molecular weight that overlaps with TaPAPhy\_b2. For this reason, an extra purification step was introduced when TaPAPhy\_b2d samples for X-ray crystallography were generated by GST-Endo F1 treatment. Recombinant TaPAPhy\_b2d was successfully purified by GST-affinity purification followed by gel filtration, obtaining results like those from Endo H treatment. When purifying TaPAPhy\_b2d batch 04, from 10 mg of Ni-NTA purified TaPAPhy\_b2 subjected to Endo F1 treatment, 9.9 mg were recovered after GST-affinity purification, and 5.7 mg after gel filtration. TaPAPhy\_b2d batch 07 yielded 7.1 mg after GST-affinity purification, and 3.9 mg after gel filtration.

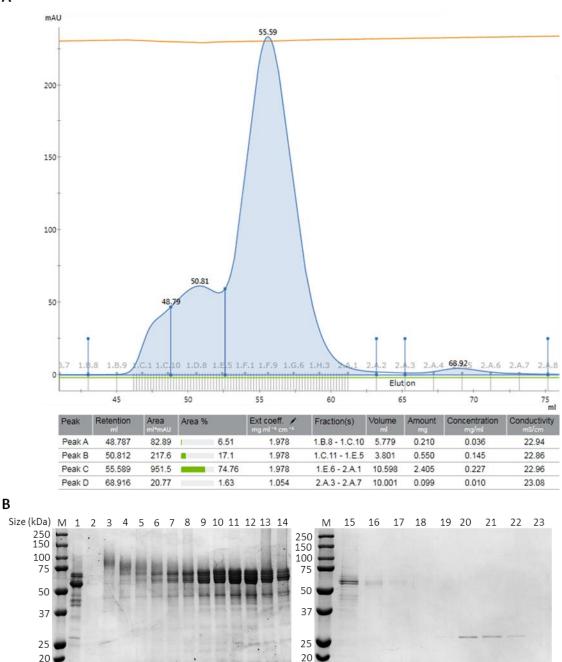


Figure 39. Gel filtration purification of partially deglycosylated TaPAPhy\_b2d with Endo H

(A) Amplified region of the chromatogram generated by the ÄKTA Pure chromatography system (GE Healthcare). Blue line, UV trace; orange line, conductivity trace. A single peak of 30 mL volume corresponding to TaPAPhy\_b2 begins to elute at a retention volume of 45 mL. The peak can be split into main peak fractions (75%) and higher molecular weight shoulder fractions (25%), the latter corresponding to hyperglycosylated recombinant protein. A second peak corresponding to Endo H can be observed at a retention volume around 69 mL. (B) SDS-PAGE (10% (v/v) acrylamide) with peak fractions. Lane M, dual colour protein standards (BIO-RAD); lane 1, Ni-NTA purified TaPAPhy\_b2; lane 2, first shoulder (peak A) maximum (1.C2); lane 3, second shoulder (peak B) maximum (1.D8); lanes 4 to 6, interface between shoulder and main peak (even fractions from 1.E4 to 1.E8); lanes 7 to 17, main peak (peak C, even fractions from 1.E10 to 1. F10 and fractions 1.G4, 1.H1, 1.H11 and 2.A1); lanes 18 to 23, Endo H peak (peak D, fractions 2.A2 to 2.A7).

### 3.3. Conclusions

Despite the generous range of strains and conditions tested, all the recombinant PAPhy expression trials performed in *Escherichia coli* proved unsuccessful. Good levels of recombinant protein expression were obtained for HvPAPhy\_a, OsPAPhy\_b and TaPAPhy\_b2 with N-terminal 6xHis tags, although their coding sequences were not optimised for *E. coli* expression. Surprisingly, the soybean phytase GmPAPhy\_b performed the worst in the expression trials, despite being the only sequence codon optimised for *E. coli* expression of the available PAPhy. When tested for solubility, however, all the recombinant PAPhy produced in *E. coli* were recovered in the insoluble fraction. The strategy of employing a GST fusion tag instead of a 6xHis tag did not improve the solubility of PAPhy. The high level of N-glycosylation and disulfide bridge content of these enzymes, together with their dependence on metal ions, may have contributed to the formation of inclusion bodies in *E. coli* hosts, even using engineered strains designed for the expression eukaryotic proteins.

Good yields of soluble recombinant TaPAPhy\_b2 were obtained using *Pichia pastoris* as expression system, allowing for the generation of samples for X-ray crystallography after an optimised expression and purification process. The glycoengineered strain used for the recombinant expression of TaPAPhy\_b2 in *P. pastoris* did not result in the generation of completely homogeneous recombinant protein, even after two purification steps. However, although ideal, samples with 100% purity and homogeneity are often not required for crystallisation. Partially deglycosylated TaPAPhy\_b2d samples with an acceptable homogeneity degree for X-ray crystallography were also generated with commercial Endo H and recombinant GST-Endo F1 glycosidases. The fully glycosylated to extensive crystallisation screening in **Chapter 4**.

# Chapter 4. The X-ray crystal structure of a wheat PAP phytase isoform b2

After optimisation of a method for the expression and purification of the wheat PAPhy isoform b2, sufficient recombinant protein material was available to perform extensive crystallisation screening in order to initiate X-ray crystallographic structure determination.

X-ray crystallography is one of the most common methods to determine atomic structures of biomolecules, provided the biomolecule of interest can form high quality crystals that diffract to high-resolution when illuminated with X-rays. When determining the crystal structure of an eukaryotic protein, the high or heterogeneous carbohydrate content often present in these proteins is a frequently encountered problem that often requires enzymatic deglycosylation strategies (Grueninger-Leitch et al., 1996). In addition, metalloprotein crystallography usually presents challenges such as incorporation and identification of the correct metal, the possibility of X-ray induced damage to the metals or ensuring the correct refinement of the metal centre (Bowman, Bridwell-Rabb and Drennan, 2016). Computer simulation methods have become almost essential in the study of biomolecules. While a crystal structure provides a snapshot of a protein in a single conformation, molecular dynamics simulations can provide detailed information of the motion of the protein as a function of time in a realistic environment. The information obtained through molecular dynamics simulations can be used to understand structure-function relationships of proteins that prove problematic or more difficult to determine with conventional experiments.

This chapter describes the strategies followed to determine the first crystal structure of a purple acid phytase, glycosylated enzymes with two metal ions in the active site. Following crystal structure determination, the structural information acquired in combination with computer simulation methods was used to study the interactions between the TaPAPhy\_b2 enzyme and the substrate phytate.

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### 4.1. Materials and methods

### 4.1.1. Crystal growth

Crystallisation screening experiments were initiated with fully glycosylated TaPAPhy b2, freshly purified and concentrated to 6.7 - 7.9 mg mL<sup>-1</sup> as described in Chapter 3, section 3.1.2.5. and section 3.2.2.3.2. These experiments were performed at 4°C and 16°C with five commercially available screens: (1) Structure Screen<sup>™</sup> 1 and 2 Eco Screen (Jancarik and Kim, 1991); (2) JCSG-plus™ Eco Screen (Collins, Stevens and Page, 2005); (3) PACT premier<sup>™</sup> Eco Screen (Newman et al., 2005); (4) Morpheus<sup>®</sup> Screen (Gorrec, 2009); and (5) MIDAS<sup>™</sup> Screen (Grimm *et al.*, 2010); all from Molecular Dimensions. The screens were set up in 96-well 2-drop MRC plates sealed with ClearVue Sheets (Molecular Dimensions) employing an OryxNano protein crystallisation robot (Douglas Instruments Ltd.). The sitting drop vapour diffusion technique was used with a drop size of 0.5 µL containing the protein and screen solution at a 1:1 ratio, equilibrated against 50  $\mu$ L of screen solution per reservoir of the 96-well plate. The screening plates were monitored for crystal formation using a SZX9 Stereo Microscope (Olympus). Plates to optimise crystal growth were set up with screen solutions in which microcrystals were observed. The optimisation was carried out in the presence and absence of salt, varying the buffer pH  $\pm$  0.2 units and the precipitant concentration  $\pm$  2%.

Crystallisation screenings following the procedure described above were also set up with partially deglycosylated TaPAPhy\_b2d, freshly purified to concentrations ranging from 6.9 to 8.1 mg mL<sup>-1</sup> as described in **Chapter 3, section 3.1.2.5. and section 3.2.2.3.4.** Crystal growth was reproduced by setting up multiple drops containing the protein and the appropriate screen solution following the same protocol.

### 4.1.2. Crystal harvesting and cryoprotection

Single crystals formed in the different plates set up were harvested using round LithoLoops<sup>™</sup> (Molecular Dimensions) at the growth temperature. Crystals were cryoprotected prior to being stored in liquid nitrogen by soaking them for a few seconds in solutions containing the screen solution in which the crystal was formed to which had been added a cryoprotectant (i.e. 25% (v/v) PEG 400, 30% (v/v) glycerol, or 30% (w/v) sucrose). When appropriate for the experiment, variable concentrations of specific ligands were also included in the cryoprotecting solution (i.e. sodium molybdate, sodium tungstate dihydrate, or *para*-nitrophenyl sulfate), soaking the crystals for variable lengths of time ranging from minutes to over an hour. The cryoprotecting solution pH was also adjusted in some experiments to promote ligand binding.

### 4.1.3. X-ray data collection

X-ray data was collected at Diamond Light Source (DLS; Didcot, UK) on beamlines 103 (with Pilatus3 6M detector and BART sample changer) or 104 (with Pilatus 6M-F detector and BART sample changer). Single-wavelength X-ray diffraction data collection was carried out at a wavelength of 0.9763 Å (12.6994 keV) for native datasets. A wavelength of 1.7389 Å (7.1300 keV) was used for data collection at the iron edge, 0.6100 Å (20.3253 keV) for data collection at the molybdenum edge and 0.9159 Å (13.5369 keV) for data collection at the tungsten edge.

### 4.1.4. Data processing and refinement

The X-ray diffraction images collected from single crystals were scaled and integrated using the DLS automated software pipeline. Data reduction was performed with XIA2 (Winter, Lobley and Prince, 2013). Programmes from the PHENIX suite (Adams *et al.*, 2010) were used for data processing. The quality of the data was analysed with XTRIAGE (Zwart, P. H., Grosse-Kunstleve, R. W., Adams, 2005). A molecular replacement search model was generated with SCULPTOR (Bunkóczi and Read, 2011), including as input files the protein chain (containing Fe<sup>3+</sup>-Zn<sup>2+</sup> metal ions) of one subunit of the red kidney bean PvPAP1 structure (PDB accession 2QFR, Schenk *et al.*, 2008) and the sequence alignment between the red kidney bean PvPAP1, the sweet potato IbPAP1 (Schenk *et al.*, 2005) and the wheat TaPAPhy\_b2 sequences, created in **Chapter 2**, **section 2.1.3. and section 2.2.2.** to obtain a 3D homology model of TaPAPhy\_b2. SCULPTOR was run with default parameters, including the two side chain pruning methods (i.e. schwarzenbacher and similarity) and the options to remove alternate conformations and sanitize occupancies. The search model generated was further modified in PyMOL (Schrodinger LLC, 2015) according to the structure alignment

between PvPAP1, IbPAP1 and the TaPAPhy\_b2 3D homology model, and the metal content was changed to Fe<sup>3+</sup>-Fe<sup>2+</sup> (the predicted for TaPAPhy\_b2). The structures were solved by automated molecular replacement using PHASER (McCoy *et al.*, 2007) with the default settings, but preserving heteroatoms and without searching in alternative space groups. The molecular replacement solutions were subjected to several rounds of automatic refinement using PHENIX REFINE (Adams *et al.*, 2010) with the default settings (unless specified otherwise) and manual refinement using COOT (Emsley *et al.*, 2010). All atoms except water were considered anisotropic in the final stages of refinement. Ligand restraints were generated with READYSET or REEL (Adams *et al.*, 2010) and included in the refinement when needed, together with files specifying the links for the carbohydrates in the N-glycosylation sites. Metal coordination restraints were also generated with READYSET and included in the refinement for structures with a resolution lower than 1.60 Å.

### 4.1.5. TaPAPhy\_b2 metal content

X-ray fluorescence spectra were collected for various TaPAPhy\_b2d crystals at DLS beamlines IO3 or IO4 in order to determine the identity of the elements bound in the active site of the protein. In addition, element edge scans were performed to screen crystals for the presence of specific elements before collecting anomalous datasets.

A single-wavelength anomalous diffraction dataset was collected at the iron edge (Fe-SAD, 1.7389 Å or 7.1300 keV) for a TaPAPhy\_b2d crystal and molecular replacement carried out as described in **section 4.1.4.** An anomalous difference electron density map was generated using tools from the PHENIX suite (Adams *et al.*, 2010) and inspected in COOT (Emsley *et al.*, 2010).

## 4.1.6. Determination of substrate binding interactions in the TaPAPhy\_b2 active site

The binding mode of  $InsP_6$  in the TaPAPhy\_b2 active site was studied through different methodologies, with the aim to identify the structure elements responsible for the ability of this enzyme to hydrolyse phytate.

## 4.1.6.1. Determination of the X-ray crystal structure of TaPAPhy\_b2 in complex with a phytate analogue

Attempts to obtain the crystal structure of TaPAPhy\_b2 with the phytate analogue *myo*-inositol hexakissulfate (InsS<sub>6</sub>) were carried out following two different approaches. Extensive soaking experiments of TaPAPhy\_b2d crystals, grown from different recombinant protein batches, in cryoprotecting solutions including either 1 mM or 5 mM InsS<sub>6</sub> (potassium salt; Alfa Chemistry) and for different lengths of time were performed. In addition, a co-crystallisation screening experiment was set up with a protein:ligand reaction consisting of freshly-purified, partially deglycosylated TaPAPhy\_b2d concentrated to 7.3 mg mL<sup>-1</sup> (generated with recombinant GST-Endo F1 treatment) with 5 mM InsS<sub>6</sub>, as described in **section 4.1.1**.

As well as varying the concentration of InsS<sub>6</sub> and length of the soak, different cryoprotectants were tried and the pH of the cryoprotecting solution was adjusted in order to promote binding. Soaks of TaPAPhy\_b2d crystals in cryoprotecting solutions containing InsP<sub>6</sub> were also attempted.

### 4.1.6.2. Docking of phytate into the active site of TaPAPhy\_b2

Molecular docking experiments were carried out with the crystal structure of TaPAPhy\_b2 as receptor and its substrate InsP<sub>6</sub> as ligand using AutoDock Vina (Trott and Olson, 2010). The TaPAPhy\_b2 structure was stripped from all the ligands to perform the docking experiments (i.e. crystallographic water molecules, carbohydrates, phosphates and other solvent molecules), keeping the two metal ions in the active site. A model of *myo*-InsP<sub>6</sub> in the pentaequatorial (1a5e) conformation predicted to be predominant at the acidic pH optimum of PAPhy (Bohn, Meyer and Rasmussen, 2008) was used for the docking, obtaining atomic coordinates from the HIC-Up database (Kleywegt *et al.*, 2003). The structures of the ligand and receptor were prepared for the docking experiments in pdbqt format with AutoDockTools 1.5.6 (Morris *et al.*, 2009). Torsion flexibility was introduced in the InsP<sub>6</sub> ligand by allowing the free rotation of the twelve bonds involving the six phosphate groups. Polar hydrogen atoms were added to the protein and a search space was defined centred on and encompassing the active site, consisting of grid parameters x = -32; y = -26; z = 21; and grid size x = 28; y = 22;

z = 24, with all the parameters expressed in Å. A molecular docking experiment was first run with a fixed protein model, followed by a second run introducing flexibility in the side chains of specific amino acids around the active site, selected upon inspection of the binding modes obtained in the first run. Results of the molecular docking experiments were analysed in PyMOL (Schrodinger LLC, 2015).

## 4.1.6.3. Molecular dynamics simulations of TaPAPhy\_b2 in complex with phosphate and phytate

A model for the complex structure of the substrate InsP<sub>6</sub> in the binding pocket of TaPAPhy\_b2 was obtained through molecular dynamics (MD) simulations. The simulations were based on a modified version of the crystal structure of TaPAPhy\_b2 in complex with phosphate resembling substrate binding, containing the  $\mu$ -(hydr)oxo bridge in the active site. Processing of the structure prior to the MD simulations was performed in COOT (Emsley *et al.*, 2010). Residues with side chains in multiple conformations were simplified to the conformation with the highest occupancy. The conformation of unresolved residues Asp20-Arg21-Gly22, present in a flexible loop in the crystal structure, was modelled using COOT. Disordered side chains of residues Arg11, Arg18, Glu19 and Lys224, missing in the crystal structure, were also added as the most common rotamer for each amino acid. Solvent molecules were eliminated, excluding the  $\mu$ -(hydr)oxo bridge bound to the metals. Only one N-acetylglucosamine (NAG) molecule (i.e. the one directly bound to the protein through asparagine residues) was retained per N-glycosylation site in order to simplify the simulations.

The simulations were performed using the GROMACS 4.6.5 molecular dynamics package (Hess *et al.*, 2008) with the GROMOS-96 53a6 force field (Oostenbrink *et al.*, 2004). The metal ion in the MI site was modelled as Fe<sup>3+</sup>, while the one in the MII site was modelled as Fe<sup>2+</sup>. Potential errors associated with the use of the formal charges of the metal atoms in the simulations were disregarded due to the tight restraints applied to the active site (see next paragraph for more details). The bridging solvent molecule was modelled as a  $\mu$ -oxo bridge. The 53a6 force field was modified to include parameters for the Fe<sup>3+</sup>, Fe<sup>2+</sup> and  $\mu$ -oxo bridge. A modified residue for the metal ligand Tyr204 was created, consisting of a negatively charged tyrosinate residue. A second

modified residue was introduced to account for the N-glycosylation sites, consisting of an asparagine residue covalently bound to a NAG residue through an Asn N $\delta$ 2-C1 NAG bond. NAG coordinates and topology were obtained from the Automated Topology Builder (ATB) version 2.2 (Koziara *et al.*, 2014). The protein topology was generated using the pdb2gmx command in GROMACS. The MD simulations were performed at pH 5.5. The protonation state of histidine and aspartate residues was manually selected upon careful inspection of their environment. The protonation state of glutamate residues was assigned automatically. The specific protonation state of each of these residues is collected in **Appendix 2**, Table A18.

MD simulations of the enzyme-phosphate complex and the enzyme-phytate complex were performed. HPO<sub>4</sub><sup>2-</sup> coordinates and topology were generated with the PRODRG2 Server (Schüttelkopf and Van Aalten, 2004). InsP<sub>6</sub> coordinates and topology were obtained from ATB version 2.2. The InsP<sub>6</sub> was modelled as  $C_6H_{12}O_{24}P_6^{6-}$  at pH 5.5 (Veiga *et al.*, 2014), the optimum pH for the enzyme (as determined in **Chapter 5**, **section 5.2.2.1.**). The MD simulations were carried out restricting the position of the two iron ions, the amino acid residues coordinating the irons, the  $\mu$ -oxo bridge and the phosphate molecule coordinated to the metals by applying harmonic force constants of  $10^6$  kJ mol<sup>-1</sup> nm<sup>-2</sup>. In the simulations of the enzyme-phytate complex, the D-4-phosphate and the D-6-phosphate were manually docked in turn over the phosphate in the crystal structure in order to perform two separate MD runs. The rest of the InsP<sub>6</sub> molecule was rotated for its accommodation in the active site cavity, so as to avoid short van der Waals contacts.

MD simulations in aqueous solution were performed at a constant temperature of 298 K in a cubic box with 10 Å distance from the centre of the protein to the edge of the box. The box was solvated by the Simple Point Charge (SPC) 216 water model, adding sodium counter ions to ensure neutral charge of the system. Prior to the unrestrained MD simulations, the systems were subjected to a maximum of 10000 steps of energy minimisation using the steepest descent method and position restrained MD for 20 ps with force constants of 1000 kJ mol<sup>-1</sup> nm<sup>-2</sup> in order to equilibrate the water molecules in the solvation box. The equilibrated systems were subjected to 1 ns of production MD runs. Analysis of the MD runs was carried out using embedded tools in the GROMACS package. Root mean square deviation (RMSD) values and root mean square fluctuations (RMSF) of the C $\alpha$  atoms were calculated with the original model as a reference. Distances of key residues or regions of the protein to neighbouring phosphate groups of the InsP<sub>6</sub> molecule were monitored for the production MD runs.

### 4.2. Results and discussion

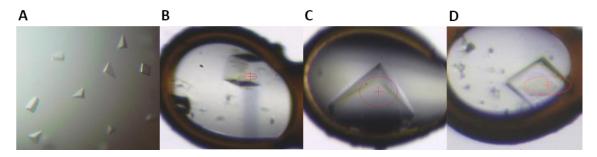
Two sets of crystallisation screening experiments were set up with fully glycosylated TaPAPhy\_b2, using two different recombinant protein batches. Microcrystals grew overnight from TaPAPhy\_b2 batch 02 (6.7 mg mL<sup>-1</sup>) in Structure Screen<sup>TM</sup> Eco Screen 1.23 drops both at 4°C and 16°C, containing 0.2 M calcium chloride dihydrate, 0.1 M HEPES pH 7.5 and 28% (v/v) PEG 400 (Figure 40A). Crystal growth was reproduced in an optimisation plate, but while the crystals formed in all the drops containing calcium chloride, none were observed in the absence of the salt. Harvesting of one crystal, cryoprotected with a solution consisting of the screen solution and 30% (v/v) glycerol, and analysis by X-ray diffraction identified the crystal form as a calcium salt.

One month after setting up, microneedles were observed in drop 1.14 of the Structure Screen<sup>™</sup> Eco Screen plate at 16°C, containing 0.2 M ammonium sulfate, 0.1 M MES pH 6.5 and 30% (w/v) PEG 8000 (Figure 40B). The crystals dissolved during harvesting, indicating a possibility of them being of protein in nature. The second set of crystallisation screen plates was set up with TaPAPhy\_b2 batch 03 (7.9 mg mL<sup>-1</sup>). Spare recombinant protein was also employed to reproduce the microneedle crystal growth in an optimisation plate. Once again, crystal formation was only observed in drops containing ammonium sulfate and not in the absence of the salt, suggesting a strong possibility of the crystals being sulfate salts despite their fragility. A new crystal form with needle morphology was observed in drop 2.44 of the Structure Screen<sup>™</sup> Eco Screen plate at 16°C, containing 0.2 M ammonium sulfate and 5% (v/v) 2-propanol (Figure 40C). The crystals were harvested in a cryoprotectant containing the screen solution and 30% (v/v) glycerol. Upon screening of one of these needle crystals a very poor diffraction pattern was obtained, although not corresponding to a salt.



Figure 40. Crystal forms observed in fully glycosylated TaPAPhy\_b2 screenings

Another two sets of crystallisation screening experiments were set up with two batches of partially deglycosylated TaPAPhy\_b2d, i.e. TaPAPhy\_b2d batch 01 (6.9 mg mL<sup>-1</sup>) and TaPAPhy\_b2d batch 03 (7.3 mg mL<sup>-1</sup>), both deglycosylated with commercial Endo H (NEB). The two batches of TaPAPhy\_b2d formed crystals in the H3 trigonal space group in drop 1.14 (B2 in the 96-well crystallisation plate) of the JCSG-*plus*<sup>TM</sup> Eco Screen at 16°C two to four days after plate set up, containing 0.2 M sodium thiocyanate and 20% (w/v) PEG 3350. Crystals of the same morphology were also observed in the equivalent drop at 4°C, but with a considerably smaller size. The H3 crystals were reproduced with two further partially deglycosylated protein batches, TaPAPhy\_b2d batch 04 (7.3 mg mL<sup>-1</sup>) and TaPAPhy\_b2d batch 07 (8.1 mg mL<sup>-1</sup>), both deglycosylated with recombinant GST-Endo F1.





(A) Drop from TaPAPhy\_b2d batch 01 screening containing 0.2 M sodium thiocyanate and 20% (w/v) PEG 3350. (B) 0.15  $\mu$ M LithoLoop<sup>TM</sup> containing crystal from TaPAPhy\_b2d batch 01 used for X-ray data collection of the TaPAPhy\_b2:PO4 complex structure resembling product binding (section 4.2.1.3.). (C) 0.2  $\mu$ M LithoLoop<sup>TM</sup> containing crystal from TaPAPhy\_b2d batch 03 used for X-ray data collection of the TaPAPhy\_b2:PO4 complex structure resembling substrate binding (section 4.2.1.4.). (C) 0.1  $\mu$ M LithoLoop<sup>TM</sup> containing crystal from TaPAPhy\_b2d batch 04 used for X-ray data collection of the TaPAPhy\_b2:PO4 complex structure resembling substrate binding (section 4.2.1.4.). (C) 0.1  $\mu$ M LithoLoop<sup>TM</sup> containing crystal from TaPAPhy\_b2d batch 04 used for X-ray data collection of the TaPAPhy\_b2:PO4 complex structure resembling enzyme regeneration (section 4.2.1.5.).

<sup>(</sup>A) Calcium salt microcrystals grown in 0.2 M calcium chloride dihydrate, 0.1 M HEPES pH 7.5 and 28% (v/v) PEG 400. (B) Sulfate salt microcrystals grown in 0.2 M ammonium sulfate, 0.1 M MES pH 6.5 and 30% (w/v) PEG 8000. (C) 0.15  $\mu$ M LithoLoop<sup>TM</sup> containing needle crystal used for X-ray data collection screen, grown in 0.2 M ammonium sulfate and 5% (v/v) 2-propanol.

Attempts to replicate the crystal growth in optimisation plates set up with isolated JCSG-*plus*<sup>™</sup> 1.14 reservoir solution were unsuccessful. The same result was observed when solution 1.14 (B2) and solution 1.26 (C2, the previous solution the robot sets up in plates containing the whole screen) were set up in alternate rows of the 96-well crystallisation plate. However, crystals were observed in solution 1.14 drops every time it was set up preceded by all the solutions located prior to 1.14 in the original 96-well crystallisation screen plate. This indicated the need for a certain degree of carry over to drops with solution 1.14 from a number of the previous reservoir solutions of the JCSG-*plus*<sup>™</sup> Eco Screen in order to reproduce crystal growth.

TaPAPhy\_b2d crystals in the H3 trigonal space group from different batches of freshly purified protein diffracted to high resolution, allowing the determination of various crystal structures of the wheat PAPhy isoform b2, as described in the following sections.

## 4.2.1. Determination of the X-ray crystal structure of TaPAPhy\_b2 in complex with phosphate in different binding poses

### 4.2.1.1. Overall structure and comparison with PAPs

Single crystals in the *H*3 space group grown with TaPAPhy\_b2d batch 01 were harvested and cryoprotected by briefly soaking them in a solution containing 0.2 M sodium thiocyanate, 20% (w/v) PEG 3350 and 25% (v/v) PEG 400. An initial dataset with resolution down to 2.64 Å was collected at DLS beamline I04. This dataset was used to perform molecular replacement with the search model described in **section 4.1.4.** A solution was found and refined to an R<sub>work</sub> of 27.09% and an R<sub>free</sub> of 33.56% before collection of a higher resolution dataset. The partial TaPAPhy\_b2 structure was used as search model to perform molecular replacement with a dataset with a resolution of 1.42 Å collected at DLS beamline I03 from the crystal shown in Figure 41B, a cube with sides of approximately 30  $\mu$ M. The final model was refined to R<sub>work</sub> and R<sub>free</sub> values of 13.22% and 15.80%, respectively, to give the TaPAPhy\_b2:PO<sub>4</sub> complex structure resembling product binding (**section 4.2.1.3.**), as shown in Figure 42. Crystal

parameters, data collection and refinement statistics for the initial and the higher resolution structures are summarised in Table 11.

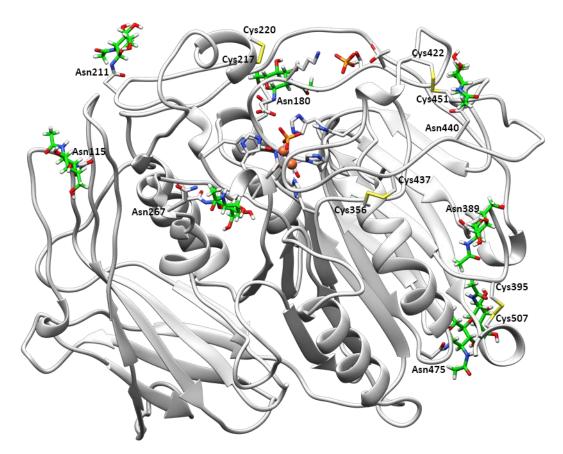


Figure 42. Cartoon representation of the overall structure of TaPAPhy\_b2 in complex with phosphate

Polypeptide chain coloured in light grey. The two iron ions are shown as brown spheres. Side chains of residues displayed as sticks are involved in metal ion coordination, ligands of phosphate molecules, cysteine residues involved in disulfide bond formation or N-glycosylated asparagine residues. Phosphates are shown as sticks and coloured by element. NAGs are displayed as sticks and coloured by element, with carbons in green. Image created with the UCSF Chimera package (Pettersen *et al.*, 2004).

One monomer of the TaPAPhy\_b2 enzyme was present in the asymmetric unit, with a solvent content of 56.6% (v/v). TaPAPhy\_b2 shares domain arrangements with the previously crystallised plant PAPs (Sträter *et al.*, 1995; Schenk *et al.*, 2005). The phytase structure consists of a smaller N-terminal domain composed mainly of two sandwiched  $\beta$ -sheets and not involved in active site interactions, and the bigger C-terminal MPE  $\alpha/\beta$  domain, composed of two  $\beta$ -sheets forming a  $\beta$ -sandwich decorated by  $\alpha$ -helices and containing the active site (Matange, Podobnik and Visweswariah, 2015). A cartoon representation of the secondary structure elements of TaPAPhy\_b2 is shown in Figure 43A.

The majority of the residues (97.23%) were found in the most favourable region of the Ramachandran plot, with no outliers present. Continuous electron density was present for the whole polypeptide excluding Glu1 at the N-terminus, Leu509, Lys510 and the 6xHis tag at the C-terminus, probably due to disorder. In addition, the side chains of the surface residues Glu19, Arg37 and Lys224 could not be modelled, as they were not defined in the electron density. A list of 24 residues were modelled with alternative conformations: Ser51, Ser56, Gln127, Arg155, Arg168, Ser183, Glu186, Ser190, Ser249, Asn267, Lys268, Met282, Ser311, Arg318, Ser330, Ser345, Glu355, Ser401, Met411, Thr414, Ser449, Val494, Glu497 and Tyr499. Of the nine cysteine residues present in the TaPAPhy b2 enzyme, eight of them formed four disulfide bridges (i.e. Cys217-Cys220, Cys356-Cys437, Cys395-Cys507 and Cys422-Cys451) with only one existing as a free cysteine (Cys139), as predicted previously (Dionisio et al., 2012). However, single difference electron density features were observed around the modelled disulfide bonds, indicating possible photoreduction of the crystal during data collection. Electron density for NAG residues was observed in the seven predicted N-glycosylation sites, i.e. Asn115, Asn180, Asn211, Asn267, Asn389, Asn440 and Asn475 (Dionisio et al., 2011, 2012). A single NAG was modelled per site except for Asn475, in which electron density for a second NAG was present with 80% occupancy, indicating the endoglycosidase treatment was inefficient in cleaving the  $\beta$ -(1,4)-glycosidic bond in that site. In addition, occupancies lower than 100% were observed for NAGs in Asn267 (81%) and Asn389 (79%).

Two iron ions were modelled in the TaPAPhy\_b2 active site, with occupancies of 47% for the iron in the MI site (44.78 Å<sup>2</sup> *B* factor) and 89% for the iron in the MII site (12.78 Å<sup>2</sup> *B* factor). The architecture of the TaPAPhy\_b2 active site was in accordance to that described for PAPs in **Chapter 1, section 1.3.3.4.2.**, with the metal ligand residues conserved (Mitić *et al.*, 2006; Schenk *et al.*, 2012; Matange, Podobnik and Visweswariah, 2015). Amino acid residues coordinating the iron in the MI site was coordinated by Asn258, His340, His377 and the bridging Asp 201. A tetrahedral and an octahedral geometry were assigned to the irons in the MI and MII sites, respectively, by the CheckMyMetal Metal Binding Site Validation Server (Zheng *et al.*, 2014).

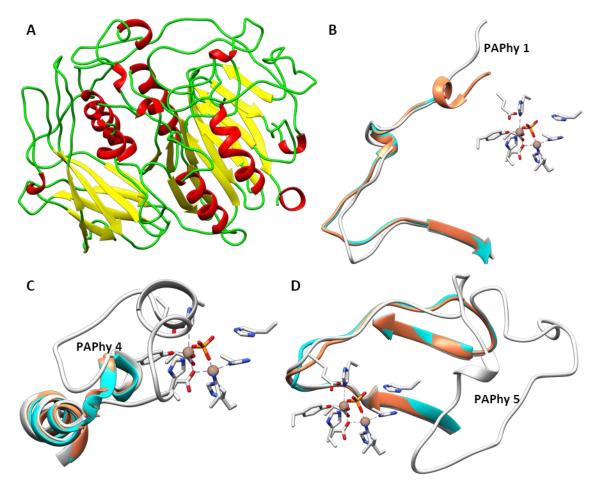


Figure 43. Cartoon representation of the TaPAPhy\_b2 secondary structure arrangements and selected PAPhy motifs

(A) Overall view of TaPAPhy\_b2 coloured by its secondary structure elements.  $\alpha$ -Helixes, red;  $\beta$ -strands, yellow; loops, green. (B) Overlapped view of PAPhy 1, (C) PAPhy 4 and (D) PAPhy 5 motifs and relative positions to the active site. TaPAPhy\_b2, light grey; red kidney bean PvPAP1, cyan; sweet potato IbPAP1, coral. Images created with the UCSF Chimera package (Pettersen *et al.*, 2004).

Electron density for two inorganic phosphate molecules bound to the TaPAPhy\_b2 structure was observed. The first phosphate was bound in the active site with 95% occupancy (29.73 Å<sup>2</sup> *B* factor), coordinated to the two iron ions and the side chains of His259, His350 and Glu409, resembling the enzyme-product complex (see **section 4.2.1.3.** for details). A second phosphate was modelled in the vicinity of the active site with an occupancy of 97% (58.12 Å<sup>2</sup> *B* factor), coordinated by residues Lys410, Met411, Thr413 and Thr414. Both phosphate molecules were presumably scavenged during recombinant protein expression, as the yeast was grown in culture media containing phosphate buffer. As well as phosphates, electron density was observed for additional solvent molecules originated from the crystal growth solution or the cryoprotectant. The TaPAPhy\_b2 structure contained 489 waters, twelve ethylene glycol

molecules (three-letter code: EDO, formula:  $C_2H_6O_2$ ), five diethylene glycol molecules (PEG,  $C_4H_{10}O_3$ ), two triethylene glycol molecules (PGE,  $C_6H_{14}O_4$ ) and a single pentaethylene glycol molecule (1PE,  $C_{10}H_{22}O_6$ ).

The crystal structure of TaPAPhy\_b2 confirmed the structural proximity to the active site of the phytase motifs PAPhy 1, PAPhy 4 and PAPhy 5 predicted on **Chapter 2**, **section 2.2.2.** upon observation of the TaPAPhy\_b2 3D homology model. The proximity to the active site of these motifs, especially PAPhy 4 and PAPhy 5, can be observed in Figure 43B, C and D, together with the lack of conservation in the phosphatase structures. PAPhy 1 motif was formed by residues Arg21 to Arg37 (Arg21-Leu50 displayed in Figure 43B). PAPhy 4 motif contains residues Asp216-His229 (Ala205-Thr247 displayed in Figure 43C). PAPhy 5 motif extends from residue Arg408 to residue Arg454 (Val398-Glu463 displayed in Figure 43D). Phytase motifs PAPhy 2 and PAPhy 3 were located in the N-terminal domain of the TaPAPhy\_b2 enzyme and, therefore, away from the active site as predicted from the 3D homology model.

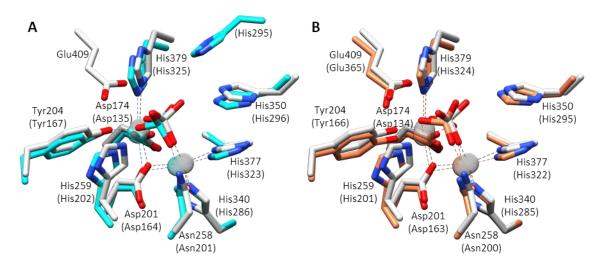


Figure 44. Conservation between the TaPAPhy\_b2 phytase and the PAPs active sites

Detailed view of the active sites of the enzymes in complex with phosphate with no bridging solvent molecule present. (A) TaPAPhy\_b2 in light grey overlapped to red kidney bean PvPAP1 phosphatase in cyan (PDB accession 4KBP). (B) TaPAPhy\_b2 in light grey overlapped to sweet potato lbPAP1 phosphatase in coral (PDB accession 1XZW). Residue labels in brackets correspond to the phosphatases. Images created with the UCSF Chimera package (Pettersen *et al.*, 2004).

A detailed comparison of the active site of the wheat TaPAPhy\_b2 phytase with the red kidney bean PvPAP1 phosphatase and the sweet potato IbPAP1 phosphatase is displayed in Figure 44A and Figure 44B, respectively. The TaPAPhy\_b2 structure was compared to those of the plant phosphatases with a phosphate molecule bound to the active site and in the absence of a solvent molecule bridging the two metal ions. PDB accessions 4KBP and 1XZW were used for the red kidney bean PvPAP1 phosphatase (Klabunde et al., 1996) and the sweet potato IbPAP1 phosphatase (Schenk et al., 2005), respectively. Little variation was observed between the three structures regarding the metal ions (Fe<sup>3+</sup>-Fe<sup>2+</sup> in TaPAPhy b2, Fe<sup>3+</sup>-Zn<sup>2+</sup> in PvPAP1 and Fe<sup>3+</sup>-Mn<sup>2+</sup> in IbPAP1) and their ligands. The amino acid residues stabilising the binding of the phosphate molecule to the active site were also conserved between TaPAPhy\_b2 (His259, His350 and Glu409) and IbPAP1 (His201, His295 and Glu365). PvPAP1 showed conservation of the two histidines coordinating the phosphate (His202 and His296) but not the glutamate residue. Instead, PvPAP1 contained an extra histidine residue (His295) in the active site with respect to the other two structures. In the PvPAP1 enzyme, His296 (His350 in TaPAPhy b2 and His295 in IbPAP1) is responsible for the protonation of the leaving group (Klabunde et al., 1996; Schenk et al., 2008). However, in the IbPAP1 enzyme this role is shared by His295 (His350 in TaPAPhy\_b2 and His296 in PvPAP1) and Glu365 (Glu409 in TaPAPhy\_b2 and not conserved in the PvPAP1). It has been proposed that at low pH Glu365 acts as proton donor for the leaving group, while at higher pH His295 performs this task (Schenk et al., 2005). Noting that these two residues are conserved in the TaPAPhy\_b2 structure, a similar mechanism is likely to occur.

#### Table 11. Data collection and refinement statistics for the TaPAPhy\_b2:PO<sub>4</sub> complex structures

The 'Initial' structure data corresponds to the initial dataset collected and first used to perform molecular replacement. The partial model obtained was the initial model for the 'Product' structure. Values in brackets correspond to the high resolution outer shell. The X-ray flux is the total experimented by the crystal during data collection, corrected for transmission. The  $R_{merge}$  value corresponds to  $R_{merge}$  (all I+ & I-). The number of reflections stated are the unique reflections used in refinement.

Structure	Initial	Product	Substrate	Regeneration
PDB ID	n/a	6GIT	6GIZ	6GJ9
Crystal parameters				
Space group	НЗ	H3	H3	H3
<i>a, b, c</i> (Å)	126.9, 126.9, 107.0	126.5, 126.5, 106.8	126.7, 126.7, 107.0	127.0, 127.0, 107.5
<i>α, β,</i> γ (°)	90, 90, 120	90, 90, 120	90, 90, 120	90, 90, 120
Data collection				
Wavelength (Å)	0.9763	0.9763	0.9763	0.9763
Ω Oscillation (°)	0.10	0.10	0.10	0.05
Total Ω (°)	147	125	120	123
Exposure (s)	0.220	0.025	0.300	0.025
Beam size (µm)	19x10	50x20	63x50	50x20
X-ray flux (ph)	4.53x10 <sup>13</sup>	4.38x10 <sup>12</sup>	5.04x10 <sup>13</sup>	5.23x10 <sup>13</sup>
Resolution (Å)	63.44-2.64 (2.69-2.64)	63.24-1.42 (1.44-1.42)	48.11-1.54 (1.57-1.54)	48.30-1.76 (1.79-1.76)
R <sub>merge</sub> (%)	13.7 (58.4)	4.7 (50.6)	5.6 (71.4)	14.6 (53.9)
$< I/\sigma(I) >$	8.8 (2.6)	14.6 (2.4)	13.4 (1.5)	8.3 (2.4)
Completeness (%)	99.5 (99.5)	92.6 (99.4)	99.8 (99.7)	99.0 (98.4)
Multiplicity	4.1 (4.2)	3.5 (3.3)	3.4 (2.9)	3.5 (3.2)
CC <sub>1/2</sub>	1.0 (0.7)	1.0 (0.7)	1.0 (0.5)	1.0 (0.8)
Wilson <i>B</i> factor (Å <sup>2</sup> )	44.7	14.5	18.8	14.2
Refinement				
Total No. of atoms	3034	5093	4915	4948
Water molecules	0	489	433	670
No. of reflections	18748	111798	94712	63506
R <sub>work</sub> (%)	27.1	13.2	13.6	14.4
R <sub>free</sub> (%)	33.6	15.8	16.7	19.6
Anisotropy	0.274	0.135	0.131	0.357
<b>RMS</b> deviations				
Bonds (Å)	0.009	0.005	0.006	0.006
Angles (°)	1.211	0.838	0.896	1.060
Planes (Å)	0.008	0.006	0.005	0.005
Ramachandran plot				
Favoured (%)	84.76	97.23	96.80	97.00
Allowed (%)	10.43	2.77	3.20	3.00
Outliers (%)	4.81	0.00	0.00	0.00
Mean <i>B</i> factors (Å <sup>2</sup> )	39	23.0	28.0	18

### 4.2.1.2. TaPAPhy\_b2 metal content

PAPs are characterised for containing  $Fe^{3+}$  in the MI site and a preference for  $Fe^{2+}$  in the MII site has been reported for the PAPhy\_b isoforms (Dionisio *et al.*, 2011, 2012).

For these reasons, sources of iron(III) and iron(II) were included in the *Pichia pastoris* culture media for the recombinant expression of TaPAPhy\_b2, and two iron ions had been modelled in the crystal structure. Further confirmation of the TaPAPhy\_b2 metal content was achieved by collecting fluorescence data of TaPAPhy\_b2d H3 crystals at DLS beamline I03. Peaks for iron were observed when recording an X-ray fluorescence spectrum (Figure 45A), while no zinc or manganese peaks were identified (the other two common metals in the MII site of PAPs). The X-ray fluorescence spectrum of the TaPAPhy\_b2d crystal suggested a small presence of gadolinium (Gd). These peaks are likely to be an artefact due to noise in the fluorescence spectrum and the iron and gadolinium edges being very similar in energy (7.1120 keV and 7.2428 keV, respectively).

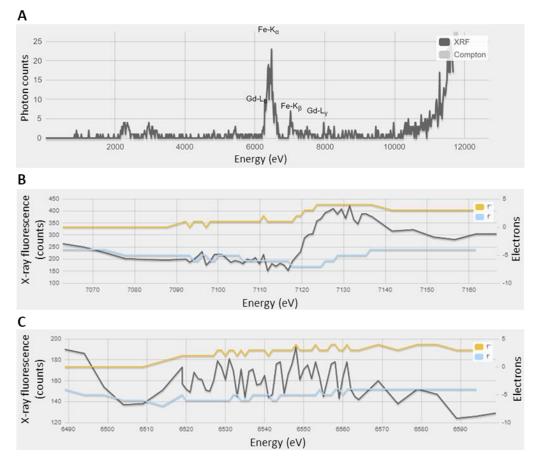


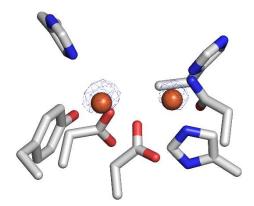
Figure 45. Fluorescence data collected from a TaPAPhy\_b2d crystal

(A) X-ray fluorescence spectrum. XRF, X-ray fluorescence. Compton, Compton scattering. (B) Iron edge and (C) Manganese edge scans. Black line, raw fluorescence. Yellow line (f''), anomalous scattering factor. Blue line (f'), dispersive scattering factor.

In addition, an iron edge scan was performed in the crystal and a peak was detected at the iron edge (1.7389 Å or 7.1300 keV), as shown in Figure 45B. However,

manganese could also give a signal in a dataset collected at the iron edge. In order to disregard the presence of manganese in the TaPAPhy\_b2d crystals, a manganese edge scan was also performed, and no peak was detected at the manganese edge (1.8897 Å or 6.5611 keV), as shown in Figure 45C.

To conclude, an Fe-SAD dataset was collected for a TaPAPhy\_b2d H3 crystals at DLS beamline I04. The anomalous difference map obtained showed two regions of strong electron density (peak heights 32  $\sigma$  and 29  $\sigma$  for sites MI and MII, respectively) around the location of the iron ions in the TaPAPhy\_b2 structure, as displayed in Figure 46.

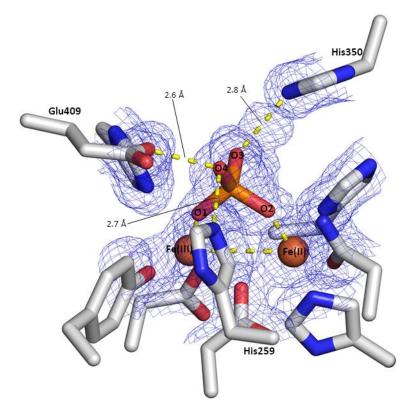


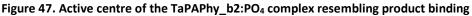
**Figure 46.** Anomalous difference electron density map from a TaPAPhy\_b2d Fe-SAD dataset Anomalous difference electron density map displayed as a blue mesh at a contour level of 10 r.m.s.d. Iron ions showed as brown spheres. Side chains of the metal ligands in the TaPAPhy\_b2 active site are shown as sticks and coloured by heteroatom. Image created with PyMOL version 1.3 (Schrodinger LLC, 2015).

### 4.2.1.3. TaPAPhy\_b2:PO<sub>4</sub> complex structure resembling product binding

A detailed overview of the catalytic mechanism of PAPs was described in **Chapter 1, section 1.3.3.4.2.**, alongside crystal structures from representative PAPs supporting most of the steps. The X-ray crystal structure of the TaPAPhy\_b2:PO<sub>4</sub> complex at 1.42 Å resolution described in the sections above resulted from a crystal soaked in the screen solution in which it was formed, with the only addition of the cryoprotectant PEG 400. This structure contains a phosphate molecule in the active site and resembles the red kidney bean PvPAP1:PO<sub>4</sub> complex structure representing the product-bound state (PDB accession 4KBP), with bidentate coordination to the metal ions and absence of a bridging solvent molecule (Sträter *et al.*, 1995; Schenk *et al.*, 2008).

Distances to phosphate ligands are depicted in Figure 47, while remaining active site distances are summarised in Table 12.





Double difference electron density map around the phosphate displayed as a blue mesh with a contour level of 1 r.m.s.d. Distances between the phosphate and the amino acid residues involved in the binding are indicated. Image created with PyMOL version 1.3 (Schrodinger LLC, 2015).

### 4.2.1.4. TaPAPhy\_b2:PO<sub>4</sub> complex structure resembling substrate binding

Single crystals in the H3 space group grown with TaPAPhy\_b2d batch 03 were harvested and cryoprotected by soaking them for a few minutes in a solution containing 0.2 M sodium thiocyanate, 20% (w/v) PEG 3350, 25% (v/v) PEG 400 and 5 mM InsS<sub>6</sub>. The non-hydrolysable phytate analogue InsS<sub>6</sub> was combined with the original screen solution and cryoprotectant mixture used to obtain the TaPAPhy\_b2:PO<sub>4</sub> product-bound structure described in the previous sections, with the aim to obtain a TaPAPhy\_b2:InsS<sub>6</sub> complex structure and gain insights into PAPhy substrate binding. A dataset with resolution down to 1.54 Å was collected at DLS beamline IO4 from crystal in Figure 41C, wedge-shaped with approximate dimensions of 135 x 60 x 30  $\mu$ M<sup>3</sup>, and the structure was solved by molecular replacement with the TaPAPhy\_b2:PO<sub>4</sub> complex structure in the product-bound state. The final model was refined to R<sub>work</sub> and R<sub>free</sub> values of 13.62% and 16.74%, respectively. Crystal parameters, data collection and refinement statistic for this structure are summarised in Table 11. The structure consisted of TaPAPhy\_b2:PO<sub>4</sub> complex, with no electron density observed for InsS<sub>6</sub> bound to the active site or anywhere else. However, upon close inspection of the active site of this new structure, it was observed that there was spherical electron density present for a solvent molecule bridging the two iron ions and that the phosphate molecule was positioned higher up in the active site (Figure 48). This TaPAPhy\_b2 crystal structure resembled the pig SsPAP5:PO<sub>4</sub> complex structure representing the substrate-bound state or catalytic complex (PDB accession 1UTE), with bidentate coordination of the  $\mu$ -hydroxide and phosphate groups to the metal ions (Guddat *et al.*, 1999; Schenk *et al.*, 2008). Selected active site distances of the TaPAP\_b2:PO<sub>4</sub> complex structure resembling substrate binding are collected in Table 12, compared to the other enzyme-phosphate complex structures.

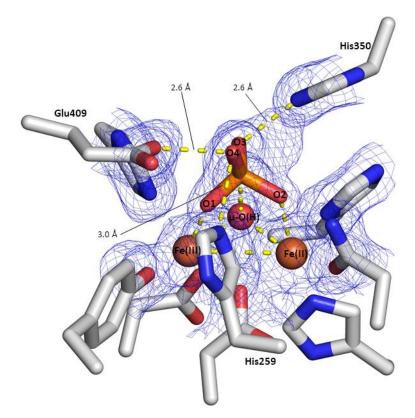


Figure 48. Active centre of the TaPAPhy\_b2:PO₄ complex resembling substrate binding

Double difference electron density map around the phosphate displayed as a blue mesh with a contour level of 1 r.m.s.d. Distances between the phosphate and the amino acid residues involved in the binding are indicated. Image created with PyMOL version 1.3 (Schrodinger LLC, 2015).

The bridging solvent molecule observed in the red kidney bean PvPAP1 phosphatase crystal structure in complex with sulfate (PDB accession 2QFR) has been identified as a  $\mu$ -hydroxide, being within hydrogen bond formation distance of the carbonyl oxygen of His323, one of the Zn<sup>2+</sup> ligands (Schenk *et al.*, 2008). The carbonyl oxygen of the equivalent residue in the present TaPAPhy\_b2 structure, His377, was also observed to be at a distance that would allow hydrogen bond formation with the bridging solvent molecule (2.35 Å) and, therefore, is likely to be a  $\mu$ -hydroxide too.

The iron ion in the MI site, modelled with an occupancy of 62% (20.09  $Å^2$ B factor), was coordinated by a nitrogen atom from the side chain of His379, oxygen atoms from the side chains of the Tyr204, Asp174, the bridging Asp201, and the bridging hydroxide. The iron ion in the MII site was modelled with an occupancy of 90% (16.66  $Å^2$ B factor) and ligated by the side chain oxygen atoms of the bridging Asp201 and Asn258, the side chain nitrogen atoms of His340 and His377, and the  $\mu$ -hydroxide. Both metals were coordinated with an octahedral geometry, as assigned by the CheckMyMetal server (Zheng et al., 2014). No Ramachandran outliers were present in the final structure, and 96.80% of the residues were found in the most favourable region of the plot. Gaps in electron density were found at Glu1 in the N-terminus; three consecutive residues Asp20, Arg21 and Gly22; and Leu509, Lys510 and the 6xHis tag at the Cterminus. The side chains of surface residues Arg11, Arg18, Glu19 and Lys224 were not defined in the electron density and, therefore, not modelled. The following 14 residues were modelled with alternative conformations: Asp26, Ser56, Gln127, Glu130, Arg168, Ser249, Asn267, Met303, Ser345, Glu353, Glu363, Thr414, Ser449 and Asp457. The disulfide bonds formed by Cys217-Cys220, Cys356-Cys437and Cys422-Cys451 displayed signs of photoreduction of the crystal during data collection. Electron density for NAG residues was observed in the seven predicted N-glycosylation sites, with a second NAG in the Asn115 and Asn180 sites with occupancies of 75 and 77%, respectively. Occupancies lower than 100% were also observed for NAGs in Asn211 (86%), Asn267 (84%), Asn389 (78%) and Asn475 (89%).

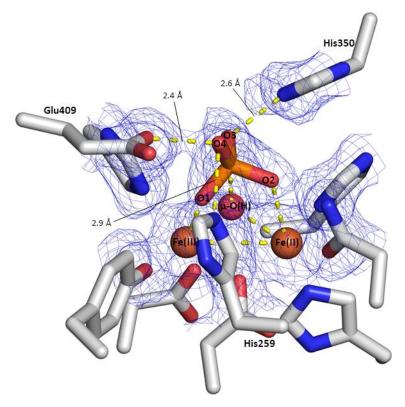
In addition to the phosphate molecule bound to the active site, with 79% occupancy (33.81 Å<sup>2</sup> *B* factor), the second phosphate in the vicinity of the active site was also bound in this structure with 91% occupancy (38.47 Å<sup>2</sup> *B* factor). Electron density for

a third inorganic phosphate molecule was observed in the protein surface, with 81% occupancy (67.11 Å<sup>2</sup> *B* factor) and coordinated by residues Ser311, Lys312 and Ser313. The TaPAPhy\_b2:PO<sub>4</sub> substrate-bound complex structure contained 433 waters, eight ethylene glycol molecules (EDO,  $C_2H_6O_2$ ), four diethylene glycol molecules (PEG,  $C_4H_{10}O_3$ ), and three triethylene glycol molecules (PGE,  $C_6H_{14}O_4$ ).

## 4.2.1.5. TaPAPhy\_b2:PO<sub>4</sub> complex structure resembling enzyme regeneration

Failing to obtain a TaPAPhy b2:InsS<sub>6</sub> complex structure by soaking crystals in a solution containing InsS<sub>6</sub>, co-crystallisation of the enzyme with the non-hydrolysable substrate analogue was attempted. Single crystals in the H3 space group resulting from the co-crystallisation of TaPAPhy b2d batch 04 and 5 mM InsS<sub>6</sub> were harvested and cryoprotected by soaking them for two minutes in a solution containing 0.2 M sodium thiocyanate, 20% (w/v) PEG 3350, 30% (w/v) sucrose and 1 mM  $InsS_6$ . A dataset with 1.76 Å resolution was collected at DLS beamline IO3 from a crystal with approximate dimensions 60 x 40 x 10  $\mu$ M<sup>3</sup> (shown in Figure 41D) and the structure was solved by molecular replacement with the TaPAPhy\_b2:PO<sub>4</sub> complex structure in the productbound state. The final model was refined to R<sub>work</sub> and R<sub>free</sub> values of 14.37% and 19.55%, respectively. Crystal parameters, data collection and refinement statistics for this structure are summarised in Table 11. Another TaPAPhy\_b2:PO<sub>4</sub> complex structure with no electron density for  $InsS_6$  apparent was obtained. Spherical electron density for a solvent molecule bridging the two iron ions was also observed for this structure, but positioned closer to the Fe(III) than to the Fe(II) (1.99 Å vs 2.31 Å) in comparison to the substrate-bound structure described in the previous section (2.13 Å vs 2.24 Å). In this case, the phosphate molecule bound to the active site seemed to be 'leaning' towards the iron ion in the MI site and the Glu409, as can be observed in Figure 49. No other PAP crystal structure was found in the PDB database with phosphate (or another tetrahedral ion) bound to the active site in a similar position and, according to the PAP catalytic mechanism described in Chapter 1, section 1.3.3.4.2., this structure could represent a stage of regeneration of the enzyme active site. However, since the differences in the active site interatomic distances between the current structure and the other TaPAPHy\_b2:PO<sub>4</sub> complex structures obtained in this project are quite subtle (especially

compared to the substrate-bound structure) and the resolution of this potential regeneration structure was slightly lower (1.76 Å *vs* 1.42 Å and 1.54 Å), the possibility that uncertainties in the position of the active site atoms may be at least partially responsible for the differences observed cannot be ignored. Nevertheless, addition of a water molecule and monodentate coordination of the phosphate to the metal in the MI site has been predicted as the first step carried out by PAP enzymes to return to their resting state (Schenk *et al.*, 2008), an interpretation that would fit with the current TaPAPhy\_b2 structure. Higher resolution structures of the PAP enzyme regeneration steps would aid in confirming this prediction.



**Figure 49.** Active centre of the TaPAPhy\_b2:PO₄ complex resembling enzyme regeneration Double difference electron density map around the phosphate displayed as a blue mesh with a contour level of 1 r.m.s.d. Distances between the phosphate and the amino acid residues involved in the binding are indicated. Image created with PyMOL version 1.3 (Schrodinger LLC, 2015).

The iron ion in the MI site was modelled with an occupancy of 63% (16.54 Å<sup>2</sup> *B* factor) and displayed octahedral coordination geometry, while the iron in the MII showed 100% occupancy (12.57 Å<sup>2</sup> *B* factor) and trigonal bipyramidal coordination geometry, as assigned by the CheckMyMetal server (Zheng *et al.*, 2014). The final structure did not contain Ramachandran outliers and 97% of the residues were found in the most favourable region of the plot. Gaps in electron density were found at Glu1 in

the N-terminus; three consecutive residues Glu19, Asp20 and Arg21; and Leu509, Lys510 and the 6xHis tag at the C-terminus. The side chains of surface residues Arg11, His23, Arg37, Lys224, Lys410 and Glu424 were not defined in the electron density and, therefore, not modelled. The following 23 residues were modelled with alternative conformations: Thr39, Ser56, Ser105, Glu111, Gln114, Arg125, Glu130, Ser164, Arg168, Ser190, Leu199, Ser249, Asn267, Met282, Ser288, Met303, Leu304, Lys322, Val331, Ser345, Glu355, Thr414 and Val494. Signs of photoreduction were only visible around the disulfide bond formed by Cys356-Cys437, and in a lower degree than in the previous datasets. Electron density for NAG residues was observed in the seven predicted N-glycosylation sites, with a second NAG in the Asn475 site modelled with 100% occupancy. Occupancies lower than 100% were observed for NAGs in Asn267 (81%) and Asn389 (74%). The phosphate molecule bound to the enzyme's active site was the only one modelled in this structure, displaying an occupancy of 72% (21.93 Å<sup>2</sup> B factor). The TaPAPhy\_b2:PO<sub>4</sub> complex structure resembling an enzyme regeneration step contained 670 waters, a single ethylene glycol molecule (EDO, C<sub>2</sub>H<sub>6</sub>O<sub>2</sub>) and a single diethylene glycol molecule (PEG, C<sub>4</sub>H<sub>10</sub>O<sub>3</sub>).

From	То	Product	Substrate	Regeneration
Fe(III)	Fe(II)	3.57	3.45	3.37
	Asp174 Οδ2	1.79	1.89	1.96
	Asp201 Οδ2	2.35	2.35	2.34
	Tyr204 O <sup>-</sup>	1.86	1.88	1.91
	His379 Nɛ2	2.75	2.42	2.48
	μ-(hydr)oxo O	n/a	2.13	1.99
Fe(II)	Asp201 Οδ2	2.25	2.21	2.16
	Asn258 Οδ1	2.18	2.13	2.10
	His340 Nɛ2	2.00	2.12	2.14
	His377 Nδ1	2.08	2.13	2.10
	μ-(hydr)oxo O	n/a	2.24	2.31
PO4 01	Fe(III)	1.49	2.27	2.03
PO4 02	Fe(II)	2.00	2.45	2.73
PO4 03	His350 Nɛ2	2.83	2.59	2.57
PO <sub>4</sub> O4	His295 Ne2	2.72	3.03	2.87
	Glu409 Οε1	2.56	2.63	2.44
μ-(hydr)oxo O	PO <sub>4</sub> P	n/a	2.63	2.51

**Table 12. Selected active site distances of the TaPAPhy\_b2:PO<sub>4</sub> complex structures** All distances are expressed in Å.

Selected active site distances of the TaPAP\_b2:PO<sub>4</sub> complex structure resembling enzyme regeneration are collected in Table 12, compared to the other enzymephosphate complex structures. The three states of the active site obtained in the different TaPAPhy\_b2:PO<sub>4</sub> complex structures are displayed superimposed in **Appendix 2**, Figure A5.

## 4.2.1.6. Determination of the X-ray crystal structures of TaPAPhy\_b2 in complex with inhibitors

Single crystals in the *H*3 space group grown with TaPAPhy\_b2d batch 07 were harvested and cryoprotected by soaking for a few min to over one hour in solutions containing 0.2 M sodium thiocyanate, 20% (w/v) PEG 3350, 25% (v/v) PEG 400 and either 1 mM sodium molybdate, 5 mM sodium tungstate dihydrate, 10 mM sodium tungstate dihydrate or 5 mM *para*-nitrophenyl sulfate (pNPS). In addition, the pH of all the cryoprotectants prepared was adjusted to 5.5 with acetate buffer (the optimum for the enzyme, as determined in **Chapter 5, section 5.2.2.1.**) in an attempt to promote ligand binding. Mo-SAD datasets, W-SAD datasets and native datasets were collected for molybdate, tungstate and pNPS soaked crystals, respectively, as well as performing fluorescence scans and element specific edge scans. All the datasets collected displayed electron density for only a phosphate molecule bound to the active site, irrespective of the ligand present in the cryoprotectant solution.

## 4.2.2. Determination of substrate binding interactions in the TaPAPhy\_b2 active site

## 4.2.2.1. Determination of the X-ray crystal structure of TaPAPhy\_b2 in complex with a phytate analogue

Following the frustrated attempts to obtain the crystal structure of TaPAPhy\_b2d in complex with the non-hydrolysable phytate analogue InsS<sub>6</sub> that resulted in the TaPAPhy\_b2:PO<sub>4</sub> complex structures described in **sections 4.2.1.4. and 4.2.1.5.**, further soaking experiments were set up with single crystals in the *H*3 space group grown with TaPAPhy\_b2d batch 07. The crystals were harvested and cryoprotected in solutions containing 0.2 M sodium thiocyanate, 20% (w/v) PEG 3350, 25% (v/v) PEG 400 and

either 1 mM InsS<sub>6</sub> or 5 mM InsS<sub>6</sub>, but with the pH adjusted to 5.5 with acetate buffer in this occasion. The crystals were soaked in the cryoprotectants for different lengths of time ranging from a few minutes to over one hour. Results of the inhibitory effect of InsS<sub>6</sub> in the phytase activity of TaPAPhy\_b2 are presented in **Chapter 5, section 5.2.2.4.** A number of crystals were also soaked in a cryoprotectant with the same composition but containing 1 mM InsP<sub>6</sub> instead of InsS<sub>6</sub> and datasets were collected but, as expected, electron density for the substrate was not observed in the active site.

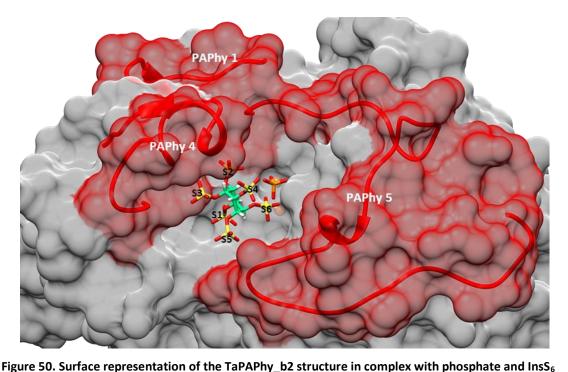
A dataset with 1.68 Å resolution was collected at DLS beamline IO3 from a wedge-shaped crystal with approximate dimensions of  $60 \times 50 \times 15 \mu M^3$ , and the structure solved by molecular replacement with the TaPAPhy\_b2:PO<sub>4</sub> complex structure in the product-bound state. The final model was refined to R<sub>work</sub> and R<sub>free</sub> values of 13.41% and 17.60%, respectively. Crystal parameters, data collection and refinement statistic for this structure are summarised in Table 13. The map obtained revealed once again electron density for a phosphate molecule bound to the active site. However, positive single difference electron density features not present in the previous datasets were also spotted in the active site. Further refinement allowed to assign this electron density to an InsS<sub>6</sub> molecule bound to the active site of the TaPAPhy\_b2 enzyme. However, no coordination to the metal ions was observed for any of the InsS<sub>6</sub> sulfate groups due to the phosphate molecule present at the active centre. It was then concluded that, although the binding of InsS<sub>6</sub> to TaPAPhy\_b2 in the position observed in this structure would have an inhibitory effect to the activity of the enzyme by blocking access to the active site, the InsS<sub>6</sub> did not mimic substrate binding. In addition, the InsS<sub>6</sub> molecule modelled in the TaPAPhy b2 structure was not in the expected *myo*-inositol pentaequatorial (1a5e) conformation. The InsS<sub>6</sub> conformation that best fitted the electron density consisted of the inverted pentaaxial (5a1e) state. Such a conformational change has been most often observed for InsP<sub>6</sub> at pH values above 9.5 (Volkmann et al., 2002; Bohn, Meyer and Rasmussen, 2008; Veiga et al., 2014), higher than the pH 5.5 of the cryoprotectant used in this case, but no similar studies were found for InsS<sub>6</sub>. Nevertheless, InsS<sub>6</sub> in the pentaaxial (5a1e) conformation has previously been found in crystal structures in complex with other phytases (Chu et al., 2004; Ariza et al., 2013).

### Table 13. Data collection and refinement statistics for the structure of TaPAPhy\_b2 in complex with phosphate and $InsS_6$

Values in brackets correspond to the high resolution outer shell. The X-ray flux is the total experimented by the crystal during data collection, corrected for transmission. The  $R_{merge}$  value corresponds to  $R_{merge}$  (all I+ & I-). The number of reflections stated are the unique reflections used in refinement.

Structure	TaPAPhy_b2d:PO₄ & InsS <sub>6</sub>		
PDB ID	6GJ2		
Crystal parameters			
Space group	H3		
<i>a, b, c</i> (Å)	126.0, 126.0, 105.9		
<i>α, β,</i> γ (°)	90, 90, 120		
Data collection			
Wavelength (Å)	0.9763		
$\Omega$ Oscillation (°)	0.10		
Total Ω (°)	180		
Exposure (s)	0.040		
Beam size (µm)	50x20		
X-ray flux (ph)	6.12x10 <sup>13</sup>		
Resolution (Å)	48.51-1.68 (1.71-1.68)		
R <sub>merge</sub> (%)	6.4 (118.4)		
$< I/\sigma(I) >$	12.6 (1.3)		
Completeness (%)	99.9 (100)		
Multiplicity	5.1 (5.1)		
CC <sub>1/2</sub>	1.0 (0.5)		
Wilson <i>B</i> factor (Å <sup>2</sup> )	26.2		
Refinement			
Total No. of atoms	4748		
Water molecules	286		
No. of reflections	71408		
R <sub>work</sub> (%)	13.4		
R <sub>free</sub> (%)	17.6		
Anisotropy	0.24		
<b>RMS</b> deviations			
Bonds (Å)	0.011		
Angles (°)	0.838		
Planes (Å)	0.006		
Ramachandran plot			
Favoured (%)	96.20		
Allowed (%)	3.60		
Outliers (%)	0.20		
Mean <i>B</i> factors (Å <sup>2</sup> )	37.0		

The binding pose of  $InsS_6$  above the active site cavity of TaPAPhy\_b2 can be observed in Figure 50, with the positions of phytase motifs PAPhy 1, 4 and 5 highlighted in the surface.



Phytase motifs PAPhy 1, 4 and 5 are highlighted in red in the surface and shown in cartoon representation. The two iron ions are shown as brown spheres. Phosphate and  $InsS_6$  molecules are displayed as sticks and coloured by element, with carbons in  $InsS_6$  coloured in lime green. Sulfate groups are numbered S1-S6. Image created with the UCSF Chimera package (Pettersen *et al.*, 2004).

The iron ions in the active site were modelled with occupancies of 70% (56.88  $Å^2$ B factor) and 71% (20.38  $Å^2$  B factor) in the MI and MII site, respectively, and the coordination geometry of both metals was classified as octahedral by the CheckMyMetal server (Zheng et al., 2014). The position of the phosphate molecule in the active site resembled that of the TaPAPhy\_b2:PO<sub>4</sub> complex structure in the product bound state (section 4.2.1.3.), with no spherical electron density for a bridging solvent molecule observed between the metals. The majority of the residues (96.20%) were found in the most favourable region of the Ramachandran plot, with no outliers present. Gaps in electron density were found at four consecutive residues Glu19, Asp20, Arg21 and Gly22; and Leu509, Lys510 and the 6xHis tag at the C-terminus. The side chains of surface residues Glu1, Arg11, Arg37 and Lys224 were not defined in the electron density and, therefore, not modelled. Seven residues were modelled with alternative conformations: Arg36, Arg85, Gln138, Ser345, Ser367, Met411 and Glu476. Signs of photoreduction were observed in the four disulfide bonds described for TaPAPhy\_b2. N-glycosylation was observed in six of the seven predicted sites, with no electron density for a NAG residue visible in the Asn267 site. A second NAG was modelled in the Asn475

site with an occupancy of 91%. Occupancies lower than 100% were observed for NAGs in Asn211 (90%) and Asn389 (74%). The phosphate molecule bound to the enzyme's active site was the only one modelled in this structure, displaying an occupancy of 100% (49.76 Å<sup>2</sup> *B* factor). The occupancy of the InsS<sub>6</sub> molecule was 95% (119.08 Å<sup>2</sup> *B* factor). The TaPAPhy\_b2structure in complex with phosphate and InsS<sub>6</sub> contained 286 waters, four ethylene glycol molecules (EDO, C<sub>2</sub>H<sub>6</sub>O<sub>2</sub>), five diethylene glycol molecules (PEG, C<sub>4</sub>H<sub>10</sub>O<sub>3</sub>), four triethylene glycol molecules (PGE, C<sub>6</sub>H<sub>14</sub>O<sub>4</sub>), and one tetraethylene glycol molecule (PG4, C<sub>8</sub>H<sub>18</sub>O<sub>5</sub>).

#### 4.2.2.2. Docking of phytate into the active site of TaPAPhy\_b2

Failing to obtain substrate utilisation information from the crystal structure of TaPAPhy\_b2 in complex with the InsS<sub>6</sub> phytate analogue, molecular docking of InsP<sub>6</sub> into the active site of the TaPAPhy\_b2:PO<sub>4</sub> product-bound complex structure was attempted. However, the results obtained both with a fixed protein model and introducing flexibility in the side chains of some active site residues were even less promising, since none of the generated InsP<sub>6</sub> binding modes included any of the phosphate groups coordinating the irons. Instead, most of the binding modes consisted of InsP<sub>6</sub> lying above the active site at distances greater than 8 Å from the iron ions. It was then suspected that the presence of two metal ions in the active site added an extra complexity to the enzyme difficult to model in molecular docking experiments and, therefore, a different approach was sought.

### 4.2.2.3. Molecular dynamics simulations of TaPAPhy\_b2 in complex with phosphate and phytate

Molecular dynamics simulations of TaPAPhy\_b2 at pH 5.5 and 298 K were performed in order to obtain a model of the enzyme-substrate complex. The starting protein model (TaPAPhy\_b2:PO<sub>4</sub> resembling substrate binding, **section 4.2.1.4.**), force field parameters and simulation settings were tested and optimised by running a simulation of the enzyme-phosphate complex prior to introduction of InsP<sub>6</sub>. Once the system was ready, starting poses for the TaPAPhy\_b2: InsP<sub>6</sub> MD runs were prepared by manually docking InsP<sub>6</sub> into the active site pocket, overlapping selected phosphate groups of InsP<sub>6</sub> onto the phosphate molecule bound to the metal ions. Wheat phytases and, in general, plant phytases are commonly classified as D-4/L-6-phytases, with a preference of hydrolysis for the D-4-phosphate in InsP<sub>6</sub> (Lim and Tate, 1973; Nakano *et al.*, 1999, 2000; Brinch-Pedersen, Sørensen and Holm, 2002; Bohn *et al.*, 2007; Rasmussen, Sorensen and Johansen, 2007; Bohn, Meyer and Rasmussen, 2008). A product profile of InsP<sub>6</sub> degradation for the TaPAPhy\_b2 enzyme was obtained in **Chapter 5, section 5.2.2.2.**, confirming TaPAPhy\_b2 can be classified into this category. However, since the technique used in this project to obtain the product profile of phytate hydrolysis cannot resolve the enantiomers D-Ins(1,2,3,5,6)P<sub>5</sub> and D-Ins(1,2,3,4,5)InsP<sub>5</sub>, starting poses for the MD runs were generated with the D-4-phosphate and the D-6-phosphate in the metallic centre.

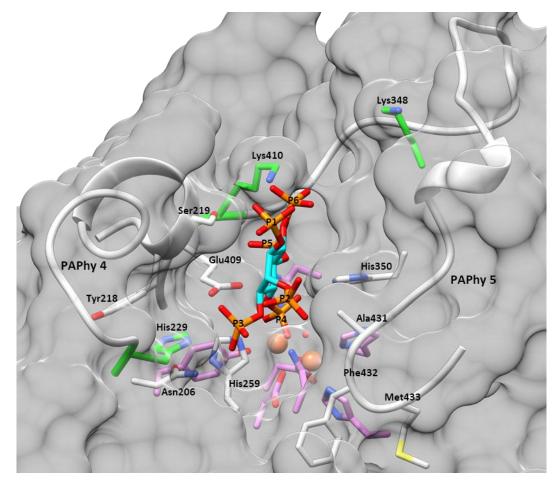


Figure 51. Energy minimised model of the TaPAPhy\_b2:InsP<sub>6</sub> complex bound in 'D-4-phytase' mode

A model for the structure of the complex of TaPAPhy\_b2 with InsP<sub>6</sub> bound so as to present the D-4-phosphate for hydrolytic removal. Motif PAPhy 4 and a fraction of PAPhy 5 are displayed in light grey with cartoon representation. The metal ions and  $\mu$ -(hydr)oxo bridge are shown as spheres and coloured by element. The docked InsP<sub>6</sub> molecule is shown as sticks and coloured by element, with carbons in cyan. Phosphate groups are numbered P1-P6. The side chains of selected amino acid residues are displayed as sticks and coloured by element. Carbons of residues involved in metal coordination are coloured purple. Carbons of basic residues in the TaPAPhy\_b2 active site pocket not conserved in PAPs without phytase activity are coloured green. Carbons of remaining residues are coloured light grey.

The TaPAPhy\_b2 model with the D-4-phosphate of InsP<sub>6</sub> docked in the active site after 10000 steps of energy minimisation is displayed in Figure 51. The active site residues involved in metal coordination, conserved in the PAPs, were highlighted in purple. An active site lined with basic residues to balance the negatively charged phosphates of InsP<sub>6</sub> is a common feature of phytases belonging to the other phosphatase families, as detailed in **Chapter 1, section 1.3.3.** Such a characteristic was not obvious in the TaPAPhy\_b2 enzyme. Although a concentration of basic residues appeared to occur in the active site cavity, the majority of them consisted of the metal (His340, His377 and His379) or the scissile phosphate ligands (His259 and His350) and, therefore, were conserved in the PAPs lacking phytase activity.

However, it was possible to identify three basic residues in the TaPAPhy\_b2 structure located in the vicinity of the docked InsP6 molecule that were conserved in PAPhy and not in the non-phytase PAPs (coloured green in Figure 51). The first of these residues was His229, located at the end of PAPhy 4 motif (an insertion absent in nonphytase PAPs) with distances of approximately 5.1 Å and 7.6 Å to the D-3-phosphate (P3) and the D-2-phosphate (P2) of the InsP<sub>6</sub> molecule, respectively (measured from the centre of the imidazole ring to the phosphorus atoms). A ring stack interaction was also observed between His229 and Tyr218 that may play a role in stabilising the PAPhy 4 motif  $\alpha$ -helix. The second residue was Lys410, located in the closest portion to the active site of the long PAPhy 5 motif (Val367 in the red kidney bean PvPAP1 and Gly366 in the sweet potato IbPAP1 phosphatases) with distances of approximately 4.1 Å and 3.5 Å to the D-5-phosphate (P5) and the D-6-phosphate (P6), respectively (measured between the NZ and the phosphorus atoms). The third and most distant residue was Lys348, located in a small unconserved region not corresponding to any PAPhy motif (Asn294 in the red kidney bean PvPAP1 and Glu293 in the sweet potato IbPAP1 phosphatases) with distances of approximately 10.9 Å and 8.5 Å to the D-1-phosphate (P1) and P6, respectively (measured between the NZ and the phosphorus atoms).

Residues Asn206 (Asp169 in PvPAP1 and Asn168 in IbPAP1 phosphatases) and Ser219 (in PAPhy 4 insertion) were also identified as close neighbours of P3 and P1, respectively, with distances of 3.9 Å (from N $\delta$ 2) and 3.6 Å (from the side chain O). In addition, it was noted that the negative charge resulting from the dipole moment at the end of the  $\alpha$ -helix in the PAPhy 4 motif could also be contributing to the stabilisation of InsP<sub>6</sub> binding in the TaPAPhy\_b2 active site, with approximate distances of 6.6 Å to P1 and 8.3 Å to P6 (measured from the centre of the amino groups of Tyr218, Ser219 and Cys220). A similar phenomenon may be occurring between P2 and residues Ala431, Phe432 and Met433 in the PAPhy 5 motif, arranged in a short  $\alpha$ -helical conformation, with an approximate distance of 7.4 Å (measured from the P2 phosphorus atom to the centre of the amino groups of Ala431, Phe432 and Met433). This last interaction between the P2 phosphate and the PAPhy 5 short  $\alpha$ -helix was not observed in the energy minimised model with P6 rather than P4 docked in the active centre (i.e. to model the enzyme acting as a D-6-phytase). In the TaPAPhy\_b2:InsP<sub>6</sub> model resulting from the docking of P6 as the scissile phosphate, P2 (axial) would be in an equivalent location to P6 in the first pose (i.e. modelling the enzyme acting as a D-4-phytase), while the location of P2 would be taken by P4 (equatorial), increasing the phosphate-helix distance to 9.4 Å. Hence, the interaction between the InsP<sub>6</sub> axial phosphate and the PAPhy 5 short  $\alpha$ -helix in the model of TaPAPhy\_b2 acting as a D-4-phytase could imply a preference of TaPAPhy b2 for the D-4-phosphate over the D-6-phosphate.

Key TaPAPhy\_b2-InsP<sub>6</sub> interactions described in the energy minimised model with P4 as the scissile phosphate were validated with a 1 ns MD run. The dynamic behaviour of the enzyme during the 1 ns simulation was examined by analysing the trajectory for root mean square deviation (RMSD) values of the C $\alpha$  atoms with the starting model as reference (Figure 52A). The structure was equilibrated after approximately 600 ps. Root mean square fluctuations (RMSF) of the C $\alpha$  atoms of each amino acid residue in the TaPAPhy\_b2 structure during the 1 ns MD run were also calculated (Figure 52B). The RMSF of key residues identified in Figure 51 was between 0.33 Å and 1.1 Å.

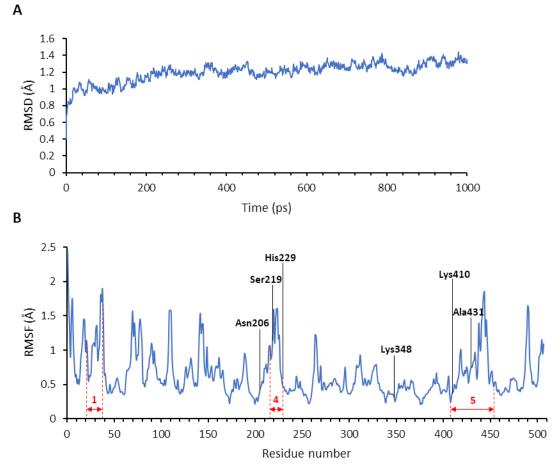
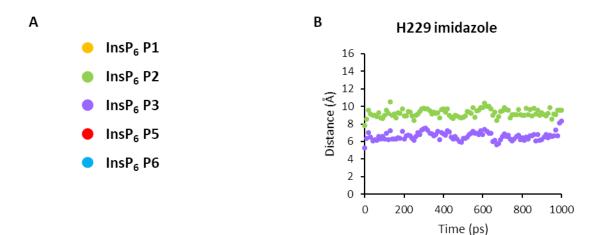
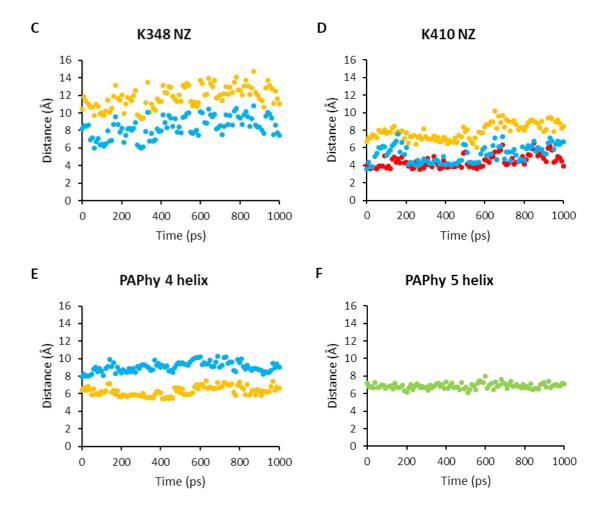


Figure 52. TaPAPhy\_b2 RMSD values and RMSF of amino acid residues for 1 ns MD run

(A) Root mean square deviation (RMSD) values of the C $\alpha$  atoms during 1 ns MD run. (B) Root mean square fluctuations (RMSF) of the C $\alpha$  atoms of each amino acid residue in the TaPAPhy\_b2 structure during 1 ns MD run. Phytase motifs PAPhy 1, 4 and 5 marked with motif number, arrows and dashed lines in red. Selected amino acid residues are labelled.

Average distances and standard deviation from His229 to the P3 and P2 phosphate phosphorus were 6.63 Å ± 0.47 Å and 9.24 Å ± 0.45 Å, respectively (Figure 53B). Distances from Lys348 to P6 and P1 phosphorus were 8.38 Å ± 1.20 Å and 11.83 Å ± 1.20 Å, respectively (Figure 53C). Distances from Lys410 to P5, P6 and P1 phosphorus were 4.43 Å ± 0.70 Å, 5.27 Å ± 0.97 Å and 7.89 Å ± 0.90 Å, respectively (Figure 53D). Distances from the PAPhy 4 helix to P1 and P6 phosphorus were 6.31 Å ± 0.53 Å and 9.06 Å ± 0.56 Å, respectively (Figure 53E). And last, the distance from the PAPhy 5 helix to P2 phosphorus was 6.87 Å ± 0.31 Å (Figure 53F). In general, the monitored interactions identified in the energy minimised TaPAPhy\_b2:InsP<sub>6</sub> model persisted over the course of the 1 ns MD simulation.





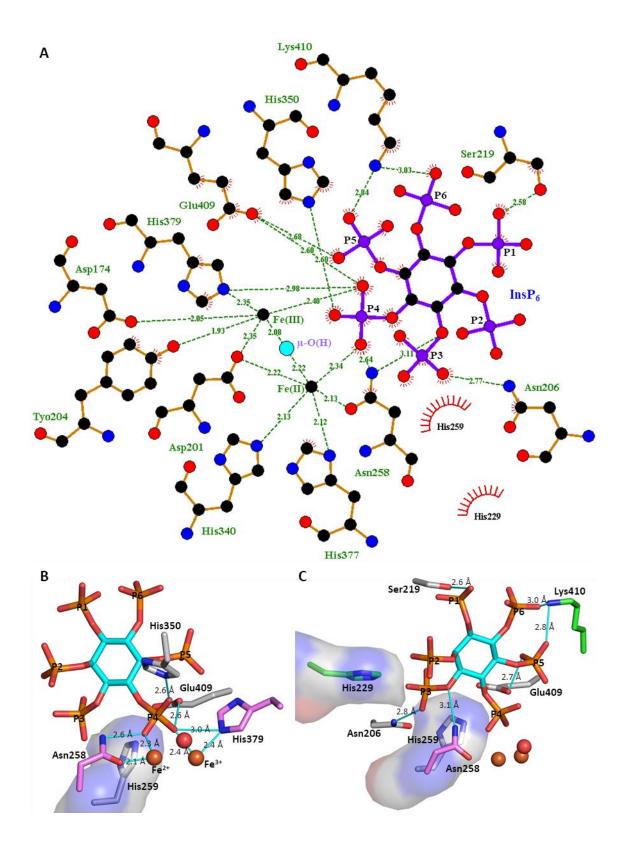


Distances were recorded every 10 ps. (A) Legend, indicating the colour in the graphs of each  $InsP_6$ D-phosphate to which the distances were monitored (to the phosphorus atom of each phosphate). (B) Distances from the centre of mass of the His229 imidazole ring to phosphorus in P2 and P3 of  $InsP_6$ . (C) Distances from the Lys348 NZ nitrogen to phosphorus in P1 and P6 of  $InsP_6$ . (D) Distances from the Lys410 NZ nitrogen to phosphorus in P1, P5 and P6 of  $InsP_6$ . (E) Distances from the centre of mass of the  $\alpha$ -helix N-terminus in PAPhy 4 to phosphorus in P1 and P6 of  $InsP_6$ . (F) Distances from the centre of mass of the Ala431-Phe432 short  $\alpha$ -helical fragment in PAPhy 5 to phosphorus in P2 of  $InsP_6$ .

#### 4.2.2.4. Identification of likely TaPAPhy\_b2 phytate-specificity pockets

Once validated through the 1 ns MD simulation, the TaPAPhy\_b2:InsP<sub>6</sub> model with P4 as the scissile phosphate was analysed in detail for ligand binding (Figure 54). For comparison, a similar analysis was performed on the TaPAPhy\_b2:InsS<sub>6</sub> structure described in **section 4.2.2.1.** (Figure 55). The analysis was carried out with the LigPlot<sup>+</sup> programme (Laskowski and Swindells, 2011), allowing the automatic generation of 2D ligand-protein interaction diagrams (Figure 54A and Figure 55A) and 3D visualisation through PyMOL (Figure 54B,C and Figure 55B) (Schrodinger LLC, 2015).

In the TaPAPhy\_b2:InsP<sub>6</sub> model, six hydrogen bonds (represented as green dashed lines in the 2D diagram and cyan lines in the 3D view) were detected between the P4 scissile phosphate and the protein: two connecting P4 oxygens to each of the iron ions; two more connecting P4 oxygens to the two metal ligands Asn258 and His379; and the last two connecting P4 oxygens to His350 and Glu409. A hydrophobic interaction (represented by red strokes radiating towards the ligand in the 2D diagram and surface representation around the residue involved in the 3D view) between P4 and His259 was also present. The interactions picked up by LigPlot<sup>+</sup> agreed with those described for the TaPAPhy\_b2:PO<sub>4</sub> structures in **section 4.2.1.** (Figure 54A and B). The P3 phosphate displayed hydrogen bonds with Asn206 and the metal ligand Asn258, and hydrophobic interactions with His259 and His229. A hydrogen bond between the P1 phosphate and Ser219 was present, while P6 formed a hydrogen bond with Lys410. The P5 phosphate formed hydrogen bonds with Glu409 and Lys410 (Figure 54A and C). Interactions between the PAPhy 4  $\alpha$ -helix and InsP<sub>6</sub> phosphates were not picked up by LigPlot<sup>+</sup>, and neither did the PAPhy 5 short  $\alpha$ -helix interaction with P2.

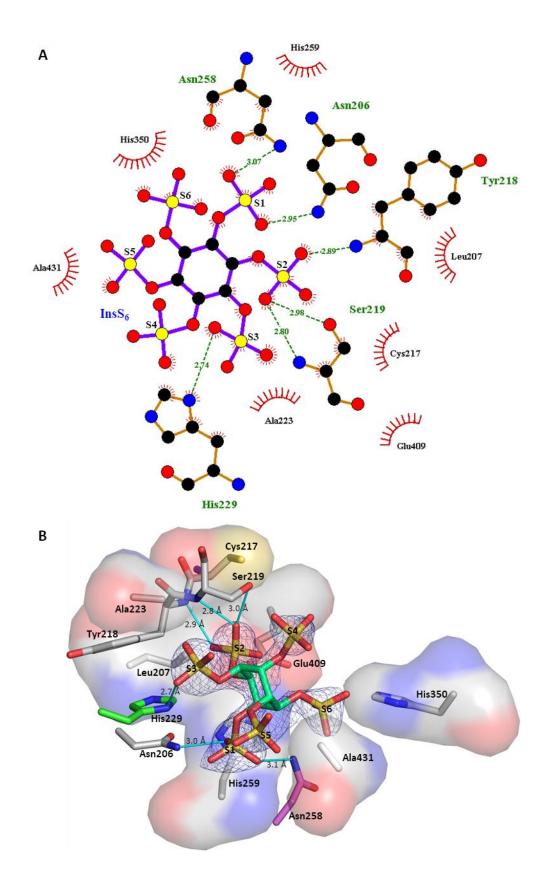


### **Figure 54. Interactions in the energy minimised model of the TaPAPhy\_b2:InsP<sub>6</sub> complex bound in 'D-4-phytase' mode** (on previous page)

Phosphate groups in InsP<sub>6</sub> are numbered P1-P6. (**A**) 2D representation generated with LigPlot<sup>+</sup> version 1.4 (Laskowski and Swindells, 2011). C, N, O and P atoms are displayed as black, blue, red and purple balls, respectively. Protein and ligand bonds are represented in brown and purple, respectively. Hydrogen bonds are represented by green dashed lines, with their lengths labelled in Å. Hydrophobic interactions are represented by red strokes radiating towards the ligand. (**B**) 3D representation of interactions involving the 4-phopshate and (**C**) the remaining phosphate groups. The metal ions and  $\mu$ -(hydr)oxo bridge are shown as spheres and coloured by element. InsP<sub>6</sub> is shown as sticks and coloured by element, with carbons in cyan. The side chains of residues involved in interactions with InsP<sub>6</sub> are displayed as sticks and coloured by element. Carbons of residues involved in metal coordination are coloured purple. Carbons of basic residues in the TaPAPhy\_b2 active site pocket not conserved in PAPs without phytase activity are coloured green. Carbons of remaining residues are coloured light grey. Hydrogen bonds are depicted as cyan lines. Hydrophobic interactions are depicted with the surface of the residue involved. Images created with PyMOL version 1.3 (Schrodinger LLC, 2015).

In the TaPAPhy\_b2:InsS<sub>6</sub> structure, hydrogen bonds were observed between oxygens in the S1 sulfate group and residues Asn206 and Asn258, together with a hydrophobic interaction with His259. S2 oxygens formed hydrogen bonds with the amino groups of Tyr218 and Ser219, the side chain oxygen of Ser219, and a hydrophobic interaction with Cys217, all residues belonging to the  $\alpha$ -helix in PAPhy 4 motif. Leu207 and Glu409 also showed hydrophobic interactions with S2. The sulfate group S3 formed a hydrogen bond with the N $\delta$ 1 nitrogen of His229 and a hydrophobic interaction with Ala223. S5 and S6 displayed hydrophobic interactions with Ala431 (forming part of the PAPhy 5 short  $\alpha$ -helix) and His350, respectively, and no interactions were picked up by Ligplot<sup>+</sup> for the S4 sulfate (Figure 55).

When the TaPAPhy\_b2:InsP<sub>6</sub> model and the TaPAPhy\_b2:InsS<sub>6</sub> structure were superimposed, none of the InsS<sub>6</sub> sulfate groups overlapped with any of the InsP<sub>6</sub> phosphates. Groups P1 and S4 were the closest, 1.62 Å apart measured between the phosphorus and sulfur atoms, located near Ser219. S1 and P3 were 2.14 Å apart, both located near Asn206. Lastly, S5 and P2 were 3.49 Å apart but in a similar orientation with respect to the PAPhy 5 short  $\alpha$ -helix formed by Ala431, Phe432 and Met433.



#### Figure 55. Interactions in the TaPAPhy\_b2:InsS<sub>6</sub> complex structure (on previous page)

Sulfate groups in  $InsS_6$  are numbered S1-S6. (A) 2D representation generated with LigPlot<sup>+</sup> version 1.4 (Laskowski and Swindells, 2011). C, N, O and S atoms are displayed as black, blue, red and yellow balls, respectively. Protein and ligand bonds are represented in brown and purple, respectively. Hydrogen bonds are represented by green dashed lines, with their lengths labelled in Å. Hydrophobic interactions are represented by red strokes radiating towards the ligand. (B) 3D representation created with PyMOL version 1.3 (Schrodinger LLC, 2015). InsS<sub>6</sub> is shown as sticks and coloured by element, with carbons in lime green. Double difference electron density around the InsS<sub>6</sub> is displayed as a blue mesh contoured to 1 r.m.s.d. Residues involved in interactions with InsS<sub>6</sub> are displayed as sticks and coloured by element. Carbons of residues involved in metal coordination are coloured purple. Carbons of basic residues in the TaPAPhy\_b2 active site pocket not conserved in PAPs without phytase activity are coloured green. Carbons of remaining residues are coloured light grey. Hydrogen bonds are depicted as cyan lines. Hydrophobic interactions are depicted with the surface of the residue involved.

Based on the analysis of the TaPAPhy\_b2:InsP<sub>6</sub> model with P4 as the scissile phosphate, the InsP<sub>6</sub> specificity pockets defined in Figure 56 are proposed for phytase enzymes belonging to the purple acid phosphatase class (with residue numbers according to the TaPAPhy\_b2 structures). The specificity pocket for the P4 scissile phosphate was named S<sub>A</sub> and consisted of the two metal ions, the  $\mu$ -(hydr)oxo bridge and residues Asn258, His259, His350, His379 and Glu409. Placing the axial phosphate group P2 towards the viewer, the remaining specificity pockets were named S<sub>B</sub>-S<sub>F</sub> anticlockwise from the scissile phosphate P4. With this nomenclature, the P3 specificity pocket S<sub>c</sub> contained the short  $\alpha$ -helical conformation formed by residues Ala431, Phe432 and Met433 in PAPhy 5 motif; the P1 specificity pocket S<sub>D</sub> was formed by Ser219 and possibly the PAPhy 4  $\alpha$ -helix comprising residues Tyr218, Ser219 and Cys220; the P6 specificity pocket S<sub>E</sub> contained the residue Lys410; and the P5 specificity pocket S<sub>F</sub> was formed by residues Glu409 and Lys410.

Rotation of the InsP<sub>6</sub> molecule in Figure 56 to place the P6 phosphate in the position of P4, i.e. in specificity pocket  $S_A$ , retains contacts of individual phosphates with all specificity pockets except  $S_C$ . In the TaPAPhy\_b2:InsP<sub>6</sub> model with P4 as the scissile phosphate, the distance  $S_C$  specificity pocket-phosphate increases by approximately 2 Å, causing a loss of the interaction between the PAPhy 5 short  $\alpha$ -helix of TaPAPhy\_b2 and the substrate due to the change in position of the axial phosphate group. The absence of this interaction may indicate that D-6-phytase activity is disfavoured over D-4-phytase activity in this enzyme.

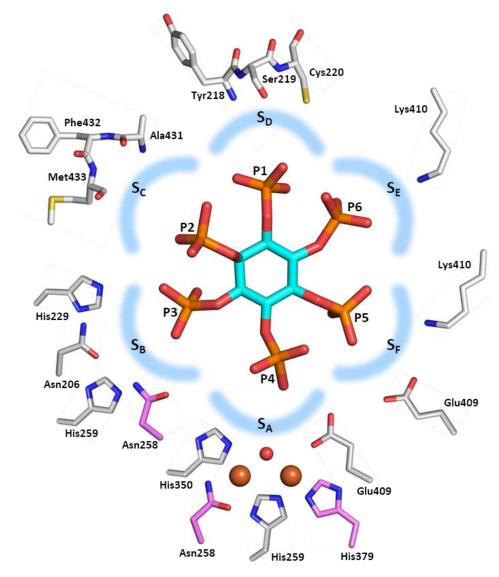


Figure 56. Schematic representation of the InsP<sub>6</sub> specificity pockets in TaPAPhy\_b2

Phosphate groups in the InsP<sub>6</sub> molecule are numbered P1-P6. Specificity pockets encompassing the amino acid residues involved in interactions with each of the phosphate groups are named  $S_A$ - $S_F$ . Iron ions are shown as brown spheres. The  $\mu$ -(hydr)oxo bridge is displayed as a red sphere. InsP<sub>6</sub> is displayed in stick representation, coloured by element and with carbons in cyan. Amino acid residues are shown in stick representation, coloured by element and with carbons in light grey. Carbons of residues involved in metal coordination are coloured purple.

#### 4.3. Conclusions

Successful determination of the high-resolution crystal structure of the wheat phytase TaPAPhy\_b2 is reported in this chapter, being the first time the structure of a purple acid phytase has been solved. The crystallographic data collected also confirms that TaPAPhy\_b2 has a diiron metal centre. Moreover, the crystal structures determined in this project of TaPAPhy\_b2 in complex with phosphate in different binding poses support the catalytic mechanism currently accepted for PAP enzymes and could provide insights into the less known enzyme regeneration steps.

Structural information in combination with computer simulations of the enzymesubstrate complex have also allowed to outline for the first time the potential specificity pockets in the active site cavity responsible for the ability of certain PAP enzymes to hydrolase phytate. In addition, the proposed active site residue interactions with InsP<sub>6</sub> provide a plausible explanation as to why TaPAPhy\_b2 may favour hydrolysis for the D-4-phosphate group over the D-6-phosphate group of the substrate. While an interaction with residues in the PAPhy 5 motif, forming the S<sub>C</sub> pocket, is present when InsP<sub>6</sub> is bound in the TaPAPhy\_b2 active centre with the D-4-phosphate presented for hydrolysis (in the S<sub>A</sub> pocket), this interaction was absent when D-6 was the scissile phosphate.

The power of 3D modelling when structures of homologues of the target protein are available is also corroborated in this chapter. Upon studying the 3D homology model created for the TaPAPhy\_b2 enzyme in Chapter 2, it was predicted that phytase motifs PAPhy 1, PAPhy 4 and PAPhy 5 were likely to form part of the active centre of the enzyme. With the addition of crystal structure information, amino acid residues belonging to PAPhy 4 and PAPhy 5 motifs have been identified to form part of phytate specificity pockets and, therefore, confirming their importance in the enzyme activity. Although no interactions between PAPhy 1 residues and the substrate were identified, the TaPAPhy\_b2 crystal structures also confirmed the position of this motif in the vicinity of the active site predicted by the model.

# Chapter 5. Site-directed mutagenesis and enzymatic characterisation of wheat PAPhy isoform b2

Based on the initiation site of phytate hydrolysis, most phytase enzymes found in grains and seeds of higher plants belong to the category of L-6-(D-4)-phytases (Chapter 1, section 1.3.2.), with a preference for the phosphate group on the carbon next to C5 of the inositol ring (Brinch-Pedersen, Sørensen and Holm, 2002; Bohn, Meyer and Rasmussen, 2008; Yao et al., 2012). Traditionally called 6-phytases (EC 3.1.3.26), with the 1L-(L) descriptor commonly omitted, the current convention names these enzymes as 4-phytases with the 1D-(D) descriptor omitted. This change in nomenclature reflects the relaxation by the IUPAC-IUBMB of previous rules for naming of *myo*-inositol phosphates (Bohn, Meyer and Rasmussen, 2008). Phytases purified from wheat bran have been classified as D-4-phytases (Tomlinson and Ballou, 1962; Lim and Tate, 1971, 1973, Nakano et al., 1999, 2000, Brinch-Pedersen et al., 2003, 2006) and are active at acidic to neutral pH. In addition, attack on the D/L-3-phosphate (Brinch-Pedersen et al., 2003, 2006; Bohn et al., 2007), 5-phosphate (Lim and Tate, 1973; Brinch-Pedersen et al., 2003, 2006) and 2-phosphate (Lim and Tate, 1973) has also been reported for wheat bran phytases. At the time of these studies, the identity of the genes encoding the characterized activities was unknown. However, since then proteins of the PAP and the MINPP class have been identified in wheat (Rasmussen, Sorensen and Johansen, 2007; Bohn, Meyer and Rasmussen, 2008; Brinch-Pedersen et al., 2014).

In this chapter, a series of biochemical and biophysical assays were employed to determine the enzymatic properties of the wild type TaPAPhy\_b2 enzyme. Using the crystal structure and substrate binding information obtained in the previous chapter, rational mutagenesis of TaPAPhy\_b2 was implemented by targeting amino acids with suggested implications in phytate utilisation. The single-site mutant proteins generated were subsequently utilised to study the structure-function relationships of TaPAPhy\_b2.

#### 5.1. Materials and methods

#### 5.1.1. Design and preparation of TaPAPhy\_b2 single-site mutants

Individual residues of TaPAPhy\_b2 chosen as targets for mutagenesis were selected through analysis of the newly solved TaPAPhy\_b2 crystal structures and computer simulation models, combined with comparison with the published structures for PAPs lacking phytase activity. The multiple sequence alignment of TaPAPhy\_b2, the red kidney bean PvPAP1 and the sweet potato IbPAP1, used to construct the TaPAPhy\_b2 homology model, was inspected in conjunction with the structures (**Chapter 2, section 2.1.3.** for method, **section 2.2.2.** for result). PyMOL (Schrodinger LLC, 2015) and UCSF Chimera (Pettersen *et al.*, 2004) molecular graphics systems were used to display and compare the structures.

#### 5.1.1.1. Generation of TaPAPhy\_b2 mutants by QuickChange<sup>™</sup> mutagenesis

Single-site mutagenesis of TaPAPhy\_b2 was performed with a modified version of the QuickChange<sup>™</sup> method, consisting on the one-step amplification of whole plasmid DNA with mutagenic primers followed by the elimination of template DNA by digestion with DpnI. The modification uses primers containing non-overlapping sequences at the 3' end and overlapping sequences at the 5' end rather than primers that overlap completely. This modification results in reduction of primer dimerization and allows newly synthesised DNA to be used as template for subsequent PCR amplification cycles (Liu and Naismith, 2008).

#### Table 14. List of TaPAPhy\_b2 single-site mutants

Mutant constructs generated from TaPAPhy_b2-pGAPZαA with the QuickChange™ modified method. The
original codons were substituted by GCT, the Pichia pastoris preferred codon for alanine.

Construct	Original residue	Original codon	Mutated codon	Mutated residue
TaPAPhy_b2_H229A-pGAPZαA	His229	1432 CAC 1435	1432 GCT 1435	Ala229
TaPAPhy_b2_K348A-pGAPZαA	Lys348	1789 AAG 1791	1789 GCT 1791	Ala348
TaPAPhy_b2_K410A-pGAPZαA	Lys410	1975 AAG 1977	1975 GCT 1977	Ala410

Three single-site mutagenesis reactions were performed to substitute residues His229, Lys348 and Lys410 with alanine residues in the TaPAPhy\_b2-pGAPZ $\alpha$ A construct (Table 14). Primers were designed by selecting an overlapping region (12-15 bp long)

centred around the single mutation with T<sub>m</sub> between 40-48°C, then extending towards the 3' end to obtain a non-overlapping region with T<sub>m</sub> 5-10°C higher than the overlapping region, when possible, and ended with C or G to promote specific binding. Primer properties were assessed using the Eurofins Genomics Oligo Analysis Tool (https://www.eurofinsgenomics.eu/en/ecom/tools/oligo-analysis.aspx). The primer sequences designed for TaPAPhy\_b2 mutagenesis are included in **Appendix 2**, Table A14.

Table 15. Reaction components for QuickChange<sup>™</sup> mutagenesis PCR with Phusion polymerase

Plasmid template was diluted to a working concentration of 10 ng  $\mu L^{\text{-}1}$ . Primer mixes were prepared in water from 100  $\mu M$  stocks.

Reagent	[Stock]	[rxn]	V for 1x 25 μL rxn (μL)
Water	n/a	n/a	15.8
Phusion HF buffer	5x	1x	5.0
DMSO	100%	4%	1.0
dNTP mix	10 mM each	0.4 mM each	1.0
Primer mix	10 µM each	$0.4\mu M$ each	1.0
Plasmid	10 ng µL <sup>-1</sup>	0.4 ng μL <sup>-1</sup>	1.0
Phusion polymerase	2 U μL <sup>-1</sup>	0.016 U μL <sup>-1</sup>	0.2
TOTAL			25.0

The construct TaPAPhy\_b2-pGAPZ $\alpha$ A purified from an *E. coli Dam*<sup>+</sup> (encoding Dam DNA methylase) strain was used as plasmid template for the mutagenesis reactions. The reactions were set up on ice as detailed in Table 15, with 25 µL final volume. The PCR protocol on Table 16 was used for the amplification with Phusion High-Fidelity DNA Polymerase (Thermo Scientific). Dimethyl sulfoxide (DMSO) was included in the PCR mix and a standard annealing temperature of 50°C was used for the three reactions. Negative control reactions were set up for each pair of primers, using water instead of plasmid DNA. An extra negative control reaction for DpnI digestion was also set up with template DNA but water instead of primers. Results of the PCR reactions were assessed on 1% (w/v) agarose gels by running 5 µL of each PCR product. The remaining volumes of the positive reactions and the DpnI control were incubated with 0.5 U µL<sup>-1</sup> of DpnI for 2 h at 37°C to eliminate template DNA before transformation into *E. coli*. A volume of 2 µL per digestion product was transformed into 20 µL of XL10-Gold ultracompetent cells (Agilent Technologies). The DNA was added to the competent cells and left to mix by diffusion for 30 min on ice, before a heat-shock at 42°C for 35 s.

Subsequently, the transformations were returned to ice for 1-2 min before adding 180  $\mu$ L of SOC medium. The transformations were then incubated at 37°C for 1 h with agitation before plating the whole volume on low salt LB agar plates with Zeocin<sup>TM</sup> (25  $\mu$ g mL<sup>-1</sup>), incubated at 37°C overnight.

#### Table 16. PCR protocol for QuickChange<sup>™</sup> mutagenesis

The plasmid template TaPAPhy\_b2-pGAPZ $\alpha$ A used was 4623 bp long. The extension time was calculated according to formula, time = (template length in kb x 1 min) + 1min.

Step	Cycles	Time	T (°C)
Initial denaturation	1	3 min	98
Denaturation		30 s	98
Annealing	25	1 min	50
Extension		6 min	68
Final Extension	1	10 min	68
Hold	1	~	4

Analysis of transformants was first carried out by colony PCR with primers designed to amplify the TaPAPhy b2 gene (TaPAPhyB-F1 and TaPAPhyB-R1, Table A14 in Appendix 2). Two single colonies of each mutant were resuspended in 25 µL of water, storing 10 µL at 4°C and denaturing the remaining 15 µL at 98°C for 10 min. Cell debris was separated by centrifugation and 1 µL of supernatant from each denatured colony was used as template in 20 µL colony PCR reactions, set up on ice as detailed in Table 17. A positive control reaction with TaPAPhy b2-pGAPZαA construct as template and a negative control reaction with water instead of plasmid DNA were also set up. The protocol of Table 18 was used for the colony PCR amplification with GoTag<sup>®</sup> G2 Flexi DNA Polymerase (Promega) and results were assessed on 1% (w/v) agarose gels by running 5 μL of each PCR product. Positive colonies for TaPAPhy b2-pGAPZαA transformation were grown in 10 mL of low salt LB liquid culture with Zeocin™ (25 µg mL<sup>-1</sup>) at 37°C and 180 rpm overnight, by inoculating the stored 10 µL of resuspended colonies. The overnight cultures were used to purify the plasmids using the QIAprep<sup>®</sup> Spin Miniprep Kit (Qiagen). The concentration of the plasmids after their isolation was calculated by absorbance measurement at  $\lambda = 260$  nm with a NanoDrop<sup>M</sup> Spectrophotometer (Thermo Scientific). The plasmid isolated from one positive colony per mutant was further analysed by sequencing with the TaPAPhy b2 gene specific primers used for the colony PCR, to confirm the presence of the desired mutations.

Stocks of the TaPAPhy\_b2 mutants in *E. coli* XL10-Gold ultracompetent cells in 30% (v/v) glycerol were prepared, snap-frozen in liquid nitrogen, and stored at -80°C. The resulting construct sequences and properties are shown in **Appendix 2**, Table A16.

#### Table 17. Reaction set up for colony PCR with GoTaq G2 Flexi polymerase

Plasmid template diluted to a working concentration of 2 ng  $\mu L^{\text{-}1}$  was used for the positive control reaction.

Reagent	[Stock]	[rxn]	V for 1x 20 μL rxn (μL)
Water	n/a	n/a	10.7
Green GoTaq Flexi Buffer	5x	1x	4.0
DMSO	100%	3%	0.6
dNTP mix	10 mM each	0.25 mM each	0.5
MgCl <sub>2</sub>	25 mM	2.5 mM	2.0
Primer mix	$10\mu\text{M}$ each	0.5 μM each	1.0
Template DNA	n/a	n/a	1.0
GoTaq G2 Flexi polymerase	5 U μL-1	0.05 U μL <sup>-1</sup>	0.2
TOTAL			20.0

#### Table 18. PCR protocol for amplification with GoTaq G2 Flexi polymerase

DMSO was included in the PCR mix and a standard annealing temperature of 55°C was used for colony PCR.

Step	Cycles	Time	т (°С)
Initial denaturation	1	3 min	95
Denaturation		30 s	95
Annealing	30	30 s	55
Extension		2 min	72
Final Extension	1	10 min	72
Hold	1	8	4

### 5.1.1.2. Transformation, expression and purification of TaPAPhy\_b2 mutants in *Pichia pastoris*

The transformation, expression and purification of the TaPAPhy\_b2 mutants was performed as for the wild type (WT) enzyme. The three TaPAPhy\_b2-pGAPZαA mutant constructs were transformed into the KM71H (*OCH1::G418R*) *Pichia pastoris* glycoengineered strain through electroporation following the protocol described for the WT construct in **Chapter 3, section 3.1.2.2.** Sufficient plasmid DNA of each mutant for *P. pastoris* transformation was purified from 100 mL overnight cultures using the Plasmid Midi Kit (Qiagen).

Six *P. pastoris* transformed colonies per mutant were subjected to a small volume expression trial in a 24-well plate. The selected colonies were monitored by pNPP assay for the production of secreted recombinant protein in 2 mL cultures for four days, following the protocol described for the WT enzyme in **Chapter 3, section 3.1.2.3.** A WT culture and an untransformed KM71H (*OCH1::G418R*) strain culture were set up alongside the mutants as expression controls. The highest expressing transformants for each TaPAPhy\_b2 mutant were selected for further protein expression, storing them at 4°C and -20°C in 1 M sorbitol and 10% (v/v) glycerol, respectively.

Expression was carried out in 100 mL of buffered minimal glucose medium, distributed in 250 mL conical flasks with 50 mL per flask, for four days under continuous shaking (200 rpm) at 26°C, adding 100  $\mu$ M iron(II) sulfate and 100  $\mu$ M iron(III) citrate daily. The enzymes were harvested, purified by nickel-affinity chromatography and concentrated in the same way as the WT medium scale expression experiment described in **Chapter 3, sections 3.1.2.4.** and **3.1.2.5.** Individual new 1 mL HisTrap HP columns (GE Healthcare) were used for the purification of each TaPAPhy\_b2 mutant, at a flow rate of 1 mL min<sup>-1</sup>, while the column from the generation of samples for X-ray crystallography was reused for the WT. All the columns were regenerated by stripping and recharging of metal ion according to the manufacturer's instructions before storage in 20% (v/v) ethanol at 4°C.

The nickel-affinity purified TaPAPhy\_b2 WT enzyme and its three mutants were normalised to a working concentration of 150  $\mu$ M and stored in 20 mM Tris/HCl pH 8.0 at 4°C for their subsequent enzymatic characterisation.

## 5.1.2. Enzymatic characterisation of wild type TaPAPhy\_b2 and three single-site mutants

The enzymatic characterisation of recombinant TaPAPhy\_b2 WT, H229A, K348A and K410A mutants was performed with fully glycosylated proteins after the nickel-affinity chromatography purification step.

#### 5.1.2.1. The phosphate release assay

The enzymatic activity of WT TaPAPhy\_b2 was characterised alongside the three single-site mutants mainly by means of standard phosphate release assays (**Chapter 3** section 3.1.1.5) in 0.2 M acetate pH 5.5 buffer with 5 mM potassium phytate ( $\geq$ 95% purity, Sigma). Reactions (50 µL) were performed in 96-well plates for 15 min at room temperature with two to four replicates per condition, depending on the experiment layout.

Standard curves for each assay were prepared with monopotassium phosphate, carrying out serial dilutions in duplicate ranging from 1 mM down to 7.8  $\mu$ M. Buffer with InsP<sub>6</sub> and buffer only reactions were also set up, in order to determine background absorbance of small levels of contaminant inorganic phosphate present in the InsP<sub>6</sub> substrate. The reactions were stopped with 50  $\mu$ L of a colour reagent, containing four volumes of 1.5% (w/v) ammonium molybdate in a 5.5% (v/v) sulfuric acid solution and one volume of a 10.8% (w/v) iron(II) sulfate solution, that reacts with the free phosphate. Absorbance at  $\lambda$  = 700 nm was measured in a microplate reader (Hidex Sense) after colour development for 30 min.

Phosphate release was quantified by interpolation from linear least-squares regressions of plots of absorbance vs monopotassium phosphate. Raw absorbance data were processed in Microsoft Excel (2016), after subtraction of absorbances arising from InsP<sub>6</sub> and free phosphate in the InsP<sub>6</sub> substrate.

#### 5.1.2.2. Relative activity, pH and temperature profiles

Scouting assays with enzyme concentrations ranging in decades of concentration from 10  $\mu$ M to 10 nM were undertaken to evaluate differences in phytase activity of the TaPAPhy\_b2 mutants with respect to the WT enzyme. Four replicates per enzyme concentration and TaPAPhy\_b2 variant were set up. The same assay was repeated after storage of the recombinant proteins at -80°C in the presence of 30% (v/v) glycerol to evaluate their stability in those conditions.

The assay was also performed to compare phytase and phosphatase activity of the TaPAPhy\_b2 mutants, adapting the standard phosphate release assay to the

substrate pNPP. Instead of the colour reagent, 50  $\mu$ L of 1 M NaOH were used to stop the reactions, and the absorbance of the released product pNP (as phenolate) at  $\lambda$  = 405 nm was measured immediately. The standard curve was prepared with pNP in this case, although results were expressed in phosphate concentration released as for the rest of the assays.

Temperature and pH profiles for phytase activity of the recombinant proteins were obtained with 100 nM enzyme and with InsP<sub>6</sub> as substrate. For the pH profile, the following buffers were used: pH 2.0 to 3.5, 0.2 M glycine/HCl; pH 4.0 to 5.5, 0.2 M sodium acetate; pH 6.0 to 7.0, 0.2 M bis-tris or MES; and pH 7.5 to 8.5, 0.2 M Tris/HCl. Reactions were carried out in duplicate. For the temperature profile, reactions were carried out in triplicate and incubated at 16, 25, 37 and 50°C in a thermal cycler (BIO-RAD).

#### 5.1.2.3. HPLC product profiles of phytate hydrolysis

The product profiles of reaction of WT TaPAPhy\_b2 and its three single-site mutants with InsP<sub>6</sub> were obtained by separating the inositol phosphate products on high performance liquid chromatography (HPLC) after Blaabjerg *et al*. (2010). Reactions were performed at room temperature in 0.2 M acetate pH 5.5 buffer with 1  $\mu$ M enzyme and 1 mM sodium phytate (≥98% purity, Merck) as substrate. Reactions were stopped after 15, 30, 60 or 120 min by boiling at 100°C for 5 min. Reaction products were resolved by anion-exchange HPLC on a 250 x 3 mm CarboPac PA200 column (Dionex UK, Ltd) and a 50 x 3 mm guard column of the same material, injecting 20 µL of reaction per run. The elution was performed at a flow rate of 0.4 mL min<sup>-1</sup> with a gradient of methanesulfonic acid delivered from solvent reservoirs containing (A) water and (B) 600 mM methane sulfonic acid according to the following programme: time (min), % B; 0, 0; 25, 100; 38, 100. The separated inositol phosphates were mixed post-column with a solution consisting of 0.1% (w/v) ferric nitrate in 2% (w/v) perchloric acid at a flow rate of 0.2 mL min<sup>-1</sup> for their detection by UV absorbance at  $\lambda$  = 290 nm (Phillippy and Bland, 1988). Inositol phosphate standards were prepared by reflux in 1 M HCl for 24 h with subsequent rotary evaporation at 35°C to remove the HCl.

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#### 5.1.2.4. Enzyme kinetics

Kinetic parameters for the WT TaPAPhy\_b2 enzyme and its mutants were obtained performing the standard phosphate release assay at pH 5.5 and 37°C, with sodium phytate ( $\geq$ 98% purity, Merck) as substrate and reactions in triplicate. A single timepoint (10 or 90 min) and enzyme concentration (60 nM) were chosen on the basis that, when less than 10-15% of the total substrate for each substrate concentration has been consumed during the reaction, the rate obtained can be assumed to be the initial rate. The substrate concentrations used to calculate the kinetic parameters for phytate were 0, 5, 10, 25, 50, 100, 200 and 400  $\mu$ M.

Raw absorbance data was processed by linear regression in Microsoft Excel (2016). In order to avoid negative values at low substrate concentrations, the data was transformed to increments of phosphate concentration released with respect to the points with 0  $\mu$ M substrate. The results for each reaction were expressed as the rate of phosphate concentration released ( $\mu$ M) per time of the reaction (min) and amount of enzyme (0.173  $\mu$ g). To estimate enzyme kinetic parameters, the data was fitted to the Michaelis-Menten equation (substrate *vs.* velocity) by performing nonlinear regression with the least squares (ordinary) fit method using GraphPad Prism version 7.03 (GraphPad Software, La Jolla California USA).

#### 5.1.2.5. Inhibition of wild type TaPAPhy\_b2 phytase activity

The effect of the non-hydrolysable  $InsP_6$  analogue *myo*-inositol hexakissulfate (InsS<sub>6</sub>, potassium salt; Alfa Chemistry) on the phytase activity of WT TaPAPhy\_b2 was tested through a phosphate release assay. The assay was performed with 5 mM InsP<sub>6</sub> substrate and 1  $\mu$ M enzyme in the standard conditions described in **section 5.1.2.1.**, setting up reactions in triplicate in the presence of increasing concentrations of InsS<sub>6</sub>, ranging from 0 to 1 mM. Equivalent reactions in the presence of sodium molybdate, a potent inhibitor of acid phosphatases, were set up alongside for comparison.

The assay was repeated in the presence of increasing concentrations of the nonhydrolyzable pNPP analogue *para*-nitrophenyl sulfate (pNPS, Sigma), ranging from 0 to 5 mM.

#### 5.1.2.6. Thermal stability of wild type TaPAPhy\_b2

Thermostability is one of the principal characteristics desired of commercial phytases. In addition to the temperature profile described in **section 5.1.2.2.**, the thermostability of WT TaPAPhy\_b2 was tested by measuring its activity at fixed temperature after treatment at high temperature, and by determining its melting temperature. The thermal stability of TaPAPhy\_b2 was tested with partially deglycosylated samples from batch 07 used for X-ray crystallography (**Chapter 3, section 3.2.2.3.4.**).

#### 5.1.2.6.1. Recovery after heating at 80°C

The effect on phytase activity of incubation of WT TaPAPhy\_b2 at 80°C for 10 min was assessed by setting up a standard phosphate release assay alongside untreated enzyme as control. The assay was performed after cooling down the treated enzyme to 4°C before setting up four replicate reactions using 1  $\mu$ M enzyme and 5 mM InsP<sub>6</sub> as substrate in 0.2 M acetate buffer pH 5.5 for 15 min at 37°C. Results were analysed using Microsoft Excel (2016) as described in **section 5.1.2.1**.

#### 5.1.2.6.2. Differential scanning calorimetry

Differential scanning calorimetry (DSC) is a technique that can be used to determine the thermal stability of biomolecules in their native form, by measuring the heat (enthalpy) change associated with their denaturation. In the case of proteins, it is performed in a micro-differential scanning calorimeter (micro-DSC) consisting of a sample cell (with protein) and a reference cell (with its buffer) which temperature is simultaneously increased over time. The differences in composition between the sample and the reference translate into different amounts of energy needed to raise the temperature of the cells. This energy difference is measured as heat capacity by the DSC and can be correlated to properties of the sample such as the melting temperature (T<sub>m</sub>). The molar heat capacity (Cp) is the amount of heat needed to increase the temperature of one mol of a substance by one degree. The T<sub>m</sub> of a protein is the temperature at which the folded and unfolded states of the protein are in equilibrium (Gill, Moghadam and Ranjbar, 2010; Durowoju *et al.*, 2017).

The T<sub>m</sub> of WT TaPAPhy\_b2 at 1.5 mg mL<sup>-1</sup> (26.09  $\mu$ M) in 20 mM Tris/HCl pH 8.0 buffer was calculated by carrying out temperature scans from 10 to 110°C at a scan rate of 200°C h<sup>-1</sup> in a MicroCal VP-Capillary-DSC (Malvern Instruments Ltd.). Up to 20 buffer-buffer (B-B) runs with 20 mM Tris/HCl pH 8.0 in both cells were carried out overnight in order to warm up the instrument prior to the buffer-protein (B-P) runs. Three replicate B-P runs were carried out by loading fresh enzyme into the instrument sample cell in each run, followed by a rerun of the last sample in order to determine the ability of TaPAPhy\_b2 to refold after thermal denaturation. Automatic analysis of the data was performed with Origin (OriginLab Corporation).

#### 5.1.3. Crystal structure of the TaPAPhy\_b2 H229A mutant

Preparation of partially deglycosylated TaPAPhy\_b2-H229A mutant for crystallography was performed as described for the WT enzyme. Expression, purification and crystal growth was carried out alongside WT TaPAPhy\_b2d batch 07 (**Chapter 3**, **section 3.1.2.5**. and **section 3.2.2.3.4**.; **Chapter 4**, **section 4.1.1**.), using recombinant GST-Endo F1 treatment for enzymatic deglycosylation. Single crystals in the *H*3 space group were harvested following protocol in **Chapter 4**, **section 4.1.2**., using cryoprotectants containing 0.2 M sodium thiocyanate, 20% (w/v) PEG 3350, 25% (v/v) PEG 400 and either 1 mM InsP<sub>6</sub> or 1 mM InsS<sub>6</sub>, adjusting the pH to 5.5 with acetate buffer. X-ray data was collected at Diamond Light Source (DLS; Didcot, UK) on beamline I03 at a wavelength of 0.9763 Å (12.6994 keV). Data processing and structure refinement was performed as described in **Chapter 4**, **section 4.1.4**. for the WT enzyme.

#### 5.2. Results and discussion

#### 5.2.1. Design and preparation of TaPAPhy\_b2 single-site mutants

The amino acid sequence, crystal structures of TaPAPhy\_b2:PO<sub>4</sub> complexes and the TaPAPhy\_b2:InsP<sub>6</sub> model generated by MD simulations were studied and compared with the red kidney bean PvPAP1 and the sweet potato IbPAP1 phosphatases to identify candidate amino acid residues for mutagenesis. As confirmed in the previous chapter, the structure of TaPAPhy\_b2 contains features not present in the PAPs lacking phytase activity (see Figure 51 and Figure 56 **Chapter 4**), which presumably allow the enzyme to accommodate phytate in the active site and use it as substrate. Among the amino acids proposed to form part of the TaPAPhy\_b2 phytate specificity pockets, residues His229 (found in the PAPhy 4 motif) and Lys410 (found in the PAPhy 5 motif, corresponding to Val367 in PvPAP1 and Gly366 in IbPAP1) were chosen as mutagenesis targets by virtue of their basic nature and conservation in PAPhy enzymes, but not in PAPs lacking phytase activity. Although not assigned to any of the specificity pockets due to longer distances to the InsP<sub>6</sub> phosphates, the basic residue Lys348 (Asn294 in PvPAP1 and Glu293 in IbPAP1) was also selected as third target for mutagenesis to further study potential effects on activity.

The impact on the phytase activity of TaPAPhy\_b2 of these three amino acid residues was studied by individual substitution with the small neutral amino acid alanine, and subsequent characterisation of the resulting proteins alongside the WT enzyme.

#### 5.2.1.1. Generation of TaPAPhy\_b2 mutants by QuickChange<sup>™</sup> mutagenesis

Successful amplification of the entire TaPAPhy\_b2-pGAPZ $\alpha$ A construct (4623 bp) was obtained with the three sets of primers designed to introduce single-site mutations into the TaPAPhy\_b2 sequence, although less efficient in the case of the H229A mutation. No bands were observed in the negative controls, including the DpnI digestion negative control which contained template DNA but no primers (Figure 57A). The PCR products obtained were subjected to digestion by DpnI, a restriction enzyme specific for methylated DNA, before transformation into *E. coli* for plasmid amplification and storage. Through DpnI reactions, the digestion of the TaPAPhy\_b2-pGAPZ $\alpha$ A construct (methylated DNA) used as template for the mutagenesis PCR reactions is achieved, while keeping the newly synthesised mutated plasmids (non-methylated DNA) unaffected. Several colonies were observed on the plates resulting from the transformation of *E. coli* XL10-Gold ultracompetent cells with the mutated plasmids. No colonies were present on the DpnI negative control plates, indicating completed digestion of the WT template DNA.

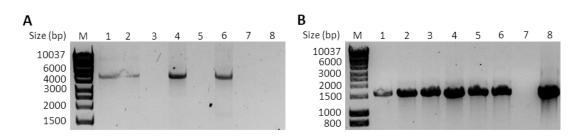
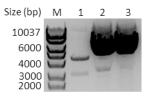


Figure 57. Results of the generation of TaPAPhy\_b2 single-site mutants by QuickChange™ mutagenesis

(A) PCR products from the QuickChange<sup>™</sup> mutagenesis reactions in a 1% (w/v) agarose gel. 5 μL samples mixed with 6x Purple Loading Dye (NEB) were loaded. Lane M, HyperLadder 1kb DNA standards (Bioline); lane 1, H229A PCR product; lane 2, leakage from lane 1; lane 3, TaB2\_H229A-F1/R1 primers negative control; lane 4, K348A PCR product; lane 5, TaB2\_K348A-F1/R1 primers negative control; lane 6, K410A PCR product; lane 7, TaB2\_K410A-F1/R1 primers negative control; lane 8, DpnI digestion negative control.
(B) Results from the colony PCR in a 1% agarose gel. 5 μL samples of each PCR product were loaded. Lane M, HyperLadder 1kb DNA standards (Bioline); lane 1, H229A colony 1; lane 2, H229A colony 2; lane 3, K348A colony 1; lane 4, K348A colony 2; lane 5, K410A colony 1; lane 6, K410A colony 2; lane 7, TaPAPhyB-F1/R1 primers negative control; lane 8, TaPAPhy\_b2-pGAPZαA positive control.

All the colonies tested by colony PCR for the incorporation of plasmids codifying for the TaPAPhy\_b2 gene were positive (1559 bp PCR product size, Figure 57B). Sequencing of plasmids purified from one colony per mutant confirmed the successful introduction of the three desired single-site mutations H229A, K348A and K410A, respectively.

### *5.2.1.2.* Transformation, expression and purification of TaPAPhy\_b2 mutants in *Pichia pastoris*



#### Figure 58. Digestion of TaPAPhy\_b2-pGAPZαA mutant constructs with AvrII

1% (w/v) agarose gel showing complete linearization of TaPAPhy\_b2-pGAPZαA mutant constructs (all 4623 bp) by digestion with AvrII in preparation for *Pichia pastoris* transformation. Lane M, HyperLadder 1kb DNA standards (Bioline); lane 1, linearized TaPAPhy\_b2\_H229A-pGAPZαA; lane 2, linearized TaPAPhy\_b2\_K348A-pGAPZαA; lane 3, linearized TaPAPhy\_b2\_K410A-pGAPZαA.

Complete linearization of the three TaPAPhy\_b2-pGAPZαA mutant constructs was achieved by digestion with AvrII. Although the same amount of plasmid was subjected to AvrII digestion for the three mutants, bands of much greater intensity were observed for K348A and K410A than for H229A when the linearized plasmids were analysed on agarose gel electrophoresis before *Pichia* transformation (Figure 58).

Nevertheless, the three linearized constructs were successfully transformed into freshly prepared KM71H (*OCH1::G418R*) *Pichia* competent cells by electroporation with similar efficiency. Single colonies were observed in all the transformation plates after three days of incubation (Figure 59).

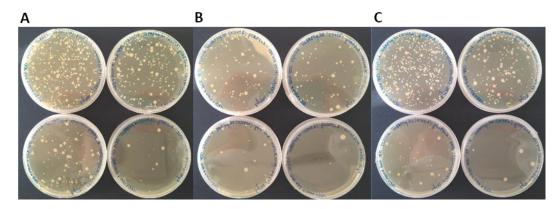


Figure 59. Selection of transformants of *P. pastoris* bearing TaPAPhy\_b2 mutants Four plates per transformation were plated with decreasing volumes of transformed cells (200  $\mu$ L, top left; 100  $\mu$ L, top right; 50  $\mu$ L, bottom left; 10  $\mu$ L, bottom right). (**A**) TaPAPhy\_b2\_H229A-pGAPZ\alphaA. (**B**) TaPAPhy\_b2\_K348A-pGAPZ\alphaA. (**C**) TaPAPhy\_b2\_K410A-pGAPZ\alphaA.

Six of the biggest colonies (i.e. highest resistance to Zeocin<sup>™</sup>) were selected for each mutant and transferred to fresh YPD agar plates, showing optimal growth levels to initiate expression trials after three days of incubation. The production of recombinant proteins in the culture media during the course of the expression trial was monitored by the presence of phosphatase activity against pNPP. As the activity assay was carried out for colony screening and not for quantification purposes, a pNP calibration curve was not included and the results were 'quantified' in absorbance units. Activity of recombinant proteins was detected for all the transformants of the three mutants and the WT control after one day of expression, and the expression patterns for each transformant were consistent across the four-day trial. Figure 60 shows the phosphatase activity against pNPP and, therefore, the expression levels for the six transformants of the K348A mutant and A of the K410A mutant displayed the highest expression levels of recombinant protein, hence were selected to produce proteins for enzymatic characterisation.

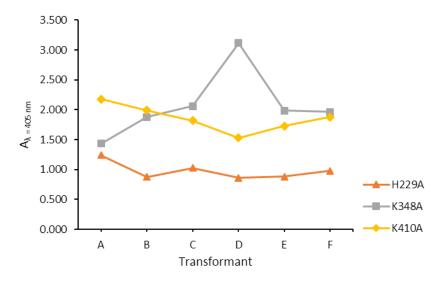


Figure 60. Enzyme activity screen of TaPAPhy\_b2-pGAPZαA mutants expression in *Pichia pastoris* KM71H (*OCH1::G418R*)

Phosphatase activity measured on the fourth day of the expression trial is displayed for six individual transformants of each of the three TaPAPhy\_b2 mutants.

TaPAPhy\_b2 WT, H229A, K348A and K410A in *P. pastoris* KM71H (*OCH1::G418R*) were successfully expressed and purified from 100 mL of culture media by nickel-affinity chromatography. The yield of recombinant TaPAPhy\_b2 WT protein obtained was 33 mg L<sup>-1</sup>, consistent with previous batches. The yields of mutant TaPAPhy\_b2 obtained were higher than the WT, with 53 mg L<sup>-1</sup> for H229A, 70 mg L<sup>-1</sup> for K348A and 47 mg L<sup>-1</sup> for K410A.

### 5.2.2. Enzymatic characterisation of wild type TaPAPhy\_b2 and three single-site mutants

#### 5.2.2.1. Relative activity, pH and temperature profiles

Differences in activity against  $InsP_6$  were observed for the mutant enzymes with respect to WT TaPAPhy\_b2, as depicted in Figure 61A. A conserved pattern by which H229A is less active, K348A is equally or more active and K410A is equally or less active than the WT was observed across all the enzyme concentrations tested. However, the relative activities against  $InsP_6$  of the three mutants compared to that of the WT varied depending on the concentration of the enzymes. At an enzyme concentration of 1 µM, the relative activities were 15% for H229A, 119% for K348A and 61% for K410A, while at 100 nM the relative activities were 49%, 100% and 82% for H229A, K348A and K410A, respectively. Concentrations of 10  $\mu$ M and 10 nM were considered too high and too low, respectively, for the detection limits of the assay. Due to an unusually high InsP<sub>6</sub> background absorbance in this experiment, results in Figure 61A are displayed without subtracting this value to avoid negative values of activity.

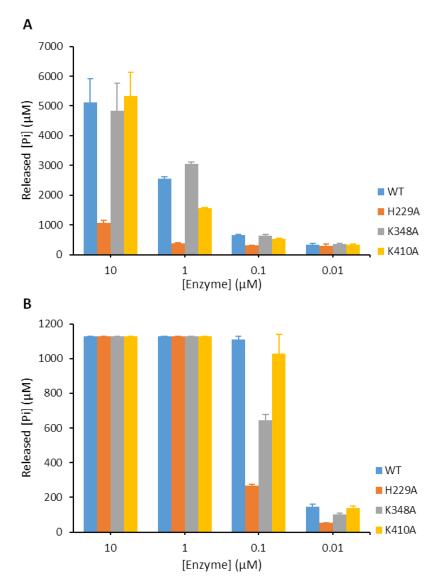


Figure 61. Phytase and phosphatase activity of WT TaPAPhy\_b2 and its mutants

(A) Phosphate release assay with 5 mM  $InsP_6$  as substrate in 0.2 M acetate buffer pH 5.5 for 15 min at room temperature. The average phosphate concentration released as a measure of phytase activity of four replicate reactions with decreasing enzyme concentrations is displayed. Error bars represent the standard deviation of the four replicates. (B) Phosphate release assay with 5 mM pNPP as substrate in 0.2 M acetate buffer pH 5.5 for 15 min at room temperature. The average phosphate concentration released as a measure of phosphatase activity of four replicate reactions with decreasing enzyme concentrations is displayed. Error bars represent the standard deviation of the four replicates activity of four replicate reactions with decreasing enzyme concentrations is displayed. Error bars represent the standard deviation of the four replicates. pNP background absorbance was subtracted from the measurements. 'Pi', inorganic phosphate.

Similar results were obtained when the assay was repeated after storage of the recombinant proteins for one month at -80°C in 20 mM Tris/HCl, pH 8.0 buffer

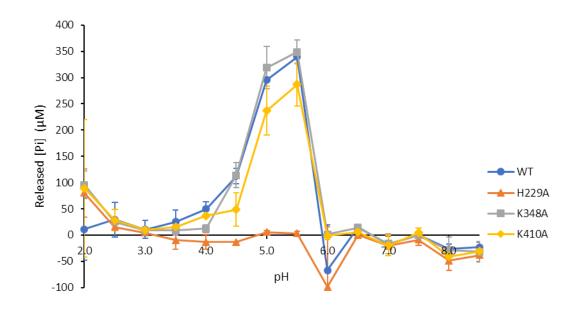
containing 30% (v/v) glycerol. The relative activity against  $InsP_6$  of the defrosted enzymes compared to the fresh ones at 100 nM-1  $\mu$ M was 88-103% for the WT, 69-72% for H229A, 92-103% for K348A and 93-110% for K410A. According to these results, 1  $\mu$ M seemed to be a suitable enzyme concentration to carry out enzymatic assays with recombinant TaPAPhy\_b2 after -80°C storage.

Differences in activity of the mutants compared to the WT enzyme were observed with pNPP as substrate (Figure 61B). In this case, both 10  $\mu$ M and 1  $\mu$ M enzyme concentrations resulted in activities higher than the detection limit of the assay. H229A and K3418A mutants were less active, while K410A activity was similar to the WT. The relative activities against pNPP also varied with the enzyme concentration, being 24%, 58% and 93% for H229A, K348A and K410A, respectively, at 100 nM, and 36%, 71% and 95% for H229A, K348A and K410A, respectively, at 10 nM.

In summary, the H229A mutation caused a 51 to 85% reduction in phytase activity against InsP<sub>6</sub>, and a 64 to 76% reduction in phosphatase activity against pNPP. The K348A mutation produced no reduction in phytase activity against InsP<sub>6</sub> and a reduction of 29 to 42% in phosphatase activity against pNPP. Finally, the K410A mutation resulted in an 18 to 39% reduction in phytase activity against InsP<sub>6</sub>, and a reduction of 5 to 7% in phosphatase activity against pNPP.

The pH profile, for phytate utilisation, of recombinant TaPAPhy\_b2 and its mutants is displayed in Figure 62. The H229A mutant showed no phytase activity across the whole pH range. No differences in the pH profile were observed for the other two TaPAPhy\_b2 mutants relative to the WT enzyme. Thus, TaPAPhy\_b2 showed phytase activity in the range of pH from 4.0 to 5.5, with an optimum at pH 5.5 and dramatic reduction at more alkaline pH. In order to confirm that the rapid drop in activity between pH 5.5 and 6.0 was actually due to pH change and not the change of buffer from 0.2 M acetate to 0.2 M bis-tris, the assay was repeated using 0.2 M MES instead of bis-tris for the pH range from 6.0 to 7.0, obtaining similar results. Although a pH optimum for TaPAPhy\_b2 has not previously been reported, similar pH profiles and pH optimum values were found in the literature for the wheat PAPhy isoforms TaPAPhy\_a1 and

TaPAPhy\_b1, with 5.5  $\pm$  0.14 and 5.0  $\pm$  0.2 optimum pH, respectively (Dionisio *et al.*, 2011).



#### Figure 62. Phytase pH profile of WT TaPAPhy\_b2 and its mutants

Enzymes were assayed with 5 mM  $InsP_6$  as substrate and 100 nM enzymes in the pH range 2.0-8.5 for 15 min at room temperature. The average phosphate concentration released as a measure of phytase activity of two measurements per pH and enzyme is displayed. Error bars represent the standard deviation of the two replicates (not displayed when smaller than the height of the symbol).  $InsP_6$  background absorbance in each buffer was subtracted from the measurements. 'Pi', inorganic phosphate.

The temperature profiles for phytate hydrolysis of WT TaPAPhy\_b2 and the three mutants generated in this project are shown in Figure 63. No activity was detected for the H229A mutant. For the WT and other mutants, phytase activity increased with temperature up to 37°C, with the activity decreasing by approximately 30% between 37°C and 50 °C for WT and K348A, but without change for the K410A mutant. The optimum temperature for phytate hydrolysis for the wheat PAPhy isoforms TaPAPhy\_a1 and TaPAPhy\_b1 has been reported to be  $55^{\circ}C \pm 1.8^{\circ}C$  and  $50^{\circ}C \pm 2^{\circ}C$ , respectively (Dionisio *et al.*, 2011).

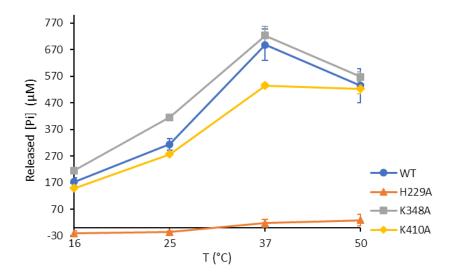


Figure 63. Phytase temperature profile of WT TaPAPhy\_b2 and its mutants

Phosphate release assay with 5 mM  $InsP_6$  as substrate and 100 nM enzymes in 0.2 M acetate buffer pH 5.5 for 15 min. The average phosphate concentration released as a measure of phytase activity of three measurements per temperature and enzyme is displayed. Error bars represent the standard deviation of the three replicates (not displayed when shorter than the height of the symbol).  $InsP_6$  background absorbance was subtracted from the measurements. 'Pi', inorganic phosphate; 'T', temperature.

#### 5.2.2.2. HPLC product profiles of phytate hydrolysis

The extent of degradation of phytate, and the pathway(s) by which dephosphorylation occurs are of great interest for the animal feed industry. The benefits obtained by the use of adjunct phytases extend to the sparing of addition of rock-phosphate to animal feed and the obviation of the antinutrient properties of dietary phytate (Blaabjerg, Hansen-Møller and Poulsen, 2010). Most commonly the pathways of dephosphorylation have been studied by anion-exchange HPLC by the method of Phillippy and Bland (1988). It is worth noting, however, that these HPLC methods are modern day iterations of the seminal work of Ballou, Cosgrove, Tate and co-workers who additionally established methods for determining the enantiomerism of inositol phosphates and the inositol phosphate products of phytate dephosphorylation (reviewed in Cosgrove, 1980).

Here, inositol phosphates were separated by acid elution from an anion exchange column and subsequent detection of inositol phosphate-ferric complexes (Phillippy and Bland, 1988). As seen in Figure 64, Figure 65 and Figure 66 (blue trace), TaPAPhy\_b2 shows a strong preference for initial hydrolysis of the phosphate in position D-4 and/or D-6 of the inositol ring. Since these columns do not resolve enantiomers it is not possible to conclude whether the product(s) contain one or both enantiomers of  $InsP_5$  product. Nevertheless, this work identifies D-Ins(1,2,3,5,6)P<sub>5</sub> and/or its enantiomer D-Ins(1,2,3,4,5)P<sub>5</sub> as first product of  $InsP_6$  hydrolysis, indicated here with a peak visible in the chromatogram after 15 min of reaction (Figure 64). The potential of marginal D-1 and/or D-3 activity was also observed. As the reaction progresses, an accumulation of the D-and/or L-Ins(1,2,5,6)P<sub>4</sub> intermediate can be observed, with smaller peaks of D-and/or L-Ins(1,2,3,4)P<sub>4</sub>, InsP<sub>3</sub> and InsP<sub>2</sub> also appearing after 15 min, 30 min and 2 h of reaction, respectively (Figure 64, Figure 65 and Figure 66, respectively).

The H229A mutant did not display phytase activity after 15 or 30 min reaction (orange trace, Figure 64 and Figure 65). No differences in the InsP<sub>6</sub> product profile of the K348A mutant were observed when compared to the WT profile (grey trace, Figure 64 and Figure 65), whereas slower reaction development with less accumulation of the D-and/or L-Ins(1,2,5,6)P<sub>4</sub> intermediate and faster progression to InsP<sub>3</sub> and InsP<sub>2</sub> could be seen for the K410A mutant when compared to the WT enzyme profile. This was particularly evident when the reactions were left to progress for 1 and 2 h (yellow trace, Figure 64, Figure 65 and Figure 66).

At extended periods of reaction (Figure 66) the great similarity of product profiles for WT and K410A mutants is especially striking. In summary, other than the H229A mutant which was inactive, not one of the individual mutations altered the specificity of attack of TaPAPhy\_b2 on InsP<sub>6</sub> or evidently on any of its hydrolysis products. That is with the caveat that the HPLC method does not distinguish between enantiomers. It remains a possibility, albeit a slight one, that individual mutations might alter the proportion of enantiomers of particular products at different stages of dephosphorylation.

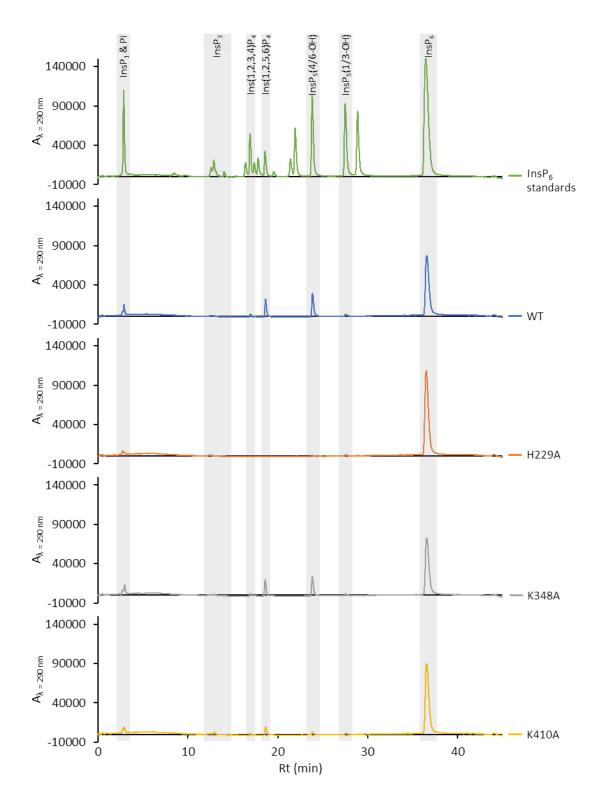


Figure 64. Product profiles of WT TaPAPhy\_b2 and its mutants after limited reaction against InsP<sub>6</sub>

Reactions were performed for 15 min at room temperature with 1 mM InsP<sub>6</sub> substrate and 1  $\mu$ M enzymes in 0.2 M acetate buffer pH 5.5. An acid hydrolysate of InsP<sub>6</sub> with relevant peaks labelled for reference is shown (InsP<sub>5</sub>s are identified by the residual hydroxyl). 'Rt', retention time.

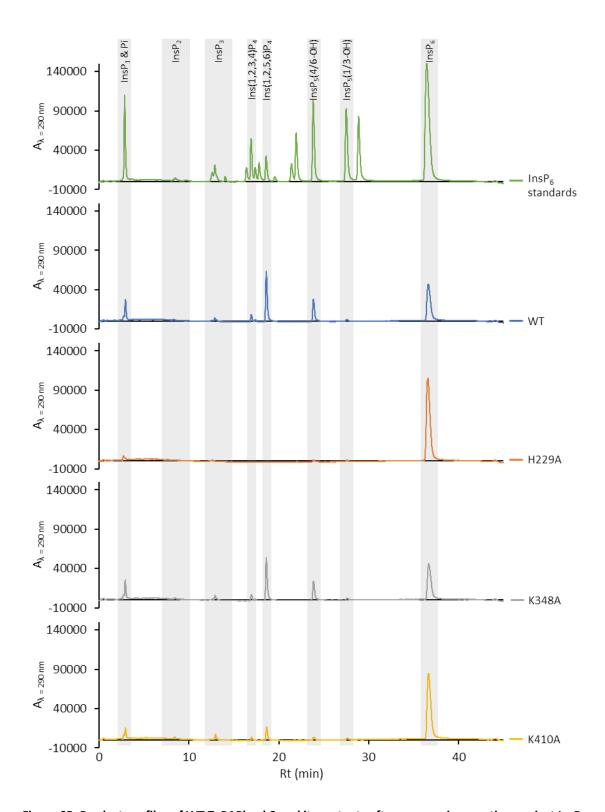
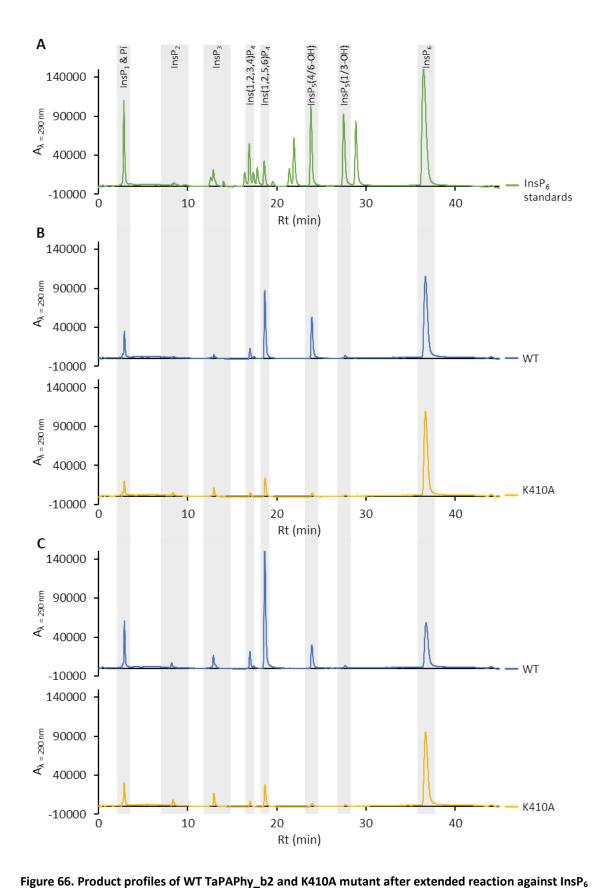


Figure 65. Product profiles of WT TaPAPhy\_b2 and its mutants after progressive reaction against InsP<sub>6</sub> Reactions were performed for 30 min at room temperature with 1 mM InsP<sub>6</sub> substrate and 1  $\mu$ M enzymes in 0.2 M acetate buffer pH 5.5. An acid hydrolysate of InsP<sub>6</sub> with relevant peaks labelled for reference is shown (InsP<sub>5</sub>s are identified by the residual hydroxyl). 'Rt', retention time.



Reactions were performed at room temperature with 1 mM InsP<sub>6</sub> substrate and 1  $\mu$ M enzymes in 0.2 M acetate buffer pH 5.5. 'Rt', retention time. (**A**) An acid hydrolysate of InsP<sub>6</sub> with relevant peaks labelled for reference is shown (InsP<sub>5</sub>s are identified by the residual hydroxyl). (**B**) 1 h reaction. (**C**) 2 h reaction.

#### 5.2.2.3. Enzyme kinetics

The enzyme kinetics of recombinant TaPAPhy\_b2 and the three mutants generated in this project was studied by means of the phosphate release assay at pH 5.5 and 37°C (Figure 67). Reactions were limited to less than 15% conversion of substrate by careful titration of the amount of enzyme. While no sensible kinetic parameters were obtained for the H229A mutant due to its lack of phytase activity, estimates of the kinetic parameters of the WT enzyme and the K348A and K410A mutants were obtained and are presented in Table 19.

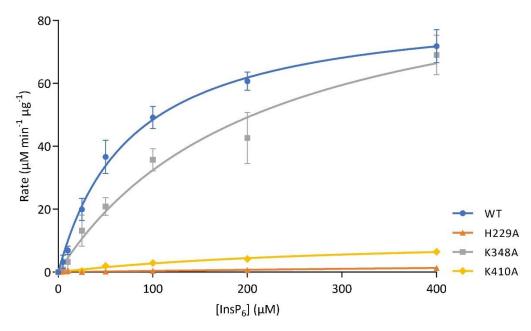


Figure 67. Michaelis-Menten kinetics of WT TaPAPhy\_b2 and its mutants against InsP<sub>6</sub>

Reactions carried out in triplicate with 60 nM enzymes and increasing concentrations of  $InsP_6$  at 37°C in 0.2 M acetate buffer pH 5.5. WT and K348A mutant, 10 min reactions. H229A and K410A, 90 min reactions. The results are the average of the three replicates per enzyme and substrate concentration, expressed as the rate of phosphate concentration released ( $\mu$ M) per time of the reaction (min) and amount of enzyme ( $\mu$ g). Error bars represent the standard deviation of the three replicates (not displayed when smaller than the height of the symbol).

 $V_{max}$  is the maximum rate of catalysis of an enzymatic reaction at a given enzyme concentration, approached when the enzyme is saturated with substrate (Lorsch, 2014). The value of  $V_{max}$  for WT TaPAPhy\_b2 was estimated as  $85.5 \pm 3.1 \,\mu$ M min<sup>-1</sup>  $\mu$ g<sup>-1</sup>, while a similar or slightly higher  $V_{max}$  of  $102.1 \pm 10.8 \,\mu$ M min<sup>-1</sup>  $\mu$ g<sup>-1</sup> was obtained for the K348A mutant, while the mutant K410A presented a much lower  $V_{max}$  of  $11.3 \pm 1.2 \,\mu$ M min<sup>-1</sup>  $\mu$ g<sup>-1</sup>. The Michaelis constant K<sub>m</sub> is the concentration of substrate required to give a rate that is half of the  $V_{max}$ , and it reflects how well the enzyme binds

a specific substrate (Lorsch, 2014). The estimated K<sub>m</sub> values for WT, K348A and K410A TaPAPhy\_b2 were 76.4  $\pm$  7.7  $\mu$ M, 214.6  $\pm$  46.6  $\mu$ M and 307.6  $\pm$  56.7  $\mu$ M, respectively, indicating that both mutations result in a much lower affinity to InsP<sub>6</sub> than the WT enzyme. High standard errors in the estimation of K<sub>m</sub> values for the K348A and K410A mutants were obtained consistently when repeating the experiment several times. The catalytic constant for the conversion of substrate to product k<sub>cat</sub>, also known as the turnover number, reflects the efficiency of the enzyme (Lorsch, 2014). Mutant K348A, with a k<sub>cat</sub> of 28.4  $\pm$  3.0 s<sup>-1</sup>, showed similar or slightly higher efficiency than the WT enzyme, with a k<sub>cat</sub> of 23.8  $\pm$  0.9 s<sup>-1</sup>. The mutation K410A resulted in a much lower efficiency than the WT, with a k<sub>cat</sub> of 3.2  $\pm$  0.3 s<sup>-1</sup>.

Table 19. Estimation of kinetic parameters of InsP<sub>6</sub> hydrolysis for WT, K348A and K410A TaPAPhy\_b2  $K_m$  values are expressed as substrate concentration ( $\mu$ M).  $V_{max}$  values are expressed as phosphate concentration release ( $\mu$ M) per time of reaction (min) and amount of enzyme ( $\mu$ g).  $k_{cat}$  values are expressed per time of reaction (s). Estimated value ± standard error is shown for each parameter. The R<sup>2</sup> of the curve fit is also included.

Parameter	wт	K348A	K410A
K <sub>m</sub> (μM)	76.4 ± 7.7	214.6 ± 46.6	307.6 ± 56.7
V <sub>max</sub> (µM min⁻¹ µg⁻¹)	85.5 ± 3.1	102.1 ± 10.8	11.3 ± 1.2
k <sub>cat</sub> (s <sup>-1</sup> )	23.8 ± 0.9	$28.4 \pm 3.0$	$3.1 \pm 0.3$
R <sup>2</sup>	0.98	0.96	0.98

#### 5.2.2.4. Inhibition of wild type TaPAPhy\_b2 phytase activity

Before the sequencing of genomes, the expression of recombinant proteins and the elaboration of protein folds underlying biochemical activity, it was common to characterize enzyme activity of partially or extensively purified proteins by simple kinetic parameters and sensitivity of activities to inhibitors and other assay factors (see Konietzny and Greiner, 2002, for a review of the characterization of phytases). Among the factors employed to distinguish activities and reaction mechanism are analogues of substrate or transition state intermediates. Molybdate and vanadate are commonly used analogues of the penta-coordinate transition state of the acid phosphatase and PAP reaction mechanisms (Ishikawa *et al.*, 2000).

Experiments were performed to determine whether TaPAPhy\_b2 is sensitive to the transition state analogue molybdate and the substrate analogue InsS<sub>6</sub>. A progressive loss of activity of recombinant TaPAPhy\_b2 was achieved with sodium molybdate

concentrations in the range  $0.1 - 100 \mu$ M, with complete inhibition at 1 mM (Figure 68 and Figure 69), as expected for a strong inhibitor of acid phosphatases. The substrate analogue, InsS<sub>6</sub>, was less potent with 75% and 28% of uninhibited activity observed in the presence of 0.1 mM and 1 mM of InsS<sub>6</sub>, respectively (Figure 68). The results of this assay, together with the structure information, suggest that InsS<sub>6</sub> is an inhibitor of PAPhy which, although not mimicking substrate binding (see Figure 50 in **Chapter 4, section 4.2.2.1.**), is able to compete with InsP<sub>6</sub> for the enzyme's active site.

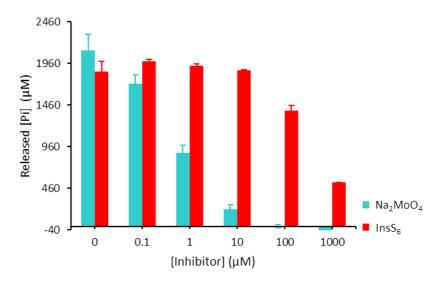


Figure 68. Inhibition of TaPAPhy\_b2 activity in the presence of myo-inositol hexakissulfate

The PAP inhibitor molybdate was used as reference. Phosphate release assay with 5 mM InsP<sub>6</sub> as substrate and 1  $\mu$ M WT TaPAPhy\_b2 in 0.2 M acetate buffer pH 5.5 for 15 min at room temperature. The average phosphate concentration released as a measure of phytase activity of three measurements per inhibitor concentration is displayed. Error bars represent the standard deviation of the three replicates. InsP<sub>6</sub> background absorbance was subtracted from the measurements. 'Pi', inorganic phosphate.

For enzymes that cleave phosphoanhydride or phosphomonoester bonds, thioesters are commonly used non-hydrolysable analogues of substrates of these enzymes. While InsS<sub>6</sub> is an analogue of the physiological substrate, InsP<sub>6</sub>, of plant phytases, *para*-nitrophenyl sulfate, pNPS, affords a non-hydrolysable analogue of the artificial substrate pNPP. Here, pNPS displayed only a very weak inhibitory effect on phytate hydrolysis of TaPAPhy\_b2 in the conditions assayed, with approximately 20% reduction of activity with 5 mM pNPS (Figure 69). The results of this assay are in accordance with the inability to obtain a crystal structure of TaPAPhy\_b2 in complex with pNPS (**Chapter 4, section 4.2.1.6.**) and probably reflect much weaker binding of pNPS, and likely pNPP, than InsP<sub>6</sub>.

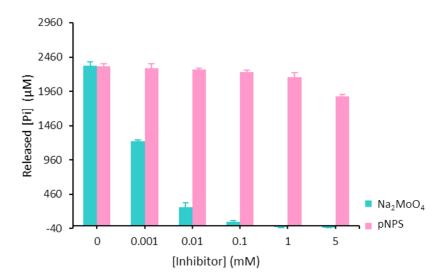


Figure 69. Inhibition of TaPAPhy\_b2 activity in the presence of para-nitrophenyl sulfate

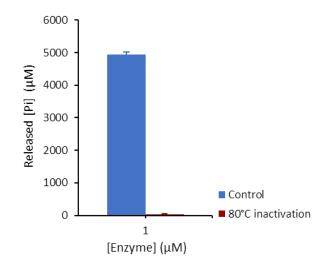
The PAP inhibitor molybdate was used as reference. Phosphate release assay with 5 mM InsP<sub>6</sub> as substrate and 1  $\mu$ M WT TaPAPhy\_b2 in 0.2 M acetate buffer pH 5.5 for 15 min at room temperature. The average phosphate concentration released as a measure of phytase activity of three measurements per inhibitor concentration is displayed. Error bars represent the standard deviation of the three replicates. InsP<sub>6</sub> background absorbance was subtracted from the measurements. 'Pi', inorganic phosphate.

#### 5.2.2.5. Thermal stability of wild type TaPAPhy\_b2

A major goal of the animal feed adjunct enzyme sector is the enhancement of thermostability of phytases added to animal feed (Lei *et al.*, 2013; Rebello *et al.*, 2017). Enhanced thermostability has the additional benefit that it is commonly accompanied by resistance to proteolytic cleavage in the gastro-intestinal tract of animals fed with phytase-supplemented feed (Menezes-Blackburn *et al.*, 2011). Thermostability is essential because the pelleting process by which raw plant-based feedstuffs are converted to feed includes a heat-treatment specific to the feed mill. Consequently, considerable effort is placed in the engineering of thermostability. Thermostability may be tested in a variety of contexts. Heat-resistance may be measured by assay of residual enzyme activity after a heat treatment and cooling. Measurement of protein melting temperature may be studied by methods including differential scanning fluorimetry (Niesen, Berglund and Vedadi, 2007) or DSC (Bruylants, Wouters and Michaux, 2005; Johnson, 2013). For this study, a DSC experiment was conducted.

#### 5.2.2.5.1. Recovery after heating at 80°C

To test the thermostability of TaPAPhy\_b2, protein was incubated at 80°C for 10 min before cooling to 4°C and subsequent assay. Complete and irreversible deactivation of TaPAPhy b2 phytase activity was observed (Figure 70).

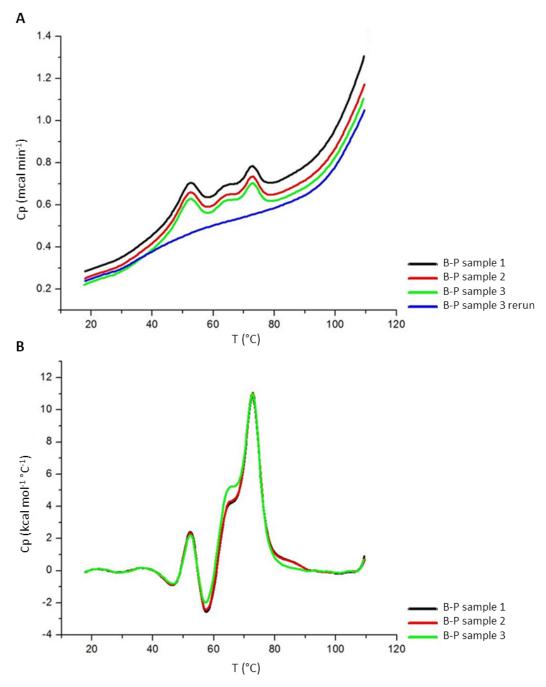


#### Figure 70. Recovery of TaPAPhy\_b2 phytase activity of after heating at 80°C

Phosphate release assay with 1  $\mu$ M WT TaPAPhy\_b2 and 5 mM InsP<sub>6</sub> as substrate in 0.2 M acetate buffer pH 5.5 for 15 min at 37°C. The enzyme was incubated at 80°C for 10 min, then cooled down to 4°C before setting up the reactions. Control enzyme was kept at 4°C. The average phosphate concentration released as a measure of phytase activity of four replicates is displayed. Error bars represent the standard deviation of the four replicates. InsP<sub>6</sub> background absorbance was subtracted from the measurements.

#### 5.2.2.5.2. Differential scanning calorimetry

When analysing the thermal denaturation of recombinant TaPAPhy\_b2 by DSC, a complex thermogram with three peaks was obtained for three replicate runs before the processing of the raw data (Figure 71A). The third replicate was tested for recovery of structure (renaturation) by subjecting the protein to a second cycle of DSC. No recovery of TaPAPhy\_b2 was observed in the rerun of the third replicate, consequently this curve was selected as baseline to subtract from the raw data in the automatic data processing.



**Figure 71. Differential scanning calorimetry thermogram of TaPAPhy\_b2** 'B', 20 mM Tris/HCl pH 8.0 buffer; 'P' WT TaPAPhy\_b2 at 1.5 mg mL<sup>-1</sup>. (**A**) Raw data. (**B**) After baseline subtraction.

The thermogram of the processed DSC data for TaPAPhy\_b2 after baseline subtraction can be observed in Figure 71B. Two melting temperatures were identified, a  $T_{m1}$  at 52.31 ± 0.11°C and a  $T_{m2}$  at 72.67 ± 0.11°C, expressed as the average and standard deviation of the three replicate runs. A lower temperature shoulder before the  $T_{m2}$  peak can also be observed at approximately 65°C. The different peaks may correspond to metal loss and unfolding of the protein chain.

#### 5.2.3. Crystal structure of the TaPAPhy\_b2 H229A mutant

Structures of phytase enzymes with the substrate InsP<sub>6</sub> as ligand are generally solved with inactive mutants (Lim et al., 2000; Gruninger et al., 2012). The difficulty to crystallise WT phytases with  $InsP_6$  may arise from substrate turnover, even in the crystal form. The H229A single-site mutant displayed virtually no phytase activity in the assays performed. In order to take advantage of this property, the TaPAPhy b2 H299A mutant was crystallised to attempt to solve its structure in complex with InsP<sub>6</sub>. Single crystals in the H3 space group grown with TaPAPhy b2d-H229A batch 02 (7.0 mg mL<sup>-1</sup>, deglycosylated with recombinant GST-Endo F1) were harvested and cryoprotected by soaking them for a few minutes in a solution containing 0.2 M sodium thiocyanate, 20% (w/v) PEG 3350, 25% (v/v) PEG 400 and 1 mM InsP<sub>6</sub>, with pH adjusted to 5.5 with acetate buffer. A dataset with 1.50 Å resolution was collected at DLS beamline I03 from a wedge-shaped crystal with approximate dimensions of  $30 \times 25 \times 10 \mu M^3$ , and the structure was solved by molecular replacement with the TaPAPhy\_b2:PO<sub>4</sub> complex structure in the product-bound state (Chapter 4, section 4.2.1.1. and 4.2.1.3.). The final model was refined to Rwork and Rfree values of 12.83% and 15.23%, respectively. Crystal parameters, data collection and refinement statistic for this structure are summarised in Table 20.

The structure consisted of TaPAPhy\_b2 with the H229A mutation in complex with phosphate, with no electron density observed for the substrate InsP<sub>6</sub> bound to the active site or anywhere else. Other datasets collected from crystals soaked in InsS<sub>6</sub> did not show electron density for this molecule either. The iron ions in the active site were modelled with occupancies of 50% (20.16 Å<sup>2</sup> *B* factor) and 100% (14.63 Å<sup>2</sup> *B* factor) in the MI and MII site, respectively, and the coordination geometry of both metals was classified as octahedral by the CheckMyMetal server (Zheng *et al.*, 2014). The position of the phosphate molecule in the active site resembled that of the TaPAPhy\_b2:PO<sub>4</sub> complex structure in the substrate-bound state (**Chapter 4, section 4.2.1.4.**), with spherical electron density for a bridging solvent molecule observed between the metals and modelled with 97% occupancy.

#### Table 20. Data collection and refinement statistics for the TaPAPhy\_b2-H229A:PO₄ complex structure

Values in brackets correspond to the high resolution outer shell. The X-ray flux is the total experimented by the crystal during data collection, corrected for transmission. The  $R_{merge}$  value corresponds to  $R_{merge}$  (all I+ & I-). The number of reflections stated are the unique reflections used in refinement.

Structure	TaPAPhy_b2d-H229A:PO <sub>4</sub>	
PDB ID	6GJA	
Crystal parameters		
Space group	НЗ	
<i>a, b, c</i> (Å)	126.0, 126.0, 106.6	
<i>α, β,</i> γ (°)	90, 90, 120	
Data collection		
Wavelength (Å)	0.9763	
$\Omega$ Oscillation (°)	0.10	
Total Ω (°)	120	
Exposure (s)	0.040	
Beam size (µm)	50x20	
X-ray flux (ph)	4.08x10 <sup>13</sup>	
Resolution (Å)	38.46-1.50 (1.53-1.50)	
R <sub>merge</sub> (%)	5.6 (59.1)	
< 1/\sigma(1) >	12.4 (1.7)	
Completeness (%)	96.6 (75.0)	
Multiplicity	3.2 (2.0)	
CC <sub>1/2</sub>	1.0 (0.4)	
Wilson <i>B</i> factor (Å <sup>2</sup> )	16.0	
Refinement		
Total No. of atoms	4940	
Water molecules	443	
No. of reflections	97457	
R <sub>work</sub> (%)	12.8	
R <sub>free</sub> (%)	15.2	
Anisotropy	0.062	
<b>RMS</b> deviations		
Bonds (Å)	0.005	
Angles (°)	0.833	
Planes (Å)	0.006	
Ramachandran plot		
Favoured (%)	96.91	
Allowed (%)	3.09	
Outliers (%)	0.00	
Mean <i>B</i> factors (Å <sup>2</sup> )	24.0	

The majority of the residues (96.91%) were found in the most favourable region of the Ramachandran plot, with no outliers present. Gaps in electron density were found at four consecutive residues Glu19, Asp20, Arg21 and Gly22; twelve consecutive residues Asp216, Cys217, Tyr218, Ser219, Cys220, Ser221, Phe222, Ala223, Lys224, Ser225, Thr226 and Pro227, constituting the majority of the PAPhy 4 motif (Figure 72); and Leu509, Lys510 and the 6xHis tag at the C-terminus. The side chains of residues Arg11, Arg37, Glu111, Ile228 and Lys410 were not defined in the electron density and, therefore, not modelled. A list of 26 residues were modelled with alternative conformations: Ser56, Asp100, Arg125, Leu126, Gln127, Glu130, Lys134, Arg155, Ser183, Ser190, Leu199, Glu244, Ser249, Ser281, Met282, Ile302, Met303, Ser330, Ser345, Glu355, Ser367, Arg408, Met411, Thr414, Ser449 and Val494. Signs of photoreduction were observed in all three disulfide bonds present in the structure (Cys217-Cys220 was in one of the gaps in electron density). N-glycosylation was observed in the seven predicted glycosylation sites. Occupancies lower than 100% were observed for NAGs in Asn267 (76%) and Asn389 (69%). Electron density for a second NAG residue linked to a  $\beta$ -D-mannose was present in the Asn475 site.

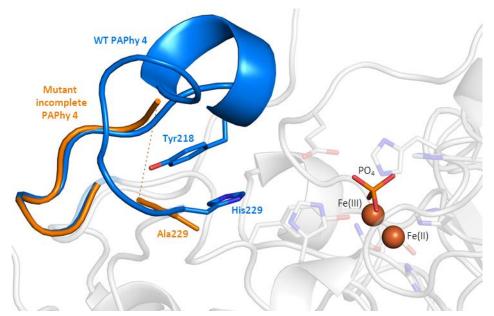


Figure 72. Disordered PAPhy 4 motif in the TaPAPhy\_b2-H229A:PO₄ complex structure

Cartoon representation of the WT structure with the PAPhy 4 motif highlighted in blue. The region corresponding to the PAPhy 4 motif in the H229A mutant structure is superimposed in orange, with the two ends of the unmodelled region (due to a gap in the electron density) connected by a dashed line. Ala229 in the mutant structure, Tyr218, His229, the metal ligands, the phosphate ion and the phosphate ligands in the WT structure are displayed in stick representation. The iron ions are shown as brown spheres. Image created with PyMOL version 1.3 (Schrodinger LLC, 2015).

Three phosphate molecules were modelled in the TaPAPhy\_b2-H229A mutant structure in the same location as in the TaPAPhy\_b2:PO<sub>4</sub> complex structure resembling substrate binding (**Chapter 4, section 4.2.1.4.**), with occupancies of 81% (23.99 Å<sup>2</sup> *B* factor, bound to the metals), 83% (65.76 Å<sup>2</sup> *B* factor, near the active site) and 75% (77.60 Å<sup>2</sup> *B* factor, in the protein surface). The TaPAPhy\_b2-H229A:PO<sub>4</sub> complex

structure contained 443 waters, eight ethylene glycol molecules (EDO,  $C_2H_6O_2$ ), five diethylene glycol molecules (PEG,  $C_4H_{10}O_3$ ), three triethylene glycol molecules (PGE,  $C_6H_{14}O_4$ ) and one 1-(2-methoxy-ethoxy)-2-{2-[2-(2-methoxy-ethoxy]-ethoxy}-ethane molecule (PG6,  $C_{12}H_{26}O_6$ ).

Figure 72 shows the unmodelled region of the mutant structure (orange) due to discontinuous electron density between residues Asp216 and Pro227, covering most of the PAPhy 4 motif, with the equivalent region in the WT structure superimposed (blue). The lack of electron density in this region of the mutant enzyme preventing model building could be explained by the introduction of disorder due to the loss of the ring stack interaction between His229 and Tyr218 (displayed as blue sticks in Figure 72) caused by the mutation of His229 to alanine (see Figure 51 in **Chapter 4, section 4.2.2.3.**).

### 5.3. Conclusions

A full characterisation of the recombinant TaPAPhy b2 wheat phytase has been completed in this project, revealing that the optimal conditions for phytate hydrolysis are pH 5.5 and 37°C, with kinetic parameters estimated in these conditions being  $K_m = 76.4 \pm 7.7 \mu M$ ,  $V_{max} = 85.5 \pm 3.1 \mu M min^{-1} \mu g^{-1}$  and  $k_{cat} = 23.8 \pm 0.9 s^{-1}$ . Although no kinetic data was found for the TaPAPhy b2 enzyme in the literature, differences in kinetic parameters were observed for TaPAPhy\_b2 compared to other wheat PAPhy isoforms. A K<sub>m</sub> of 45 ± 3.4  $\mu$ M, V<sub>max</sub> of 216 ± 12.4  $\mu$ M min<sup>-1</sup> mg<sup>-1</sup> and k<sub>cat</sub> of 270 s<sup>-1</sup> have been reported for recombinant TaPAPhy b1, while published kinetic parameters for TaPAPhy a1 were  $K_m = 35 \pm 6.8 \,\mu\text{M}$ ,  $V_{max} = 223 \pm 9.4 \,\mu\text{M}$  min<sup>-1</sup> mg<sup>-1</sup> and  $k_{cat} = 279 \,\text{s}^{-1}$ (Dionisio et al., 2011). Recombinant TaPAPhy b2 was strongly inhibited by molybdate, a known phytase inhibitor (Zhang et al., 1997). An inhibitory effect on phytase activity was also observed when carrying out the phosphate release assay in the presence of InsS<sub>6</sub>, supported by the crystal structure of its complex with the enzyme solved in the previous chapter. In addition, this study also found that TaPAPhy b2 is not a thermostable phytase, lacking recoverable phytase activity after heating at 80°C. Two melting temperatures were noted at  $52.31 \pm 0.11$ °C and  $72.67 \pm 0.11$ °C, respectively. The thermal stability data obtained through DSC explains the decrease in phytase

activity at 50°C observed in the temperature profile of this enzyme. Engineering of thermostability in TaPAPhy\_b2 would be required to make it suitable as an animal feed additive in order to survive the pelleting process.

The degradation profiles obtained for recombinant TaPAPhy b2 in this study show a clear peak of D-Ins(1,2,3,5,6)P<sub>5</sub> (or its enantiomer D-Ins(1,2,3,4,5)P<sub>5</sub>) as main product of InsP<sub>6</sub> hydrolysis, classifying the enzyme into the D-4/6-phytase category. Although a hint of a peak implying certain D-1/3 phytase activity was observed, the suspicion that this peak corresponded to a contaminant in the substrate was confirmed in the product profiles obtained in **Chapter 6**. An accumulation of the D- and/or L-Ins(1,2,5,6)P<sub>4</sub> intermediate indicating attack of the group adjacent to the D-4/6-phopshate, with a secondary smaller peak for the D- and/or L-Ins $(1,2,3,4)P_4$ intermediate, and little progression to lower inositol phosphates even after 2 h reaction completed the findings of this project regarding the TaPAPhy\_b2 preference of InsP<sub>6</sub> hydrolysis. Similar phytate degradation pathways have been reported for wheat phytases previously (Tomlinson and Ballou, 1962; Nakano et al., 1999, 2000; Bohn et al., 2007), while those studies showing a wider variety of InsP<sub>5</sub> intermediates are suspected to belong to wheat MINPPs or a mix of PAPhy and MINPP enzymes (Lim and Tate, 1971, 1973, Brinch-Pedersen et al., 2003, 2006). The inefficiency of the TaPAPhy b2 phytase to remove more than two phosphate groups from the inositol ring of phytate could be the consequence of losing a subset of the interactions identified in the previous chapter that contribute to stabilise InsP<sub>6</sub> binding in lower inositol phosphates (see Figure 56, in Chapter 4 section 4.2.2.4.).

Mutation of residues His229, Lys348 or Lys410 in the TaPAPhy\_b2 enzyme still produced viable protein, able to fold into a soluble enzyme, containing metal ions and conserving different degrees of phytase or phosphatase activity. The mutation H229A significantly inactivated the protein, confirming the importance of residue His229 in InsP<sub>6</sub> binding or catalysis suggested in **Chapter 4** through the specificity pocket S<sub>B</sub> (3-phosphate). Besides direct interaction with the substrate, the crystal structure of the mutant H229A solved in this chapter revealed perhaps a more or equally important role of this residue. Mutation of His229 to alanine interrupted the aromatic ring stacking with Tyr218, present in the WT enzyme structures. Such interruption resulted in the

instability of the whole PAPhy 4 motif insertion, proposed to have an essential role in binding the substrate in a productive mode in the active site and, therefore, likely to account for the loss of activity of this mutant.

The mutation K348A produced an enzyme with similar relative phytase activity, pH optimum, temperature optimum and product profile to the WT. A reduction in relative phosphatase activity was observed compared to the WT, as well as differences in their kinetic parameters at least with regards to affinity for InsP<sub>6</sub>. Mutation of Lys348 to alanine resulted in an enzyme with lower affinity for InsP<sub>6</sub>, indicating it may provide indirect contributions to the  $S_E$  (6-phosphate) or  $S_D$  (1-phosphate) specificity pockets. To conclude, the mutation K410A produced an enzyme with lower relative phytase activity and similar relative phosphatase activity to the WT protein, sharing the same pH and temperature optimum for phytate hydrolysis. Subtle differences in the product profile of InsP<sub>6</sub> were observed with respect to the WT. Although slower in InsP<sub>6</sub> degradation than the WT, the mutant K410A did not seem to accumulate the D- and/or L-Ins(1,2,5,6)P<sub>4</sub> intermediate as much as the WT enzyme. Looking at the kinetic parameters, mutation of Lys410 to alanine resulted in an enzyme with a much lower maximum rate of catalysis, efficiency and affinity for InsP<sub>6</sub>. The observed effects in phytase activity confirmed the importance of this residue in InsP<sub>6</sub> hydrolysis by the TaPAPhy\_b2 phytase, forming part of the  $S_E$  (6-phosphate) and  $S_F$  (5-phosphate) specificity pockets.

## Chapter 6. Comparison of TaPAPhy\_b2 with other plant PAP phytases

Plasmid DNA for the expression of seven different plant PAPhy was acquired for this project, including wheat phytases TaPAPhy\_a1, TaPAPhy\_b1 and TaPAPhy\_b2, barley phytase HvPAPhy\_a, rice phytase OsPAPhy\_b, maize phytase ZmPAPhy\_b, and soybean phytase GmPAPhy\_b. Six of these targets were put aside after failed attempts to produce soluble recombinant protein in *Escherichia coli* strains, to move onto an eukaryotic expression system with the wheat enzyme TaPAPhy\_b2. After successful expression of TaPAPhy\_b2 in *Pichia pastoris*, leading to subsequent purification, structural and enzymatic characterisation, advantage of the knowledge acquired was taken for further work on the remaining plant PAPhy targets.

The information gathered from the newly solved crystal structures of TaPAPhy\_b2 was used in conjunction with the data obtained from the characterisation of the enzyme and single-site mutants to determine common characteristics or specific properties between PAPhy isoforms or PAPhy from different plant species. In particular, 3D homology models of plant PAPhy with unknown structure were generated based on the TaPAPhy\_b2 fold, in order to compare their active site architecture with TaPAPhy\_b2 and with each other. Structure-function relationships of the PAPhy active site were further examined by generating recombinant samples of a subset of plant PAPhy enzymes and obtaining their phytate hydrolysis product profiles.

### 6.1. Materials and methods

# 6.1.1. Protein homology modelling of plant PAPhy based on the TaPAPhy\_b2 structure

Homology models of TaPAPhy\_a1, TaPAPhy\_b1, HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b were produced using the SWISS-MODEL automated protein structure homology-modelling server employed in user template mode (Biasini *et al.*, 2014). The structure of TaPAPhy\_b2 in complex with phosphate resembling product binding was used as template for homology modelling (**Chapter 4, section**)

**4.2.1.1.** and **4.2.1.3.**). Pairwise sequence alignments of TaPAPhy\_b2 with each of the proteins being modelled, as well as a MSA including the seven proteins, were created using the T-Coffee server (Notredame, Higgins and Heringa, 2000) with default parameters. The MSA was analysed with Jalview (Waterhouse *et al.*, 2009), while the 3D homology models were analysed with the UCSF Chimera package (Pettersen *et al.*, 2004).

To compare the plant PAPhy structure and models, amino acid residues falling within at least one of the following criteria were selected: (1) non-conserved residues within 10 Å of the phosphate ion in the TaPAPhy\_b2 structure, (2) non-conserved residues forming part of PAPhy motifs or in their vicinity, and (3) non-conserved residues forming part of PAP motifs or in their vicinity. Plant PAPhy targets to produce recombinant protein for phytase activity studies were chosen after inspection of the amino acid conservation in the selected positions.

## 6.1.2. Gateway<sup>™</sup> cloning of soybean PAPhy for expression in *Pichia pastoris*

Of the plant PAPhy targets selected for recombinant expression after inspection of their active centres, the only enzyme not available in a construct for *Pichia pastoris* expression was the soybean GmPAPhy\_b phytase. For this purpose, the Gateway<sup>M</sup> cloning system was used to sub-clone GmPAPhy\_b into a Gateway-compatible pPICZ $\alpha$ -DEST vector. The GmPAPhy\_b-pOPINB construct was employed as template for the cloning. Since the coding region of GmPAPhy\_b-pOPINB had been codon optimised for *E. coli* expression (see **Chapter 3, section 3.1.1.2.**), a rare codon analysis for expression in *Pichia pastoris* was performed prior the cloning process using the GenScript Rare Codon Analysis Tool (https://www.genscript.com/tools/rare-codonanalysis).

The Gateway<sup>™</sup> technology is a high-fidelity and high-efficiency cloning method based on the bacteriophage λ site-specific recombination system. It allows the transfer of DNA fragments from an entry vector to different expression vectors in a standardised manner, maintaining the orientation of the DNA fragment (Hartley, Temple and Brasch, 2000). The insertion of the gene of interest into the vectors takes place through two recombination reactions, based on the presence of specific recombination sites in the vectors and flanking the gene of interest. The first recombination reaction, known as the BP reaction, inserts the gene of interest into an entry vector. It consists of the recombination of *att*B sequences, flanking a PCR fragment containing the gene sequence, and *att*P sequences, present in the cloning site of the entry vector. After the BP recombination reaction, the gene of interest is flanked by *att*L sequences in the entry vector (Figure 73B). The target gene can then be easily transferred from the entry vector to different destination vectors for recombinant protein expression through a second recombination reaction known as the LR reaction. This reaction takes place by the recombination of the *att*L sequences, flanking the gene in the entry vector, and *att*R sequences, present in the cloning site of the gene in the gene flanked again by *att*B sequences in the destination vector (Figure 73C).

For the cloning of GmPAPhy\_b, the vector pDONR 207, encoding gentamycin and chloramphenicol resistance, was used as entry vector, and the vector pPICZ $\alpha$ -DEST, encoding Zeocin<sup>TM</sup> and chloramphenicol resistance, was used as destination vector. The destination vector pPICZ $\alpha$ -DEST is a modified pPICZ $\alpha$  *Pichia pastoris* methanol-inducible expression vector, in which the Gateway<sup>TM</sup> cassette containing the specific recombination sites has been inserted to make it compatible with the Gateway<sup>TM</sup> cloning system (Sasagawa *et al.*, 2011).

#### Table 21. Reaction set up for Gateway™ adapter PCRs with Phusion polymerase

Plasmid template for adapter 1 PCR was diluted to a working concentration of 2.5 ng  $\mu$ L<sup>-1</sup>. Adapter 1 PCR product was used as template for adapter 2 PCR reactions, setting up reactions with undiluted product, diluted 1:20 and diluted 1:50. Primer mixes were prepared in water from 100  $\mu$ M stocks.

Reagent	[Stock]	[rxn]	V for 1x 20 μL rxn (μL)
Water	n/a	n/a	13.5
Phusion HF buffer	5x	1x	4
DMSO	100%	2%	0.4
dNTP mix	10 mM each	0.2 mM each	0.4
Primer mix	10 µM each	$0.25\mu\text{M}$ each	0.5
Template DNA	n/a	n/a	1
Phusion polymerase	2 U μL <sup>-1</sup>	0.02 U µL <sup>-1</sup>	0.2
TOTAL			20

Primers were designed to perform two adapter PCRs in order to extract the GmPAPhy\_b coding region from the GmPAPhy\_b-pOPINB construct, with the addition of the sequence encoding for a C-terminal 6xHis tag, the *P. pastoris* preferred stop codon TAA, and flanking *att*B recombination sites (Figure 73A). The reactions for the two adapter PCRs were set up on ice as detailed in Table 21. Primers attB1\_GmPAPhy-F1 and CHis\_GmPAPhy-R1 (see Table A14 in **Appendix 2**) were used for adapter 1 PCR, introducing the first half of the *att*B1 site at the 5' end, and the 6xHis tag and stop codon at the 3' end of the GmPAPhy\_b sequence. Primers attB1 and CHis-attB2-pPICZ (see Table A14 in **Appendix 2**) were used for adapter 2 PCR, introducing the second half of the *att*B1 site at the 5' end. The PCR protocol on Table 22 was used for the amplification. Negative control reactions were included in both PCRs, using water instead of plasmid DNA. Results of the PCR reactions were assessed on 1% (w/v) agarose gels containing ethidium bromide.

**Table 22. PCR protocol for amplification with Phusion polymerase in the Gateway™ adapter PCRs** A standard annealing temperature of 50°C was used for the adapter PCR reactions.

Step	Cycles	Time	т (°С)
Initial denaturation	1	3 min	98
Denaturation		30 s	98
Annealing	30	30 s	50
Extension		1 min	72
Final Extension	1	10 min	72
Hold	1	~	4

A BP reaction was set up to transfer the PCR-generated GmPAPhy\_b construct to the pDONR 207 entry vector through the recombination of sites *att*B (PCR fragment) and *att*P (entry vector), as represented in Figure 73B. The reaction was set up with 2 µL of 50 ng µL<sup>-1</sup> pDONR 207, 1 µL of adapter 2 PCR product, 1 µL of BP Clonase<sup>™</sup> II Enzyme mix (Invitrogen) and 1 µL of 1x TE Buffer (10 mM Tris/HCl pH 8.0, 1 mM EDTA). The reaction was incubated for 2 h at 25°C in a thermal cycler (BIO-RAD). A volume of 0.5 µL of Proteinase K (Invitrogen) was mixed into the BP reaction for a 10 min incubation at 37°C, before transformation of the total volume of the reaction into 50 µL of DH5α Library Efficiency competent cells (Invitrogen). Protocol on **Chapter 3, section 3.1.1.3.** was followed for the transformation. Selection of colonies was performed in LB agar plates with gentamycin (20 µg mL<sup>-1</sup>). Analysis of transformants was first done by colony PCR with primers designed to amplify the *att*L recombination sites, followed by sequencing of one positive colony. Protocol on **Chapter 5, section 5.1.1.1.** was followed.

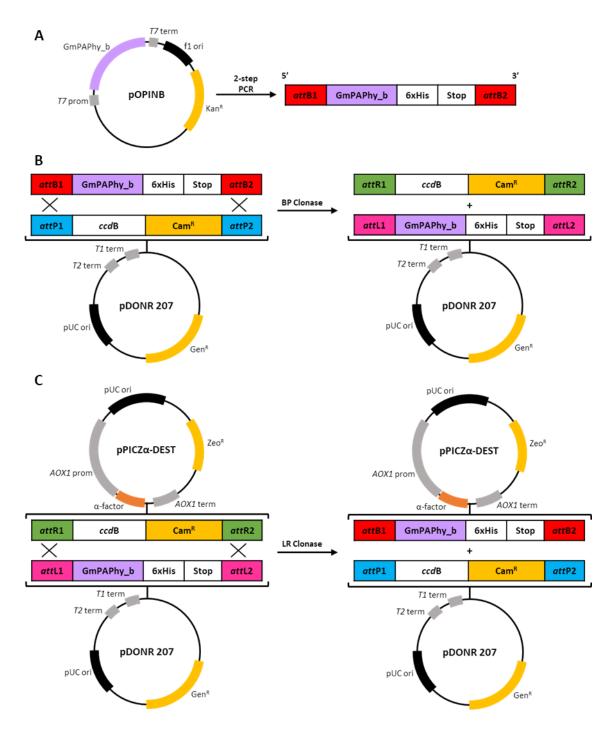


Figure 73. Gateway™ cloning of GmPAPhy\_b into pPICZα-DEST for expression in Pichia pastoris

(A) Two-step adapter PCR to introduce *att*B recombination sites, C-terminal 6xHis tag and stop codon in the GmPAPhy\_b sequence, using GmPAPhy\_b-pOPINB construct as template. (B) BP reaction to introduce the GmPAPhy\_b gene into the pDONR 207 entry vector through the recombination of *att*B and *att*P sites. (C) LR reaction to transfer the GmPAPhy\_b gene from the pDONR 207 entry vector to the pPICZ $\alpha$ -DEST destination vector through the recombination of *att*R sites.

A LR reaction was set up to transfer the GmPAPhy\_b construct from the pDONR 207 entry vector to the pPICZ $\alpha$ -DEST expression vector, through the recombination of sites *att*L (pDONR 207) and *att*R (pPICZ $\alpha$ -DEST), as represented in Figure 73C. The reaction was set up with 1 µL of 100 ng µL<sup>-1</sup> pPICZ $\alpha$ -DEST, 1 µL of 100 ng µL<sup>-1</sup> GmPAPhy\_b-pDONR207, 0.5 µL of LR Clonase<sup>TM</sup> II Enzyme mix (Invitrogen) and 2.5 µL of 1x TE Buffer (10 mM Tris/HCl pH 8.0, 1 mM EDTA). The same procedure described above for the BP reaction was followed for the LR reaction, performing the selection of transformants in LB agar plates with Zeocin<sup>TM</sup> (25 µg mL<sup>-1</sup>) and using primers designed to amplify the *att*B recombination sites for the colony PCR and sequencing.

## 6.1.3. Transformation, expression and purification of HvPAPhy\_a, OsPAPhy b, ZmPAPhy b and GmPAPhy b in *Pichia pastoris*

The transformation, expression and purification of HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b was performed as for WT TaPAPhy\_b2 enzyme and its three mutants. The four PAPhy-pPICZα constructs were transformed into the KM71H (*OCH1::G418R*) *Pichia pastoris* glycoengineered strain through electroporation following the protocol described for the WT TaPAPhy\_b2 construct in **Chapter 3, section 3.1.2.2.** Sufficient plasmid DNA of each construct for *P. pastoris* transformation was purified from 100 mL overnight cultures using the Plasmid Midi Kit (Qiagen). In preparation for *P. pastoris* transformation, pPICZα constructs were linearized with Dral (NEB) at 37°C overnight, setting up reactions as detailed in Table 23.

Reagent	[Stock]	[rxn]	V for 1x 20 µL rxn (µL)
Water	n/a	n/a	Variable*
CutSmart buffer	10x	1x	2
pPICZa construct	Variable*	500 ng µL <sup>-1</sup>	Variable*
Dral	20 U μL <sup>-1</sup>	1 U μL <sup>-1</sup>	1
TOTAL			20

(\*) Depending on the concentration of the plasmid stock used for each digestion.

Table 23. Reaction set up for the digestion of pPICZa vector with Dral

Six *P. pastoris* transformed colonies per PAPhy construct were subjected to a small volume expression trial in a 24-well plate. The selected colonies were monitored by pNPP assay for the production of secreted recombinant protein in 2 mL cultures during a five-day expression trial, consisting of one day of pre-growth in buffered

minimal glycerol medium (1.34% (w/v) yeast nitrogen base, 2% (w/v) casamino acids, 2% (v/v) glycerol, 100 mM phosphate buffer pH 5.0, 100  $\mu$ g mL<sup>-1</sup> kanamycin, 100  $\mu$ M zinc sulfate), followed by four days of expression in buffered minimal methanol medium (1.34% (w/v) yeast nitrogen base, 2% (w/v) casamino acids, 2% (v/v) methanol, 100 mM phosphate buffer pH 5.0, 100  $\mu$ g mL<sup>-1</sup> kanamycin, 100  $\mu$ M iron(II) sulfate, 100  $\mu$ M iron(III) citrate). For the expression of the PAPhy\_a isoform HvPAPhy\_a, 100  $\mu$ M manganese(II) sulfate and Complete Mini EDTA-free Protease inhibitor cocktail tablets (Roche) were also added to the buffered minimal methanol medium. The expression trial was set up and production of recombinant protein monitored as described for TaPAPhy\_b2 in **Chapter 3, section 3.1.2.3.** Cultures were topped up daily with 1% (v/v) methanol and the appropriate metals, as well as extra medium to compensate for loss by evaporation (approximately 100  $\mu$ L per day) and the samples taken to check for phosphatase activity. The highest expression, storing them at 4°C and -20°C in 1 M sorbitol and 10% (v/v) glycerol, respectively.

Expression of the plant PAPhy enzymes was performed in 100 mL of buffered minimal glycerol/methanol medium, distributed in 250 mL conical flasks with 50 mL per flaks, for five days under continuous shaking (200 rpm) at 26°C, adding 1% (v/v) methanol and the appropriate metals daily. The enzymes were harvested, purified by nickel-affinity chromatography and concentrated in the same way as the TaPAPhy\_b2 medium scale expression experiment described in **Chapter 3, sections 3.1.2.4.** and **3.1.2.5.** Individual 1 mL HisTrap HP columns (GE Healthcare) regenerated by stripping and recharging were used for the purification of each protein, at a flow rate of 1 mL min<sup>-1</sup>. All the columns were regenerated by stripping and recharging of metal ion according to the manufacturer's instructions before storage in 20% (v/v) ethanol at 4°C.

The nickel-affinity purified plant PAPhy enzymes were normalised to a working concentration of 20  $\mu$ M and stored in 20 mM Tris/HCl pH 8.0 buffer containing 30% (v/v) glycerol at -80°C.

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## 6.1.4. Phytase activity and HPLC product profiles of HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b

The phytase activity of HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b, alongside TaPAPhy\_b2, was assessed by means of a standard phosphate release assay in 0.2 M acetate pH 5.5 buffer with 5 mM potassium phytate ( $\geq$ 95% purity, Sigma) for 15 min at room temperature, as described in **Chapter 5, section 5.1.2.1.** Scouting assays with enzyme concentrations ranging in decades of concentration from 2  $\mu$ M to 10 nM were undertaken to evaluate differences in phytase activity of the four new enzymes with respect to TaPAPhy\_b2, setting up four replicates per enzyme concentration.

The product profiles of the five phytases were obtained as described in **Chapter 5, section 5.1.2.3.**, setting up reactions at room temperature in 0.2 M acetate pH 5.5 buffer with 1 mM sodium phytate ( $\geq$ 98% purity, Merck) as substrate. Enzyme concentrations used for the reactions ranged from 650 nM to 2  $\mu$ M.

### 6.2. Results and discussion

# 6.2.1. Protein homology modelling of plant PAPhy based on the TaPAPhy\_b2 structure

A very high conservation of the primary structure was observed for the plant PAPhy studied in this project (i.e. TaPAPhy\_a1, TaPAPhy\_b1, TaPAPhy\_b2, HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b). With sequence identities compared to TaPAPhy\_b2 ranging from 70 to 98%, the remaining plant PAPhy constituted ideal targets for 3D homology modelling.

The QMEAN scores of the 3D homology models generated for six plant PAPhy based on the TaPAPhy\_b2 structure are displayed in Table 24. According to the QMEAN scoring function, the six models generated were of good quality. A clear correlation between percentage of sequence identity and higher QMEAN score was observed, indicating that model quality improves as the sequence identity of the target protein with the template used to originate the model increases. The two metal ions in the active site were automatically modelled as irons for TaPAPhy\_a1, HvPAPhy\_a,

OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b. As a preference for Mn<sup>2+</sup> in the MII site has been reported for the PAPhy\_a isoforms (Dionisio *et al.*, 2011), the 3D models of TaPAPhy\_a1 and HvPAPhy\_a were modified accordingly. Only Fe<sup>3+</sup> in the MI site was automatically modelled in the TaPAPhy\_b1 active centre, due to the lack of conservation of one of the metal ligands in the MII site of TaPAPhy\_b2 described in **Chapter 2, section 2.2.1.2.** While PAPs in general present a histidine residue in PAP IV motif (His340 in the TaPAPhy\_b2 structure), a tyrosine residue appears in this position in the TaPAPhy\_b1 enzyme. This mutation would likely disrupt the PAP active site, indicating that an error in determining the amino acid sequence of TaPAPhy\_b1 at this position may have occurred.

QMEAN Enzyme % Sequence identity TaPAPhy\_a1 90.32 -0.68 TaPAPhy\_b1 98.42 -0.43 HvPAPhy\_a 90.91 -0.67 OsPAPhy\_b 88.51 -1.01 ZmPAPhy\_b 85.38 -0.84 GmPAPhy b 71.60 -1.74

The homology models were based on the TaPAPhy\_b2 structure in complex with phosphate resembling

 Table 24. Sequence identity and QMEAN scores of 3D homology models of plant PAPhy

product binding.

The conservation of active site residues of the six plant PAPhy analysed in comparison to TaPAPhy\_b2 is collated in **Appendix 2**, Table A19. Snapshots of the plant PAPhy active sites can be observed in Figure 74, highlighting the specific residues that were not conserved in each enzyme with respect to TaPAPhy\_b2 (Figure 74A). Aside from the metal ligand exception noted above, TaPAPhy\_b1 was identical to TaPAPhy\_b2 in all the residues studied and, therefore, the TaPAPhy\_b1 homology model was not included in the figure. TaPAPhy\_a1 (Figure 74C) showed conservation with the wheat PAPhy\_b isoforms in 16 of the 33 positions studied, while three more residues were conserved in HvPAPhy\_a (Figure 74D). Excluding the three extra residues in HvPAPhy\_a showing conservation with the wheat PAPhy\_b isoforms (i.e. Ser203, Thr215 and Ser221), the residues in the remaining 30 positions compared were conserved between TaPAPhy\_a1 and HvPAPhy\_a1, i.e. Cys203, Ala215 and Ala221 (appearing in place of Ser203, Thr215 and Ser221), were conserved in ZmPAPhy\_b (Figure 74F), indicating a

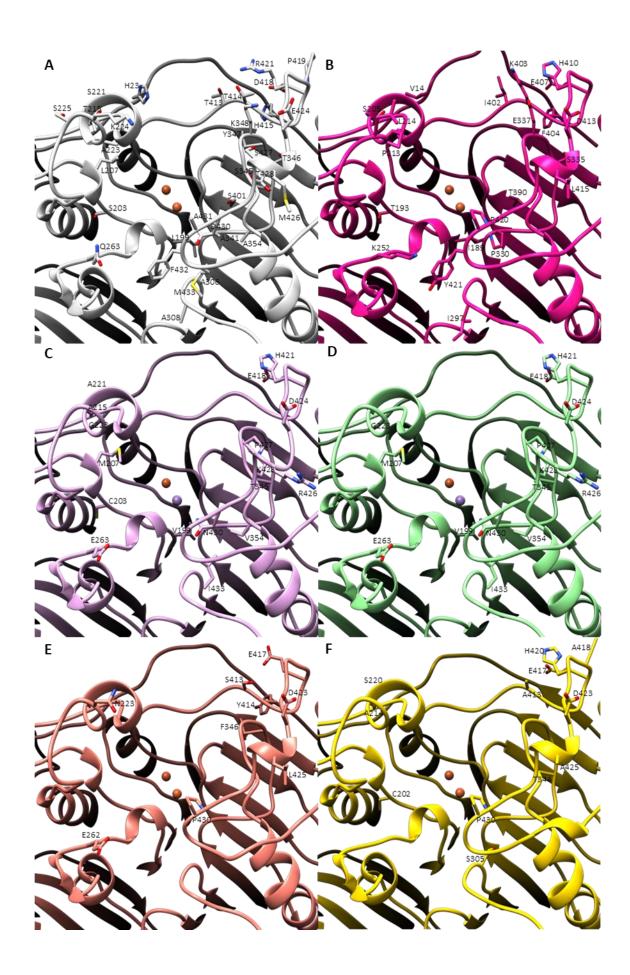
lack of correlation of these mutations with the PAPhy isoform. The ZmPAPhy\_b enzyme showed conservation with the wheat PAPhy\_b isoforms in 21 of the 33 amino acids compared, while 24 residues were conserved in the OsPAPhy\_b enzyme (Figure 74E). In contrast, only 11 residues out of the 33 compared were conserved in GmPAPhy\_b with respect to the wheat PAPhy\_b isoforms (Figure 74B).

Overall, no differences in the active site of the seven plant PAPhy compared seemed major enough to have a dramatic impact in their phytase activity, as the likely substrate specificity pockets proposed in **Chapter 4**, **section 4.2.2.4**. for TaPAPhy\_b2 remained mostly unaffected in the rest of the enzymes (see Figure 56). Differences in substrate specificity pocket amino acids were only observed in the PAPhy 5 motif located in the S<sub>c</sub> (2-phosphate) pocket, affecting residues Ala431 (proline in OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b), Phe432 (tyrosine in GmPAPhy\_b) and Met433 (isoleucine in TaPAPhy\_a1 and HvPAPhy\_a). Nevertheless, the contribution of these residues is believed to be through their amino groups rather than their side chain and, therefore, such changes were not expected to interfere.

In general, six consistent changes between PAPhy\_b and PAPhy\_a isoforms were observed among the seven enzymes analysed: L207M, A354V, S427P, T428K, D430N and M433I, with TaPAPhy\_b2 being the reference structure. Little difference was observed between TaPAPhy\_a1 and HvPAPhy\_a. In order to also take into account potential differences in phytase activity between PAPhy from different plant species, HvPAPhy\_a was chosen over TaPAPhy\_a1 for further experiments. GmPAPhy\_b was selected for activity assays for having the lowest conservation with TaPAPhy\_b2 in the active site and for being the only non-cereal PAPhy available for the project.

Figure 74. Differences in the plant PAPhy active centre with TaPAPhy\_b2 as reference structure (on the next page)

The TaPAPhy\_b2 structure and the plant PAPhy 3D models are displayed in cartoon representation, with metal ions shown as spheres and coloured by element (i.e. Fe, brown; Mn, lilac). Residues that are not conserved in one or more of the enzymes analysed with respect to TaPAPhy\_b2 are shown as sticks, coloured by element and labelled. Images created with the UCSF Chimera package (Pettersen *et al.*, 2004). (A) TaPAPhy\_b2. (B) GmPAPhy\_b. (C) TaPAPhy\_a1. (D) HvPAPhy\_a. (E) OsPAPhy\_b. (F) ZmPAPhy\_b.



Changes in ten positions with potential interest were observed between the six cereal PAPhy and GmPAPhy\_b: (1) His23 to Val14 in PAPhy 1 motif; (2) Ala/Gly223 to Pro213, (3) Lys/Asn224 to Leu214 and (4) Ser225 to deletion, corresponding to the region in PAPhy 4 motif before His229 (S<sub>B</sub> pocket); (5) Gln/Glu263 to Lys252, a residue near His229 in the PAPhy structures; (6) Lys348 to Glu337, a residue which mutation to alanine in the TaPAPhy\_b2 enzyme results in lower substrate affinity; (7) Thr413 to Ile402 and (8) Thr/Ser/Ala414 to Lys403, residues near Lys410 (S<sub>E</sub> and S<sub>F</sub> pocket) in the PAPhy structures and described as a phosphate binding site (TaPAPhy\_b2:PO<sub>4</sub> complex structures in **Chapter 4, section 4.2.1.1. and 4.2.1.4.**); (9) Ala431 to Pro420 and (10) Phe432 to Tyr421, residues belonging to PAPhy 5 motif in the S<sub>C</sub> specificity pocket. In addition, ZmPAPhy\_b and OsPAPhy\_b were both selected for expression and activity assays, for presenting some unique mutations in the positions analysed and for being from different plant species.

# 6.2.2. Gateway<sup>™</sup> cloning of soybean PAPhy for expression in *Pichia pastoris*

The rare codon analysis carried for the GmPAPhy\_b sequence, codon optimised for *E. coli* expression, predicted a chance of poor expression of recombinant protein in *Pichia pastoris* due to a Codon Adaptation Index (CAI) of 0.61. The CAI is a common measure of codon usage bias, useful to predict the likely success of heterologous gene expression (Sharpl and Li, 1987). A protein coding gene with a CAI bigger than 0.8 is considered good for expression in the desired host, with 1.0 being the ideal value. However, an even lower CAI of 0.52 was obtained when the same analysis was performed on the TaPAPhy\_b2-pGAPZαA sequence. Despite no codon optimisation for *P. pastoris* expression had been carried out for TaPAPhy\_b2, good levels of expression were achieved from this construct and, therefore, expression of GmPAPhy\_b in *P. pastoris* was attempted with the current sequence.

The GmPAPhy\_b gene with a C-terminal 6xHis tag, a stop codon and the flanking *att*B recombination sites was successfully amplified in a two-step PCR (Figure 75). The PCR product of the adapter 2 PCR amplified from a 1:20 dilution of the adapter 1 PCR product was chosen to carry out the BP reaction with pDONR 207.

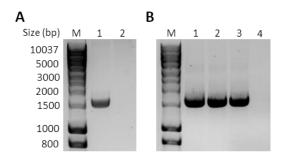


Figure 75. Adapter PCRs for the Gateway™ cloning of GmPAPhy\_b into pPICZα-DEST

Results of the two adapter PCRs in 1% (w/v) agarose gels. 5  $\mu$ L samples mixed with 6x Purple Loading Dye (NEB) were loaded. Lane M, HyperLadder 1kb DNA standards (Bioline). (A) Lane 1, adapter 1 PCR product (1541 bp); lane 2, attB1\_GmPAPhy-F1 and CHis\_GmPAPhy-R1 primers negative control. (B) Lane 1, adapter 2 PCR product (1548 bp) with undiluted adapter 1 PCR product as template; lane 2, adapter 2 PCR product (1548 bp) with 1:20 dilution of adapter 1 PCR product as template; lane 3, adapter 2 PCR product (1548 bp) with 1:50 dilution of adapter 1 PCR product as template; lane 4, attB1 and CHis-attB2-pPICZ primers negative control.

Several colonies resulting from the transformation of the BP reaction into *E. coli* DH5 $\alpha$  Library Efficiency competent cells were observed after gentamycin selection in LB agar plates (and no colonies in the negative control plate). Two of the four colonies tested by colony PCR presented bands corresponding to the GmPAPhy\_b insert (Figure 76A). Sequencing of the plasmid extracted from the first of these colonies confirmed the successful cloning of GmPAPhy\_b into pDONR 207 and was subjected to the LR reaction with pPICZ $\alpha$ -DEST.

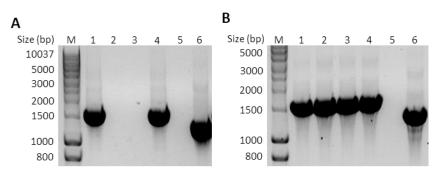


Figure 76. Colony PCRs from the Gateway™ cloning of GmPAPhy\_b into pPICZα-DEST

Results from the two colony PCRs in 1% (w/v) agarose gels. 5  $\mu$ L samples of each PCR product were loaded. Lane M, HyperLadder 1kb DNA standards (Bioline). (**A**) GmPAPhy\_b-pDONR207 colony PCR. Lane 1, colony 1; lane 2, colony 2; lane 3, colony 3; lane 4, colony 4; lane 5, SeqLA and SeqLB primers negative control; lane 6, positive control. (**B**) GmPAPhy\_b-pPICZ $\alpha$ -DEST colony PCR. Lane 1, colony 1; lane 2, colony 2; lane 3, colony 4; lane 5, attB1 and attB2 primers negative control; lane 6, positive control.

Several colonies were also observed as a result of the transformation of the LR reaction into *E. coli* DH5α Library Efficiency competent cells after Zeocin<sup>™</sup> selection. All

the colonies tested by colony PCR displayed bands corresponding to the GmPAPhy\_b insert (Figure 76B). Further confirmation by sequencing of the plasmid extracted from the first of the colonies indicated the successful cloning of the gene encoding the GmPAPhy\_b phytase into pPICZ  $\alpha$ -DEST.

# 6.2.3. Transformation, expression and purification of HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b in *Pichia pastoris*

Complete linearization of the four plant PAPhy constructs was achieved by digestion with Dral (Figure 77). The four linearized constructs were successfully transformed by electroporation into freshly prepared KM71H (*OCH1::G418R*) *Pichia* competent cells with similar efficiency, showing single colonies in all the transformation plates after three days of incubation. Six of the biggest colonies (i.e. highest resistance to Zeocin<sup>™</sup>) were selected for each PAPhy and transferred to fresh YPD agar plates, showing optimal growth levels to initiate expression trials after three days of incubation. The production of recombinant proteins in the culture media during the course of the expression trial was monitored by the presence of phosphatase activity against pNPP. As the activity assay was carried out for colony screening and no with quantification purposes, a pNP calibration curve was not included and the results were 'quantified' in absorbance units.

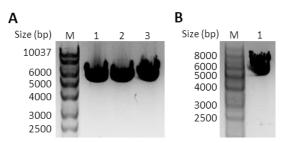


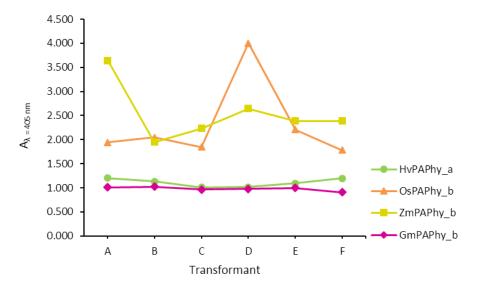
Figure 77. Digestion of PAPhy in pPICZ $\alpha$  constructs with Dral

1% (w/v) agarose gels showing complete linearization of PAPhy-pPICZ $\alpha$  constructs by digestion with Dral in preparation for *Pichia pastoris* transformation. Lane M, HyperLadder 1kb DNA standards (Bioline). (A) Lane 1, linearized HvPAPhy\_a-pPICZ $\alpha$ A; lane 2, linearized OsPAPhy\_b-pPICZ $\alpha$ A; lane 3, linearized ZmPAPhy\_b-pPICZ $\alpha$ A. (B) Lane 1, linearized GmPAPhy\_b-pPICZ $\alpha$ -DEST.

Figure 78 shows the phosphatase activity against pNPP and, therefore, the expression levels for the six transformants of each enzyme, on the last day of the trial. Activity of recombinant OsPAPhy\_b, ZmPAPhy\_b and the TaPAPhy\_b2 control was

detected after one day of expression, and the expression patterns for each transformant were consistent across the duration of the trial. All transformants of HvPAPhy\_a and GmPAPhy\_b displayed phosphatase activity levels similar or only slightly higher than the untransformed strain control across the duration of the trial, indicating poor expression of these enzymes in *Pichia pastoris* in the conditions tested.

Transformants OsPAPhy\_b-D and ZmPAPhy\_b-A displayed the highest expression levels of recombinant protein and, hence were selected to produce proteins for phytase activity assays. Transformants HvPAPhy\_a-A and GmPAPhy\_b-B were also selected to attempt to obtain recombinant material of these enzymes in a medium scale expression trial.



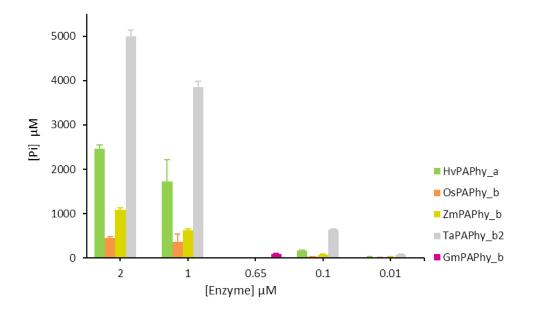
**Figure 78. Enzyme activity screen of plant PAPhy expression in** *P. pastoris* **KM71H** (*OCH1::G418R*) Phosphatase activity measured on the fifth day of the expression trial is displayed for six individual transformants of each of the four plant PAPhy enzymes.

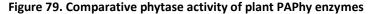
Recombinant expression of HvPAPhy\_a, OsPAPhy\_b and ZmPAPhy\_b was achieved from 100 mL of *P. pastoris* KM71H (*OCH1::G418R*) culture media. The enzymes were purified by nickel-affinity chromatography with a yield of 1.7 mg L<sup>-1</sup> for HvPAPhy\_a, 6.7 mg L<sup>-1</sup> for OsPAPhy\_b and 14.1 mg L<sup>-1</sup> for ZmPAPhy\_b. With the same expression conditions and purification method, an approximate yield of only 141  $\mu$ g L<sup>-1</sup> was achieved for GmPAPhy\_b.

## 6.2.4. Phytase activity and HPLC product profiles of HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b

Activity against InsP<sub>6</sub> was observed for all the plant PAPhy purified (Figure 79). TaPAPhy\_b2 was included in the assay to serve as reference of activity, displaying significantly higher phytase activity than the other enzymes tested. The relative activity of HvPAPhy\_a was 49% and 45% at enzyme concentrations of 2  $\mu$ M and 1  $\mu$ M, respectively. The relative activity of OsPAPhy\_b was 9% both at 2  $\mu$ M and 1  $\mu$ M concentration. ZmPAPhy\_b relative activity was 22% and 16% when tested at concentrations of 2  $\mu$ M and 1  $\mu$ M, respectively. The enzyme concentrations 100 nM and 10 nM were considered too low for the detection limits of the assay.

Due to the low recovery yield of recombinant GmPAPhy\_b, phytase activity for this enzyme was only tested at one concentration, approximately 650 nM, and setting up reactions in duplicate. Although very low, phytase activity in the presence of GmPAPhy\_b was detected over the InsP<sub>6</sub> background absorbance, equivalent to approximately 3.6% of the predicted TaPAPhy\_b2 activity at the same concentration.





Phosphate release assay with 5 mM  $InsP_6$  as substrate in 0.2 M acetate buffer pH 5.5 for 15 min at room temperature. The average phosphate concentration released as a measure of phytase activity of four replicate reactions with decreasing enzyme concentrations is displayed. Error bars represent the standard deviation of the four replicates. A unique concentration with two replicate reactions was assayed for GmPAPhy\_b.  $InsP_6$  background absorbance was subtracted from the measurements. 'Pi', inorganic phosphate.

Product profiles resulting from InsP<sub>6</sub> degradation by the recombinant plant PAPhy enzymes are shown in Figure 80 (TaPAPhy\_b2), Figure 81 (HvPAPhy\_a), Figure 82 (ZmPAPhy\_b), Figure 83 (OsPAPhy\_b) and Figure 84 (GmPAPhy\_b). Background InsP<sub>6</sub> control reactions in the absence of enzyme were set up in parallel for the identification of contaminant peaks not resulting from enzymatic hydrolysis. Product profiles of recombinant TaPAPhy\_b2 were obtained again alongside the remaining PAPhy for comparison. The InsP<sub>6</sub> product profile obtained for TaPAPhy\_b2 assayed at 1  $\mu$ M concentration for 15 and 30 min reaction was consistent with the results presented in **Chapter 5, section 5.2.2.2.** However, the possibility of TaPAPhy\_b2 presenting marginal D-1 and/or D-3 phytase activity was discarded, as the peak for D-Ins(2,3,4,5,6)P<sub>5</sub> and/or its enantiomer D-Ins(1,2,4,5,6)P<sub>5</sub> observed in the enzyme's product profile was also present in the InsP<sub>6</sub> non-enzyme control (Figure 80).

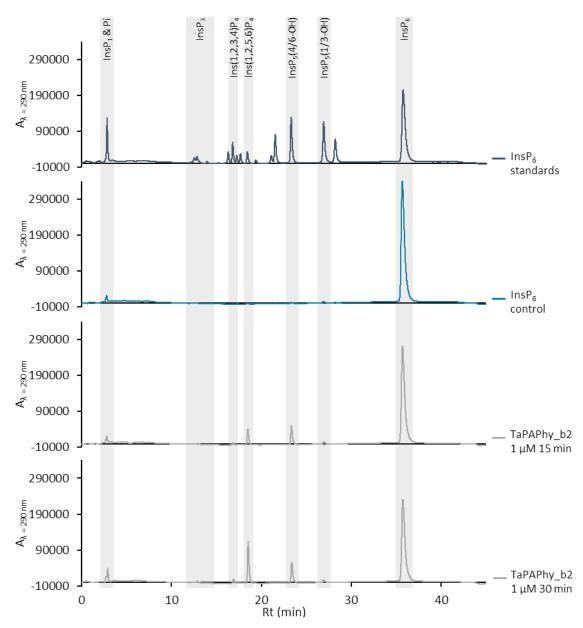


Figure 80. Product profile of TaPAPhy\_b2 after limited and progressive reaction against InsP<sub>6</sub>

Reactions were performed for 15 and 30 min at room temperature with 1 mM InsP<sub>6</sub> substrate and 1  $\mu$ M enzyme in 0.2 M acetate buffer pH 5.5. A control reaction in the absence of enzyme was included. An acid hydrolysate of InsP<sub>6</sub> with relevant peaks labelled for reference is shown (InsP<sub>5</sub>s are identified by the residual hydroxyl). 'Rt', retention time.

The same intermediates of  $InsP_6$  hydrolysis as in the TaPAPhy\_b2 reactions were obtained in reactions performed with 1 µM HvPAPhy\_a (Figure 81). It was also noted that, despite HvPAPhy\_a displaying lower phytase activity than TaPAPhy\_b2 in the phosphate release assay (Figure 79), higher levels of  $InsP_6$  hydrolysis were observed for HvPAPhy\_a in the HPLC product profile experiment under the same reaction conditions.

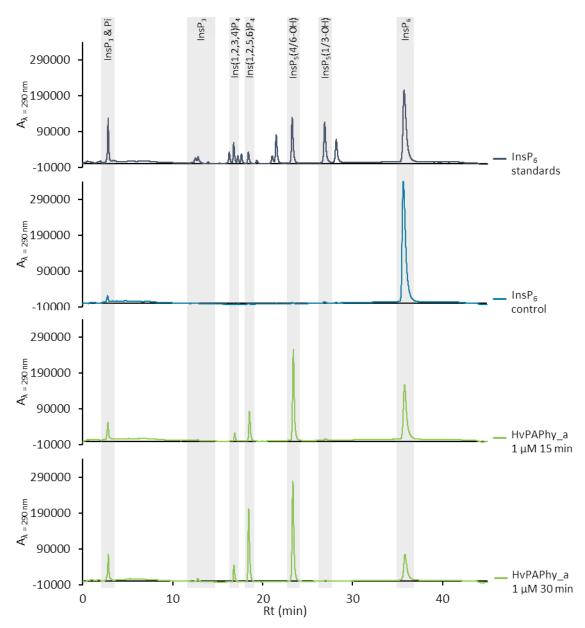


Figure 81. Product profile of HvPAPhy\_a after limited and progressive reaction against InsP<sub>6</sub>

Reactions were performed for 15 and 30 min at room temperature with 1 mM InsP<sub>6</sub> substrate and 1  $\mu$ M enzyme in 0.2 M acetate buffer pH 5.5. A control reaction in the absence of enzyme was included. An acid hydrolysate of InsP<sub>6</sub> with relevant peaks labelled for reference is shown (InsP<sub>5</sub>s are identified by the residual hydroxyl). 'Rt', retention time.

A higher enzyme concentration (2  $\mu$ M) and longer reaction time (2 h) were needed in order to obtain a product profile of InsP<sub>6</sub> hydrolysis for the ZmPAPhy\_b enzyme. Despite its lower phytase activity, the profile of InsP<sub>6</sub> degradation obtained for ZmPAPhy\_b displayed the same intermediates as TaPAPhy\_b2 and HvPAPhy\_a (Figure 82).

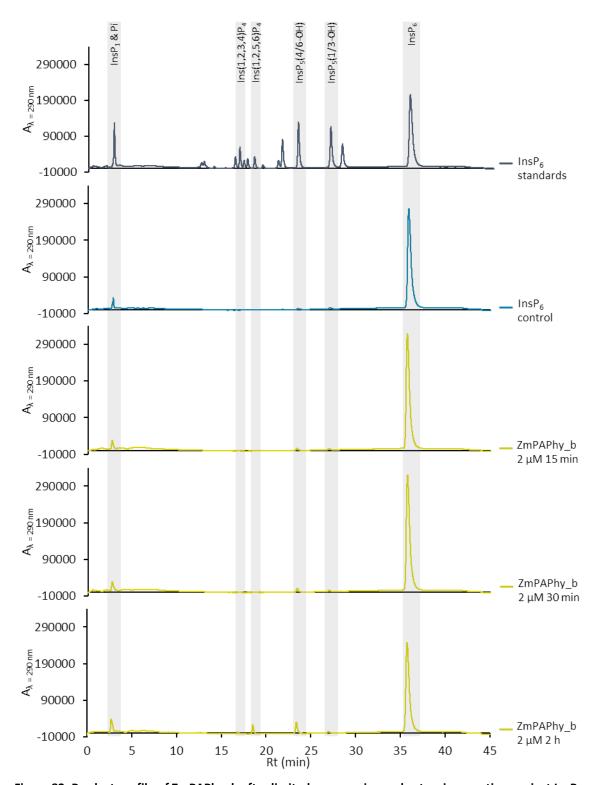


Figure 82. Product profile of ZmPAPhy\_b after limited, progressive and extensive reaction against InsP<sub>6</sub> Reactions were performed for 15 min, 30 min and 2 h at room temperature with 1 mM InsP<sub>6</sub> substrate and 2  $\mu$ M enzyme in 0.2 M acetate buffer pH 5.5. A control reaction in the absence of enzyme was included. An acid hydrolysate of InsP<sub>6</sub> with relevant peaks labelled for reference is shown (InsP<sub>5</sub>s are identified by the residual hydroxyl). 'Rt', retention time.

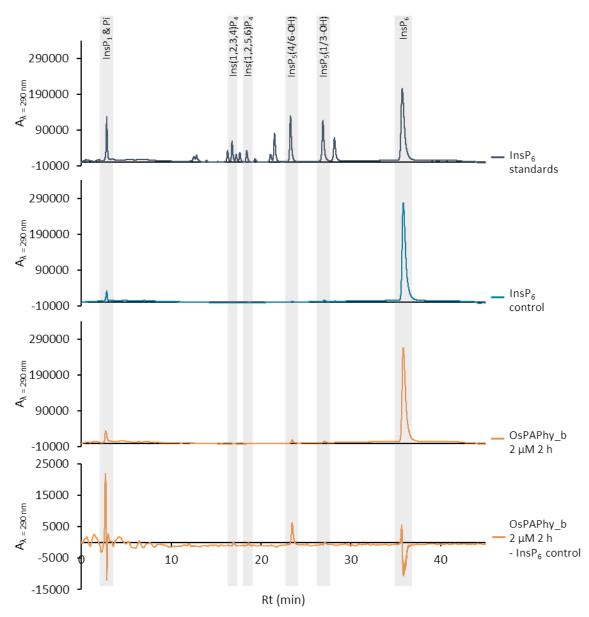


Figure 83. Product profile of OsPAPhy\_b after extensive reaction against InsP<sub>6</sub>

Reactions were performed for 2 h at room temperature with 1 mM InsP<sub>6</sub> substrate and 2  $\mu$ M enzyme in 0.2 M acetate buffer pH 5.5. A control reaction in the absence of enzyme was included. The absorbance of the 1 mM InsP<sub>6</sub> control reaction was subtracted from the OsPAPhy\_b reaction for peak identification. An acid hydrolysate of InsP<sub>6</sub> with relevant peaks labelled for reference is shown (InsP<sub>5</sub>s are identified by the residual hydroxyl). 'Rt', retention time.

OsPAPhy\_b had to be assayed in the same conditions as ZmPAPhy\_b, at a concentration of 2  $\mu$ M and with a reaction time of 2 h. However, this enzyme displayed such a low activity even in these conditions that accurate peak identification proved challenging. However, after subtraction of the InsP<sub>6</sub> non-enzyme control absorbance, it was possible to identify again a clear D-4 and/or D-6 phytase activity for the rice phytase, together with very subtle peaks starting to appear which correspond to the same InsP<sub>4</sub> intermediates generated by the previously characterised PAPhy (Figure 83).

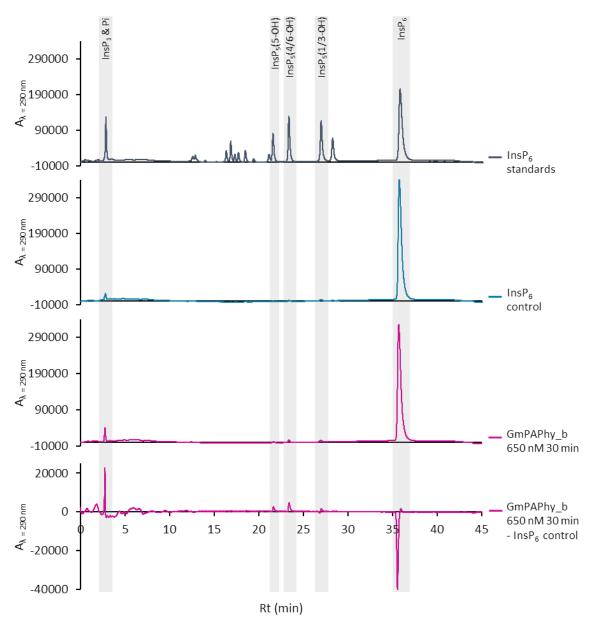


Figure 84. Product profile of GmPAPhy\_b after progressive reaction against InsP<sub>6</sub>

Reactions were performed for 30 min at room temperature with 1 mM InsP<sub>6</sub> substrate and 650 nM enzyme in 0.2 M acetate buffer pH 5.5. A control reaction in the absence of enzyme was included. The absorbance of the 1 mM InsP<sub>6</sub> control reaction was subtracted from the GmPAPhy\_b reaction for peak identification. An acid hydrolysate of InsP<sub>6</sub> with relevant peaks labelled for reference is shown (InsP<sub>5</sub>s are identified by the residual hydroxyl). 'Rt', retention time.

The HPLC assays carried out with GmPAPhy\_b were limited by the scarce recombinant protein produced. GmPAPhy\_b was assayed at the highest concentration available, approximately 650 nM, and product profiles of InsP<sub>6</sub> hydrolysis were obtained after 15 and 30 min reactions (Figure 84). The phytase activity displayed was too low for accurate peak identification, and there was not enough recombinant enzyme left to set up a longer reaction. Nevertheless, after subtraction of the InsP<sub>6</sub> non-enzyme control absorbance, it was possible to identify three distinct InsP<sub>5</sub> peaks. These peaks suggest

that the GmPAPhy\_b enzyme can initiate InsP<sub>6</sub> hydrolysis by attack of the usual D-4 (and/or D-6) phosphate, but also by attack of the D-1 (and/or D-3) phosphate and the 5-phosphate of the inositol ring, making it more promiscuous than the other plant PAPhy tested above.

### 6.3. Conclusions

Recombinant versions of five plant PAPhy enzymes have been produced in Pichia *pastoris* in this project. Expression and purification under the described conditions only produced a good yield of TaPAPhy b2. Nevertheless, even lower yields have been reported previously (Dionisio et al., 2011). The low expression levels of HvPAPhy a can be explained by our collaborators experience that PAPhy a isoforms are attacked by Pichia pastoris endogenous proteases (unpublished data). Protease inhibitors were added to the culture media in an attempt to improve the yield of recombinant HvPAPhy a, but this proved to be an insufficient measure. Another factor influencing the HvPAPhy a expression levels could be the metal preference of this enzyme. A preference for manganese in the MII site has been described for PAPhy a isoforms (Dionisio et al., 2011). Both iron(II) and manganese(II) sources were provided in the culture media for the expression of HvPAPhy a in Pichia pastoris, following our collaborators advice that P. pastoris has been observed to be less efficient in incorporating manganese than iron into metalloproteins and, therefore, providing an alternative metal source would be beneficial for the expression of these enzymes (unpublished data). In general, optimisation of the expression and purification conditions of each individual PAPhy may result in better yields of recombinant protein.

HvPAPhy\_a, OsPAPhy\_b, ZmPAPhy\_b and GmPAPhy\_b displayed lower levels of phytase activity than TaPAPhy\_b2 when tested in phosphate release assays. However, it is worth to point out that all the enzymes were assayed at pH 5.5, the optimum for TaPAPhy\_b2 activity, and a full characterisation of the remaining plant PAPhy would help to identify optimal assay conditions for each enzyme that may improve their activity. HvPAPhy\_a, OsPAPhy\_b and ZmPAPhy\_b resulted in the same product profile of InsP<sub>6</sub> hydrolysis than that described for TaPAPhy\_b2 in **Chapter 5**. Despite some consistent amino acid variations between the active sites of the PAPhy\_a and the PAPhy\_b isoforms, all the plant PAPhy from cereal sources assayed in this work presented the same phytate degradation profile, regardless of the plant species or the enzyme isoform.

Despite the limited recombinant protein available to test the phytase activity of GmPAPhy b, it was possible to determine that this enzyme appears to show positional promiscuity in the first step of phytate hydrolysis as opposed to the conserved D-4/6-phytase activity displayed by the PAPhy from cereal sources, generating up to three different InsP<sub>5</sub> intermediates in similar proportions. Such a profile of phytate degradation is reminiscent of that arising from MINPP phytase activity, known for their positional promiscuity towards InsP<sub>6</sub> hydrolysis (Craxton *et al.*, 1997; Stentz *et al.*, 2014). A conclusive explanation for the soybean phytase positional promiscuity was not found in the structure analysis performed in this chapter. The residues proposed to form the substrate specificity pockets in TaPAPhy\_b2 (see Chapter 4, Figure 56) are all conserved in GmPAPhy\_b with the exception of Ala431 (Pro420 in soybean, but also in rice and maize phytases) and Phe432 (Tyr421 exclusively in the soybean phytase). Both amino acids form part of the PAPhy 5 short  $\alpha$ -helix in the S<sub>c</sub> pocket (2-phosphate), believed to contribute to InsP<sub>6</sub> binding through their amino groups rather than through side chain interactions. Differences are also observed in the PAPhy 4  $\alpha$ -helix (S<sub>D</sub>, 1-phosphate pocket), but the unconserved residues in GmPAPhy\_b are at the other end of the  $\alpha$ -helix of those identified in TaPAPhy b2 as contributors to the specificity pocket. The PAPhy 4  $\alpha$ -helix in TaPAPhy b2 is formed by residues Try218-Ser219-Cys220-Ser221-Phe222-Ala223-Lys224-Ser225, while GmPAPhy\_b contains Try208-Ser209-Cys210-Ser211-Phe212-Pro213-Leu214-deletion. In addition, the soybean phytase has a glutamate residue in the position of Lys348, a residue that when mutated to alanine in the wheat phytase is largely indistinguishable from the WT except with regards to affinity for phytate (see **Chapter 5**). Optimisation of the expression and purification of GmPAPhy b would be necessary to perform in-depth studies that may allow for conclusive findings with regards to the particular activity and structure features of this enzyme. In addition,

other PAPhy from non-cereal plant species could be subjected to a similar analysis, in order to determine if the GmPAPhy\_b characteristics are conserved in other plant phytases from the PAP class.

## **Chapter 7.** General conclusion and future work

This thesis presents the results of structure-function studies of phytases of the purple acid phosphatase class. Phytases are considered one of the most effective and lucrative additives in the animal feed industry due to their role in improving animal nutrition and preventing environmental pollution, as well as having additional industrial applications in food or biofuel production (Rebello *et al.*, 2017). Consequently, they are the focus of extensive research, with efforts directed to the discovery of novel phytases or to the improvement of the characteristics of existing ones (Lei *et al.*, 2013). Of the four structural classes of phytases, HAPhy are the subject of most of the progress achieved in phytase research, with the PAPhy being very much at the other end of the spectrum.

This thesis presents for the first time the crystal structure of a purple acid phytase, that of the wheat TaPAPhy\_b2 enzyme, together with a model of the enzyme-substrate complex revealing the residues contributing to its substrate specificity pockets. Furthermore, the multiple structures of TaPAPhy\_b2 in complex with phosphate solved by X-ray crystallography provide new insights to the PAP catalytic mechanism (Schenk *et al.*, 2008), by delivering snapshots of the substrate- and product-bound forms, and that of the complex during enzyme regeneration (states **c**, **e** and **f-g** in Figure 12).

Maximum phytase activity at pH 5.5 and 37°C, with thermal denaturation just over 50°C, have also been determined through the full characterisation of this enzyme, indicating that TaPAPhy\_b2 is an acid phytase moderately sensitive to thermal deactivation. The reaction intermediates identified in this project for the hydrolysis of InsP<sub>6</sub> by the TaPAPhy\_b2 phytase indicate the production of D/L-Ins(1,2,3,5,6)P<sub>5</sub> as first product and only InsP<sub>5</sub>, followed by rapid accumulation of D/L-Ins(1,2,5,6)P<sub>4</sub> with some D/L-Ins(1,2,3,4)P<sub>4</sub> and slower progression to lower inositol phosphates. Therefore, the hydrolysis of phytate by TaPAPhy\_b2 starts with the attack of the D-4 or D-6-phosphate and progresses through sequential attack to the D-3 or D-1-phosphate in a major route, or through a minor route attacking the 5-phosphate. Since the technique used in this work does not resolve enantiomers of InsP, it is not possible to conclude whether the first attack to InsP<sub>6</sub> happens at the D-4 or D-6-phosphate on the basis of the obtained product profile alone. However, earlier studies of the InsP<sub>6</sub> hydrolysis pathway by reaction with wheat phytases, in which the enantiomers of InsP were resolved, have determined that the initial attack occurs at the phosphate in the D-4 position (Tomlinson and Ballou, 1962; Lim and Tate, 1971, 1973). A finding of this project that would be in agreement with this specificity is the interaction between the axial 2-phosphate and a region with short  $\alpha$ -helical conformation observed when the D-4-phosphate is placed for InsP<sub>6</sub> hydrolysis in the TaPAPhy\_b2 active centre (specificity pocket S<sub>A</sub>, Figure 56), absent when the D-6-phosphate is the scissile phosphate instead. In conclusion, the enzyme-substrate complexes generated through computer simulations in this thesis, together with earlier studies of wheat phytases, may point to the D-4-phosphate over the D-6-phosphate as preferred initiation site of InsP<sub>6</sub> hydrolysis by the wheat TaPAPhy\_b2 enzyme.

Although TaPAPhy\_b2 is the main subject of this project and a need for optimisation of the expression and purification process for other PAPhy has been identified in order to obtain good yields of recombinant protein, preliminary work has been achieved with four more plant PAPhy. The data obtained points to a conserved phytate hydrolysis pathway in the cereal PAPhy, while positional promiscuity such as the MINPP enzymes appears to be displayed by the soybean PAPhy (Craxton *et al.*, 1997; Stentz *et al.*, 2014).

The findings in this thesis regarding TaPAPhy\_b2 do not appear to be compatible with direct applications of this enzyme in animal feed supplementation, implying a need to engineer thermal stability and higher catalytic efficiency in the wheat PAPhy for such purpose (Rebello *et al.*, 2017). The structural information, optimised computer simulation parameters, conditions for phytase activity, product profile and DSC assays achieved in this work may provide useful tools that can be employed in the future to improve PAPhy enzymes for potential industrial applications. In general, the work performed on this project provides a strong basis for further investigation of phytase activity of enzymes of the PAPhy class, either from plant enzymes such as those studied in this thesis, or by using the information acquired to pursue the finding of novel targets in other organisms.

Improving the fully characterised wheat PAPhy, other plant PAPhy enzymes or potential novel candidates in different organisms, may result in proteins suitable to be used as feed additives either alone or in conjunction with other phytases.

# Appendix 1. Tables and figures from Chapter 2

#### Table A1. Purple acid phosphatase sequences used in bioinformatics analysis

Collection of the purple acid phosphatase sequences, with and without phytase activity, that were analysed in **Chapter 2**. PAPhy, pink shading. Plant PAPs, lilac shading. Animal PAPs, orange shading. Microalgal PAPs, green shading. Fungal PAPs, yellow shading. Bacterial PAPs, blue shading. Sequences excluded during the analysis, red shading. 'n/a', not applicable. PAPhy sequences are separated in characterised (PAPhy), predicted by sequence homology (Predicted PAPhy) and sequence outliers (PAPhy outlier). Plant and animal PAP sequences are separated in HMW and LMW.

Name	Organism	Group	Alternative names	UniProt ID
AtPAP15	Arabidopsis thaliana	PAPhy	n/a	Q9SFU3
GmPAPhy_b	Glycine max	PAPhy	GmPhy	Q93XG4
HvPAPhy_a	Hordeum vulgare	PAPhy	(Hv)P2	C4PKL2
HvPAPhy_b1	Hordeum vulgare	PAPhy	(Hv)P1	C4PKL3
HvPAPhy_b2	Hordeum vulgare	PAPhy	(Hv)P1	C4PKL4
LaPAPhy	Lupinus albus	PAPhy	LASAP3	D2YZL4
MtPAPhy	Medicago truncatula	PAPhy	MtPHY1	Q3ZFI1
NtPAPhy	Nicotiana tabacum	PAPhy	NtPAP	A5YBN1
OsPAPhy_b	Oryza sativa	PAPhy	(Os)F1, (Os)F2, OsPAP5	D6QSX9
PtPAP3	Poncirus trifoliata	PAPhy	n/a	V9LXK5
TaPAPhy_a1	Triticum aestivum	PAPhy	(Ta)PHYI	С4РКК7
TaPAPhy_b1	Triticum aestivum	PAPhy	n/a	С4РКК9
TaPAPhy_b2	Triticum aestivum	PAPhy	n/a	C4PKL0
ZmPAPhy_b	Zea mays	PAPhy	n/a	C4PKL6
AtaPAPhy_a1	Aegilops tauschii	Predicted PAPhy	n/a	F6MIX0
AtaPAPhy_b1	Aegilops tauschii	Predicted PAPhy	n/a	F6MIX1
PvPAPhy	Phaseolus vulgaris	Predicted PAPhy	n/a	V7B3Z4
ScPAPhy_a1	Secale cereale	Predicted PAPhy	n/a	F6MIX2
ScPAPhy_a2	Secale cereale	Predicted PAPhy	n/a	F6MIX4
ScPAPhy_b1	Secale cereale	Predicted PAPhy	n/a	F6MIX5
TaPAPhy_a2	Triticum aestivum	Predicted PAPhy	(Ta)PHYII	С4РКК8
TaPAPhy_a3	Triticum aestivum	Predicted PAPhy	n/a	F6MIW2
TaPAPhy_b3	Triticum aestivum	Predicted PAPhy	n/a	F6MIW6
TmPAPhy_a1	Triticum monococcum	Predicted PAPhy	n/a	F6MIW8
TmPAPhy_b1	Triticum monococcum	Predicted PAPhy	n/a	F6MIW9
VrPAPhy	Vigna radiata	Predicted PAPhy	VrPAP1	B5ARZ7
AtPAP23	Arabidopsis thaliana	PAPhy outlier	AtPAP_c	Q6TPH1
GmPAP4	, Glycine max	, PAPhy outlier	n/a	V9HXG4
AcPAP	Allium cepa	HMW Plant PAP	ACPEPP	Q93WP4
AIPAP15	Arabidopsis lyrata	HMW Plant PAP	n/a	D7L636
AoPAP32	Anchusa officinalis	HMW Plant PAP	n/a	Q9XF09
AtPAP10	Arabidopsis thaliana	HMW Plant PAP	n/a	Q9SIV9
AtPAP11	Arabidopsis thaliana	HMW Plant PAP	n/a	Q95I18
AtPAP12	Arabidopsis thaliana	HMW Plant PAP	n/a	Q38924
AtPAP13	Arabidopsis thaliana	HMW Plant PAP	n/a	048840
AtPAP20	Arabidopsis thaliana	HMW Plant PAP	n/a	Q9LXI7
AtPAP21	Arabidopsis thaliana	HMW Plant PAP	n/a	Q9LXI4
AtPAP22	Arabidopsis thaliana	HMW Plant PAP	n/a	Q8S340
AtPAP25	Arabidopsis thaliana	HMW Plant PAP	ll/d	023244
AtPAP25 AtPAP26	Arabidopsis thaliana Arabidopsis thaliana		n/a n/a	
AtPAP25 AtPAP26 AtPAP5	Arabidopsis thaliana Arabidopsis thaliana Arabidopsis thaliana	HMW Plant PAP HMW Plant PAP HMW Plant PAP	n/a n/a	Q949Y3 Q9C927

Name	Organism	Group	Alternative names	UniProt ID
GmPAP1	Glycine max	HMW Plant PAP	n/a	Q09131
GmPAP3	Glycine max	HMW Plant PAP	n/a	Q6YGT9
HvPAP_c	Hordeum vulgare	HMW Plant PAP	n/a	C4PKL5
IbPAP1	Ipomoea batatas	HMW Plant PAP	SpPAP2	Q9SE00
IbPAP2	Ipomoea batatas	HMW Plant PAP	SpPAP3	Q9SDZ9
IbPAP3	Ipomoea batatas	HMW Plant PAP	SpPAP1	Q9ZP18
LaAP1	Lupinus albus	HMW Plant PAP	n/a	Q93VM7
LaAP2	Lupinus albus	HMW Plant PAP	n/a	Q9XJ24
LIAP1	Lupinus luteus	HMW Plant PAP	(LI)AP1; acPase1	Q8L5E1
LIAP2	Lupinus luteus	HMW Plant PAP	(LI)AP2; acpase2	Q8L6L1
LIPPD1	Lupinus luteus	HMW Plant PAP	PPD1	Q8VX11
LIPPD2	Lupinus luteus	HMW Plant PAP	PPD2	Q8VXF6
LIPPD4	Lupinus luteus	HMW Plant PAP	PPD4	Q8VXF4
LpPAP	Landoltia punctata	HMW Plant PAP	n/a	Q9MB07
MtPAP1	Medicago truncatula	HMW Plant PAP	n/a	Q4KU02
NtPAP	Nicotiana tabacum	HMW Plant PAP	n/a	Q84KZ3
OsPAP2	Oryza sativa	HMW Plant PAP	n/a	Q8S505
OsPAP3	Oryza sativa	HMW Plant PAP	Os08g0280100	Q6ZCX8
OsPAP4	Oryza sativa	HMW Plant PAP	Osl_28583	B8B909
PpPAP	Physcomitrella patens	HMW Plant PAP	n/a	A9SPI2
PvPAP1	Phaseolus vulgaris	HMW Plant PAP	PvPAP_tIII	P80366
PvPAP2	Phaseolus vulgaris	HMW Plant PAP	KeACP; PvPAP_tIV	Q764C1
RcPAP1	Ricinus communis	HMW Plant PAP	RCOM_1019210	B9RWG6
RcPAP2	Ricinus communis	HMW Plant PAP	RCOM_0003680	B9SXP8
RcPAP3	Ricinus communis	HMW Plant PAP	RCOM_0003560	B9SXP6
SbPAP	Sorghum bicolor	HMW Plant PAP	SORBI_3007G091100	A0A1Z5R9T8
StPAP3	Solanum tuberosum	HMW Plant PAP	n/a	Q6J5M8
ТаАСР	Triticum aestivum	HMW Plant PAP	n/a	C4PKL1
VvPAP	Vitis vinifera	HMW Plant PAP	VITISV_037278	A5BGI6
ZmPAP_c	Zea mays	HMW Plant PAP	n/a	C4PKL7
AtPAP17	Arabidopsis thaliana	LMW Plant PAP	AtACP5	Q9SCX8
AtPAP3	Arabidopsis thaliana	LMW Plant PAP	n/a	Q8H129
AtPAP7	Arabidopsis thaliana	LMW Plant PAP	n/a	Q8S341
AtPAP8	Arabidopsis thaliana	LMW Plant PAP	n/a	Q8VYZ2
BrPAP17_1	Brassica rapa	LMW Plant PAP	n/a	D6MW88
GmPAP2	Glycine max	LMW Plant PAP	n/a	Q9LL80
IbPAP4	Ipomoea batatas	LMW Plant PAP	n/a	Q9LL81
LIACP3	Lupinus luteus	LMW Plant PAP	n/a	Q707M7
LIPPD3	Lupinus luteus	LMW Plant PAP	PPD3	Q8VXF5
OsPAP1	Oryza sativa	LMW Plant PAP	OSJNBa0023I19.10	Q7XH73
PvPAP3	Phaseolus vulgaris	LMW Plant PAP	n/a	D2D4J4
PvPAP4	Phaseolus vulgaris	LMW Plant PAP	n/a	Q9LL79
PvPAP5	Phaseolus vulgaris	LMW Plant PAP	n/a	E2D740
StPAP1	Solanum tuberosum	LMW Plant PAP	n/a	Q6J5M7
ZmPAP	Zea mays	LMW Plant PAP	n/a	C4IZM1
AgPAP	Anopheles gambiae	HMW Animal PAP	Aga_PAPL1	Q7PUN5
AmPAP	Apis mellifera	HMW Animal PAP	Ame_PAPL1	A0A087ZWE4
CePAP1	Caenorhabditis elegans	HMW Animal PAP?	CELE_F02E9.7	001320
CePAP3	Caenorhabditis elegans	HMW Animal PAP	Cel_PAPL3	Q9NAM9
DmPAP1	Drosophila melanogaster	HMW Animal PAP	Dme_PAPL1; DmPAP_b	Q9VZ56
DmPAP2	Drosophila melanogaster	HMW Animal PAP	Dme_PAPL2	Q9VZ58
DmPAP3	Drosophila melanogaster	HMW Animal PAP	Dme_PAPL3; DmPAP_a	Q9VZ57
HsPAP7	Homo sapiens	HMW Animal PAP	Hsa_PAPL1; HsACP7	Q6ZNF0

Name	Organism	Group	Alternative names	UniProt ID
MmPAP7	Mus musculus	HMW Animal PAP	Mmu_PAPL1; MmACP7	Q8BX37
TnPAP1	Tetraodon nigroviridis	HMW Animal PAP	Tni_PAPL1	Q4RLR4
DrPAP1	Danio rerio	LMW Animal PAP	Dre_PAP1; DrACP5a	Q6DHF5
DrPAP2	Danio rerio	LMW Animal PAP	Dre_PAP2; DrACP5a	Q7SXT1
HsPAP5	Homo sapiens	LMW Animal PAP	Hsa_ACP5	P13686
MmPAP5	Mus musculus	LMW Animal PAP	Mmu_ACP5	Q05117
RnPAP5	Ratus novergicus	LMW Animal PAP	Rn_ACP5	P29288
SsPAP5	Sus scrofa	LMW Animal PAP	Ss_ACP5	P09889
TnPAP2	Tetraodon nigroviridis	LMW Animal PAP	n/a	Q4S7S5
XIPAP1	Xenopus laevis	LMW Animal PAP	Xla_PAP1; XIACP5	Q6GNG2
XIPAP2	Xenopus laevis	LMW Animal PAP	Xla_PAP2; XIACP5	Q6IP56
XtPAP5	Xenopus tropicalis	LMW Animal PAP	XtACP5	Q66IG6
CrPAP1	Chlamydomonas reinhardtii	Microalgal PAP	Cre16.g672250.t1.3	n/a
CrPAP2	Chlamydomonas reinhardtii	Microalgal PAP	Cre13.g578350.t1.2	n/a
CrPAP3	Chlamydomonas reinhardtii	Microalgal PAP	Cre11.g476700.t1.2	n/a
CrPAP4	Chlamydomonas reinhardtii	Microalgal PAP	Cre11.g468500.t1.3	n/a
CrPAP5	Chlamydomonas reinhardtii	Microalgal PAP	Cre12.g500200.t1.3	n/a
CrPAP6	Chlamydomonas reinhardtii	Microalgal PAP	Cre06.g259650.t1.2	n/a
MpPAP1	Micromonas pusilla	Microalgal PAP	MpPAP(3567)	n/a
MpPAP2	Micromonas pusilla	Microalgal PAP	MpPAP(48357)	n/a
MpPAP3	Micromonas pusilla	Microalgal PAP	MpPAP(57207)	n/a
MpPAP4	Micromonas pusilla	Microalgal PAP	MpPAP(146371)	n/a
OIPAP1	Ostreococcus lucimarinus	Microalgal PAP	OIPAP(1604)	n/a
OIPAP2	Ostreococcus lucimarinus	Microalgal PAP	OIPAP(2983)	n/a
AfPAP	Aspergillus ficuum	Fungal PAP	AphA; APase6; AfPAPhyC	Q12546
AnidPAP	Aspergillus nidulans	Fungal PAP	suApacA	Q92200
BcPAP	Burkholderia cenocepacia J2315	Bacterial PAP	BCAM1663	B4EKR2
BmaPAP	Burkholderia mallei ATCC 23344	Bacterial PAP	BMA0259	A0A0H2WHP3
BpsPAP	Burkholderia pseudomallei K96243	Bacterial PAP	BPSL0702	Q63X35
LePAP	Lysobacter enzymogenes	Bacterial PAP	phoA	Q05205
MbPAP	Mycobacterium bovis AF2122/97	Bacterial PAP	BQ2027_MB2608	A0A1R3Y2F9
MtubPAP	Mycobacterium tuberculosis H37Rv	Bacterial PAP	Rv2577	P9WL81

### Figure A1. Colour key for Chapter 2 MSAs

PAPhy sequences are separated in characterised (PAPhy), predicted by sequence homology (Predicted PAPhy) and sequence outliers (PAPhy outlier). Signal peptide was only displayed when the information was available from the UniProt database.

## Horizontal groups

## **Vertical features**

PAPhy
Predicted PAPhy
PAPhy Outliers

Plant PAPs

Animal PAPs

Microalgal PAPs

Fungal PAPs

**Bacterial PAPs** 

Signal peptide

PAP motifs I to V

PAPhy motifs 1 to 4

Proposed PAPhy motif 5

Figure A2. PAPhy vs HMW PAPs MSA (See Figure A1 for key)

HvPAPhy_a/C4PKL2//1-544	1		22
TaP APhy_a1 C4PKK7 /1-550	1	MWMWR GSLLLLLLAAAV	18
TaP APhy_b1/C4PKK9//1-538	1	MWMWR - GSLPLLLLAAAV	17
TaP APhy_b2   C4PKL0  /1-537	1	MWMWR GSMPLLLLAPAA	17
HvPAPhy_b2 C4PKL4 /1-537	1		17
HvPAPhy_b1 C4PKL3 /1-536	1		17
OsP APhy_b   D6QSX9   /1-539	1		17
ZmP APhy_b   C4PKL6   /1-544	1		18
MtP APhy   Q3ZFI 1   / 1-543	1	MGSVLVHTHVVTLCMLLLSLSS	22
PtPAP3/V9LXK5//1-564	- 1	MASSSLPSISLPVNV FELNNILSLVLKLTITLILLANGA	39
NtP APhy   A5YBN1   /1-551	1		27
LaP APhy   D2 YZL4   / 1-543	1		19
GmPAPhy_b Q93XG4 /1-547	1	MASITFSLLQFHRAPILLLILLA	23
AtP AP 15   Q9 SFU3   /1-532	1	<mark>MTFLLLLFCFL</mark>	12
AtaPAPhy_a1/F6MIX0//1-549	1		16
ScPAPhy_a2 F6MIX4 /1-543	1	MP S N MWL - G S L R L L L L L A A A	19
TmP APhy_a 1   F6MI W8   /1-545	1		15
TaP APhy_a3   F6MIW2   /1-539	1	GSLRLLLLAAA	15
TaP APhy_a2   C4PKK8   / 1-549	1		17
ScP APhy_a1/F6MIX2//1-541	1	MWR - GSLR LLLLLAAA	15
TaP APhy_b3 (F6MIW6 // 1-536	1	MGIWR - GSLPLLLLAAAA	17
TmP APhy_b1/F6MIW9//1-539	1	MWIWR - GSLPLLLLAAAA	17
AtaPAPhy_b1/F6MIX1//1-538	1		17
ScP APhy_b1/F6MIX5//1-538	1		17
RcP AP 1 / B9R W G6 / /1-566		MNPLFLDSCSFMQGLQYNRCNMGLLSVPVFALSFYVLLS	39
VvP AP (A5BGI6)/1-540	1		18
1 17			
PvPAPhy/V7B3Z4//1-546	1		23
VrP APhy   B5 AR Z7   /1-547	1	<mark>MKICTTL</mark> CMLAMVLVMMST	20
AIP AP 15   D7L636   /1-532	1	MTFLLLLFCFL	12
AtP AP 23   Q6TPH 1   / 1-458	1		21
GmP AP 4   V9H XG4   /1-442	1	MELKQQKLLLVLILTLLF	18
ZmP AP_c   C4PKL7   /1-566	1	<mark></mark> MATPTSTVTRGGNRHWHCTQVLPLLLLVPL	30
5bP AP   A0 A1Z5R9T8   / 1-566	1	<mark>MATPTRTVAAGGSSHRHWHCIQVLQLLLLVQC</mark>	32
HvP AP_c   C4PKL5   /1-564	1		27
PpP AP   A9 SPI 2   / 1-557	1		27
0sP AP 3   Q6ZCX8   /1-622	1	MAAP AAACD LR F L LV G L L LV VV V G	24
OsP AP 4   B8 B909   /1-622	1	MA A P A A A G D L R F L L V G L L L V V V V G	24
AtP AP 5   Q9 C9 27   /1-39 6	-		
AtP AP 20   Q9 LXI 7   /1-427	1		17
1	1		15
AtP AP 22   Q85340   / 1-434	1		12
IbP AP3   Q9ZP 18   /1-427			
AtP AP 2 1   Q9 LXI4   / 1-437	1		19
		MARLY LAVMELLNAAI	
LpP AP   Q9MB07  /1-455	1		16
RcPAP2 B95XP8 /1-463	1		18
R c P AP 2   B9 5XP 8   / 1-4 63   bP AP 2   Q9 5D Z9   / 1-4 65	1 1		18 18
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q95I 18  /1-441	1		18 18 12
R c P AP 2   B9 5XP 8   / 1-4 63   bP AP 2   Q9 5D Z9   / 1-4 65	1 1		18 18
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q95I 18  /1-441	1 1 1		18 18 12
RcP AP 2   B95XP8  /1-463  bP AP 2   Q95D29  /1-465 AtP AP 11   Q95  18  /1-441 GmP AP 1   Q09 13 1  /1-464	1 1 1 1	MR LVRVIVTLWFVLLGFA         MGASRTGCYLLAVVLAAV         MGASRTGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MRMNK         ILLVFVFLSIAT         MSSRSDLKIKRVSLIIFLLSVLV	18 18 12 17
R cP AP 2   895XP 8  /1-463 IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q95I 18  /1-441 GmP AP 1   Q09 I 31  /1-464 AtP AP 25   O23244  /1-466	1 1 1 1		18 18 12 17 17
R.CP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   095I 18  /1-441 GmP AP 1   009 I 31  /1-464 AtP AP 25   023244  /1-469 AtP AP 12   038924  /1-469	1 1 1 1 1	MR LVRVIVTLWFVLLGFA         MGASRTGCYLLAVVLAAV         MGASRTGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MRMNK         ILLVFVFLSIAT         MSSRSDLKIKRVSLIIFLLSVLV	18 18 12 17 17 23
R.CP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   095 I 8  /1-441 GmP AP 1   009 I 3 1  /1-464 AtP AP 25   023244  /1-469 AtP AP 12   038924  /1-469 IttP AP   084K23  /1-461	1 1 1 1 1	MR LVRVIVTLWFVLLGFA         MGASRTGCYLLAVVLAAV         MGASRTGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MRMNK         ILLVFVFLSIAT         MSSRSDLKIKRVSLIIFLLSVLV	18 12 17 17 23 17
R.cP AP 2   895XP 8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   095I 18  /1-441 GmP AP 1 (009131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 IttP AP 0 8844 (23  /1-461 MtP AP 1   04KU02  /1-465 OSP AP 2   085505  /1-476	1 1 1 1 1	MR LVRVIVTLWFVLLGFA         MGASRTGCYLLAVVLAAV         MGASRTGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MRMNK         ILLVFVFLSIAT         MSSRSDLKIKRVSLIIFLLSVLV	18 12 17 17 23 17 13
R.CP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   095 18  /1-441 GmP AP 1   009 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038824  /1-469 I \tP AP   084K25  /1-461 MtP AP 1   04KU02  /1-465	1 1 1 1 1 1 1	MR LVRVIVTLWFVLLGFA         MGASRTGCYLLAVVLAAV         MELSHLALVCAA         MGVVEGGLALALVLSAC         MRMNK_ILLVFVFLSIAT         MSSRSDLKIKVSLIIFLLSVLV         MGFLHSLLLAFTN         MGFLHSLLLALCL	18 12 17 17 23 17 13 17 18
R.CP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   09518  /1-464 AtP AP 12   09518  /1-464 AtP AP 25   023244  /1-469 IttP AP 1 084K23  /1-465 OSP AP 1   04KU02  /1-465 OSP AP 2   085505  /1-476 La AP 1   093VM7  /1-460 P vP AP 2   0764 C1  /1-457	1 1 1 1 1 1 1 1 1 1 1	MR LVRVIVTLWFVLLGFA         MGASRTGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MRMNK         MSSRSDLKIKRVSLITFLLSVLV         MGFLHSLLLFITN         MGYSFVAILLFITN         MGYSFVAILLLFITN         MGYSFVAILLFITN         MGRYSFVAILLFITN	18 12 17 17 23 17 13 17 18 18
R.CP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11 (095 18  /1-441 GmP AP 11 (095 18  /1-464 AtP AP 25   023244  /1-469 NtP AP 12   038924  /1-469 NtP AP 1 (04K:U02  /1-465 OSP AP 2   085505  /1-476 La AP 1 (095 VM7  /1-460 P vP AP 2   0764 C1  /1-457 UAP 2   08L6L1  /1-463	1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLG FA         MGAS R TG CYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MRMNK         MS S R SD LK I K RVS LI I FLLSVLV         MG I SW         FYVAILLFITN         MGWR FALLLHVLLQLV         MG VS FVAIALLHVLCLV         MG VS FVAIALLMSVVV         MG NS S FVAIALLMSVVVL	18 12 17 17 23 17 13 17 18 18 20
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 AtP AP 11   09 SI 8   /1-441 GmP AP 1   00 9 I 31   /1-464 AtP AP 25   023244   /1-466 AtP AP 12   038324   /1-461 MtP AP 1 04KU02   /1-465 OSP AP 2   085505   /1-476 La AP 1 0 05 V7   /1-460 P vP AP 2   0764 C1   /1-453 UAP 2   08 SL 1   /1-463 AtP AP 10   09 SI V9   /1-468	1 1 1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLG FA         MGASR TGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MR MNK         MSSRSDLKIKKVSLIFLSVLV         MGISW         FYVAILLFITN         MGYSFVAILLFITN         MGYSFVAILLFITN         MGYSFVAILLFITN         MGYSFVAILLFITN         MGRYSFVAILLFITN         MGRSFVAILLFNUCCU         MGRSFVAILLFNUCCU         MGRVKAILLFVLCU         MGRVKAILLFVLASFV	18 12 17 17 23 17 13 17 18 18
R.CP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   095 I 8  /1-441 GmP AP 1   009 I 3 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 INP AP 1 04KU02  /1-465 OSP AP 2   085505  /1-476 La AP 1 (093VM7  /1-460 P vP AP 2   0764C1  /1-457 UAP 2   08L6L1  /1-463 AtP AP 10   093V9  /1-468 P vP AP 1   P80366  /1-459	1 1 1 1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLG FA         MGASR TGCYLLAVVLAAV         MGASR TGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MR MNK         MSSRSDLKIKVSLIIFLLSVLV         MGVFLSUVVL         MGRVFALLLFITN         MGWR FALLLLHVLCLV         MGYSSFVAIALLMSVVVV         MGRVFALLLKVLASFV         MGRVFALLLLVVVV	18 12 17 17 23 17 13 17 18 20 18 18
R.CP AP 2   895XP8   / 1-463 IbP AP 2   095D29   / 1-465 AtP AP 11   095 I 8   / 1-441 GmP AP 1   009 I 3 1   / 1-464 AtP AP 25   023244   / 1-466 AtP AP 12   038924   / 1-469 I ttP AP   084K23 / 1-461 MtP AP 1   04KU02   / 1-465 OSP AP 2   085505   / 1-476 La AP 1   093VM7 / / 1-460 P vP AP 2   0764 C 1   / 1-457 UAP 2   08L6L1   / 1-463 AtP AP 10   09V9 / / 1-468 P vP AP 1   P80366   / 1-459 Ta ACP   04PKL1   / 1-477	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLG FA         MGASR TGCYLLAVVLAAV         MELSHLALVCAA         MGNVE         GLLALALVLSAC         MRMNK         MSSRSDLKIKVSLIIFLLSVLV         MGISW         FYVVAILLFITN         MGYSFVAILLFITN         MGYSFVAILLLHVLCLV         MGYSFVAILLLHVLCLV         MGYSFVAILLLNVVV         MGYSFVAILLLNVVV         MKMGNSFVAILLLNVVV         MKMGNSFVAIALLMSVVV         MKMGNSFVAIALLMSVVV         MKMGNSFVAIALLNVVV         MKMGNSFVAIALLNVVV         MKRVKSLALALVVVV         MRGVKKSLALALVVVV	18 12 17 17 23 17 13 17 18 18 20 18 18 18
R.CP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 AtP AP 11   095 I18   /1-441 GmP AP 1   009 I13   /1-464 AtP AP 25   023244   /1-469 IttP AP 1 084K23   /1-461 MtP AP 1 04KU02   /1-465 OSP AP 2   085505   /1-476 La AP 1   093VV7   /1-460 P vP AP 2   025K01   /1-457 UAP 2   0816L1   /1-463 AtP AP 10   095VV   /1-468 P vP AP 1   P80366   /1-459 Ta ACP   C4PKL1   /1-476	111111111111111111111111111111111111111	MR LV RV IVT LWFVLLG FA         MGASR TGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLALALVLSAC         MRMNK         MSSRSDLKIKRVSLIIFLLSVLV         MGFLHSLLALCL         MGFLHSLLALCL         MGYSSFVAIALLHVLCLV         MGYSFVAILLFITN         MGYSFVAILLFITN         MGYSFVAILLFITN         MGYSFVAILLHVLCLV         MGYSFVAIALLMSVVV         MGYSFVAIALLMSVVV         MGYSFVAIALLNSVVV         MGYSFVAIALLNVLCLV         MGYSFVAIALLNSVVV         MGYSFVAIALLNSVVV         MKMGNSFVAIALLNSVVV         MGVVKGLALALVLNVVV         MGVKGLALALVLNVVV         MRGLGFAALSLHVLCLA         MKNLVIFAFLFLS	18 12 17 17 13 17 18 18 20 18 18 18 18 18
R.CP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 AtP AP 11   095 I 8   /1-441 GmP AP 1   009 I 3 I   /1-464 AtP AP 25   023244   /1-469 NtP AP 1 0   084KZ3   /1-461 MtP AP 1 04KU02   /1-465 OSP AP 2   08505   /1-476 La AP 1   095VM7   /1-460 P VP AP 2   0764 C 1 / /1-457 UAP 2   08 L6L1   /1-463 AtP AP 10   095V9   /1-468 P VP AP 1   P80366   /1-459 Ta ACP   C4PKL1   /1-477 AtP AP 6   09 C5 10   /1-461 AcP AP   093WP4   /1-481	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLG FA         MGASR TGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MR MK         MS SR SDLK I KRVSLII FLLSVLV         MG I SW         FYVAILLFITN         MG FLHSLLALCL         MG SS FVAIALLHVLCCV         MG RV R FALLLHVLCCV         MG RV R FALLLHVLCCV         MG RV R FALLLMSVVV         MG RV R KSD FGS IVLVLCC         MG RV R KSD FGS IVLVLCC         MG RV R KSD FGS IVLVLCC         MR GLG FAALSLHVLLCLA         MR N K NU V FAFLFLS	18 12 17 17 23 17 13 17 18 20 18 18 18 18 18 13 18
R.CP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11 (095 I18 //1-441 GmP AP 11 (095 I18 //1-444 AtP AP 25   023244 //1-466 AtP AP 12   038924 //1-469 ItP AP 1 04K:002 //1-465 OSP AP 2   085505 //1-476 La AP 11 (0951V9 //1-460 P vP AP 2   0764C1 //1-457 UAP 2   08L6L1 //1-463 AtP AP 10   0951V9  /1-468 P vP AP 10   0951V9 //1-468 P vP AP 10 (0951V9 //1-468 P vP AP 6   09 C510 //1-461 AtP AP 6   09 C510 //1-481 AoP AP 32   09XF09 //1-470	111111111111111111111111111111111111111	MR LV RV IVT LWFVLLG FA         MGASR TGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MR MNK         ILVFVFLSIAT         MG ISW         FYVAILLFITN         MGYSFVAILLHVLCLV         MGYSFVAILLHVLCLV         MGYSFVAILLHVLCLV         MGYSFVAILLHVLCLV         MGRVR FALLLHVVLSVV         MGRVR FALLLHNSVVV         MGRVR KSDFGSIVLVLCC         MGVK KSDFGSIVLVLCC         MGVK KSLALALVNVV         MR GLG FAALSLHVLLCLA         MR VK SD FGSIVLVLCC         MR VK SD FGSIVLVLCC         MR VK SD FGSIVLVLCLA         MR VL FAFLFLS         MV LIPK TKNLIIFVLLFHI	18 12 17 17 23 17 13 17 18 20 18 18 18 18 13 18
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 AtP AP 11 ( 09 SI 18   /1-441 GmP AP 1   00 91 31   /1-464 AtP AP 25   023244   /1-466 AtP AP 12   038324   /1-461 MtP AP 1 04K U02   /1-465 OSP AP 2   08505   /1-476 La AP 1 0 09 SVM7   /1-460 P VP AP 2   0764 C1   /1-457 UAP 2   08 SLE1   /1-463 AtP AP 10   09 SV 9   /1-468 P VP AP 1   P80366   /1-459 Ta ACP   C4PKL1 / /1-477 AtP AP 6   09 C5 10   /1-466 AcP AP 2   09 SV09 / /1-470 StP AP 3   06 J5M8   /1-477	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLGFA         MGASR TGCYLLAVVLAAV         MELSHLALVCAA         MGVVE         GLLALALVLSAC         MR MNK         MSSRSDLKIKRVSLIFLSVLV         MGISW         FYVVAILLFITN         MGYSFVAILLFITN         MGYSFVAILLFITN         MGYSFVAILLFITN         MGRVR FALLLLHVLCLV         MGRVR FALLLHVVLCLV         MGRVR FALLLHVVVV         MGRVR FALLLHVVVV         MFRRVQTMLLKFVLASFV         MKMNSSFVAIALLMSVVVV         MKNNSSFVAIALLMSVVV         MKNNSSFVAIALLMSVVV         MKNNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNVITALVNVV	18 12 17 17 23 17 13 17 18 18 18 18 18 18 18 18 18 12
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 ArtP AP 11   09 SI 8   /1-441 GmP AP 1   00 91 31   /1-464 ArtP AP 25   02 32 44   /1-466 ArtP AP 12   03 83 24   /1-461 MrtP AP 1 04KU02   /1-465 OsP AP 2   08 5505   /1-476 La AP 1   09 SVM7   /1-460 P vP AP 2   07 64 C1   /1-457 UAP 2   08 S505   /1-476 La AP 1 0 09 SVM7   /1-468 P vP AP 1   P803 66   /1-459 Ta ACP   C4PKL1   /1-477 ArtP AP 6   09 C5 10   /1-466 AcP AP 3   09 SVM9   /1-471 AoP AP 3 2   02 SF09   /1-470 StP AP 3   06 J5M8   /1-477 IbP AP 1   09 SE00   /1-473	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLGFA         MGASR TGCYLLAVVLAAV         MELSHLALVCAA         MGVE         GLALALVLSAC         MRMNK         MSSRSDLKIKVSLIIFLLSVLV         MGISW         FYVVAILLFITN         MGVKFALLLLFITN         MGYSSFVAIALLMSVVV         MGRVR FALLLLHVLCLV         MGVK FALLLLVVVAILUSVVV         MGVK FALLLLNVVV         MGVK FALLLLNVVV         MGVK FALLLLNVVV         MGVK FALLLLHVLCLV         MGVK FALLLLHVLCLV         MGVK FALLLLHVLCLV         MGVK FALLLLHVLCLV         MGVK FALLLHVLCLA         MKMGNSSFVAIALLMSVVV         MKNLV FASLF         MKNLV FASLF         MKNLV FASLF         MKNLV FASLF         MKNLV FASLF         MKNLV FASLF         MKLVV GLWCLILGL	18 12 17 17 23 17 13 17 18 18 18 18 18 18 18 18 18 18 12 15
R.CP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 AtP AP 11   095 I18   /1-441 GmP AP 1   009 I13   /1-464 AtP AP 25   023244   /1-469 IttP AP 1 084K23   /1-461 MtP AP 1 04KU02   /1-465 OSP AP 2   08505   /1-476 La AP 1   093VV3   /1-465 P vP AP 2   095VV5   /1-463 AtP AP 10   09SIV5   /1-463 AtP AP 10   09SIV5   /1-465 P vP AP 10   09SIV5   /1-466 AtP AP 00   02FKL1   /1-477 AtP AP 6   09 C5 10   /1-466 AcP AP 32   093KP5   /1-477 IbP AP 1   093S00   /1-473 AtP AP 2   093S00   /1-475 AtP AP 2 6   0949Y3   /1-475	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLG FA         MGASR TGCYLLAVVLAAV         MGVVE         GLLALALVLSAC         MR MN K         ILVFVFLSIAT         MR MN K         MG ISW         FYVAILLFITN         MGVFFALLLHVLCLV         MG ISW         FYVAILLFITN         MG SSFV         MG SSFV         MG SSFV         MG SSFV         MG SSFV         MG NSSFV         MG RV K SDFGSIVLVVCC         MR MG NSSFVAIALLMSVVV         MK MG NSSFVAIALLMSVVVL         MK MG NSSFVAIALLMSVVL         MK MG NSSFVAIALLMSVVVL         MK NLVIFALSVE         MK NLVIFALSVE         MR NLVIFALSVE         MR NLVIFALSVE         MK NLVIFALSVE         MK NLVIFALSVE         MK NLVIFALSVE         MK NLVIFALSVE         MK NLVIFALSVE         MK NLVVYGLULL	18 12 17 17 13 17 18 20 18 18 18 13 18 12 15 16
R.CP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 AtP AP 11   095 I18   /1-441 GmP AP 11   009 I13   /1-464 AtP AP 25   023244   /1-469 ItP AP 1 084K23   /1-461 MtP AP 1 04KU02   /1-465 OSP AP 2   08505   /1-476 La AP 1 0   095 V9   /1-465 P VP AP 2   08L6L1   /1-463 AtP AP 10   095 V9   /1-468 P VP AP 10   095 V9   /1-468 P VP AP 10   095 V9   /1-466 AtP AP 00   095 V9   /1-466 AtP AP 0   095 V9   /1-466 AtP AP 3   08500   /1-470 StP AP 3   08500   /1-477 IbP AP 1   095 E00   /1-475 RCP AP 3   895XP 6   /1-488	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	MR LV R V I V T LWFV LLG FA         MGAS R TG CYLLAVVLAAV         MGVV E         GLLALALVLSAC         MR MK L         MR MN K         ILV FV FLSIAT         MG I SW         MG I SW         FYVAILLFITN         MG V K         MG F LHSLLALCL         MG S S FVAIALLHVLCCV         MG S S FVAIALLMSVVV         MG RV R FALLLHVVLCLV         MG NS S FVAIALLMSVVVL         MG RV R KSD FGSIVLVLCC         MG RV R KSD FGSIVLVLCC         MG RV R KSD FGSIVLVLCC         MR NL V FAFLER         MR NL V FAFLER         MR LV V GLLALSLY         MR N R LV V FAFLER         MR N R V R KSD FGSIVLVLCC         MG RV R KSD FGSIVLVLCC         MR N R S S FVAIALLMSVVVL         MR N R LV V FAFLER         MR LH V T S S C FYLLLFHI         MR LH V T S S C FYLLLFHI         MR LV V Y GWCLILGL         MR LV V GWCLILGL         MR LV V T K MMQ YMLILAFV	18 12 17 17 23 17 13 17 18 20 18 18 13 18 18 13 18 12 15 16 18
R.CP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 AttP AP 11   095 I18   /1-441 GmP AP 11   009 I13   /1-464 AttP AP 25   023244   /1-469 NttP AP 10   084K23   /1-461 MttP AP 1 (04KU02   /1-465 OSP AP 2   085505   /1-476 La AP 1   095V07   /1-460 P vP AP 2   0764 C1   /1-477 UAP 2   08L6L1   /1-463 AttP AP 10   095V9   /1-468 P vP AP 2   095V0   /1-477 AttP AP 6   09 C5 10   /1-477 AttP AP 32   095K09   /1-470 SttP AP 3 ( 0455M8   /1-477 IbP AP 1   095E00   /1-473 AttP AP 2   095E00   /1-475 RcP AP 3   855XP 6   /1-488 UAP 1   08L5E1   /1-477	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLGFA         MGASR TGCYLLAVVLAAV         MELSHLALVVLAAV         MGVVE         GLLALALVLSAC         MR MNK         ILVFVFLSIAT         MGISW         MGISW         FYVAILLFITN         MGYVE         MGISW         MGYVE         MGISW         MGRVR         MR         MR         MR         MR         MR	18 12 17 17 23 17 13 17 18 18 18 18 18 18 18 18 18 18 18 12 15 16 18 14
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 AtP AP 11   09 SI 8   /1-441 GmP AP 11   09 SI 8   /1-444 AtP AP 25   02 3244   /1-466 AtP AP 12   03 8324   /1-469 ItP AP 1 04K U02   /1-465 OsP AP 2   08 505   /1-476 La AP 11 04K U02   /1-465 OsP AP 2   07 64 C1   /1-457 UAP 2   07 64 C1   /1-457 UAP 2   08 L6L   /1-463 AtP AP 10   09 SI V9   /1-468 P VP AP 1   P803 66   /1-459 Ta ACP   C4PK L1   /1-477 AtP AP 6   09 C5 10   /1-466 AcP AP 32   09 XF09   /1-470 StP AP 3   06 J5M8   /1-477 IbP AP 1 ( 09 SLV9   /1-473 AtP AP 26   09 SXP 6   /1-488 UAP 1   08 L5 E1   /1-477 GmP AP 3   06 YGT9   /1-512	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	MR LV RV IVT LWFVLLGFA         MGASR TGCYLLAVVLAAV         MGASR TGCYLLAVVLAAV         MGVE         GLALALVLSAC         MR MN K         ILVFVFLSIAT         MG ISW         FYVAILLFITN         MG FLHSLLALCL         MG FLHSLLLALCL         MG ISW         MG FLHSLLLALCL         MG SS FVAIALLHVUCCV         MG RV R FALLLHVUCCV         MG RV R FALLLHVUCCV         MGRV R SS FVAIALLMSVVVU         MGRV R KSD FGS IVLVUCCC         MGRV R KSD FGS IVLVUCC         MGVV K GLALALVNVVV         MR LVIFAFLFLF         MR LVIFAFLFLF         MR LVIFAFLFLF         MR LVVVGLUCH         MR LVVVGLUCH         MR LVVVGLUCH         MR LVVUGUCH         MR LVVUGUCH         MR LVVULASFV         MR LVVLLYVLASFV         MR LVVLLASFV         MR LVVLLASFV	18 12 17 17 23 17 18 18 18 18 18 18 18 18 18 18 18 18 18
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 ArP AP 11 ( 09 SI 18   /1-441 GmP AP 1   00 91 31   /1-464 ArP AP 25   02 32 44   /1-466 ArP AP 12   03 89 24   /1-469 IvP AP 1 ( 04 KU02   /1-465 OSP AP 2   08 505   /1-476 La AP 1   04 KU02   /1-465 OSP AP 2   07 64 C1   /1-457 UAP 2   07 64 C1   /1-457 UAP 2   08 SL61   /1-468 P vP AP 1   P803 66   /1-459 Ta ACP   C4Pr L1   /1-477 ArP AP 6   09 C5 10   /1-466 ArC P AP 3   08 JSM9   /1-471 IbP AP 3   08 JSM9   /1-477 IbP AP 3   08 JSM9   /1-477 IbP AP 3   09 SWP 4   /1-481 UAP 1   09 SED0   /1-473 ArP AP 2 6   09 9 SXP 6   /1-488 UAP 1   08 L5E1   /1-477 GmP AP 3   06 JST 9   /1-512 La AP 2   09 XJ24   /1-638	111111111111111111111111111111111111111	MR LV RV IVT LWFVLLGFA         MGASRTGCYLLAVVLAAV         MGASRTGCYLLAVVLAAV         MGYVE         GLLALALVLSAC         MRMNK         MRNK         MSSRSDLKIKRVSLIFLSVLV         MGISW         MGYSLIFLSVLV         MGYSSFVAIALLFITN         MGYSSFVAIALLHVLCLV         MGYSSFVAIALLHVLCLV         MGRVRFALLLHVLCLV         MGRVRFALLLHVVLCCV         MGRVRFALLLHVVLCCV         MGYSSFVAIALLMSVVV         MGRVRFALLLHVLCLV         MGRVRFALLLHVVLCCV         MGRVRFALLLHVVLCCV         MGRVRFALLLHVVLCLA         MKMGNSSFVAIALLMSVVV         MRNKSSFVAIALLNSVVV         MRNKSSFVAIALLNSVVV         MRNKSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MRNKSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNSSFVAIALLNSVVV         MKNNSSFVAIALLNSVVV         MKNVYSKSTALLNSVVV	18 12 17 17 13 17 18 18 18 18 18 18 18 18 18 18
R.CP AP 2  895XP8 /1-463 IbP AP 2  095D29 /1-465 AtP AP 11 09518 /1-441 GmP AP 1 09518 /1-464 AtP AP 25] 023244 /1-469 IttP AP 108924 /1-469 IttP AP 108924 /1-465 OSP AP 2 08505/1-476 La AP 1 093VV3/1-460 P vP AP 2 08505/1-476 La AP 10 095VV3/1-460 P vP AP 200510 /1-463 AtP AP 10 095VV3/1-468 P vP AP 10 095VV3/1-466 AtP AP 000510 /1-466 AcP AP 000510 /1-470 StP AP 3 06508/1-477 IbP AP 10 295X03/1-475 RcP AP 3 095XP6 /1-475 RcP AP 3 095XP6 /1-475 RcP AP 3 095XP6 /1-475 RcP AP 3 095XP6 /1-488 LIAP 108L5E1/1-477 GmP AP 3 067G79 /1-512 La AP 2(09XXF4)/1-629	111111111111111111111111111111111111111	MR LV R V IVT LWFV LLG FA         MGAS R TG CYLLAVVLAAV         MGAS R TG CYLLAVVLAAV         MGVV E         GLLALALVLSAC         MR MN K         ILV FV FLSIAT         MR MN K         MG ISW         FYVAILLFITN         MG V K         MG ISW         FYVAILLFITN         MG S SFVAIALLHVLCLV         MG SS FVAIALLMSVVV         MG SS FVAIALLMSVVV         MG RV K SD FGSIVLVLCC         MK MG NSS FVAIALLMSVVVL         MR MG NS FVAIALLMSVVVL         MG RV K SD FGSIVLVLCC         MK MG NS FVAIALLMSVVVL         MR GLG FAALSLHVLCLA         MR NLV I FAFLFLS         MR NLV I FAFLS         MR NLV I FAFLFLS         MR NLV I FAFLFLS         MR NLV I FAFLFLS         MR NLV I FAFLFLS         MR NLV I FAFLS         MR NLV V SUNN <td< td=""><td>18 12 17 17 17 17 17 17 18 18 18 18 18 18 18 18 18 18</td></td<>	18 12 17 17 17 17 17 17 18 18 18 18 18 18 18 18 18 18
R.CP AP 2  895XP8 /1-463 IbP AP 2  095D29 /1-465 AtP AP 11 09518 /1-441 GmP AP 11 09518 /1-464 AtP AP 25] 023244 /1-469 NtP AP 12 038924 /1-469 NtP AP 10 08505 /1-476 La AP 10 08505 /1-476 La AP 10 0951V9 /1-463 AtP AP 10 0951V9 /1-468 P vP AP 10 0951V9 /1-468 P vP AP 10 0951V9 /1-468 P vP AP 10 0951V9 /1-466 AtP AP 00 054V1 /1-457 Ta ACP  04FL1 /1-477 AtP AP 6 09C510 /1-476 AtP AP 6 09C510 /1-476 AtP AP 6 09C510 /1-476 AtP AP 6 09500 /1-477 IbP AP 1 085500 /1-475 RcP AP 3 895XP 6 /1-488 UAP 1 08L512 /1-477 GmP AP 3 06V519 /1-477 La AP 2 09X124 /1-638 UPP D4 08VX11/1-615	111111111111111111111111111111111111111	MR LV RV IVT LWFVLLGFA         MGASRTGCYLLAVVLAAV         MGVVE         GLLALALVLSAC         MRWNK         MSSRSDLKIKRVSLIIFLLSVLV         MGVVE         MGVVE         MGVVE         MGVVE         MGVVE         MGVVE         MRWNK         MGVVE         MGVVE         MGTUN         MGSSSV         MGVVAILLFITN         MGVVK         MGVK         MGRV         MKMGNSS         MGRV         MKMGNSS         MK NLV         MK MGNSS         MKNLV         MGRV         MK NLV         MGRV         MGRV         MGRVK         MR         MK NLV	18 12 17 17 13 17 18 20 18 18 18 18 18 18 18 18 18 18
R.CP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 AtP AP 11   095 I 8   /1-441 GmP AP 11   095 I 8   /1-441 GmP AP 12   038924   /1-469 NtP AP 12   038924   /1-469 NtP AP 10   04KU02   /1-465 OSP AP 2   08505   /1-476 La AP 1   095V9   /1-465 OSP AP 2   0764 C 1 / /1-457 UAP 2   0764 C 1 / /1-457 UAP 2   0764 C 1 / /1-457 UAP 2   0764 C 1 / /1-457 Ta ACP   09 SI V9   /1-468 P vP AP 1   09 SI V9   /1-468 P vP AP 1   09 SI V9   /1-468 AtP AP 10 ( 09 SI V9   /1-468 ACP AP 2   09 SI V9   /1-477 AtP AP 3 ( 045 I 0) /1-477 IbP AP 3   095E00   /1-477 IbP AP 3   095E00   /1-477 RcP AP 3   095E00   /1-477 GmP AP 3   06YGT9   /1-512 La AP 2   09XV74   /1-638 UPP D1   08VX11   /1-615 UPP D2   08VXF6   /1-612		MR LV RV IVT LWFVLLGFA         MGASRTGCYLLAVVLAAV         MGVE         GLLALALVLSAC         MRWK         MRWK         MSSRSDLKIKRVSLIIFLUSVLV         MGISW         MGISW         MGVE         MGISW         MRWK         MGISW         MRWK         MGISW         MGISW         MGYVE         MGISW         MGYVALLKFVE         MGISS         MGYK         MGYK         MGYK         MGYK         MGYK         MGRVK         MR         MR         MK         MR         MR	18 18 12 17 17 13 17 18 20 18 18 18 13 18 13 18 12 15 16 18 14 39 18 40 20 26
R.CP AP 2  895XP8 /1-463 IbP AP 2  095D29 /1-465 AtP AP 11 09518 /1-441 GmP AP 11 09518 /1-464 AtP AP 25] 023244 /1-469 NtP AP 12 038924 /1-469 NtP AP 10 08505 /1-476 La AP 10 08505 /1-476 La AP 10 0951V9 /1-463 AtP AP 10 0951V9 /1-468 P vP AP 10 0951V9 /1-468 P vP AP 10 0951V9 /1-468 P vP AP 10 0951V9 /1-466 AtP AP 00 054V1 /1-457 Ta ACP  04FL1 /1-477 AtP AP 6 09C510 /1-476 AtP AP 6 09C510 /1-476 AtP AP 6 09C510 /1-476 AtP AP 6 09500 /1-477 IbP AP 1 085500 /1-475 RcP AP 3 895XP 6 /1-488 UAP 1 08L512 /1-477 GmP AP 3 06V519 /1-477 La AP 2 09X124 /1-638 UPP D4 08VX11/1-615	111111111111111111111111111111111111111	MR LV RV IVT LWFVLLGFA         MGASR TGCYLLAVVLAAV         MGVVE         GLLALALVLSAC         MRMNK         ILVFVESIAT         MGVSSFVAILLVISIAT         MGVSSFVAILLVUCU         MGVSSFVAILLVUCU         MGVSSFVAILLVUCU         MGVSSFVAIALLNVUCU         MGRVRFALLULVUCU         MGRVRFALLULVUCU         MGVSSFVAIALLNVUCU         MGRVRFALLULVUCU         MGRVRFALLULVUCU         MGRVSSFVAIALLNSVVV         MRGRVRSFVAIALLNSVVV         MRGNSSFVAIALLNSVVV         MRGNSSFVAIALLNSVVV         MRGNSSFVAIALLNSVVV         MRGNSSFVAIALLNSVVV         MRGNSSFVAIALLNSVVV         MRGNSSFVAIALLNSVVV         MRGNSSFVAIALLNSVVV         MRRNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNNN	18 12 17 17 13 17 18 20 18 18 18 18 18 18 18 18 18 18
R.CP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 AtP AP 11   095 I 8   /1-441 GmP AP 11   095 I 8   /1-441 GmP AP 12   038924   /1-469 NtP AP 12   038924   /1-469 NtP AP 10   04KU02   /1-465 OSP AP 2   08505   /1-476 La AP 1   095V9   /1-465 OSP AP 2   0764 C 1 / /1-457 UAP 2   0764 C 1 / /1-457 UAP 2   0764 C 1 / /1-457 UAP 2   0764 C 1 / /1-457 Ta ACP   09 SI V9   /1-468 P vP AP 1   09 SI V9   /1-468 P vP AP 1   09 SI V9   /1-468 AtP AP 10 ( 09 SI V9   /1-468 ACP AP 2   09 SI V9   /1-477 AtP AP 3 ( 045 I 0) /1-477 IbP AP 3   095E00   /1-477 IbP AP 3   095E00   /1-477 RcP AP 3   095E00   /1-477 GmP AP 3   06YGT9   /1-512 La AP 2   09XV74   /1-638 UPP D1   08VX11   /1-615 UPP D2   08VXF6   /1-612		MR LV RV IVT LWFVLLGFA         MGASRTGCYLLAVVLAAV         MGVE         GLLALALVLSAC         MRWK         MRWK         MSSRSDLKIKRVSLIIFLUSVLV         MGISW         MGISW         MGVE         MGISW         MRWK         MGISW         MRWK         MGISW         MGISW         MGYVE         MGISW         MGYVALLKFVE         MGISS         MGYK         MGYK         MGYK         MGYK         MGYK         MGRVK         MR         MR         MK         MR         MR	18 18 12 17 17 13 17 18 20 18 18 18 13 18 13 18 12 15 16 18 14 39 18 40 20 26
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 AtP AP 11   09 SI 8   /1-441 GmP AP 11   09 SI 8   /1-444 AtP AP 25   02 3244   /1-466 AtP AP 12   03 89 24   /1-469 ItP AP 10   04 KU32   /1-461 MtP AP 10   04 S505   /1-465 OSP AP 2   08 5505   /1-476 La AP 10   09 SI V9   /1-468 P VP AP 2   07 64 C1   /1-457 UAP 2   08 L6L1   /1-463 AtP AP 10   09 SI V9   /1-468 P VP AP 2   07 64 C1   /1-477 AtP AP 6   09 C5 10   /1-466 ACP / C4P KL1   /1-477 AtP AP 3   09 SWP 4   /1-481 AOP AP 32   09 XF09   /1-473 AtP AP 3   09 SE0   /1-473 AtP AP 3   09 SE0   /1-475 R CP AP 3   09 SXP 6   /1-488 UAP 1   08 L5 E1   /1-477 GmP AP 3   06 YGT9   /1-512 La AP 2   09 XXF6   /1-638 UPP D4   08 XXF6   /1-612 TnP AP 1   04 RLR4   /1-378		MR LV RV IVT LWFVLLGFA         MGASR TGCYLLAVVLAAV         MGVVE         GLLALALVLSAC         MRMNK         ILVFVESIAT         MGVSSFVAILLVVSIA         MGVSSFVAILLVVLV         MGVSSFVAILLVVLV         MGVSSFVAIALLNVLCU         MGVSSFVAIALLNVVV         MR MR SSFVAIALLNVVV         MGRVR FALLLLVVLCU         MGRVSSFVAIALLNVVV         MR MGNSSFVAIALLNVVV         MR MGNSSFVAIALLNVVV         MR MGNSSFVAIALLNVVV         MR MGNSSFVAIALLNSVVV         MR MGNSSFVAIALLNSVVV         MR MGNSSFVAIALLNSVVV         MR MGNSSFVAIALLNSVVV         MR MN NV SVAL         MR NV V SVAL         MN NV V SVAL         MN V V V SVAL	18 18 12 17 17 23 17 13 17 18 20 18 18 13 18 18 12 15 16 18 18 18 18 18 18 18 18 18 18
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 AtP AP 11   09 SI 8   /1-441 GmP AP 11   09 SI 8   /1-444 AtP AP 25   02 32 44   /1-466 AtP AP 12   03 83 24   /1-467 IdP AP 1 04K U02   /1-465 OSP AP 2   08 SD35   /1-461 MtP AP 1 04K U02   /1-465 OSP AP 2   07 54 C1   /1-457 UAP 2   07 54 C1   /1-457 UAP 2   07 54 C1   /1-457 Ta ACP   C4PK L1   /1-477 AtP AP 6   09 SI V9   /1-468 P VP AP 3   05 SD   /1-476 ACP AP 32   09 SI V9   /1-466 ACP AP 32   09 SI V9   /1-466 ACP AP 32   09 SI V9   /1-477 StP AP 3   06 J5M8   /1-477 IbP AP 3   08 J558   /1-473 AtP AP 26   09 SI V9   /1-512 La AP 2   09 XJ 24   /1-538 UPP D4   08 VXF4   /1-629 UPP D4   04 VXF4   /1-637 UPP D2   04 VXF4   /1-637 HSP AP 7   06 ZI F0   /1-438		MR LV RV I VT LWFVLLGFA MGAS RTGCYLLAVVLAAV MGAS RTGCYLLAVVLAAV MGAS RTGCYLLAVVLAAV MGAS RTGCYLLAVVLAAV MGYS FVALALVCAA MGVE GLLALALVLSAC MGVE GLLALALVLSAC MGS SRS DLK I KRVSLIIFLLSVLV MGFLHSLLLALCL MGS FRALLLHVLLCLV MGYS FVAIALLMSVVVV MER RVQTMLLK FVLAS FV MK MGNSS FVAIALLMSVVVL MGRVR KSDFGSIVLVLCC MK MGNSS FVAIALLMSVVVL MGVK GLLALALVLNVVV MGVK GLLALALVLNVVV MR GLGFAALSLHVLLCLA MVLIFK KNLIFFLSSVLL MVLIFK KNLIFFLSSVLL MVLIFK KNLIFFLSSVLL MR LVVVGLUCLIGL MNHLVIISVFLSSVLL MR LVVVGLUCLIGL MNHLVISVFLSSVLL MR VVLLYLVLSFV MR GVRK SRWFLSVLVLC MR VVLLYLVLSFV MR LVVVGLUCLIGL MVLAS FRSLLCKCFIFWL-GLCRLIKTLIP MR VVLLYLVLSFV MGYSIYCLIVLVVVF MGVSKFVFLYLLVVV MGVSKFVFLYLLVAT MGDSKFVFLYLLVSVL MHPLPGYWS	18 18 12 17 17 13 17 18 18 18 18 18 18 18 18 18 18
R.CP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 AtP AP 11   095 I18   /1-441 GmP AP 1   095 I18   /1-441 GmP AP 12   038924   /1-469 ItP AP 12   038924   /1-469 ItP AP 1 04KU02   /1-465 OSP AP 2   08505   /1-476 La AP 1   04KU02   /1-465 OSP AP 2   08505   /1-476 La AP 1   093VV   /1-468 P vP AP 2   095VV   /1-468 P vP AP 10   095VV   /1-468 P vP AP 10   095VV   /1-466 AtP AP 00   095VV   /1-466 AtP AP 00   095VV   /1-466 AtP AP 00   095VV   /1-466 AtP AP 10   095VV   /1-468 P vP AP 1   80366   /1-459 Ta ACP (24PKLL1 / 1-477 AtP AP 6   09 C5 10   /1-476 StP AP 3   065DM8   1-477 IbP AP 1   095XVP   /1-475 R CP AP 3   895XP 6   /1-478 LAP 1 08 L5 E1   /1-477 GmP AP 3   067GT9   1-512 La AP 2 (09XV21 / 1-613 UPP D4   08VXF4   /1-629 UPP D4   08VXF4   /1-629 UPP D4   08VXF4   /1-378 HSP AP 7   062 IF0   /1-418 CeP AP 3   091HAM9   /1-418		MR LV RV IVT LWFVLLGFA MGASRTGCYLLAVVLAAV MELSHLALVCAA MGVVE GLLALALVLSAC MRMNKE ILVFVFLSIAT MSSRSDLKIKRVSLIIFLLSVLV MGISWEFYVAILLFITN MGSSSFVAIALLHVUCCV MGYSSFVAIALLHVUCCV MGYSSFVAIALLHVVVC MKMGNSSFVAIALLMSVVVV MERRVQTMLLKFVLASFV MKMGNSSFVAIALLMSVVVV MRGLGFAALSLHVLLCL MGVVKGLLALALVLNVVV MRGLGFAALSLHVLLCL MKNLVIFAFLFLS MKNLVIFAFLFLS MKILFFLSLE MKILFFLSLE MKILFFLSLE MKILVVGLWCLILGE MKILVFFLSSVLL MKILFFLSSVLL MKILFFLSSVLL MKILFFLSSVLL MKILVFFLSSVLL MKILFFLSSVLL MKILFFLSSVLL MKNLVFFLSSVLL MKILFFLSSSVLL MKILFFLSSVLL MKILFFLSSSVLL MKILFFLSSSVLL MKILFFLSSSVLL MKILFFLSSSVLL MKILFFLSSSVLL MKILFFLSSSVLL MKILFFLSSSVLL MKILFFLSSSVLL MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSS MKILFFLSSSSS MKILFFLSSSS MKILFFLSSSSS MKILFFLSSSS MKILFFLSSSSS MKILFFLSSSSS MKILFFLSSSSS MKILFFLSSSSS MKILFFLSSSSS MKILFFLSSSSSS MKILFFLSSSSSS MKILFFLSSSSSSSS MKILFFLSSSSSSSSSSSSSS MKILFFLSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSSS	18 18 12 17 23 17 13 17 18 18 18 18 18 18 18 18 18 18
R.CP AP 2   B95XP8   /1-463 IbP AP 2   Q95D29   /1-465 AtP AP 11   Q95 ID 2   /1-465 AtP AP 11   Q95 ID 2   /1-464 AtP AP 25   Q23244   /1-469 ItP AP 1 Q 4KU23   /1-461 MtP AP 1 Q 4KU23   /1-461 MtP AP 1 Q 4KU23   /1-465 OSP AP 2   Q8505   /1-476 La AP 1 Q 92 V 9   /1-463 AtP AP 10   Q95 V 9   /1-468 P VP AP 1   P80366   /1-457 Ta ACP   C4PKL1   /1-477 AtP AP 6   Q9 C5 10   /1-466 AcP AP   Q93 V 9   /1-466 AcP AP 2   Q95K09   /1-470 StP AP 3   Q85D0   /1-475 RCP AP 3   Q95X9   /1-475 RCP AP 3   B95XP 6   /1-488 UAP 1   08 L5 E1   /1-477 GmP AP 3   Q6 GT 9   /1-477 GmP AP 3   Q8 L5 E1   /1-477 GmP AP 3   Q8 L7   /1-438 C8 AP AP 3   Q9 L4 L7   /1-438 C8 P AP 3   Q9 L4 AP   /1-438 C8 P AP 3   Q8 L7   /1-438		MR LVR V IVT LWFVLLGFA         MGASR TGCYLLAVVLAAV         MGLSHLALVCAA         MGVE         GLLALALVLSAC         MRNKLILVFVFLSIAT         MSSRSDLKIKRVSLIIFLLSVLV         MGISW         MGFLHSLLLVFVFLSIAT         MGSSFVAILLFITN         MGFLHSLLLLLVVLCLV         MGFLHSLLLLVVLCLV         MGFLSVFVAILLHVLCLV         MGFLSVFVAILLHVULCLV         MGYKFALLLHVULCLV         MGYKKSFVAIALLMSVVV         MKRVVKGLALALVINVV         MKNLVIFAFLFLS         MKNLVIFAFLFLS         MRVVKGLLALALVINVVV         MRGLGFAALSLHVULCLA         MRNNKNUFFSCHUST         MRNNKNUFFSCHUST         MR VIFSCHULFHIS         MKNUVFSCHULFHIS         MN LVFKKSCHULFHIS         MN LVFKKSCHULFHIS         MN LVVSLVFULSSVLIL         MN LVVSLVFULSSVLIL         MR VVLLYLVLVSLSSVLIL         MN LVVSLKSSFSV <td><math display="block">\begin{array}{c} 18\\ 12\\ 17\\ 23\\ 17\\ 13\\ 17\\ 18\\ 20\\ 18\\ 18\\ 18\\ 12\\ 15\\ 16\\ 18\\ 14\\ 39\\ 20\\ 26\\ 19\\ 15\\ 15\\ \end{array}</math></td>	$\begin{array}{c} 18\\ 12\\ 17\\ 23\\ 17\\ 13\\ 17\\ 18\\ 20\\ 18\\ 18\\ 18\\ 12\\ 15\\ 16\\ 18\\ 14\\ 39\\ 20\\ 26\\ 19\\ 15\\ 15\\ \end{array}$
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 AtP AP 11   09 SI 8   /1-441 GmP AP 11   09 SI 8   /1-441 AtP AP 25   02 3244   /1-466 AtP AP 12   03 89 24   /1-469 ItP AP 10   04 KU32   /1-461 MtP AP 10   04 S505   /1-465 OSP AP 2   08 5505   /1-476 La AP 10   09 SI V9   /1-468 P VP AP 2   07 64 C1   /1-457 UAP 2   08 L6L1   /1-463 AtP AP 10   09 SI V9   /1-468 P VP AP 2   07 64 C1   /1-477 AtP AP 6   09 C510   /1-468 P VP AP 2   09 SI V9   /1-468 P VP AP 2   09 SI V9   /1-481 AOP AP 32   09 XF09   /1-470 StP AP 3   09 SE0   /1-477 IbP AP 1   09 SE0   /1-477 R CP AP 3   09 SXP 6   /1-488 UAP 1   08 L5 E1   /1-477 GmP AP 3   09 SXP 6   /1-488 UPP D4   08 VXF4   /1-638 UPP D4   08 VXF4   /1-638 UPP D4   04 KXF4   /1-378 HSP AP 7   04 RLR4   /1-378 HSP AP 7   04 RLR4   /1-378 HSP AP 7   04 RX37   /1-438 DmP AP 2   09 VZ56   /1-450		MR LVR V IVT LWFVLLGFA         MGASR TGCYLLAVVLAAV         MGASR TGCYLLAVVLAAV         MGVVE         GLLALALVLSAC         MRNK         MSSRSDLK IKRVSLIFLLSVLV         MGISW         FYVVAILLFITN         MGVK         MGVK         MGSSRSDLK         MGSSRSDLK         MGSSRSDLK         MGVK         MGSSSV         MGVK         MGVK         MGVK         MGVK         MGRV         MGVK         MK         MK         MK <td>18 12 17 17 13 17 18 20 18 18 12 15 18 10 10 10 10 10 10 10 10 10 10</td>	18 12 17 17 13 17 18 20 18 18 12 15 18 10 10 10 10 10 10 10 10 10 10
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 AtP AP 11   09 SI 8   /1-441 GmP AP 11   09 SI 8   /1-441 AtP AP 25   02 3244   /1-466 AtP AP 12   03 8324   /1-461 MtP AP 1 04K U02   /1-465 OSP AP 2   08 505   /1-476 La AP 11 09 SI V9   /1-468 P VP AP 2   07 64 C1   /1-457 UAP 2   08 L6L1   /1-463 AtP AP 10   09 SI V9   /1-468 P VP AP 2   07 64 C1   /1-477 AtP AP 6   09 C5 10   /1-466 ACP AP 09 SI V9   /1-466 ACP AP 2   09 SI V9   /1-468 P VP AP 2   09 SI V9   /1-468 P VP AP 1   09 SI V9   /1-470 StP AP 3   06 J5 M8   /1-477 IbP AP 1   09 SED   /1-477 AtP AP 6   09 C5 10   /1-473 AtP AP 2   09 SXF 0   /1-475 R CP AP 3   89 SXP 6   /1-488 UAP 1   08 L5 E1   /1-477 GmP AP 3   06 V5 T9   /1-512 La AP 2   09 XX F6   /1-615 UPP D4   08 XXF 6   /1-615 UPP D4   08 XXF 6   /1-418 MCP AP 7   08 BX 7   /1-418 MCP AP 7   08 BX 7   /1-418 MCP AP 2   09 VZ56   /1-438 DCP AP 2   09 VZ56   /1-438 DCP AP 2   09 VZ56   /1-438 DCP AP 2   09 VZ58   /1-438 DCP AP		<pre></pre>	18 18 12 17 17 13 17 18 20 18 18 18 12 15 16 18 14 39 18 10 26 19 21 15 18 18 18 18 18 18 18 18 18 18
R.CP AP 2   B95XP 8   /1-463 IbP AP 2   Q95D29   /1-465 AtP AP 11   Q95 118   /1-441 GmP AP 1   Q09 131   /1-464 ArP AP 25   Q23244   /1-469 ItP AP 1 Q 4KU02   /1-465 OSP AP 2   Q8505   /1-476 La AP 1   Q4KU02   /1-465 OSP AP 2   Q8505   /1-476 La AP 1   Q93VV   /1-466 P vP AP 2   Q95V0   /1-463 AtP AP 10   Q93VV   /1-468 P vP AP 10   Q93VV   /1-468 P vP AP 10   Q93VV   /1-466 AcP AP 0   Q93VV   /1-466 AcP AP 0   Q93VV   /1-466 AcP AP 10   Q93VV   /1-468 P vP AP 1   R80366   1-459 Ta ACP   C4PKL1   /1-477 AtP AP 6   Q9 C5 10   /1-466 AcP AP 2   Q93VF0   /1-470 StP AP 3   Q65D8   1-477 IbP AP 1   Q95XV   /1-451 La AP 2 (Q94Y13   1-475 R cP AP 3   Q95XVP 6   /1-488 UAP 1   Q8 L5 E1   /1-477 GmP AP 3   Q67G19   1-512 La AP 2   Q9XV24   /1-638 UPP D4   Q8VXF4   /1-629 UPP D4   Q8VXF4   /1-629 UPP D1   Q8VXF6   /1-418 MmP AP 7   Q8 BX37   /1-418 MmP AP 7   Q8 BX37   /1-418 DmP AP 1   Q9VZ56   /1-438 DmP AP 1   Q9VZ56   /1-438 DmP AP 1   Q0VZ56   /1-438 DmP AP 1   Q0VZ56   /1-438 DmP AP 1   Q0VZ58   /1-450 AmP AP 1   Q005 Z00   /1-413 CeP AP 1   001320   /1-419		MR LVR V IV T LWFV LLGFA         MGAS R T G CY LLAVV LAAV         MGAS R T G CY LLAVV LAAV         MG VY E         GLLALAU LAV LAAV         MG VY E         GLLALAU LAV LAAV         MG V E         GLLALAU LAV LAAV         MS S R D LK IK RVS LITF LLSV LV         MG S S R D LK IK RVS LITF LLSV LV         MG FLHS LLLALULAV         MG V K S FVA I AL LMSV VV         MG V F V A TALL KV LV LC LV         MG WR FALLL HV LC LV         MG RV R KS DF GS IV LV LC L         MG RV R KS DF GS IV LV LC LA         MG RV R KS DF GS IV LV LC LA         MR GL G FAALS LHV LNV VV         MR GL G FAALS LHV LL LLAV         MR LV I FAF LFLS         MF I YT S R S C FY LL FH I         MV L I PK TK NL I I FV S LL L         MR LV I PK TK NL I I FV S LL L         MR LV I PK TK NL I I FV S LL L         MR LV I PK TK NL I I FV S LL L         MR LV V V C LW V LY LY VAS FV         MR LV I PK TK NL I I FV S LL L         MR LV I PK TK NL I I FV S LL L         MR LV I PK TK ML I I FV S LL L         MR LV I PK TK NL I I FV S LS VL         MR LV I PK TK NL I I FV S LS VL         MR S F S S LL CK C F I P RWL G LC LL I K TT LIP         MG S V S I Y C LI V V V V F	18 12 17 17 13 17 18 12 17 18 18 18 18 18 18 18 18 18 18
R.CP AP 2   89 SXP 8   /1-463 IbP AP 2   09 SD29   /1-465 AtP AP 11   09 SI 8   /1-441 GmP AP 11   09 SI 8   /1-441 AtP AP 25   02 3244   /1-466 AtP AP 12   03 8324   /1-461 MtP AP 1 04K U02   /1-465 OSP AP 2   08 505   /1-476 La AP 11 09 SI V9   /1-468 P VP AP 2   07 64 C1   /1-457 UAP 2   08 L6L1   /1-463 AtP AP 10   09 SI V9   /1-468 P VP AP 2   07 64 C1   /1-477 AtP AP 6   09 C5 10   /1-466 ACP AP 09 SI V9   /1-466 ACP AP 2   09 SI V9   /1-468 P VP AP 2   09 SI V9   /1-468 P VP AP 1   09 SI V9   /1-470 StP AP 3   06 J5 M8   /1-477 IbP AP 1   09 SED   /1-477 AtP AP 6   09 C5 10   /1-473 AtP AP 2   09 SXF 0   /1-475 R CP AP 3   89 SXP 6   /1-488 UAP 1   08 L5 E1   /1-477 GmP AP 3   06 V5 T9   /1-512 La AP 2   09 XX F6   /1-615 UPP D4   08 XXF 6   /1-615 UPP D4   08 XXF 6   /1-418 MCP AP 7   08 BX 7   /1-418 MCP AP 7   08 BX 7   /1-418 MCP AP 2   09 VZ56   /1-438 DCP AP 2   09 VZ56   /1-438 DCP AP 2   09 VZ56   /1-438 DCP AP 2   09 VZ58   /1-438 DCP AP		MR       UV V V V T LWFV LLGFA         MG AS R T GC Y LLAVV LAAV         MG V V E         MG V V E         GLLALALV LSAC         MR S R S D LK I K RV S LI I F LLSV LV         MG I SW         MG I SW         MG V K E         MG N S F S D LK I K RV S LI I F LLSV LV         MG I SW         MG I SW         MG S S F VA I ALLMS VV VV         MG Y S F VA I ALLMS VV VV         MG R S F VA I ALLMS VV VV         MG N S F VA I ALLMS VV VV         MG Y S F VA I ALLMS VV VV         MG V K S D F GS I V V LCC         MG V K GL ALALV LNV VV         MG V K S D F GS I V V LCC         MG V K GL ALALV LNV VV         MG V S S F VA I ALLMS VV VL         MG V S S F V I I ALLMS VV VV         MG V K GL ALALV LNV VV         MG V S S F V I ALLS S F V         MG V S S F V I ALLS S F V         MG V S S F V I ALLY V L L AS F V         MG V S S F V I ALLY V L L AS F V         MN LV I P K TKN LI I F F L L S L F F S S V L L         MN H V I S S F S S S V L L S L S V F S S N L L L A S L	18 18 12 17 23 17 13 17 18 18 13 18 12 17 18 18 18 13 18 18 18 13 18 18 19 10 18 18 18 19 19 19 10 10 10 10 10 10 10 10 10 10

44	23		45
50	19	A A A A A E P A S T L T G P S R P V T V A L R E D	42
38	18	A A A A E P A S T L E G P S R P V T V P L R E D	41
37	18	AVA EPASTLEGPSRPVTVPLRED	40
37		A T A E P A S M L E G P S G P V T V L L Q E D	40
36			40
39		A	40
44		VAA TAVPAEPASTLSGPSRPVTVAIG-D	45
43			47
		MAMA I P T T L D G P F K P V T I P L D E S	
64			62
51		IPTTVDGPFKPVTVPLDQS	46
43			44
47		<mark> </mark>	48
32		<u>SPAISSA</u> HSIPSTLDGPFVPVTVPLDTS	40
49	17	<mark>V A A A</mark> A E P A S T L T G P S R P V T V A L R E D	41
43	20		44
45	16	A A E P A S T L T G P S R P V T V A L R K D	37
39	16		40
49			41
41			40
36	18	A A E P A S T L E G P S WP V T V P L R E D	39
39			42
		AAAA EPASTLEGFSRPVTVPLRED	41
38			
38			41
66		SATLAAAHGHIPTTLEGPFKPRTVPLDQS	68
40		IHAR I P T T L D G P F X P V T V P F D Q S	41
46		<mark>G F S H C</mark> R V P S T L E G P F D P V T V P F D H S	48
47		<mark>FITVMA</mark> VTESHIPTTLDGPFEPVTRRFDPT	50
32		<mark>SPAIFFA</mark> DSIPSTLDGPFVPVTVPLDTS	40
58	22		40
42		<mark>A T A</mark> T P D S E Y V R P L P R K	34
66		C F A L L V E S G G I P T T L D G P F P P A T R A F D R A	59
66	33	FALLVECGGIPTTLDGPFPPATRAFDRA	60
64	28	PIAFLLVDGGGIPTTLDGPFTPATRAFDRS	57
57	28		49
22		S R L V R P P D G G G I P T T L D G P F E P A T R A F D R A	54
22		<mark>S</mark> RLVRPPDGGGIPTKLDGPFEPATRAFDRA	54
96			2.
27	18		34
34	10		33
	10		22
27	~ ~	P FV C Q A N Y D S N F T R P P P R	37
37			
55			29
63		KNGNGGITSSFIRS	32
65			33
41		<mark>I A F S S I F V V S Q A</mark> G I T S T HAR V	33
64		V MC N G G S S S P F I R K	31
66			30
69			37
61			33
65	14		32
76	18		31
60	19		30
57	19		37
63	21		32
68			36
59			31
77			
66			29
81			37
70		A FNAATLCNGGITSR FVRK	
77		LTFIDNGSAGITSAFIRT	30
73		ILNPTK FCDAGVTSSYVRK	30
		LYRGESGITSSFIRS	
75		LLD FV NNANAGITSS FIRS	31
88			37
77		LLSSIKDGSAGITSSFIRS	33
12		MLLNLVLAS FV F LS F I R D G S A G I T S S F I R S	
38			30
29		L S K I A I Y S T V L A L H S <mark>S A S I T A</mark> S P F S L G N S N E G D D	74
15		FQQAVSDDTQPLSKVAIHKTVFAIDEHAYIKATPNVLGFEG	61
12		HPLSKVSIHRASLSLLDLAHIKVSPPILGLQGQT	60
78	20		23
38			
18			
38	16	PFSPG	20
58		LPG	21
50		L P G	21
38			
19			
53	19		21
63	13		21
~			

HvPAPhy\_a|C4PKL2|/1-54 TaP APhy\_a 1 | C4PKK7 | /1-5 TaP APhy\_b1|C4PKK9|/1-5 TaP APhy\_b2 | C4PKL0 | /1-5 HvPAPhy\_b2|C4PKL4|/1-5 HvPAPhy\_b1/C4PKL3//1-5 OsP APhy\_b | D6QSX9 | /1-5 ZmP APhy\_b | C4PKL6 | /1-5-MtP APhy | Q3ZFI 1 | / 1-54 PtPAP3/V9LXK5//1-5 NtP APhy | A5 YBN1 |/1-5 LaP APhy/D2YZL4//1-5 GmP APhy\_b | Q93XG4 |/1-5-AtP AP 15 | Q9 SFU3 | /1-5 AtaP APhy\_a 1/F6MIX0 //1-54 ScP APhy\_a2 |F6MIX4 |/1-54 TmP APhy\_a1/F6MIW8//1-5 TaP APhy\_a3 | F6MI W2 | /1-5 TaP APhy\_a2 | C4PKK8 | /1-5 ScP APhy\_a 1/F6MIX2 //1-54 TaP APhy\_b3 | F6MIW6 | /1-5 TmP APhy\_b1/F6MIW9//1-5 AtaPAPhy\_b1/F6MIX1//1-5 ScP APhy\_b1/F6MIX5//1-5 RcP AP 1 | B9R W G6 | / 1-5 VvP AP | A5 BGI 6 | / 1-5 PvPAPhy/V7B3Z4//1-54 VrP APhy | B5 AR Z7 | / 1-54 AIP AP 15 | D7L636 | /1-5 AtP AP 23 | Q6TPH 1 | / 1-4: GmP AP 4 | V9H X G4 | / 1-4-ZmPAP\_c/C4PKL7//1-5 SbP AP | AO A1Z5R9 T8 | /1-5 HvPAP\_c/C4PKL5//1-5 PpP AP | A9 SP12 |/1-5. OsP AP 3 | Q6ZCX8 | /1-62 OsP AP 4 | B8 B909 | /1-62 AtP AP 5 | Q9 C927 | /1-3 AtP AP 20 | Q9 LXI 7 | /1-4 AtP AP 22 | Q85340 |/1-4 IbP AP3 | Q9ZP 18 | /1-4 AtP AP 2 1 | Q9 LXI4 | / 1-4 LpP AP | Q9MB07 | /1-4 RcP AP 2 | B9 SXP 8 |/1-4 IbP AP 2 | Q9 SDZ9 |/1-4 AtP AP 11 | Q9 SI 18 | / 1-4-GmP AP 1 | Q09 13 1 | / 1-4 AtP AP 25 | 023244 | /1-4 AtP AP 12 | Q38924 | / 1-4 NtP AP | Q84KZ3 |/1-4 MtP AP 1 | Q4KU02 | / 1-4 0sPAP2|Q85505|/1-4 La AP 1 | Q93VM7 | /1-4 PvPAP2|Q764C1|/1-4 UAP2/Q8L6L1//1-4 AtP AP 10 | Q9 SI V9 | / 1-4 PvPAP1/P80366//1-4 Ta ACP | C4PKL1 | / 1-4 AtP AP 6 | Q9 C5 10 | / 1-4 AcP AP | Q93WP4 | / 1-4 AoP AP 32 | Q9 XF0 9 | / 1-4 StP AP 3 | Q6J5M8 | /1-4 16P AP 1 | Q9 SE00 | /1-4 AtP AP 2 6 | Q949 Y3 | / 1-4 RcP AP 3 | B9 5XP 6 | / 1-4 UAP1/Q8L5E1//1-4 GmP AP 3 | Q6YGT9 | /1-5 La AP 2 | Q9 XJ24 | /1-63 UPP D4 | Q8 VXF4 | / 1-62 UPP D1/Q8VX11//1-6 UPP D2 | Q8 VXF6 | /1-6 TnP AP 1 | Q4R LR 4 | / 1-3 HsP AP 7 | Q6Z VF0 | /1-4 CeP AP 3 | Q911AM9 | /1-4 MmP AP 7 | Q8 BX 37 | /1-4 DmP AP 1 | Q9 VZ56 | / 1-4 DmP AP 2 | Q9 VZ58 | /1-4 AmP AP | AO AO 872W E4 | / 1-4 CeP AP 1 | 00 1320 | /1-4 DmP AP3 | Q9 VZ57 | /1-4 AgP AP | Q7P UN5 | /1-4

HvP APhy_a   C4PKL2   /1-544			
	46	R G H A V D L P D T D P R V Q R R - A T G WA P E Q V	71
TaP APhy a 1/C4PKK7//1-550		R G H A V D L P D T D P R V Q R R - A T G WA P E Q I	68
/ <b>_</b> / //		R G H A V D L P D T D P R V Q R R - V T G WA P E Q I	67
TaP APhy_b1/C4PKK9//1-538			
TaP APhy_b2   C4PKL0   /1-537		<mark>R G H A V D L P D T D P R V Q R R</mark> - V T G WA P E Q I	66
HvPAPhy_b2 C4PKL4 /1-537		<mark>R G H A V D L P D T D P R V Q R R</mark> - <b>V</b> T G WA P E Q I	66
HvPAPhy_b1 C4PKL3 /1-536		<mark>R G H A V D L P D T D P R V Q R R</mark> - V T GWA P E Q I	66
OsP APhy_b   D6QSX9   /1-539	41	<mark>R G H A V D L P D T D P R V Q R R</mark> - V K G WA P E Q I	66
ZmP APhy_b   C4PKL6   /1-544	46	<mark>R G H A V D L P D T D P R V Q R R</mark> - V T G WA P E Q V	71
MtP APhy/Q3ZFI 1 // 1-543	48	F R G N A V D I P D T D P L V Q R N - V E A F Q P E Q I	74
PtPAP3/V9LXK5//1-564	63	FR GNT I D L P D T D P R V Q R T - V E G F K P E Q I	89
NtP APhy A5YBN1 1/1-551	47	FR GHAVD L P D T D P R V Q R T - V K G F E P E Q I	73
LaP APhy   D2 YZL4   /1-543		LPTVSIDLPDTDPRVRRN-VHGFQPEQI	71
GmPAPhy b/Q93XG4//1-547		L R G V A V D L P E T D P R V R R - V R G F E P E Q I	75
AtP AP 15 / Q95FU3 / /1-532		L R G Q A I D L P D T D P R V R R R - V I G F E P E Q I	67
1			
AtaP APhy_a 1/F6MIX0//1-549		R G H A V D L P D T D P R V Q R R - A T G WA P E Q I	67
ScPAPhy_a2/F6MIX4//1-543		<mark>R G H A V D L P D T D P R V Q R R</mark> - A N G WA P E Q I	70
TmP APhy_a1/F6MIW8//1-545		<mark>R G H A V D L P D T D P R V Q R R</mark> - A T G WA P E Q I	63
TaP APhy_a3   F6MIW2   /1-539	41	<mark>R G H A V D L P D T D P R V Q R R</mark> - A T G WA P E Q I	66
TaP AP hy_a2   C4P KK8   /1-549	42	<mark>R G H A V D L P D T D P R V Q R R</mark> - V T G W A P E Q I	67
ScP APhy_a1/F6MIX2 //1-541	41	<mark>R G H A V D L P D T D P R V Q R R</mark> - A N G WA P E Q I	66
TaP APhy_b3   F6MIW6   /1-536	40	<mark>R G H A V D L P D T D P R V Q R R</mark> - V T G W A P E Q I	65
TmP APhy_b1/F6MIW9//1-539	43	R G H A V D L P D T D P R V Q R R - V T G WA P E Q I	68
AtaP APhy_b1/F6MIX1//1-538		<mark>R G H A V D L P D T D P R V Q R R</mark> - <b>V T G W</b> A P E Q I	67
ScP APhy_b1/F6MIX5//1-538		R G H A V D L P D T D P R V Q R R - V T G WA P E Q I	67
RcP AP 1/B9RWG6//1-566		FR GHAIDLPDSDPRVQRT-VRDFEPEQI	95
VvP AP   A5 BGI 6   / 1-540		L R G K A V D L P D T D P R V R R R - V K G F E P E Q I	68
PvPAPhy/V7B3Z4//1-546		L <mark>R GNAV D L P P S D P R V R R R</mark> - <b>V R G F E P E Q I</b>	75
VrP APhy   B5 AR Z7   / 1-547		L <mark>R R G S D D L P M T H P R L R K N</mark> - V T L N F P E Q I	77
AIP AP 15   D7L636   /1-532		L <mark>R GKA I D L P D T D P R V R R R</mark> - V T G F E P E Q I	67
AtP AP 23   Q6TPH 1   / 1-458		L <mark>R R G S D D L P MD H P R L R K R</mark> N V S S D F P E Q I	68
GmP AP4   V9HXG4   /1-442	35	<mark>T L T T I P W D S I S K</mark> A H S S Y P Q Q V	55
ZmP AP_c   C4PKL7   / 1-566	60	L	86
SbP AP   A0 A1Z5R9T8   /1-566	61	L R Q G S D D V P L T D P R L V P R - V Q P P A P E Q I	87
HvP AP_c / C4PKL5 //1-564	58	L R R G S E D V P L S D P R L A P R - A R P P S P E Q I	84
PpPAP   A9SPI2  /1-557		L R R G S V D L L P T D P R V A K T - V V G D A P E Q I	76
OsP AP 3   Q6ZCX8   /1-622		L R Q G S D D V P L T D P R L A P R - A R P P A P E Q I	81
OsP AP 4   B8 B909   / 1-622		L R Q G S D E V P I T E P R L A P C - A R T P A P E Q I	81
AtP AP 5   Q9 C927   / 1-396			18
AtP AP 20   Q9 LXI 7   /1-427		P T N E D D P T F P D Q V	47
AtP AP 22   Q85340  /1-434		<mark>PIVFVHNDRS</mark> KSDPQQV	50
IbP AP 3   Q9ZP 18   / 1-427		<mark>DMP L D S D V F R V P</mark> - P G Y N V P Q Q V	21
AtP AP 2 1   Q9 LXI 4   / 1-437		<mark> P L F I V S H G R P</mark> K F Y P Q Q V	54
LpP AP   Q9MB07   /1-455	30	<mark>Q E S A V DMP L H A D V F R MP</mark> - P G Y N A P Q Q V	55
RcP AP 2   B9 5XP 8   / 1-463			
KC/ A 2 1000M 0 // 1-00	33	<mark>A F P S T D I P L D D P V F A S P</mark> - A G Y N A P H Q V	58
IbP AP 2   Q9 SDZ9   /1-465		<mark>A FP S T D I P L D D P V F A S P</mark> - A G Y N A P H Q V	58 59
	34		
IbP AP 2   Q9 SD Z9   / 1-465 AtP AP 11   Q9 SI 18   / 1-441	34 34	<mark>V EK T V DMP L D S <u>D V</u> F R V P</mark> - P G Y N A P Q Q V	59
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q95I 18  /1-441 GmP AP 1   Q09 131  /1-464	34 34 32	<mark>V EK TV DMP L D S DV FR V P</mark> - P G Y N A P Q Q V	59 57
1bP AP 2   Q9 SD 29   /1-465 AtP AP 11   Q9 SI 18   /1-441 GmP AP 1   Q0 9 13 1   /1-464 AtP AP 25   023244   /1-466	34 34 32 31	<mark>V EK TV DMP L D S DV FR V P</mark> - P G Y N A P Q Q V S E P S E EMS L E T <mark></mark> F P P P - A G Y N A P E Q V V EK TV DMP L D S DV F A V P - P G Y N A P Q Q V A Q P S T EMS L E T <mark> F P S P</mark> - A G H N A P E Q V	59 57 57 54
IbP AP2   Q9SDZ9  /1-465 AtP AP 11   Q9SI 18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   Q38924  /1-469	34 34 32 31 38		59 57 57 54 63
IbP AP 2   Q9SDZ9  /1-465 AtP AP 11   Q9SI 18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 IVtP AP   Q84KZ3  /1-461	34 34 32 31 38 34	<mark>V EK T V DMP L D S D V F R V P</mark> - P G Y N A P Q Q V S E P S E EMS L E T F P P P - A G Y N A P E Q V V EK T V DMP L D S D V F A V P - P G Y N A P Q Q V A Q P S T EMS L E T - F P S P - A G H N A P E Q V S D L P D D MP L D S D V F E V P - P G P N S P Q Q V V E S S E <mark>-</mark> D MP L D S D V F R V P - H G Y N A P Q Q V	59 57 57 54 63 59
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 11   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 INP AP   Q84KZ3  /1-461 MtP AP 1   Q4KU02  /1-465	34 32 31 38 34 33		59 57 54 63 59 58
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   Q03244  /1-466 AtP AP 12   Q38924  /1-469 NtP AP   Q84KZ3  /1-461 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476	34 32 31 38 34 33 32		59 57 54 63 59 58 58 57
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   Q38924  /1-469 IVtP AP   Q84KZ3  /1-461 MtP AP 1 Q4KKU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460	34 32 31 38 34 33 32 31	-       V EK TV DMP LDS DV FRVP       - P GYNAP QQV         -       S EP S E EMS L ET       - F P P P       - A GYNAP E QV         -       V EK TV DMP LDS DV FAVP       - P GYNAP QQV         -       V EK TV DMP LDS DV FAVP       - P GYNAP QQV         -       A QP S T EMS L ET       - F P S P         -       A QP S T EMS L ET       - F P S P         -       S D L P D DMP LD S DV F EVP       - A GH NA P E QV         -       S D L P D DMP LD S DV F EVP       - P G P N S P Q QV         -       V EK T D MP LD S DV F F VP       - H G Y NA P Q QV         -       V EK T I DMP LD S DV F D VP       - S G Y NA P Q QV         -       E YP S T D I P L ES EWF AVP       - N G Y NA P Q QV         -       L I EK PV DMP LD S DA FA I P       - P G Y NA P Q QV	59 57 54 63 59 58 57 57
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 INTP AP 1   Q4KU02  /1-465 OsP AP 2   Q8505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457	34 32 31 38 34 33 32 31 38	-       V EK TV DMP LDS DV FRVP       - P GYNAP QQV         -       S EP S E EMS L ET       - F P P P       - A GYNAP E QV         -       V EK TV DMP LDS DV FAVP       - P GYNAP QQV         -       A QP S T EMS L ET       - F P S P       - A GHNAP E QV         -       A QP S T EMS L ET       - F P S P       - A GHNAP E QV         -       A QP S T EMS L ET       - F P S P       - A GHNAP E QV         -       S D L P D DMP LD S DV F EVP       - P G P NS P Q QV         -       V ES S E       DMP LD S DV F R VP       - H G Y NAP Q QV         -       V EK T I DMP LD S DV F DVP       - S G Y NAP Q QV         -       E YP S T D I P L ES E WFAVP       - N G Y NAP Q QV         -       L I EK P V DMP LD S DA FA I P       - P G Y NAP Q QV         -       EWP AV D I P LD H EA FAVP       - K G Y NAP Q QV	59 57 54 63 59 58 57 57 63
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q95 18  /1-441 GmP AP 1   Q09 131  /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   O38924  /1-469 INTP AP 1 Q84KZ3  /1-461 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q8505  /1-476 La AP 1   Q93 VM7  /1-460 P vP AP 2   Q764 C1  /1-453 UAP 2   Q8L6L1  /1-463	34 32 31 38 34 33 32 31 38 33	-       V EK TV DMP LDS DV FRVP       - P G Y NAP Q Q V         -       S EP S E EMS L ET       - F P P P       - A G Y NAP E Q V         -       V EK TV DMP LDS DV FAVP       - P G Y NAP Q Q V         -       A Q P S T EMS L ET       - F P S P       - A G H NAP E Q V         -       A Q P S T EMS L ET       - F P S P       - A G H NAP E Q V         -       A Q P S T EMS L ET       - F P S P       - A G H NAP E Q V         -       S D L P D DMP LD S D V F E V P       - P G P N S P Q Q V         -       V ES S E       - DMP LD S D V F V P       - H G Y NAP Q Q V         -       V EK T I DMP LD S D V F D V P       - S G Y NAP Q Q V         -       E Y P S TD I P L E S EWFAV P       - N G Y NAP Q Q V         -       L I E K P V DMP LD S D A F A I P       - P G Y NAP Q Q V         -       EWP A V D I P LD H E A FAV P       - K G Y NAP Q Q V         -       L I Q N P V DMP LD S D A F A I P       - P G Y NAP Q Q V	59 57 54 63 59 58 57 57 63 59
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 11   Q9518  /1-441 GmP AP 25   O23244  /1-466 AtP AP 25   O23244  /1-466 INP AP 1 Q84KZ3  /1-461 MtP AP 1   Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q86L11  /1-463 AtP AP 10   Q95V9  /1-468	34 32 31 38 34 33 32 31 38 33 37	V EK TV DMP LDS DV FRVP       P G Y NAP QQV         S EP S E EMS L ET       FP P P         A QP S T EMS L ET       FP P P         A QP S T EMS L ET       FP S P         A QP S T EMS L ET       FP S P         A QP S T EMS L ET       FP S P         A QP S T EMS L ET       FP S P         A QP S T EMS L ET       FP S P         S D L P D DMP LDS DV FEVP       P G P NS P Q QV         S S E       DMP LDS DV FEVP         V EK T I DMP LDS DV FEVP       S G Y NAP Q QV         V EK T I DMP LDS DV FEVP       S G Y NAP Q QV         E Y P S TD I P L ES EWFAVP       N G Y NAP Q QV         L I EK PV DMP LDS DA FA I P       P G Y NAP Q QV         EWP AVD I P LD H EA FAVP       K G Y NAP Q QV         L I Q NV P MMP LDS DV FR VP       C G Y NAP Q QV         L I A TV DMP LDS DV FR VP       C G Y NAP Q QV         L I EA TV DMP LDS DV FR VP       C G Y NAP Q QV	59 57 54 63 59 58 57 57 63 59 62
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-411 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-466 MtP AP 1   Q4K23  /1-461 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VW7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q95V9  /1-468 P vP AP 1   P80366  /1-459	34 32 31 38 34 33 32 31 38 33 37 32	V EK TV DMP LDS DV FRVP       P G Y NAP QQV         S EP S E EMS L ET       FP P P         A QP S T EMS L ET       FP P P         A QP S T EMS L ET       FP S P         A QP S T EMS L ET       FP S P         A QP S T EMS L ET       FP S P         - S D L P D DMP LD S DV F EV P       P G Y NAP Q Q V         - S D L P D DMP LD S DV F EV P       P G P N S P Q Q V         - V ES S E       DMP LD S DV F EV P         - V ES S E       DMP LD S DV F EV P         - V ES S E       DMP LD S DV F EV P         - V ES S E       DMP LD S DV F EV P         - V ES T D I P L E S EWFAV P       N G Y NAP Q Q V         - L I EK P V DMP LD S DA FA I P       P G Y NAP Q Q V         - L I QNP V DMP LD S DA FA I P       P G Y NAP Q Q V         - L I QNP V DMP LD S DV F R V P       C G Y NAP Q Q V         - L I QNP V DMP LD S DV F R V P       P G Y NAP Q Q V         - L I QNP V DMP LD S DV F R V P       P G Y NAP Q Q V         - L I QNP V DMP LD S DV F R V P       P G Y NAP Q Q V         - L I N K NR DMP LD S DV F R V P       P G Y NAP Q Q V	59 57 54 63 59 58 57 63 59 62 57
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   Q38924  /1-466 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8 L6L1  /1-463 AtP AP 10   Q95V9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP (C4PKL1  /1-477	34 32 31 38 34 33 32 31 38 33 37 32 33	V EK TV DMP LDS DV FRVP       P GYNAP QQV         S EP S E EMS L ET       FP PP         A QP ST EMS L ET       FP PP         A QP ST EMS L ET       FP SP         S D LP DDMP LDS DV FAVP       P GYNAP QQV         S D LP DDMP LDS DV FFVP       P GP NS P QQV         V ES S E       DMP LDS DV FFVP         V EX ST D IP LDS DV FFVP       N GYNAP QQV         V EX T DMP LDS DV FFVP       N GYNAP QQV         V EX T DMP LDS DV FFVP       N GYNAP QQV         V EX T DMP LDS DV FFVP       N GYNAP QQV         E YP S T D IP L ES EWFAVP       N GYNAP QQV         L I EK PV DMP LDS DA FA IP       P GYNAP QQV         E WP AVD IP LD H EA FAVP       - K GYNAP QQV         L I QNPV DMP LDS DV FRVP       - P GYNAP QQV         L EA TV DMP LDS DV FRVP       - P GYNAP QQV         T NK NR DMP LDS DV FRVP       - P GYNAP QQV         T NK NR DMP LDS DV FRVP       - P GYNAP QQV         EFP S TDMP LDS EWFATP       - K GYNAP QQV	59 57 54 63 59 58 57 63 59 62 57 58
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-411 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-466 MtP AP 1   Q4K23  /1-461 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VW7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q95V9  /1-468 P vP AP 1   P80366  /1-459	34 32 31 38 34 33 32 31 38 33 37 32 33 30	<ul> <li>V EK TV DMP LDS DV FRVP</li> <li>P G Y NAP QQV</li> <li>S EP S E EMS L ET</li> <li>FP P P</li> <li>A G Y NAP E QV</li> <li>V EK TV DMP LDS DV FAVP</li> <li>P G Y NAP QQV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>P G Y NAP Q QV</li> <li>V ES S E</li> <li>D MP LDS DV F E VP</li> <li>P G P N S P Q QV</li> <li>V ES S E</li> <li>D MP LDS DV F E VP</li> <li>S G Y NAP Q QV</li> <li>V E Y S T D I P L ES EWFAVP</li> <li>N G Y NAP Q QV</li> <li>E Y P S T D I P LD A FA I P</li> <li>P G Y NAP Q QV</li> <li>L I Q N P V D MP LD S DA FA I P</li> <li>P G Y NAP Q QV</li> <li>L EA TV D MP LD S DV FR V P</li> <li>C G Y NAP Q QV</li> <li>T N K N R D MP LD S DV FR V P</li> <li>P G Y NAP Q QV</li> <li>T N K N R D MP LD S DV FR V P</li> <li>P G Y N AP Q QV</li> <li>A LP S I EMS LD T</li> <li>FP S T D P LD E WFA TP</li> <li>G G Y N TP E QV</li> </ul>	59 57 54 63 59 58 57 63 59 62 57
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   Q38924  /1-466 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8 L6L1  /1-463 AtP AP 10   Q95V9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP (C4PKL1  /1-477	34 32 31 38 34 33 32 31 38 33 37 32 33 30	V EK TV DMP LDS DV FRVP       P GYNAP QQV         S EP S E EMS L ET       FP PP         A QP ST EMS L ET       FP PP         A QP ST EMS L ET       FP SP         S D LP DDMP LDS DV FAVP       P GYNAP QQV         S D LP DDMP LDS DV FFVP       P GP NS P QQV         V ES S E       DMP LDS DV FFVP         V EX ST D IP LDS DV FFVP       N GYNAP QQV         V EX T DMP LDS DV FFVP       N GYNAP QQV         V EX T DMP LDS DV FFVP       N GYNAP QQV         V EX T DMP LDS DV FFVP       N GYNAP QQV         E YP S T D IP L ES EWFAVP       N GYNAP QQV         L I EK PV DMP LDS DA FA IP       P GYNAP QQV         E WP AVD IP LD H EA FAVP       - K GYNAP QQV         L I QNPV DMP LDS DV FRVP       - P GYNAP QQV         L EA TV DMP LDS DV FRVP       - P GYNAP QQV         T NK NR DMP LDS DV FRVP       - P GYNAP QQV         T NK NR DMP LDS DV FRVP       - P GYNAP QQV         EFP S TDMP LDS EWFATP       - K GYNAP QQV	59 57 54 63 59 58 57 63 59 62 57 58
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   Q38924  /1-469 NtP AP 1   Q4K23  /1-461 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-463 AtP AP 10   Q95V9  /1-468 P vP AP 1   P83056  /1-459 Ta ACP (C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466	34 32 31 38 34 32 31 38 37 32 33 37 32 33 30 38	<ul> <li>V EK TV DMP LDS DV FRVP</li> <li>P G Y NAP QQV</li> <li>S EP S E EMS L ET</li> <li>FP P P</li> <li>A G Y NAP E QV</li> <li>V EK TV DMP LDS DV FAVP</li> <li>P G Y NAP QQV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>P G Y NAP Q QV</li> <li>V ES S E</li> <li>D MP LDS DV F E VP</li> <li>P G P N S P Q QV</li> <li>V ES S E</li> <li>D MP LDS DV F E VP</li> <li>S G Y NAP Q QV</li> <li>V E Y S T D I P L ES EWFAVP</li> <li>N G Y NAP Q QV</li> <li>E Y P S T D I P LD A FA I P</li> <li>P G Y NAP Q QV</li> <li>L I Q N P V D MP LD S DA FA I P</li> <li>P G Y NAP Q QV</li> <li>L EA TV D MP LD S DV FR V P</li> <li>C G Y NAP Q QV</li> <li>T N K N R D MP LD S DV FR V P</li> <li>P G Y NAP Q QV</li> <li>T N K N R D MP LD S DV FR V P</li> <li>P G Y N AP Q QV</li> <li>A LP S I EMS LD T</li> <li>FP S T D P LD E WFA TP</li> <li>G G Y N TP E QV</li> </ul>	59 57 54 63 59 58 57 63 59 62 57 58 57 58 53
IbP AP 2   Q95DZ9  /1465 AtP AP 11   Q9518  /1441 GmP AP 1   Q09131  /1464 AtP AP 25   O23244  /1466 AtP AP 12   Q38924  /1469 INTP AP   Q84KZ3  /1461 MrP AP 1   Q4KU02  /1465 OsP AP 2   Q85505  /1476 La AP 1   Q93VM7  /1460 P vP AP 2   Q764 C1  /1457 UAP 2   Q816L1  /1463 AtP AP 10   Q95V9  /1468 P vP AP 1   P80366  /1459 Ta ACP / C4FKL1  /1477 AtP AP 6   Q9 C510  /1466 AcP AP   Q93WP4  /1481	34 32 31 38 34 33 32 31 38 37 32 33 30 38 38	<ul> <li>V EK TV DMP LDS DV FRVP</li> <li>P G Y NAP QQV</li> <li>S EP S E EMS L ET</li> <li>FP PP</li> <li>A G Y NAP E QV</li> <li>V EK TV DMP LDS DV FAVP</li> <li>P G Y NAP QQV</li> <li>A QP ST EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP ST EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP ST EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP ST EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP ST EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP ST EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP ST EMS L ET</li> <li>FP SP</li> <li>P G P NS P QQV</li> <li>V EK T I DMP LDS DV F VP</li> <li>S G Y NAP QQV</li> <li>V EK T I DMP LDS DV F P VP</li> <li>S G Y NAP QQV</li> <li>V EK T I DMP LDS DA FA I P</li> <li>P G Y NAP QQV</li> <li>E V P ST D MP LDS DV F R VP</li> <li>C G Y NAP QQV</li> <li>T NK NR DMP LDS DV FR VP</li> <li>G G Y NAP QQV</li> <li>E FP ST DMP LD S WF ATP</li> <li>K G Y NAP QQV</li> <li>A L P S I EMS L D - FP SP</li> <li>G G Y N P QQV</li> <li>A L P S I EMS L D - FP SP</li> <li>G G Y N TP E QV</li> </ul>	59 57 54 63 59 58 57 63 59 62 57 58 59 62 58 53 63
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 11   Q9518  /1-441 GmP AP 11   Q9111  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38242  /1-461 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q8505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q8611  /1-463 AtP AP 10   Q95V9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP (C4PKL1  /1-463 AtP AP 6   Q9 C510  /1-466 AcP AP 2   Q95K09  /1-470 StP AP3   Q6J5M8  /1-477	34 34 32 31 38 33 32 31 38 33 37 32 33 30 38 38 38 38 38 31	<ul> <li>V EK TV DMP LDS DV FRVP</li> <li>P G Y NAP QQV</li> <li>S EP S E EMS L ET</li> <li>FP P P</li> <li>A G Y NAP QQV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP QQV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP QQV</li> <li>S D L P D DMP LD S DV F EV P</li> <li>P G P NSP QQV</li> <li>S D L P D DMP LD S DV F EV P</li> <li>P G Y NAP QQV</li> <li>V ES E</li> <li>D MP LD S DV F EV P</li> <li>P G Y NAP QQV</li> <li>V ES T D I P L ES EWFAVP</li> <li>N G Y NAP QQV</li> <li>E Y P S T D I P L ES EWFAVP</li> <li>N G Y NAP QQV</li> <li>E Y P S T D I P L D H EA F AV P</li> <li>K G Y NAP QQV</li> <li>L I QNP V DMP LD S DV F RV P</li> <li>P G Y NAP QQV</li> <li>L I QNP V DMP LD S DV F RV P</li> <li>P G Y NAP QQV</li> <li>E FP S T D MP LD S DV F RV P</li> <li>P G Y NAP QQV</li> <li>E FP S T D MP LD S DV F RV P</li> <li>A G Y NAP QQV</li> <li>E FP S T D MP LD S DV F RV P</li> <li>A G Y NAP QQV</li> <li>E FP S T D MP LD S DV F RV P</li> <li>A G Y NAP QQV</li> <li>E FP AVD I P LD S EF AV P</li> <li>K G Y NAP QQV</li> <li>E FP AVD I P LD S EF AV P</li> <li>K G Y NAP QQV</li> <li>E FP AVD I P L D S EF AV P</li> <li>K G Y NAP QQV</li> <li>A L P S I EMS LD T</li> <li>FP S V D I P L EN EV S V P</li> <li>N G Y NAP QQV</li> <li>A A T D MP LN S DV FR V P</li> <li>N G Y NAP QQV</li> <li>Q FP S V D I P L EN EV S V P</li> <li>N G Y NAP QQV</li> </ul>	59 57 54 63 59 58 57 63 59 62 57 63 59 62 57 63 63 63 63 63 63
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-411 GmP AP 11   Q9518  /1-411 GmP AP 12   Q38924  /1-466 AtP AP 25   023244  /1-466 MtP AP 12   Q38924  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VW7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q95V9  /1-476 AtP AP 6   Q95V9  /1-476 AcP AP   Q93 WP4  /1-481 AoP AP 32   Q3XF09  /1-477 StP AP3   Q65500  /1-473 IbP AP 1   Q95E00  /1-473	34 34 32 31 38 34 33 32 31 38 33 37 32 33 30 38 38 38 31 38	<ul> <li>V EK TV DMP LDS DV FRVP</li> <li>P G Y NAP QQV</li> <li>S EP S E EMS L ET</li> <li>FP P P</li> <li>A Q Y NAP QQV</li> <li>A Q P S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP QQV</li> <li>A Q P S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP QQV</li> <li>A Q P S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP QQV</li> <li>A Q P S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP QQV</li> <li>A Q P S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP QQV</li> <li>A Q P S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP QQV</li> <li>A Q P S T EMS L ET</li> <li>FP S P</li> <li>F Q P S T EMS L ET</li> <li>F Y P S T D I P L DS DV F EVP</li> <li>F Q Y NAP QQV</li> <li>S G Y NAP QQV</li> <li>C L I EK P V DMP LDS DA FA I P</li> <li>P G Y NAP QQV</li> <li>L I Q N P V DMP LD S DA FA I P</li> <li>P G Y NAP QQV</li> <li>L I Q N P V DMP LD S DV F EVP</li> <li>C G Y NAP QQV</li> <li>C L A TV DMP LD S DV F R VP</li> <li>P G Y NAP QQV</li> <li>C L A TV DMP LD S DV F R VP</li> <li>P G Y NAP QQV</li> <li>C E FP S T DMP LD S DV F R VP</li> <li>P G Y NAP QQV</li> <li>A L P S I EMS LD F</li> <li>F S P S V D I P L DS EWFA VP</li> <li>K G Y NAP QQV</li> <li>L A A T DMP LD S DV F R VP</li> <li>P G Y NAP QQV</li> <li>A L P S V D I P L S DV F R VP</li> <li>P G Y NAP QQV</li> <li>A L P S V D I P L S DV F R VP</li> <li>S G Y NAP QQV</li> <li>A L P N A EDV DMP US DV F A VP</li> <li>S G Y NAP QQV</li> </ul>	59 57 54 63 59 58 57 63 59 62 57 58 53 63 63 63 56 66
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q9518  /1-441 GmP AP 1   Q9318  /1-444 AtP AP 25   Q23244  /1-466 AtP AP 12   Q38924  /1-469 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q95V9  /1-468 AtP AP 10   Q95V9  /1-465 AcP AP 6   Q9 C5 10  /1-466 AcP AP 6   Q9 C5 10  /1-467 AtP AP 3 2   Q9XF09  /1-470 StP AP 3   Q6J5M8  /1-477 IbP AP 1   Q95E00  /1-473 AtP AP 2 6   Q949Y3  /1-475	34 34 32 31 38 34 33 32 31 38 33 37 32 33 30 38 38 38 31 38 31 38 32	<ul> <li>V EK TV DMP LDS DV FRVP</li> <li>P GYNAP QQV</li> <li>S EP S E EMS L ET</li> <li>FP P P</li> <li>A GYNAP QQV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A GYNAP QQV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A GHNAP QQV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A GHNAP QQV</li> <li>A QP S T EMS L ET</li> <li>FP S P</li> <li>A GHNAP QQV</li> <li>S D L P D DMP LD S DV F EVP</li> <li>P G P NS P QQV</li> <li>V ES S E</li> <li>DMP LD S DV F EVP</li> <li>P G Y NAP QQV</li> <li>V EK T I DMP LD S DV F EVP</li> <li>N G Y NAP QQV</li> <li>E Y P S T D I P L ES EWFAVP</li> <li>N G Y NAP QQV</li> <li>L I EK P V DMP LD S DA FA I P</li> <li>P G Y NAP QQV</li> <li>L I QNP V DMP LD S DA FA I P</li> <li>P G Y NAP QQV</li> <li>L I QNP V DMP LD S DV F R VP</li> <li>C G Y NAP QQV</li> <li>L EA TV DMP LD S DV F R VP</li> <li>C G Y NAP QQV</li> <li>TNK NR DMP LD S DV F R VP</li> <li>G G Y N AP QQV</li> <li>A LP S I EMS LD T</li> <li>FP S V D I P L S K EFA VP</li> <li>K N Q F S P QQV</li> <li>LAAA T DMP LNS DV F R VP</li> <li>P G Y NAP QQV</li> <li>ALP NA ED V DMP LD S DV F R VP</li> <li>K G Y NAP QQV</li> <li>ALP NA C DV DMP LNS DV F AVP</li> <li>S G Y NAP QQV</li> <li>ALP NA C DV DMP WD S DV F AVP</li> <li>K G Y NAP QQV</li> <li>EWP AV D I P L DH HV F KVP</li> <li>K G Y NAP QQV</li> </ul>	59 57 54 63 59 58 57 63 59 62 57 63 59 62 57 58 53 63 63 63 63 63 56 65 57
IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   Q38924  /1-469 INP AP   Q84KZ3  /1-461 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P VF AP 2   Q764 C1  /1-457 UAP 2   Q764 C1  /1-457 UAP 2   Q764 C1  /1-457 Ta ACP   C93VM7  /1-468 P VF AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP   Q93 WP4  /1-481 AoP AP 3   Q615M8  /1-477 IbP AP 1   Q95K09  /1-473 AtP AP 2 6   Q949Y3  /1-475 RcP AP 3   B95XP 6  /1-488	34 32 31 38 34 33 32 31 38 33 37 32 33 30 38 38 38 38 38 38 38 38 32 38	<ul> <li>V EK TV DMP LDS DV FRVP</li> <li>P G Y NAP QQV</li> <li>S EP S E EMS L ET</li> <li>FP PP</li> <li>A Q Y NAP QQV</li> <li>V EK TV DMP LDS DV FAVP</li> <li>P G Y NAP QQV</li> <li>A QP S T EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP SP</li> <li>A G H NAP E QV</li> <li>A QP S T EMS L ET</li> <li>FP S T D IP LDS DV F E VP</li> <li>P G P N S P Q QV</li> <li>V EK T I DMP LDS DV F F VP</li> <li>S G Y NAP Q QV</li> <li>V EK T I DMP LDS DA FA I P</li> <li>P G Y NAP Q QV</li> <li>E WP A VD IP LD H EA FA VP</li> <li>K G Y NAP Q QV</li> <li>L EA TV DMP LDS DV FR VP</li> <li>P G Y NAP Q QV</li> <li>T NK NR DMP LDS DV FR VP</li> <li>P G Y NAP Q QV</li> <li>T NK NR DMP LDS DV FR VP</li> <li>P G Y NAP Q QV</li> <li>T NK NR DMP LDS DV FR VP</li> <li>P G Y NAP Q QV</li> <li>T NK NR DMP LDS EWFATP</li> <li>K G Y NAP Q QV</li> <li>A LP S I EMS L DT</li> <li>FP S V D IP L EN EV L S VP</li> <li>N G Y NAP Q QV</li> <li>A LP NA E DV DMP WS DV FA VP</li> <li>S G Y NAP Q QV</li> <li>A LP NA E DV DMP WS DV FA VP</li> <li>K G Y NAP Q QV</li> <li>EWP A V D IP L DH HV FK VP</li> <li>K G Y NAP Q QV</li> <li>EWP A V D IP L DH HV FK VP</li> <li>K G Y NAP Q QV</li> <li>EWP A V D IP L DH HV FK VP</li> <li>K G Y NAP Q QV</li> <li>EWP A V D IP L DH HV FK VP</li> <li>K G Y NAP Q QV</li> </ul>	59 57 54 63 59 58 57 63 59 62 57 63 59 62 57 58 53 63 63 63 56 65 7 63 56 63 57 63 57 58 57 57 57 57 57 57 57 57 57 57 57 57 57
IbP AP 2   Q95D29  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   Q38924  /1-469 INTP AP   Q84K-23  /1-461 MTP AP   Q84K-23  /1-461 D8P AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P VP AP 2   Q764 C1  /1-457 UAP 2   Q8 L6L1  /1-463 AtP AP 10   Q95V9  /1-468 P VP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C510  /1-466 AcP AP   Q93WP4  /1-481 AoP AP 32   Q9XF09  /1-473 AtP AP 2   Q95D0  /1-473 AtP AP 2   Q949Y3  /1-475 RcP AP 3   B95XP 6  /1-488 UAP 1   Q8L5E1  /1-477	34 32 31 38 34 33 32 31 38 33 30 38 33 30 38 38 31 38 32 38 32 38 34	<ul> <li>V EK TV DMP L DS DV FRVP</li> <li>P G Y NAP Q Q V</li> <li>S EP S E EMS L ET</li> <li>FP P P</li> <li>A G Y NAP Q Q V</li> <li>A Q P S T EMS L ET</li> <li>FP S P</li> <li>A G Y NAP Q Q V</li> <li>A Q P S T EMS L ET</li> <li>FP S P</li> <li>A G H NAP E Q V</li> <li>S D L P D DMP L DS DV F EV P</li> <li>P G P NS P Q Q V</li> <li>S D L P D DMP L DS DV F EV P</li> <li>P G Y NAP Q Q V</li> <li>V ES S E</li> <li>D MP L DS DV F EV P</li> <li>H G Y NAP Q Q V</li> <li>V ES S E</li> <li>D MP L DS DV F EV P</li> <li>S G Y NAP Q Q V</li> <li>V ES S E</li> <li>D MP L DS DV F EV P</li> <li>S G Y NAP Q Q V</li> <li>V EK T I D MP L DS DV F AV P</li> <li>N G Y NAP Q Q V</li> <li>V EK T I D MP L DS DA FAI P</li> <li>P G Y NAP Q Q V</li> <li>E WP AV D I P L D H EA FAV P</li> <li>K G Y NAP Q Q V</li> <li>L I Q N V D MP L DS DA FAI P</li> <li>P G Y NAP Q Q V</li> <li>L I A TV D MP L DS DV F R V P</li> <li>C G Y NAP Q Q V</li> <li>T NK NR D MP L DS DV F R V P</li> <li>C G Y NAP Q Q V</li> <li>T NK NR D MP L DS DV F R V P</li> <li>P G Y NAP Q Q V</li> <li>T NK NR D MP L DS DV F R V P</li> <li>P G Y NAP Q Q V</li> <li>T NK NR D MP L DS DV F R V P</li> <li>P G Y NAP Q Q V</li> <li>T NK NR D MP L DS DV F R V P</li> <li>P G Y NAP Q Q V</li> <li>T NK NR D MP L DS DV F R V P</li> <li>P G Y NAP Q Q V</li> <li>A L P S I EMS L D T</li> <li>F P S Y D MP L D S K E F A V P</li> <li>N G Y NAP Q Q V</li> <li>Q F P S V D I P L E N E V L S V P</li> <li>N G Y NAP Q Q V</li> <li>Q F P S V D I P L D H V F X V P</li> <li>S G Y NAP Q Q V</li> <li>E WP A V D I P L D H W F X V P</li> <li>S G Y NAP Q Q V</li> <li>E WP A V D I P L D H W F X V P</li> <li>K G Y N A P Q Q V</li> <li>E WP A V D I P L D H W F A V P</li> <li>K G Y N A P Q Q V</li> <li>E F P S T D I P L D H W F A V P</li> <li>K G Y N A P Q Q V</li> <li>E F P S T D I P L D H W F A V P</li> <li>K G Y N A P Q Q V</li> <li>E F P S T D I P L D H W F A V P</li> <li>K G Y N A P Q Q V</li> <li>E F P S T D I P L D H W F A V P</li> <li>K G Y N A P Q Q V</li> </ul>	59 57 54 63 59 58 57 63 59 62 57 63 59 62 57 63 56 63 63 56 63 57 63 59 58 57 58 57 58 59 58 57 59 58 57 57 57 57 57 57 57 57 57 57 57 57 57
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7 5 5 5 7 4 4 6 9 9 7 6 9 7 6 1 0 7 8 8 9 7 6 1 0 7 8 8 9 7 6 1 0 7 8 5 8 9 7 6 1 0 7 8 8 9 9 7 6 1 1 9 7 8 8 9 9 7 6 1 1 9 7 8 8 9 9 7 6 9 7 8 8 9 9 7 6 9 7 7 8 8 9 9 7 6 9 7 7 8 8 9 9 7 6 9 7 7 8 8 9 9 7 6 9 7 7 8 8 9 9 7 6 9 7 6 9 7 7 8 8 9 9 7 6 9 7 7 8 8 9 9 7 6 9 7 7 8 8 9 9 7 7 6 9 7 7 8 8 9 9 7 7 6 9 7 7 8 8 9 9 7 8 8 9 7 8 8 9 9 7 8 8 9 9 7 8 8 9 9 7 8 8 9 9 7 8 8 9 7 8 8 9 7 8 8 9 7 8 8 9 7 8 8 9 7 8 8 9 7 8 8 9 7 8 8 9 9 7 8 8 9 9 7 8 8 9 7 8 8 9 7 8 8 9 7 8 8 9 7 8 8 9 7 8 8 9 7 8 8 8 9 9 7 8 8 8 9 9 7 8 8 8 8	YKYANHSDSNYVKTGKATLKFQLINQRADFAFALFSGGLSNPNLVAVSNNISFVNP         YKYANHSDSNYVKTGKATLKFQLINQRSDFSFALFTGGLTNPKLIAVSNKVSFVNP         YKYANHSDSNYVKTGKATLKFQLINQRSDFSFALFTGGLTNPKLIAVSNKVSFVNP
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7 5 5 6 9 1 5 6 6 9 7 5 5 6 1 0 7 3 8 9 9 7 6 1 0 7 3 8 9 9 7 6 1 0 7 3 8 9 9 7 6 1 0 7 3 8 9 9 7 6 1 1 7 3 8 9 9 7 6 9 9 7 5 5 8 9 9 7 7 3 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 8 9 9 9 7 7 8 8 9 9 7 7 8 8 9 9 7 7 8 8 9 9 9 7 7 8 8 9 9 7 7 8 8 9 9 7 7 8 8 9 9 7 7 8 8 9 9 9 7 7 8 9 9 7 7 8 8 9 9 7 7 8 8 9 9 9 7 8 8 9 9 9 7 8 8 9 9 9 7 7 8 9 9 9 7 8 9 9 9 9	Y K Y A N H S D S N Y V K T G K A T L K F Q L I N Q R A D F A F A L F S G G L S N P N L V A V S N N I S F V N P Y K Y A N H S D S N Y V K T G K A T L K F Q L I N Q R A D F A F A L F S G G L S N P N L V A V S N N I S F V N P Y Q Y A N Y S N F Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G G L S N P K V V A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G G L S N P K V V A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G G L S N P K V V A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G G L S N P K V V A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G G L S N P K V V A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G G L S N P K V V A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G G L S N P K V V A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G G L S N P K V V A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G G L S N P K V Y A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G C L S N P K V Y A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G C L S N P K V Y A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K L Q L I N Q R S D F S F A M F S G C L S N P K Y Y A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K Q L I N Q R S D F S F A M F S G C L S N P K Y Y A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I L K Q L I N Q R S D F S F A M F S G C L S N P K Y Y A I S N K I S F A N P Y Q Y A N Y S N P Q Y S A T G K G I K Y Y Y Y A I S N K Y S Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y
7 5 5 5 6 9 7 5 6 9 7 5 5 6 9 7 7 3 5 5 8 9 7 7 3 5 5 8 9 7 7 3 5 5 8 9 7 7 3 5 5 1 1 9 9 7 7 3 5 5 1 1 9 9 7 6 9 9 7 6 9 9 7 7 3 5 5 9 9 7 7 3 8 9 9 7 7 6 9 9 7 7 3 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 9 9 7 7 8 8 9 9 7 8 8 9 9 9 7 8 8 9 9 9 7 8 8 9 9 9 7 8 8 9 9 7 8 8 9 9 7 8 8 9 9 7 8 8 9 9 7 8 8 9 9 7 8 8 8 9 9 7 7 8 8 9 9 7 8 8 9 9 7 8 8 9 9 9 7 8 9 9 9 9	YKYANHSDSNYVKTGKATLKFQLINQRADFAFALFSGGLSNPNLVAVSNNISFVNP         YKYANHSDSNYVKTGKATLKFQLINQRADFAFALFSGGLSNPNLVAVSNNISFVNP         YGYANFSSHSYKDTGKGSLKLQLINQRSDFSFALFTGGLTNPKLIAVSNKVSFVNP         YQYANYSNPQYSATGKGILKLQLINQRSDFSFAMFSGGLSNPKVVAISNKISFANP
7 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	YK YA NHS DS NYVK T GKAT LK FQL I NQRAD FA FAL FS GG LS NP NLVAVS NN I S FVNP           YK YA NHS DS NYVK T GKAT LK FQL I NQRAD FA FAL FS GG LS NP NLVAVS NN I S FVNP           YG YA NFS SHS YK DT GK GS LK LQL I NQRS D FS FAL FT GG LT NP KLI AVS NKVS FVNP           YG YA NYS NP QYSAT GK GI LK LQL I NQRS D FS FAMFS GG LS NP KVVA I S NK I S FANP           166
7 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5	YK YA NHS DS NYVK T GKAT LK FQL I NQRAD FA FAL FS GG LS NP NLVAVS NN I S FVNP           YK YA NHS DS NYVK T GKAT LK FQL I NQRAD FA FAL FS GG LS NP NLVAVS NN I S FVNP           YG YA NFS SHS YK DT GK GS LK LQL I NQRS D FS FAL FT GG LT NP KLI AVS NKVS FVNP           YG YA NYS NP QYSAT GK GI LK LQL I NQRS D FS FAMFS GG LS NP KVVA I S NK I S FANP           166

HvPAPhy\_a/C4PKL2//1-544 TaP APhy\_a1|C4PKK7|/1-550 TaP APhy\_b1/C4PKK9//1-538 TaP APhy\_b2 | C4PKL0 |/1-537 HvPAPhy\_b2|C4PKL4|/1-537 HvP APhy\_b1|C4PKL3|/1-536 OsP APhy\_b | D6QSX9 |/1-539 ZmP APhy\_b | C4PKL6 |/1-544 MtP APhy/Q3ZFI1//1-543 PtPAP3/V9LXK5//1-564 NtP APhy A5YBN1 //1-551 LaP APhy/D2YZL4//1-543 GmP APhy\_b | Q93XG4 | /1-547 AtP AP 15 | Q9 SF U3 | / 1-532 AtaP APhy\_a 1/F6MIX0 //1-549 ScPAPhy\_a2|F6MIX4|/1-543 TmP APhy\_a 1 | F6MIW8 | /1-545 TaP APhy\_a3 | F6MIW2 | /1-539 TaP APhy\_a2 | C4PKK8 | /1-549 ScP APhy\_a1/F6MIX2//1-541 TaPAPhy\_b3/F6MIW6//1-536 TmP APhy\_b1/F6MIW9//1-539 AtaP APhy\_b1/F6MIX1//1-538 ScP APhy\_b1/F6MIX5//1-538 RcP AP 1 | B9R W G6 | /1-566 VvP AP | A5 BGI 6 | /1-540 PvPAPhy/V7B3Z4//1-546 VrP APhy | B5 AR Z7 | /1-547 AIP AP 15 | D7L636 | /1-532 AtP AP 23 | Q6TPH 1 | / 1-458 GmP AP 4 | V9HXG4 | /1-442 ZmP AP\_c | C4PKL7 | /1-566 SbP AP | AO A1Z5R9 T8 | /1-566 HvP AP\_c / C4PKL5 //1-564 PpP AP | A9 SP12 |/1-557 OsP AP3 | Q6ZCX8 |/1-622 OsP AP 4 | B8 B909 | /1-622 AtP AP 5 | Q9 C927 | /1-396 AtP AP 20 | Q9 LXI7 | /1-427 AtP AP 22 | Q85340 |/1-434 IbPAP3 | Q9ZP18 | /1-427 AtP AP 2 1 | Q9 LXI4 | / 1-437 LoP AP | Q9MB07 | /1-455 RcP AP 2 | B9 5XP 8 | /1-463 IbP AP 2 | Q9 SD Z9 |/1-465 AtP AP 11/Q95/18//1-441 GmP AP 1 | Q09 13 1 | / 1-4 64 AtP AP 25 | 023244 | / 1-466 AtP AP 12 | Q38924 | / 1-469 NtP AP | Q84KZ3 | /1-461 MtP AP 1 | Q4KU02 | / 1-465 OsP AP 2 | Q85505 | / 1-476 La AP 1 | Q93VM7 | / 1-460 PvPAP2/Q764C1//1-457 UAP2|Q8L6L1|/1-463 AtP AP 10 | Q9 SI V9 | / 1-4 68 PvPAP1/P80366//1-459 Ta ACP | C4PKL1 |/1-477 AtP AP 6 | Q9 C5 10 | / 1-4 66 AcP AP | Q93WP4 | /1-481 AoP AP 32 | Q9 XF0 9 |/1-470 StP AP 3 | Q6J5M8 | /1-477 IbP AP 1 | Q95E00 | /1-473 AtP AP 26 | Q949 Y3 | /1-475 RcP AP 3 | B9 SXP 6 | /1-488 UAP 1/Q8L5E1//1-477 GmP AP 3 | Q6YGT9 |/1-512 La AP 2 | Q9 XJ 24 | / 1-638 UPP D4 | Q8 VXF4 | /1-629 UPP D1/Q8VX11//1-615 UPP D2 | Q8 VXF6 | /1-612 TnP AP 1 | Q4R LR 4 | / 1-378 HsP AP 7 | Q6Z/VF0 | /1-438 CeP AP 3 | Q9 NAM9 | / 1-418 MmP AP 7 | Q8 BX 37 | /1-438 DmP AP 1 | Q9 VZ56 | / 1-458 DmP AP 2 | Q9 VZ58 | / 1-450 AmP AP | A0 A087ZW E4 | /1-438 CeP AP 1 | 00 1320 | /1-419 DmPAP3|Q9VZ57|/1-453 AgP AP | Q7P UI\\5 | /1-463

HvP APhy_a   C4PKL2  /1-544	72	AVALSAAP-TSAWVSWITGEFQMG-GTVKPLDPRTVG	SVVRY		111
TaP APhy_a1/C4PKK7//1-550		AVALSAAP - TSAWVSWITGEFQMG - GTVKPLDPGTVG			
TaP APhy b1/C4PKK9//1-538		AVALSAAP - TSAWVSWITGDFQMG - GAVKPLDPGTVG			
· · · ·		AVALSAAP - TSAWVSWITGDFQMG-GAVKFLDFGTVG			
TaP APhy_b2   C4PKL0   /1-537					
HvPAPhy_b2 C4PKL4 /1-537		AVALSAAP - TSAWVSWITGDFQMG - GAVKPLDPGTVG			
HvPAPhy_b1/C4PKL3//1-536		AVALSAAP - TSAWVSWITGDFQMG - GAVKPLDPGTVG			
OsP APhy_b   D6Q5X9  /1-539		A V A L S A A P - S S A WV S WV T G D F Q MG - A A V E P L D P T A V A			
ZmP APhy_b   C4PKL6   /1-544	72	A V A L S A S P - T S A WV S W I T G D Y Q MG - G A V E P L D P G A V G	SVVRY		111
MtP APhy/Q3ZFI 1//1-543	75	S L S L S T S H - D S V W I S W I T G E F Q I G - E N I E P L D P E T V G	sivqy		114
P tP AP 3   V9 LXK 5   / 1-564	90	S V S L S S T H - D S V W I S W I T G E F Q I G - N N L K P L D P K S V A	SVVRY		129
NtP APhy   A5YBN1   /1-551	74	S V S L S S T Y - D S V W I S W I T G E Y Q I G - D N I K P L D P S K V G	svvqv		113
LaP APhy   D2 YZL4   /1-543	72	S L S L S T S H - H S L W V S W I T G E F Q I G - Y N I K P L D P K T V S	зννн		111
GmPAPhy_b/Q93XG4//1-547	76	SVSLSTSH-DSVWISWVTGEFQIG-LDIKPLDPKTVS	svvan		115
AtP AP 15   Q95FU3   /1-532	68	SLSLSSDH-DSIWVSWITGEFQIG-KKVKPLDPTSIN	SVVQF		107
AtaPAPhy a1/F6MIX0//1-549	68	AVALSAAP - TSAWVSWITGEFQMG - GTVKPLDPGTVG	SVVRY		107
ScP APhy_a2  F6MIX4  /1-543		AVALSAAP - TSAWVSWITGEFQMG - GTVKPLDPGTVG			
TmP APhy_a1/F6MIW8//1-545		TVALSAAP - TSAWVSWITGEFQMG - GTVKPLHPGTVA			
		AVALSAAP - TSAWVSWITGEFQMG - GTVKPLDPGTVA			
TaP APhy_a3   F6MIW2   /1-539					
TaP APhy_a2   C4PKK8   /1-549		AVALSAAP - TSAWVSWITGDFQMG - GAVKPLDPGTVG			
ScPAPhy_a1/F6MIX2//1-541		AVALSAAP - TSAWVSWITGEFQMG - GTVKPLDPGTVG			
TaP APhy_b3   F6MIW6   /1-536		AVALSAAP - TSAWVSWITGDFQMG - GAVKPLDPGTVG			
TmP APhy_b1 F6MIW9 /1-539		AVALSAAP - TSAWVSWITGDFQMG - GAVKPLDPGTAG			
AtaPAPhy_b1/F6MIX1//1-538		AVALSAAP - TSAWVSWITGDFQMG - GAVKPLDPGTVG			
ScPAPhy_b1/F6MIX5//1-538	68	AVALSAAP - TSAWVSWITGDFQMG - GAVKPLDPGTVG	SVVRY		107
RcP AP 1   B9R WG6   / 1-566	96	S V S L S S T H - D S V W I S W I T G D Y Q I G - D N I K P L N P S A T A	SVVLY		135
VvP AP   A5 BGI 6   / 1-540	69	S V A L S A S F - D S V W I S W I T G E F Q I G - Y N I K P L N P K T V S	SVVRY		108
PvP APhy/V7B3Z4//1-546	76	S L S L S T T H - D S V W I S W I T G E F Q I G - F D I K P L D P Q T V S	svvan		115
VrP APhy   B5 AR Z7   / 1-547		A LA ISS - P - T SMWV SWV T G D A Q I G - L N V T P V D P A S I G			
AIP AP 15   D7L636   /1-532		SLSLSSDH-DSIWVSWITGEFQIG-KKVKPLDPTSIK			
AtP AP 23   Q6TPH 1   / 1-458		A L A L S T - P - T S MWV S WV T G D A I V G - K D V K P L D P S S I A			
GmP AP4   V9HXG4   /1-442		HISLAGDKHMRVTWITDDKHSP			82
ZmP AP c/C4PKL7//1-566					
- ' ''		A LAASADA - DS LWV SWV T GRAR V GS S N LAP L DP AAAG			
SbP AP   A0 A1Z5R9T8  /1-566		A L A A S A D A - D S L W V S W V T G R A Q V G - S N L A P L D P A A V R			
HvP AP_c   C4PKL5  /1-564		A L A A S A D P - I S L W V S W V T G R A Q I G - S H L T P L D P T A I R			
PpPAP   A9SPI2  /1-557		A L A L S T - P - D A MWV S WV T G D A Q I G - S Q V T P L D P S T V G			
0sP AP 3   Q6ZCX8  /1-622		A L A A S S D A - T S V WV S WV T G E A Q V G - S H L T P L D P S T V R			
0sP AP 4   B8 B909  /1-622		A L A A S S D A - T S V WV S WV T G E A Q V G - S H L T P L D P S T V R			129
AtP AP 5   Q9 C9 2 7   / 1-39 6	19	H I T Q G D H N G R G M I I S WV T S L N E D G S	ΝΥΥΤΥ		48
AtP AP 20   Q9 LXI 7   / 1-42 7	48	HISLVGPDKMRISWITQSSIS	PSVVY		73
AtP AP 22   Q85340   / 1-434	51	HISLAGKDHMRVTFITEDNKVE	SVVEN		77
IbP AP 3   Q9ZP 18   /1-427	22	HITQGDYEGKGVIISWVTPE-EPGS	ктуул		50
AtP AP 2 1   Q9 LXI4   / 1-437		H I S L A G K D H M R V T Y T T D D L N V A			81
LpP AP   Q9MB07   /1-455		HITQGDHEGRSIIVSWITP-SEKGS			84
RcP AP 2   B9 5XP 8   / 1-463		HITQGDYNGTAVIISWVTPD-EPGS			87
IbP AP 2   Q9 5 D 29   /1-465		HITQGDHVGKAMIVSWVTVD-EPG			88
AtP AP 11   Q9 SI 18   / 1-441		HITQGDNAGRAMIISWVMPLNEDG			87
GmP AP 11 (009 131) / 1-464					86
1		HIVQGD1VGRAVIVSWVTV-DEFG			84
AtP AP 25   023244   / 1-466					
AtP AP 12   Q38924   / 1-469					92
NtP AP   Q84KZ3  /1-461		H L T Q G D H V G K G V I V S WV T MD - E P G			88
MtP AP 1   Q4KU02   /1-465		H I T Q G D H V G K A V I V S WV T E D - E P G S			87
0sP AP 2   Q85505  /1-476		H I T Q G D Y N G K A V I V S WV T V A - E P G T			86
La AP 1   Q93 VM7   / 1-460		H I T Q G D L V G Q A M I I S WV T V - D E P G S			86
PvPAP2 Q764C1 /1-457		H I T Q G D Y D G K A V I I S WV T P D - E P G P			92
UAP2 Q8L6L1 /1-463		H I T Q G D H V G Q A M I I S WV T V - D E P G S			88
AtP AP 10   Q95/V9  /1-468		H I T Q G D V E G K A V I V S WV T Q - E A K G S			91
PvPAP1/P80366//1-459	58	H I T Q G D L V G R A M I I S WV T M - D E P G S	SAVRY		86
Ta ACP   C4PKL1  /1-477	59	H I T Q G D Y D G K A V I V S WV T P - S E P A P	SQVEY		87
AtP AP 6   09 C5 10   / 1-4 66		H L T Q G D H D G R G M I V S WV T P L N L A G S			83
ACP AP   Q93WP4   / 1-481		HITQGDYDGKAVIVSWVTF-IDPGK			92
AoP AP 32   Q9 XF0 9   / 1-470	64	HITQGDLEGEAMIISWVRM-DEPGS	SKVLY		92
StP AP 3   Q6J5M8   /1-477		HITQGDYDGEAVIISWVTAD-EPGS			85
IbP AP 1   Q95E00   /1-473		H I T Q G D Y E G R G V I I S WT T P Y D K A G A			96
AtP AP 2 6   Q9 4 9 Y3   /1-475		HITQGDYDGKAVIISWVTPD-EPG			86
RcP AP 3   B95XP 6   / 1-488					92
UAP 1/08L5E1//1-477		HITQGDTNGKAVITSWVTFD-EFGP			88
1		HITQGD7DGKAVIVSWVTTE-EPG			124
GmP AP 3   Q6YGT9   / 1-512					
La AP 2   Q9XJ24  /1-638		H I T Q G D L V G K A V I V S WV T V D - E P G			85
UPP D4   Q8VXF4   /1-629		K V P V Y P R L A L G K S W - D E M T V T W T S G - Y N I D E A V			219
UPPD1/Q8VX11//1-615		NAPVYPRLAQGKTW-DEITVTWTSG-YDINDAE			205
UPP D2   Q8VXF6 /1-612		NAPVYPRLAMGKLW-NEMTVTWTSG-YGINEAD			202
TnP AP 1   Q4R LR 4   / 1-378		H L S Y P G V P - G S M T V T W T T F N K T E			58
HsPAP7 Q6Z\\F0 /1-438		H L S Y P G E P - G S M T V T W T T W V P T R			62
CeP AP 3   Q91\AM9   /1-418		H L S L S G N P - N EMV V T W L T Q N P L P N V T			54
MmP AP 7   Q8 BX37   /1-438		H L S Y L G E P - G T M T V T W T T WA P A R			62
DmP AP 1   Q9 VZ5 6   / 1-458		H L S F G E R T D S E I V V T W S T R S L P P D Q E V G A V			76
DmP AP 2   Q9 VZ58  /1-450	42	H L S F G D N L - R D I V V T W S T R S S P N A	S V V К Р		69
AmP AP   A0 A087ZW E4   / 1-438	29	H L A Y G D N I - H D I V V T W N T K N N T Q E		••••••••••••••••••••••••••••••••••••••	56
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DmP AP 3   Q9 VZ57   / 1-453	42	HLS FG ETV - LD I V V TWN TR D N T N E	SICER		69
AgP AP   Q7P UN5  /1-463	36	H L S F G E S P - L E I V V T W S T M T A T N E	SIVEN		63

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			G L A A - D S L - V R Q A - S G D A L V Y S Q L Y P F E G L Q N Y T S G I I H H V R L Q G 150
			GLAA - DS L - AR EA - T GEALVYS QL YP F E GLQNYT S G I I H H V R I L G 149
· · · ·			GLAA - DS L - V R EA - T GDA L V YS QL YP F E G L QN YT S G I I H H V R L Q G 148
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			GLAA - DS V - V R EA - T GDA L V Y S QL Y P F E G L QN Y T S G I I H H V R L QG 148
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			GLAA - DA L - DHEA - TGES LVYS QL YP FEGLQNYTS GI I HHVRLQG 148
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			GR FG - RS M - NGQA - VGYS LVYS QL YP FEGLQNYTS GI I HHVR LTG 156
			GTRR-SQL-NRKA-TGRSLVYSQLYPFLGLQNYTSGIIHHVRLTG 171
			GKDK - SS L - RHKA - IGESLIYNQL YP FEGLQNYTSGIIHHVQLTG 155
· · · · ·			GTSR - TA L - VREA - RGQSLIYNQL NPYEGLQNYTSGIIHHVQLRG 153
			GTSR - FE L - VHEA - R GQSLIYNQL YP FEGLQNYTSGIIHHVQLKG 157
			GTLR - HS L - SHEA - KGHSLVYSQL YP FDGLLNYTSGIIHHVRITG 149
			GLAA - DS L - VR QA - SGDA LVYSQL YP FEGLQNYTSGI I HHVR LQG 149
/_ / //			GLAA - DS L - VRVA - TGDA LVYSQL YP FEGLQNYTSGI I HHVRLQG 152
			GLAA - DS L - V R EA - T G D A L V Y S Q L Y P F E G L Q N Y T S G I I H H V R L Q G 145
			G L A A - D S L - V R Q A - T G D A L V Y S Q L Y P F E G L Q N Y T S G I I H H V R L Q G 148
/= / //			G L A A - D S L - V R E A - T G D A L V Y S Q L Y P F E G L Q N Y T S G I I H H V R L Q G 149
· - · · ·			GLAA - DS L - V R V A - T G D A L V Y S Q L Y P F E G L Q N Y T S G I I H H V R L Q G 148
			GLAA - DS L - VR EA - TGDALVYSQL YP FEGLQNYTSGI I HHVRLQG 147
· · · · · ·			G L A A - D S L - V R E A - T G D A L V Y S Q L Y P F E G L Q N Y T S G I I H H V R L Q G 150
· - · · ·			G L A A - D S L - A R E A - T G E A L V Y S Q L Y P F E G L Q N Y T S G I I H H V R I L G 149
			G L A A - D S L - V R E A - T G D V L V Y S Q L Y P F E G L Q N Y T S G I I H H V R L Q G 149
1 17			G R S I - F P L - T H Q A - T G Y S L V Y N Q L Y P F E G L K N Y T S G V I H H V R L T G 177
			G T L R - Y P L - R R K V - MG Y S L V Y N Q L Y P F E G L Q N Y T S G I I H H V R L A G 150
			G T S R - F D L - V H E A - R G Q S L I Y S Q L Y P F D G L Q N Y T S G I I H H V R L I G 157
21 12			G K E S - G K Y - T S V G - K G D S V V Y S Q L Y P F E G L WN Y T S G I I H H V K L E G 158
1 10			<mark>GTLR-HSL-SHEA-KGHSLVYSQLYPFDGLLNYTSGIIHHVRITG</mark> 149
			GKEK-GNY-MLKK-KGNATVYSQLYPSDGLLNYTSGIIHHVLIDG 149
GmP AP4   V9HXG4   /1-442	83		GTLP-GRY-DSIA-EGECTSYNYLLYSSGKIHHAVIGP 117
ZmP AP_c   C4PKL7   /1-566	128		GERS - AADAAS - Y - P HVV - T G S A EV Y S Q L Y P Y P G L L N Y T S G A I H H V R L R G 173
56P AP   A0 A1Z5R9T8   /1-566	128		GERS - AADAAS - Y - P H V A - T G S A EV Y S Q L Y P Y P G L L N Y T S G A I H H V R L R G 173
HvP AP_c   C4PKL5   /1-564	125		GERP - A S A D T V G H - P H V A - R G S A E V Y S Q L Y P Y P G L L N Y T S G V I H H V R L V G 171
PpPAP A9SP12 /1-557	116		GLAP - GV Y - T F E S P P G T S L V Y S Q L Y N F P G L R N Y T S G I I H H V R L T G 158
OsP AP 3   Q6ZCX8   / 1-622	130	AAA	G D V S - G H Y - P H V A - R G K A E V Y S Q L Y P Y P G L L N Y T S G A I H H V R L R G 174
OsP AP 4   B8 B909  /1-622	130	A A A	5 D V S - G H Y - P H V A - R G K A E V Y S Q L Y P Y P G L L N Y T S G A I H H V R L R G 174
AtP AP 5   Q9 C9 2 7   / 1-39 6	49		NIASSDGS-DNKSVIATTSSYRYFDYTSGYLHHAIIKE 85
AtP AP 20   Q9 LXI 7   / 1-42 7	74		GTVS-GKY-EGSA-NGTSSSYHYLLIYRSGQINDVVIGP 109
AtP AP 22   Q85340   / 1-434	78		GK Q P - G K Y - D G K A - T G E C T S Y K Y F F Y K S G K I H H V K I G P 112
IbP AP3   Q9ZP 18   / 1-427	51		NA EN - S S V - K R R A - D G V V T Y K Y Y N Y T S G Y I H H C T I K D 85
AtP AP 21   Q9 LXI4   / 1-437	82		G K H P - K K Y - D K K T - A G E S T S Y T Y F F Y N S G K I H H V K I G P 116
LpP AP   Q9MB07   /1-455	85		G T S E - N K L - D Q H A - E G T V T M Y K F Y T Y T S G Y I H H C V L T D 119
RcP AP 2   B95XP8   / 1-463	88		G K S E - K H Y - D S V A - E G T
IbP AP 2   Q9 SD Z9   / 1-465	89		NS EN - S Q H - K K V A - R G N I R T Y T Y F N Y T S G Y I H H C T I R N 123
AtP AP 11   Q95 18   / 1-44 1	88		NIASSDG SDNKNA - IATTSSYRYF NYTSGYLHHATIKK 124
GmP AP 1   Q09 13 1   / 1-4 64	87		NS EN - S D K - K K I A - E G K L V T Y R F F N Y S S G F I H H T T I R N 121
AtP AP 25   023244   / 1-466	85		KAVDGD VKPKKK - RGHASTSSYR FYDYTSGFLHHATIKG 123
AtP AP 12   Q38924   /1-469	93		C E N - E K S - R K Q A - E A T V N T Y R F F N Y T S G Y I H H C L I D D 127
IVtP AP   Q84KZ3   /1-461	89		NEFN-SKI-KQIA-KGTVSTYKYHTYNSGYIHHCTIQN 123
MtP AP 1   Q4KU02   / 1-465	88		SKN-SKQ-KRLA-KGKIVTYRFFNYTSGFIHHTTIRN 122
0sP AP 2   Q85505   / 1-476	87		GKNE-HQY-DQRV-EGTVTNYTFYDYKSGYIHHCLVDG 121
La AP 1   Q93VIM7   / 1-460	87		NS D S - S L Q - N F T A - E G E V F T Y T Y Y N Y T S G F I H H T T I T N 121
PvPAP2/Q764C1//1-457			GTSE-SKF-QTSL-EGTVTNYTFYEYKSGYIHHCVIEG 127
UAP2/08L6L1//1-463			SNS-SLQ-NFTA-EGEVFTYTYYNYTSGFIHHTNITN 123
AtP AP 10   Q95/V9  /1-468			K E N - S T K - K H K A - H G K T N T Y K F Y N Y T S G F I H H C P I R N 126
PvPAP1/P80366//1-459			NS EK - N G R - K R I A - K G K M S T Y R F F N Y S S G F I H H T T I R K 121
Ta ACP   C4PKL1 /1-477			K E E - N R Y - D Q K A - E G T M T N Y T F Y D Y K S G Y I H H C L V D G 122
AtP AP 6   Q9 C5 10   / 1-466			NIA T N G S D V K P - A - K K R A - H A S T K S Y R F Y D Y S S G F L H H A T I K G 123
AcP AP   Q93WP4   / 1-481	93		G T S P - N S Y - D H S A - Q G K T T N Y T Y Y D Y T S G Y I H H C L L D K 127
AoP AP 32   Q9 XF09   /1-470			NID G - S N Q - K H S A - N G K I T K Y K Y Y N Y T S G F I H H C T I R R 127
StP AP3   Q6J5M8   /1-477	86		G L S E - G K Y - D V T V - E G T L N N Y T F Y K Y E S G Y I H Q C L V T G 120
IbP AP 1   Q95E00   / 1-473			NS EN - SK S - QKRA - MGTVV TYKYY NYTSA FIHHCTIKD 131
AtP AP 26   0949 Y3   /1-475			GAVQ - GK Y - EFVA - QGTYHNYTFY
RcP AP 3   B9 SXP 6   / 1-488	93		GVSE-NKY-DFIA-EGTARNYTFYQYKSGYIHQCLIDD 127
UAP 1/08L5E1//1-477			G T S E - N K F - Q T S A - E G T V S N Y T F Y K Y K S G Y V H H C L I E G 123
GmP AP 3   Q6YGT9  /1-512			GTSE-NKF-QTSE-EGTVTNYTFHKYKSGYIHHCLIEG 159
La AP 2   Q9 XJ24  /1-638			NS D K - H S H D K K S A - H G K I V T Y R F F N Y T S G F I H H - T I K H 120
UPP D4   Q8 VXF4   / 1-629			G P T G - G R K - T R S P - A G T L T F D R N S L C G E P A R T V G W R D P G F I H T S F L K E 264
UPP D1   Q8VX11   /1-615			G P K E - G N L - V K T P - A G T L T F D R N T M C G A P A R T V G W R D P G Y I H T S F L K E 250
UPP D2   Q8VXF6 /1-612			g P K G - G D H - I H S P - A G T L T F T K D S L C G A P A R T V G W R D P G F I H T S Y L K E 247
TnP AP 1   Q4R LR4   / 1-378			GLLG-GRLFEKRA-KGESTLFVDSGVEKRKMFIHRVTLTG 96
HsP AP 7   Q6Z VF0   /1-438			G L Q P S G P L - P L R A - Q G T F V P F V D G G I L R K L Y I H R V T L R K 100
CeP AP 3   Q911AM9   /1-418	55		G V S Q - D S L - R F T A - K G N T T G WA D Q G K H K T M R Y T H R A T M Q N 91
MmP AP 7   Q8 BX 37   / 1-438	63		G S Q L S G P L - P F R A - H G T A R A F V D G G V L R K L Y I H R V T L R K 100
DmP AP 1   Q9 VZ56   / 1-458	77		G Q L V - D G Q V R L - T Q Q A - R G K A T K F V D G G H K Q A T Q F I H R V T L R D 116
DmP AP 2   Q9 VZ58  /1-450	70		S R N Y L - K D E P - I MV N G T WQ R F V D G G K K A R T Q Y I H N V E L K D 107
AmP AP   A0 A087ZW E4   / 1-438	57		GINGL-ILTA-TGNSTLFVDGGNEKQKQYIHRVWLKN 91
CeP AP 1/00 1320 //1-419	26		- QK - VK
DmP AP 3   Q9 VZ57   / 1-453			G I D G L - H Q R V - K A T Q M P T K F V D G G A K K A T Q Y I H R V T L S H 106
AgP AP   Q7P UI\15   /1-463	64		GIGGL-ILSA-TGTETK FVDGGPAKRTQYIHRVVLRD 98

In+PMPs_210P121/254       154       IP OT EXTYQ C OD A IF G.       MOA VH A E TOW A D OF S Y G R IA VV G G G G       D1         ISPATPS_210P121/S125       154       IP OT EXTYQ C OD A IF G.       MOA VH A E TOW VV G G F S Y G R IA VV G G G       D1         ISPATPS_210P121/S125       154       IP OT EXTYQ C OD A IF G.       MOA VH A E TOW VV G S Y G R IA VV G G G       D1         ISPATPS_210P121/S125       154       IF OT EXTYQ C OD A IF G.       MOA VH A E TOW VV G S Y G R IA VV G G G       D1         ISPATPS_210P121/S125       154       IF OT EXTYQ C OD A IF G.       MOA VH A E TOW VV G S Y G R IA VV G G G       D1         ISPATPS_210P121/S125       154       IF OT EXTYQ C OD A IF G.       MOA VH A E TOW VV G S Y G R IA VV G G G       D1         ISPATPS_210P121/S125       154       IF OT EXTYQ C OD A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G       D1         ISPATPS_210P121/S125       154       IF OT EXTYQ C OD A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G G A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G G A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G G A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G G A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G G A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G G A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G G A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G A IF G.       MOA VH A E TOW VV G G F G R IA VV G G G A IF G.       MOA VH A E TOW VV G G F			
Tot APPU, 21 (CH12)/1530         S15         L P A TE YUY QC OD A LP 6.         MM A VH A F TU W V D F 5 YF G1 A VV OD 0         IST           Tot APPU, 21 (CH12)/138         S16         L P O TE YUY QC OD A LP 6.         MM A VH A F TU W V D F 5 YF G1 A VV OD 0         IST           Tot APPU, 21 (CH12)/138         S16         L P O TE YUY QC OD A LP 6.         MM A VH A F TU W V D F 5 YF G1 A VV OD 0         IST           Tot APPU, 21 (CH12)/138         S16         L P O TE YUY QC OD A LP 6.         MM O LH A F TU W V D F 5 YF G1 A VV OD 0         IST           Tot APPU, 21 (CH21)/138         S16         L P O TE YUY QC OD A LP 6.         MM O LH A F TU W V D F 5 YF G1 A VV OD 0         IST           Tot APPU, 21 (CH21)/134         S17         L P F TU YUY QC OD F 1.G         MO D U H F TU W V D F 5 YF G1 A VV OD 0         IST           Tot APPU, 21 (CH21)/134         S16         L P TU YUY QC OD F 1.G         MD D U Y F TU W I S D F S YF G1 A VV OD 0         IST           Tot APPU, 21 (CH24)/134         S16         L P TU YUY QC OD F 1.G         MD D U Y F TU W I S D F S YF G1 A VV OD 0         IST           Tot APPU, 21 (CH24)/134         S16         L P TU YUY QC OD F 1.G         MD U Y F TU W I S D F S YF G1 A VV OD 0         IST           Tot APPU, 21 (CH24)/134         S16         L P TU YUY QC OD A LP G.         MA V H F TU W V D F S YF G1 A VV OD 0           Tot APPU, 21 (CH24)/13	HvPAPhy a/C4PKL2//1-544	154 LEPGTKYYYQCGDPAIPG -	- <mark>A M S A V H A F R T M P</mark> A A G P R S Y P G R I A V V <mark>G D L G</mark> 201
TorAmby_21(GMU3)/333       150       LP TO TY YY QC DD A LP 6.       MA A H + 6 TT MY V D D' S Y 6 TA IV V G LO       357         TorAmby_21(GMU3)/333       140       LP OT TY YY QC DD A LP 6.       MA A H + 6 TT MY V QC BY 8 Y 6 TA VV G LO       355         Ger Mey_13(GMU3)/334       140       LP OT TY YY QC DD A LP 6.       MO A H + 6 TT MY V QC BY 7 6 TA VV G LO       355         Jone May_13(GMU3)/343       150       LP OT TY YY QC DD A LP 6.       MO G VH + 6 TT MY V QC BY 7 6 TA VV G LO       355         Jone May_13(GMU3)/343       152       LP OT TY YY C DD A LP 6.       MO G VH + 6 TT MY V QC BY 7 6 TA VV G LO       353         Methy_13(GMU3)/343       152       LP OT TY YY C DD A LP 6.       MO G VH + 6 TT MY V G DD A LP 6.       MO G VH + 6 TT MY V G DD A LP 6.       353         Methy_13(GMU3)/343       150       LP T T VY Y C DD A LP 6.       MO G VH + 6 TT MY V G DD A LP 6.       353         Methy_13(GMU3)/343       150       LP A T VY Y C DD A LP 6.       MA A H + 6 TT MY V C DA S Y 6 TA A VV 0 L 0.       357         SerAmy_13(GMU3)/343       150       LP A T VY Y C DD A LP 6.       MA A H + 6 TT MY V C DA S Y 6 TA A VV 0 L 0.       357         Methy_12(GMU3)/343       150       LP A T VY Y C DD A LP 6.       MA A H + 6 TT M V Y C DA S Y 6 TA A VV 0 L 0.       357         Methy_12(GMU3)/343       150       LP A T Y Y Y C DA A LP 6. <td></td> <td></td> <td></td>			
The PerpL_21 (DPFLD)(J-S32         LEP G TK YY Y C C DP A IP 6         NG A VH A T THE A VG P K Y P C H A VY D C G         Set           Her PerpL_21 (DPFL2)(J-S32         LEP G TK YY Y C C DP A IP 6         NG A VH A T THE A VG P K Y P C H A VY D C G         Set           Def PerpL_21 (DPFL2)(J-S34         LEP G TK YY Y C C DP A IP 6         NG A VH A T THE A VG P K Y G H A VY D C G         Set           Def PerpL_21 (DPFL2)(J-S44         LEP G TK YY Y C C DP A IP 6         NG A VH A T THE A VG P K Y G H A VY D C G         Set           Def PerpL_21 (DPFL2)(J-S44         LEP G TK YY Y C C DP S L F         NG A VH A T THE A VG P K Y G H A VY D C G         Set           JAPPEPL_21 (DPFL2)(J-S44         LE K K T T V Y Y C C DP S L F         NG Y Y F T H A VY D C G F K Y F R L A VY D C G         Set           JAPPEPL_21 (DPFL2)(J-S44         LE K K T T V Y Y C C DP S L F         NG Y Y F T H A VY D C G D S L F         NG Y Y F T H A VY D C G D S L F           JAPPEPL_21 (DPFL2)(J-S44         LE F A T K YY C C DP S L F         NG Y Y F T H A VY D C G D S L F         NG Y Y F T H A VY D C G D S L F           JAPPEPL_21 (DPFL2)(J-S44         LE F A T K YY C C DP A L F         NG Y Y F T H A VY D C G D S L F         NG Y Y F T H A VY D C G D S L F           JAPPEPL_21 (DPFL2)(J-S44         SE K Y F T H A VY D C G D A L F         NG Y F T H A VY D C G D A L F         NG Y F T H A VY D C G D A L F           JAPPEPL_21 (DPFL2)(JS S S L Y Y F T H Y Y Y C C DP A L F         <			
HP#P#p_12(PDENL_1/1532       10       EFGTKYYY 0.000A JPC       MA AV HAFTKYM AV GPRSYDEI AV DCC       155         D#P#P_12(DACOS)(JS33       10       EFGTKYYY 0.000A JPC       MA D WAFTKYM AV GPRSYDEI AV DCC       156         D#P#P_12(DACOS)(JS33       12       EFGTKYYY 0.000A JPC       156       156         D#P#P_12(DACOS)(JS33       12       EFGTKYYY 0.000A JPC       156       156         D#P#P_12(DACOS)(JS33       12       EFGTKYYY 0.000A JPC       156       157       156			
mp#Pm_j_alp(PHU3/j_353       126       E F G T T Y Y Y C G D A I P A       N A V A V A T T MP A V G P S Y O S I A V D G G       355         DmPM_j_alp(PHU3/j_344)       151       E F G T T Y Y Y C G D A I P A       N A V A V D G G Y Y G I A V D G G       323         MmPM_j_alp(PHU3/j_343)       151       E F G T T Y Y Y C G D Y A P A       N A V A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G I A V D G G Y Y G Y A V D G G Y Y G I A V D G G Y Y G Y A V D G G Y Y G Y A V D G G Y Y G Y A V D G G Y Y G Y A V D G G Y Y G Y A V D G G Y Y G Y A V D G G Y Y G Y A V D G G Y Y G Y A V D G G Y Y G Y A V V D G G Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y Y	·= · · · ·	-	
OP ##PH_D (DEQ201/J333         125         E F G TE YY N C G D A IP D.         NUD U H A TIME A UF B S TO K I A IV D C G         325           D## PH_D (DEX)/545         155         F F D T Y V Y C G D F S L         AD U H F TIME A UF G S Y F G I A V V C G G         323           P# PH (DX)/1364         127         F F H T Y V C G D F S L         AD U H F TIME A UF G S Y F G I A V V C G G         323           ILD PHW (DX22L/J-343         125         E F S T L Y V C G D F S L         AD U H F TIME A UF A U			
2m+PH_2         2m+PH_2 <t< td=""><td>HvPAPhy_b1 C4PKL3 /1-536</td><td>149 LEPGTKYYYQCGDPAIPG-</td><td>- AMSAVHAFRTMPAVGPRSYPGRIAVVGDLG 196</td></t<>	HvPAPhy_b1 C4PKL3 /1-536	149 LEPGTKYYYQCGDPAIPG-	- AMSAVHAFRTMPAVGPRSYPGRIAVVGDLG 196
Mick Public 1023711/543         157         KK P D T L VY C C D P S L S         NG D V H F T NIP V S D K X Y B K A V D D C O         233           Ind Public VX V S V S V V V C C D P S L S         NG D V H F T NIP V S D K X Y B K A V D D C O         233           Ind Public VX V S V V S V V C C D P S L S         NG V V F T T NIP V S D K X Y B K A V D D C O         233           Ind Public VX V S V V S V V V C C D P S L S         NG V V F T T NIP V S D K X Y B K A V D D C O         233           Ind Public VX V S V V S V V V V V V V V V V V V V	OsP APhy_b   D6QSX9   / 1-539	149 LEPGTEYFYQCGDPAIPA-	- A MS D I H A F R T MP A V G P R S Y P G K I A I V G D L G 196
Mick Public 1023711/543         157         KK P D T L VY C C D P S L S         NG D V H F T NIP V S D K X Y B K A V D D C O         233           Ind Public VX V S V S V V V C C D P S L S         NG D V H F T NIP V S D K X Y B K A V D D C O         233           Ind Public VX V S V V S V V C C D P S L S         NG V V F T T NIP V S D K X Y B K A V D D C O         233           Ind Public VX V S V V S V V V C C D P S L S         NG V V F T T NIP V S D K X Y B K A V D D C O         233           Ind Public VX V S V V S V V V V V V V V V V V V V	ZmP APhy b   C4PKL6   /1-544	154 LEPGTRYVYRCGDPAIPD -	- <mark>A M S G V H A F R T M P</mark> A V G P G S Y P G R I A V V <mark>G D L G</mark> 201
PP#P#j         PVMSJ         INP DWJ         I			
IbP#Phy_102101/L53       15       L PP TV, YY QC GD PS LQ       MAD T V PT RTM       IS S PKS YF RAI LA LY QC G       200         GmP #Ph_2102304()/L33       IS       L PP TV, YY QC GD PS LQ       MAD T V PT RTM       IS S PKS YF RAI LA V C GL G       200         AdP H2) (D3304()/L33       IS       L PP TV YY QC GD PS LQ       MAD T V PT RTM       IS S PKS YF RAI LAV C GL G       200         AdP H2) (D4304()/L33       IS       L PP AT I YY AC GD PS LQ       MAD T V PT RTM       X V S PS YF RAI LAV C GL G       200         TMP #Ph_21(PD400()/L33       IS       L PP AT I YY AC GD PA LP G       MAS VI AF RTM       X V S PS YF RAI LAV C GL G       200         TMP #Ph_21(PD4002()/L33       IS       L PP AT I YY AC GD PA LP G       MAS VI AF RTM       X V S PS YF RAI LAV C GL G       200         TMP #Ph_21(PD4002()/L33       IS       L PP AT I YY AC GD PA LP G       MAS VI AF RTM A V O PS YF RAI LAV C GL G       200         TMP #Ph_21(PD4002()/L33       IS       L PP AT I YY AC GD PA LP G       MAS VI AF RTM A V O PS YF RAI LAV V O LG       200         TMP #Ph_21(PD4002()/L33       IS       L PP AT I YY AC GD PA LP G       MAS VI AF RTM A V O PS YF RAI LAV V O LG       200         S C PP AF LAV C RUMALS       IS       L P AT I YY AF C RAI LAV AF AF RTM A V O PS YF RAI LAV V O LG       200       200       200			
Los Physion 20126/1/243         15         L F S T LY VY Q G G D F S Q         M G U Y T F T M I         IS G S LS F G V G V V V V U G L G			
om/PMP_b1033461/1-37         155         LEPSTLYVY0CGDPSA         AMS 01VYERTMU 15 055 YF GK 14VV 00 0			
APP         Display         LEP II IVV COD F AP LO         Main H R TAU Y S P S Y D G L AVV COL C         357           APP PM_D21/F6MAN (J/143         15         LEP AT KYV Q CO D P A P C         MAX AV A P R TV A A V O P S Y D G L AVV COL C         357           APP PM_D21/F6MAN (J/143         15         LEP AT KYV Q CO D P A P C         MAX AV A P R TV A V O P S Y D G L AVV COL C         357           TAPPM_D21/F6MAN (J/143         15         LEP AT KYV Q CO D P A P C         MAX AV A P R TV A V O P S Y D G L AVV COL C         357           TAPPM_D21/F6MAN (J/143         154         LEP AT KYV Q CO D P A P C         MAX AV A P R TV A V O P S Y D G L AVV COL C         357           TAPPM_D21/F6MAN (J/143)         154         LEP AT KYV Q CO D P A P C         NAX AV A P R TVA V O P S Y D G L AVV COL C         357           TAPPM_D21/F6MAN (J/143)         154         LEP GT KYV Q CO D P A P C         NAX AV A P R TVA V O P S Y D G L AVV COL C         357           TAPPM_D21/F6MAN (J/143)         154         LEP GT KYV Q CO D P A P C         NAX AV A P R TVA V O V O S Y D G L AVV COL C         357           TAPPM_D21/F6MAN (J/143)         154         LEP GT KYV Q CO CA P A P C         NAX AV A P R TVA V O V O V O C         357           TAPPM_D21/F6MAN (J/143)         LEP GT KYV V CO CO D A LO         NAX AV A P R TVA V O V O V O C         357           TAPPM_D21/F6MAN (J/144)			
Amp Pmy_s1/FEMAND (1-24)         SD         LFP ATK, YY YU CG DP ALP C-         MGA AV AF R TMA AV OP RS YF GA I AVV OD C         300           The Phys_s1/FEMAND (1-24)         SE L FP ATK, YY YU GG DP ALP C-         MGA AV AF R TMA AV OP RS YF GA I AVV OD C         330           The Phys_s1/FEMAND (1-24)         SE L FP ATK, YY YU GG DP ALP C-         MGA AV AF R TMA AV OP RS YF GA I AVV OD C         335           The Phys_s1/FEMAND (1-24)         SE L FP ATK, YY YU GG DP ALP C-         MGA AV AF R TMA AV OP RS YF GA I AVV OD C         335           The Phys_s1/FEMAND (1-24)         SE L FP ATK, YY YU GG DP ALP C-         MGA AV AF R TMA AV OP RS YF GA I AVV OD C         336           The Phys_s1/FEMAND (1-24)         SE L FP ATK, YY YU GG DP ALP C-         MGA AV AF R TMA AV OP RS YF GA I AVV OD C         336           The Phys_s1/FEMAND (1-24)         SE L FP ATK, YY YU GG DP ALP C-         MGA AV AF R TMA AV OF RS YF GA I AVV OD C         336           The Phys_s1/FEMAND (1-24)         SE L FP ATK, YY YU GC DP ALP C-         MGA AV AF R TMA AV AV AT R TMA AV AF R TMA AV AV AF R			
SchPapi_api_ExploreMay [1:43]       151       LEP TIK YY QC QC P A IP -       MG A VH A F TIM, A V Q PR S Y PG RI AVV QD LG       333         The Phby_api_ExploreMay [1:43]       164       LEP TIK YY Y QC QC P A IP -       MG A VH A F TIM, A V Q PR S Y PG RI AVV QD LG       353         The Phby_api_ExploreMay [1:43]       164       LEP TIK YY Y QC QC P A IP -       MG A VH A F TIM, A V Q PR S Y PG RI AVV QD LG       357         SchPapi_api_ExploreMay [1:43]       164       LEP TIK YY QC GD P A IP -       MG A VH A F TIM, A V Q PR S Y PG RI AVV QD LG       357         SchPapi_api_ExploreMay [1:43]       151       LEP TIK YY QC GD P A IP -       MG A VH A F TIM, A V Q PR S Y PG RI AVV QD LG       358         The Phby_api_ExploreMay [1:43]       151       LEP TIK YY QC GD P A IP -       MG A VH A F TIM, A V Q PR S Y PG RI AVV QD LG       357         SchPapi_BiBSG MAY [1:43]       151       LEP TIK YY QC GD P A IP -       MG A VH A F TIM A V Q PR S Y PG RI AVV QD LG       357         SchPapi_BiBSG MAY [1:43]       151       LEP TIK YY QC GD P A IP -       MA VH A F TIM A V C PR S Y PG RI AVV QD LG       357         SchPapi_BiBSG MAY [1:43]       LEP TIK YY QC GD P A IP -       MA VH A F TIM A VA PA A PA PA A PA A PA A PA A PA A			
The Pert, all FONN Val. 73-51         16         LEFA TLY YU G G D P G I P G.         MAS VU AF R TUP YU G R SY P G I AVU G D L G.         135           The Pert, all FONN Val. 73-39         15         LEFA TLY YU G G D P A I P G.         MAS VU AF R TUP YU G R SY P G I AVU G D L G.         135           The Pert, all FONN Val. 73-39         15         LEF G TLY YU G G D P A I P G.         MAS VU AF R TUP YU G R SY P G I AVU G D L G.         136           The Pert, all FONN Val. 73-56         16         LEF G TLY YU G G D P A I P G.         TTA AVU AF R TUP YU G R SY P G I AVU G D L G.         136           The Pert, all FONN Val. 73-56         15         LEF G TLY YU G G D P A I P G.         TTA AVU AF R TUP YU G R SY P G I AVU G D L G.         136           The Pert, all FONN Val. 73-56         16         LEF G TLY YU G G D P A I P G.         TTA AVU AF R TUP YU G R SY P G I A VU G D L G.         137           SERP TLY ISON VAL. 73-50         15         LEF G TLY YU G G D P A I P G.         MAS O' Y FR TUP Y S G R SY P K K G I A VU G D L G.         136           SERP TLY ISON VAL. 73-70         15         LEF TLY YU R G G SS I P G.         MAS O' Y FR TUP Y S G R SY P K K G I A VU G D L G.         136           SERP TLY ISON VAL. 74-70         15         LEF TLY YU R G G SS I P G.         MAS O' Y FR TUP YS G R SY P K K G I A VU G D L G.         136           SERP TLY ISON VAL P R SY YU R G G SS I P G.         MAS O' Y FR TUP YS Y	AtaP APhy_a 1   F6MIX0   /1-549	150 LEPATKYYYQCGDPALPG-	- <mark>A MS A V H A F R T MP</mark> A V G P R S Y P G R I A V V <mark>G D L G</mark> 197
ToPP#p_alple         ToPP#p_alple<	ScP APhy_a2 (F6MIX4 )/1-543	153 LEPGTKYYYQCGDPALPG -	- TMS AV HAFR TMP AV GPR SYP GRIAV V GD L G 200
ToPP#p_alple         ToPP#p_alple<	TmP APhy a1/F6MIW8//1-545	146 LEPATKYYYQCGDPGIPG -	- <mark>A M S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G</mark> 193
ToP-Pmp_2/CPRIX2/J-349       150       LEP OT KY YY 0.G GO PA IP G.       MMS VY HAF TIVP V VG R SY 0 G IA VY 0 C LG 0.       157         ToP-Pmp_15/FGMVW/J-339       150       LEP OT KY YY 0.G GO PA IP G.       T SA VY HAF TIVP V VG R SY 0 G IA VY 0 C LG 0.       158         ToP-Pmp_15/FGMVW/J-339       150       LEP OT KY YY 0.G GO PA IP G.       T SA VY HAF TIVP V VG R SY 0 G IA VY 0 C LG 0.       158         AmP-Pm_21/FGMX1/J-339       150       LEP OT KY YY 0.G GO PA IP G.       MMS VY HAF TIVP V VG R SY 0 G IA VY 0 C LG 0.       157         R.P-Pm_15/FGMX1/J-338       150       LEP OT KY YY 0.G GO PA IP G.       MMS VY HAF TIVP V VG R SY 0 G IA VY 0 C LG 0.       137         R.P-Pm_15/FGMX1/J-349       150       LEP OT KY YY 0.G GO PA IP G.       MMS VY HAF TIVP V VG R SY 0 G IA VY 0 C LG 0.       137         R.P-Pm_15/FGMX1/J-349       150       LEP OT KY YY 0.G GO PA IP G.       MMS VY HAF TIVP V VG R SY 0 G IA VY 0 C LG 0.       137         R.P-PM 1/5820/J-340       150       LEP OT TAY YR 0.G GO PA IP G.       MMS 0'H FAF TIVP V VG R SY 0 G IA VY 0 C LG 0.       137         R.P-PM 1/5820/J-340       150       LEP OT TAY YR 0.G CO PA I P G.       MMS 0'H FAF TIVP V VG R GO V IA GY 0.       137         R.P-PM 1/5820/J-340       120       LEP TT YY VG CO SY F.       MMS 0'H FAF TIVP VG R GY 0'H AF HA IA VY 0'LG 0.       136         R.P-PM 1/5920/PA/STATTY YR CO CO S			
Schwp			
ToPPP_12F(FANNE/1.336       150       LEP OT KYYY 0 C G DP A IP 0.       T 5 A VH A FR TWP A VG R SYP G R I AV 0 D L 0       155         Fin PPP_15(FANNE/1.538       55       LEP OT KYYY 0 C G DP A IP 0.       MMS VH AFR TWP V V G R SYP G R I AV 0 D L 0       137         RePP1_15(FANNE/1.538       55       LEP OT KYYY 0 C G DP A IP 0.       MMS VH AFR TWP V V G R SYP G R I AV 0 D L 0       137         RePP1_15(FANNE/1.538       LEP OT KYYY 0 C G DP A IP 0.       MMS VH AFR TWP V V G R SYP G R I AV 0 D L 0       137         RePP1_15(FANNE/1.536       LEP OT KYYY 0 C G DP A IP 0.       MMS V H AFR TWP V V G R SYP G R I AV 0 D L 0       137         RePP1_15(FANNE/1.546       LEP ST KYYY 0 C G DP A I 0.       MMS V H AFR TWP V S G R SYP G K I AV 0 D L 0       137         RePP110(71838)(7340       SL KP ST TYYY 0 C G DP S I 0.       MM 0 G R P F P F SP NHW K I 0 I 0 D L 0       135         Am P2310(71480)(1345       SL KP ST TYYY 0 C G DS S R 0.       MM 0 G R P F F F SP NHW K I 0 D L 0       135         SMP A (ALTANY)(1350)(1340)       SL KP ST TYYY 0 C G DS S R 0.       1400 E L 0 E E T TYYY N C G DS S S R 0.       1400 E L 0 E E T TYYY N C G DS S R 0.       1400 E L 0 E E T TYY N R 0 D S S R 0.       1500 E S FT I P A A AY F R NAVV 0 D L 0       155         SMP A (ALTANY)(1340)(135)       LEP T TYYY R C G DS S R 0.       1400 E L 0 E S FT I P A F A AY Y R R A AV 0 D L 0       121         MPPA 2 (OPAL)(1355) <td></td> <td></td> <td></td>			
The Perk, 21/FORM 9/1/339         151         LEP GT KLYYN QC GOP ALP C.         TAX VHA FT TUM AV GT RS YF GH LAVY BO LO         138           Amp Perk, 21/FORM 5/1/381         150         LEP GT KLYY QC GOP ALP C.         MAS AV HA FT TUM AV GT RS YF GH LAVY BO LO         137           SchPark, 21/FORM 5/1/381         151         LEP GT KLYY QC GOP ALP C.         MAS AV HA FT TUM AV GT RS YF GH LAVY BO LO         137           SchPark, 12/FORM 5/1/381         151         LEP ST RLYY QC GOP ALP C.         MAS AV HA FT TUM AV GT RS YF GH LAVY BO LO         137           Pri APR/13/107381/1/345         151         LEP ST RLYY QC GOP ST G         MAS AV HA FT TUM Y S GP RS YF GH LAVY BO LO         136           Gm Park 1/38/R2/1/347         151         LEP ST RLYY QC GOP ST G         MAS AV HA FT TUM Y S GP RS YF GH LAVY BO LO         136           Gm Park 1/38/R2/1/347         151         LEP ST RLYY QC GOP ST G         MAS AV HA FT TUM Y S GP RS YF GH LAVY BO LO         136           Gm Park 1/38/R2/1/347         151         LEP TR YY KC GO SS VF         MAS AV HA FT TUM Y S GP RS YF GH LAVY BO LO         136           Shar A FT AT MY SC GOP SS VF GH LAVY CO COP ST GF GF TT F         SAAAAPK AV KO LO         137         138           Shar A FT AT MY KC GOP SS VF GH LAVY CO COP ST GF GF TT F         157 AFT AT MY AV CO LO         137           Shar A FT AT MY KC GOP SS VF GH LAVY CO COP ST GF GF TT F	· · · · ·		
Aub Philip Ji (FRMX J) (1-38)         151         LEP GT KLYY Q C OP A LP C-         MXX AV A CP TUM D'O SP SY P G H A VY D'O C         377           RcPAP J (388WG) (1-56)         170         LKP NTT Y Y Q C OP S LP         MXX D'V H F TUM A S O F SY P G H A VY D'O C         377           RcPAP J (388WG) (1-56)         170         LKP NTT Y Y Q C OP S LP         MXX D'V H F TUM A S O F SY P G H A VY D'O C         377           PrAP JS (1-56)         151         LKP S T LYY Q C OP S LP         MXX D'V F F TUM I'S C LNS Y P G K A VY D'O C         376           PrAP JS (1-7456)         151         LF S T LYY Q C OP S LP         MXX D'V F F TUM I'S C LNS Y P G K A VY D'O C         376           APP 315 (07456)         151         LF S T LYY Q C OP S R         MXX B LH F T TUP A'S O P S R P G H I A A VY D'O C         376           APP 315 (07456)         LF D E T TYY R C OP S S R         MXX B LH F A T M A VY S D C C         375         376           Brance (CHXL/1/1-42         LE P T TYY R C OP S S R         MXX B LH F A T M A VY D O C C         351         377         376         377         376 <td< td=""><td></td><td></td><td></td></td<>			
schwig			
Ref# 21/88W 06/1-56         172         LK N TTY Y V C GO PS LP         MSS 1 Y HE FT TM A S G P KS P G KL G LI N V G CU G         224           We# ApsG6/1-540         151         LK PS T TY V C G O P L Q         MSS 1 Y HE FT TM Y S G PS Y P KL G I L O L         235           P## Aps/15/07L856/1-323         151         LF S T TY V C G O S P K R         MSS 0 L Y F FT TM Y S G N Y P KL AV V O L O         236           A## 231 (07L856/1-323         151         LF S T TY V R C G O S P K R         MSS 0 L Y F FT TM Y S C N Y P KL AV V O L O         235           3m# 2 (0FKL7/1-424         13         LE DE T TY V R C G O S S LP 6         LS D E KS T TY A T G A O C Y P R A AV V I D L O         231           Sm# 2 (0FKL7/1-424         13         LE DE T TY V R C G O S S LP 6         LS D E KS T TY P A T G A C Y P R A AV V I D L O         231           B# AP (ADL258/S R) (-155)         L R P A T R Y V R C G O S S LP 6         LS D E KS F TT L P A T G A A C Y P R A AV V I D L O         231           B# AP (ADL258/S R) (-155)         L R P A T R Y V R C G O S S LP 6         LS D E KS F TT L P A T G A A C Y P R A AV V I D L O         231           B# AF A I N Y V R C G O S S LP 6         LS D E KS F TT L P A T G A A Y P R V A V O D L O         234           O# AP (ADL258/S R) (-152)         L R P A T R Y V R C G O S S V R G A LI O S LE F TT L P A T G A A Y P R V A V O D L O         234           D# AP (21) (ADL27)/1-27         L R P	AtaPAPhy_b1/F6MIX1//1-538	150 LEPGTKYYYQCGDPAIPG-	- <mark>A MS A V H A F R T MP</mark> D V G P R S Y P G R I A V V <mark>G D L G</mark> 197
w.P.#. JABGEG/J.1-40         151         LKS TT VY N C GOP T IG         MSS I Y S F TT VY S G P S Y F R (I I 0 L C	ScP APhy_b1/F6MIX5//1-538	150 LEPGTKYYYQCGDPAIPG-	- AMSAVHAFRTMPAVGPRSYPGRIAVVGDLG 197
w.P.#. JABGEG/J.1-40         151         LKS TT VY N C GOP T IG         MSS I Y S F TT VY S G P S Y F R (I I 0 L C	RcP AP 1/B9RWG6//1-566	178 LKPNTTYFYQCGDPSIP	- AMS DI YH FR TMP AS GP KS FP GK I AI V GD L G 224
PP#Phy//7852/1/1246         158         LEPSTLVYVGCODPALQ         AMSDIYYERTM         ISGLHSYPARIAVYOLO         205           P#PEJS(D7L656/L-352         150         LEPSTLVYVGCODPAR         AMSDIYERTFTFF         YSPSSYPARIAVYOLO         356           A#PEJS(D7L656/L-352         150         LEPSTLVYVGCODPAR         AMSSIHHERTTFTF         YSPSSYPARIAVYOLO         356           B#PAEJS(D7L656/L-352         150         LEPSTLVYVGCODSSIPG         AMSSIHHERTTFTF			
WP#PbyB3AE271/547       159       150       LP DT IVYK COD DS IF       AMS CEF FET FF K PS PN VP PARIAVY OLG       2016         AP#230(GSTP11/1-458       150       LP DT IVYK COD DS VP       AMS CEI S FET L       LP SK DAY PHR IA FV OLG       356         GMP AP (VMHC41/1-428       150       LE DT TAY VK COD S VP       AMS CEI S FET L       LP SK DAY PHR IA FV OLG       355         SPM PL_COPKC1/1-566       174       LP AT R YVK COD S LP G       015 0 EHS FTT L       ATGA CYP RRAAVY OLG       2211         HP PL_COPKC1/1-566       174       LP AT R YVK COD S LF G       015 0 EHS FTT L       ATGA CYP RRAAVY OLG       2211         HP PL_COPKC1/1-566       174       LP AT R YVK COD S LF G       015 0 EHS FTT L       ATGA CYP RRAAVY OLG       016       2211         HP PL_COPKC1/1-566       175       LP AT RYVK COD S LVG GS LK G       015 0 ELS FT LP S AAAAYP RAVY OLG       016       224         ADP421(B305)/1-522       175       LP AT RYVK COD S LVG GG LS GET LP S AAAAYP RAVAVY OLG       016       224         ADP423(B305)/1-522       175       LP AT RYVK COD S LVG GG LS GET LP S AAAAYP RAVAVY OLG       016       224         ADP423(B305)/1-522       175       LP AT RYVK COD S LVG GG LS GET LP S AAAAYP RAVAVY OLG       016       224         ADP423(B305)/1-521       100       LV TVYVK CG GD S			
AP#21507L656()-1532       150       LF PT KIY VY R C GD PS RA       AMS I I H H FT TM       VS PS S V P G AL AVY       OL 6       156         GMP#4()SHX6()/L42       118       LE DITA Y V R C GD S L       OK 6 A EF L KT TP A       OF A L A C A S A A V P R I A Y V C I G       155         DITA Z (PML)/L56       174       LR A TR YV R C GD S L F G G V P R A AVV (OL 6       251         DIFA Z (PML)/L56       174       LR A TR YV R C GD S L F G G V P R A AVV (OL 6       251         DIFA Z (PML)/L57       155       LG P TV R C GD S S F G A G G G S G S G F TT L A PA D A V P R A AVV (OL 6       250         DIFA Z (PML)/L57       155       LG P TV R C GD S S F G A G G G S G S G F TT L A PA D A V P R A AVV (OL 6       254         OP#44 (ASD2G)/L-52       175       LR P A TR YV R C GD S S F G A G G G S G S G L F T L I S A A A V P R N AVV (OL 6       254         OP#44 (ASD2G)/L-52       175       LR P A TR YV R C G D S S F G A G G G S G S G F F T P S       S A A A V P R N AVV (OL 6       254         OP#44 (ASD2G)/L-52       175       LR P A TR YV R C G D S S R G A G S G S G F F T P S       S A A V P R N AVV (OL 6       254         OP#44 (ASD2G)/L-52       175       LR P A TR YV R C G D S S R G A G S G S F F T P S       S A A V P R N AVV (OL 6       254         OF#44 (ASD2G)/L-52       175       LR N TV Y V R G G D S T F F T P S       S A A V P R N AVV (OL 6       257			
AP#2310GTPH1/L+38       150       150       ED FTR TY YR CG DS SY P       ANS EE IS FET LY       P K N AY PH K A FY N CG DS S       155         DP#P 2_COPKCJY/J-56       174       LB A T R YYR CG DS S LP G       0.150       0.150       155         DSPP 2_COPKCJY/J-56       174       LB A T R YYR CG DS S LP G       0.150       156       157       167       167       157         DSPP 2_COPKCJY/J-56       174       LB A T R YYR CG DS S LV G       0.150       158       171       LA GG CYP R RA XVY OL G       211         HP#P2_COPKCJY/J-56       172       LB P S T R YYR CG DS S LV GS S K GG A LISG EL S FET LY       S AA AYP R R VA VY OL G       212         D2# AP 30(ASTCAT/Y)       175       LB A T R YYR CG DS S VR GG A LISG EL S FET LY       S S AA AYP R R VA VY OL G       224         D2# AP 30(ASTCAT/Y)       101       LR NTYYR CG DS S VR GG A LISG EL S FET LY       S S AA AYP R R VA VY OL G       224         AP 4P 30(DST//1-327       101       LR NTYYR CG CD S S VR GG A LISG EL S FET LY       S S AA AYP R R VA VY OL G       224         AP 4P 30(DST//1-327       101       LR NTYYYR CG CD S AA AYP R P AYP R AY			
OnP #4 (VPM:K4)/L442         LED NTAY FYN CG.G			
DP PP_2(ICPRC)[1/1-56       14       IF A T IN YY NG CO S LP G       0.1 SO EH S FT TL P A G A OC YP RR AVV G D L G       211         HP PP_2(ICPRC)[1/1-56       171       IF A T S TH YY NG CO S S LK G       0.1 SO ER S FT TL P A F A D A YF R W A VV G D L G       213         PPPP/105203       175       L F N T H YY NG CO S S W R G A D LS O ER S FT TL P A F A D A YF R W A VV G D L G       235         OP PA106203       175       L F N T H YY NG CO S W R G A D LS O ELS F E TL P S S A A A Y P R W A VV G D L G       224         OP PA106203       175       L F N T H YY NG CO S W R G A D LS O ELS F E TL P S A A A Y P R W A VV G D L G       224         AP A 20106027       175       L F N T Y Y F C G O S W R G A D LS O ELS F E TL P S A A A Y P R W A VV G D L G       224         AP A 20106027       174       174       L F N T Y Y Y C G G O S W R G A D LS O ELS F E TL P S A A A Y P R W A VV G D L G       224         AP A 20106027       174       174       L F N T Y Y Y C G G O S W R G A D LS O ELS F E TL P S A A A Y P R W A VV G D L G       226         AP A 20106027       174       174       L F N T Y Y K C G O S W R G A D LS O ELS F T T Y Y F A V A V G O L G       226         AP A 20106027       174       174       174       L K N T X Y Y Y K C G O S W R G A D LS O ELS F T Y Y Y K C G O S W G A D L A A A Y P R V A V A O L G       226         AP A 20106027       174       174       1			
SpP#/P         Description         Description <thdescription< th=""> <thdescription< th=""> <thd< td=""><td></td><td></td><td></td></thd<></thdescription<></thdescription<>			
Prive Act (CHRUS)/LISE       LR P S TR Y YR C C D S LK G       OLS D E RS FR TLP AF AP DY P R C AP VR AV Y G D L G       215         DP AP3 (DCCGA)/LISE       150 L R P AT R YY YR C D D S VR G G A       LS O E LS FE TLP S SA AA AY P R VA VV G D L G       224         DP AP3 (DCCGA)/LISE       150 L L P AT R YY YR C D D S VR G G A       LS O E LS FE TLP S SA AA AY P R VA VV G D L G       224         DP AP3 (DCCG37 //LISE       150 L L P AT R YY YR C D D S VR G G A       LS O E LS FE TLP S SA AA AY P R VA VV G D L G       224         AP AP3 (DCCG37 //LISE       150 L L YR TR YY YR C D D S VR G G A       LS O L S D E S FE TLP S SA AA AY P R VA VV G D L G       224         AP AP3 (DCCG37 //LISE       150 L L YN YY YK C G D S VR G G A       LS O L S P S R F T P K S P V F Y F VA VA V G D L G       150         AP AP3 (DCCG37 //LISE       110 L K P NT YY YK C G D S       D K K D C FE S KHT P S       FF P LK F P V F A V S O L G       150         AP AP3 (DCCG37 //LISE       110 L K P NT YY YK L G G C       D AK R G PW V TP F K S O PV P Y T F G L I G D L G       152         IP AP3 (DCCG37 //LISE S)       110 L K Y V K Y V K L G C       D AK R G PW V TP F W N P D V P Y T F G L I G D L G       152         IP AP3 (DCCG37 //LISE S)       110 L K Y V K Y V K L G C       D A A L FW K Y T P E L O P V P Y T F G L I G D L G       152         IP AP3 (DCCG37 //LISE S)       110 L K Y Y K Y V K U G G       N T R G W W T P F E V A D V P Y T F G L I G D L G <td></td> <td></td> <td></td>			
Pp <sup>7</sup> P <sup>3</sup> /P <sup>3</sup>	56P AP   A0 A1Z5R 9 T8  /1-566	174 LRPATRYYYRCGDSSLPG -	- <mark>G L S D E R S F T T L P</mark> A T G A G C Y P R R V A V V <mark>G D L G</mark> 221
OpPAP3 (GECCG)/L+22       175 LR PATRY YR C C D S VR G G A GL S G E L S E E L P S SAAAAY PR RV AV V G D L G       224         OPPAP3 (GECG27/)/L39       85 L E YK TK Y YR C D S VR G G A GL S G E L S E T L P S SAAAAY PR RV AV V G D L G       227         APPAP3 (GECG27/)/L39       85 L E YK TK Y YR C D G S VR G G A GL S G E L S E T L P S SAAAY PR RV AV V G D L G       227         APPAP3 (GECG27/)/L427       110 LK P NT VY YK C G G P       5 T Q E F S R T P F S       F F P K F A I V G D L G       129         APPAP3 (GECG27/)/L427       110 LK P NT VY YK C G G P       5 T Q E F S R T P F S       F F P K F A I V G D L G       120         APPAP3 (GECG27/)/L435       120 L K V D K V Y V K L G G G       0 A K Q E V F V T P K C O P V P Y T F G L I G D L G       128         APPAP2 (GMA07/)/L455       120 L K V D K V Y V K L G G G       0 S K R E F W C O T P W N N P V - P Y T F G L I G D L G       122         IbPAP2 (GMS07/)/L455       124 L E YN T K Y Y W C Q G G       N T T R S F W T D P E V O P V P V T F G L I G D L G       126         APPAP3 (GS232/)/L465       124 L E YN T K Y Y W C Q G G       N T T R S F W T D P E G D D V - P Y T F G L I G D L G       126         APPAP3 (GS232/)/L465       124 L E YN T K Y Y W E V G G G       N T T R S F W T D P E G D D V - P Y T F G L I G D L G       126         Gm P A 1 (O9318/)/L44       125 L E YN T K Y Y W E V G G G       N T R R S F T D P K V D P V Y P Y F G L I G D L G       126	HvPAP_c C4PKL5 /1-564	172 LRPSTRYYYRCGDSSLKG -	- GLSDERSFRTLPAPAPDAYPRRVAVVGDLG 219
Op# AP4 [88:809]/L622       175       IR P A TRY YVR C G D S VR G G G       01 S G L S G L S F LT P S XVR P K VA VP R V A V A V A V A V A V A V A V A V A V	PpP AP   A9 SP12   / 1-557	159 LQPNTRYYFQCGDAATD	- TFSAEHSFTTLPLPSPSAYPARIAIVGDLG 205
APP AP3 (09:027)(J-396       BS L EYY TK KY YE LG TG	0sP AP 3   Q6ZCX8   /1-622	175 LRPATRYYYRCGDSSVRGG	A <mark>G L S G E L S F E T L P</mark> S S A A A A Y P R R V A V V <mark>G D L G</mark> 224
APP AP3 (09:027)(J-396       BS L EYY TK KY YE LG TG	OsP AP 4   B8 B909   /1-622	175 LRPATRYYYRCGDSSVRGG	A <mark>G L S G E L S F E T L P</mark> S S A A A A Y P R R V A V V <mark>G D L G</mark> 224
APP AP20 (02UV7)/L427       111       L K P NTV Y Y K G G P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S T G E F S F N P P       S F P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P S F N P P       S F N P P S F N P P       S F N P P S F N P P V F F S F N P P V F F S F N P P V F F S F N P P V F F S F N P P V F F S F N P P V F F S F N P P V F F S F N P P V F F N F S F N P P V F F S F N P V F F S F S P N V F F S F			
AP AP210(38340/1/434)       111       LQA NTTYYYR CG			
IbP #3 (ag2) als/1-427       B6       LEY D TK YY Y E LG LG       D K K 0 E WF Y T P K G P D V - P Y T FG L I G D L G			
APP A21/02/04/01/-437       117       LK P N TK YY YK C G G G G G G G G G G G G G G G G G G			
LpP AP (05M007)/L455       120       K Y D R K Y F Y K V G E G	1 4 10		
ibPAP2/gSS08//1463       12       -YDTKYYYKLGEG			
IbP#2/05020//L465       12       LEYNTKYYYEVGIG       ITTRSFWFTTP       EVGPDV-PYTFGLIGDLG       147         GmP#21(039131/L464       122       LEYNTKYYYEVGLG       NTTR0PWFVTP       FLGPDV-PYTFGLIGDLG       166         ARP #21(039232/L465       124       LEYNTKYYYEVGLG       SVR0FSFTSPFVTP       FLGPDV-PYTFGLIGDLG       160         ARP #22(03232/L465       124       LEYNTKYYYEVGLG       SVR0FSFTSPFVFP       FLGPDV-PYTFGLIGDLG       160         MR#AP1(04502/L465       124       LEYNTKYYYEVGLG       SVR0FSFTSPFVFP       FVF0PV-PYTFGLIGDLG       160         MR#AP1(04502/L465       124       LEYNTKYYYEVGLG       NTTR0FWFTTP       FLOPDV-PYTFGLIGDLG       160         MP#2/02(03505/L467       122       LEFDTKYYYEVGLG       NTTR0FWFTTP       FLOPDV-PYTFGLIGDLG       160         MP#2/02(03505/L467       122       LEFDTTYYYEVGLG       NTTR0FWFTTP       FU/DA-SYTFGLIGDLG       160         MP#2/0203507/L468       124       LEFNTTYFVVGGLG       NTTR0FWFTTP       FU/DA-SYTFGLIGDLG       160         MP#2/030507/L468       124       LEFNTTYFVVGGLG       NTTR0FWFTTP       FU/DA-SYTFGLIGDLG       160         MP#2/030507/L473       122       LEYNTKYYVEVGLG       NTTR0FWFTP       FU/DA-SYTFGLIGDLG       160       160       160 <t< td=""><td></td><td></td><td></td></t<>			
AtP # 11 (09318)/1-441       122       LE Y D T K Y Y Y E V G L G       TT R Q F W F Y P E I G P D V P Y T F G L I G D L G       164         AtP & #1 (003824)/1-460       124       LE Y D T K Y I Y E V G L G       G V R Q F S F T S P F K V G P D V P Y T F G L I G D L G       166         AtP & #1 (038324)/1-460       124       LE Y D T K Y I Y E V G L G       KW S R R F W F I P K S G P D V - Y T F G L I G D L G       166         AtP & #1 (038324)/1-460       124       LE Y D T K Y I Y E V G L G       HS R R F W F Y P P K S G P D V - Y T F G L I G D L G       160         MP & #1 (034X7)/1-460       122       LE Y N T K Y Y W V G L G       NT R Q F W F T P P I G P D V - Y T F G L I G D L G       166         M & # M (1034W7)/1-460       122       LE Y N T K Y Y W V G L G       D S A R E F W F E T P A I D P D A - S Y T F G I G D L G       164         P & P & P & 2 (036/C 4 C I / 1-457       128       LE Y K T K Y Y W V G G G       NT T R Q F W F T P P E V G I D V - Y Y T F G L I G D L G       166         M & P & P & 2 (036/C 4 C I / 1-457       128       LE Y K T K Y Y W U G G G       NT T R Q F W F T P P E Y G I D V - Y Y T F G L I G D L G       166         M & P & P & P & 2 (035) / 1-466       124       LE Y N T K Y Y V U G V G R       NT R R G F F T P P X V D P A - S Y F G I G D L G       166         M & P & P & 2 (035) / 1-466       124       LE Y N T K Y Y Y U K G G G       0 S R E F W F T P P X I G D D A -			
GmPAP1[Q09131]/1-46       122       LEYYTKYYYEVGLG       NTTRQFWFYTPP       EIGPDV-PYTFGLIGDLG       164         ARPA23[Q23244]/1466       124       LEYDTKYIYEVGLG       SVRQFSFPFPPKVGPDV-PYTFGLIGDLG       160         ARPA21[Q38244]/1465       124       LEYDTKYIYEIGSG       SVRQFSFPFPFPKVGPDV-PYTFGLIGDLG       160         INPAP1[Q4KU22]/1465       123       LEYNTKYYVEVGLG       NTTRQFWFTPP       FIPPKSFPVFPVPVFFGLIGDLG       165         MPAP1[Q4KU22]/1465       123       LEYNTKYYVEVGLG       NTTRQFWFTPP       FIPPKFFFP       FIFQL       160       166         MPAP1[Q4KU22]/1465       124       LEYNTKYYVEVGLG       DSAREFWFFTPP       FIPPKVDPVYFFGLIGDLG       164         LAP1[Q35WM7]/1460       122       LEFNTTYYVEVGLG       NTTRQFWFTPP       FVFGTP       FIFGLIGDLG       160         MPAP1[Q35WS]/1475       122       LEFNTTYYVEVGLG       NTTRQFWFTPP       FVFGTP       FIFGLIGDLG       160       160         MPAP2[Q764C1]/1477       128       LEYNTKYVVEVGLG       NTTRQFWFTPP       FVFGTP       FIFGLIGDLG       160       160       170         MAP2[Q35US]/1476       122       LEYNTKYVVEVGLG       NTTRQFWFTPP       FVFGTP       FIFGLIGDLG       160       160       160       160       160       170 </td <td>1bP AP 2   Q9 SD 29  /1-465</td> <td>124 L E Y N T K Y Y Y E V G I G</td> <td>- NTTRSFWFTTPPEVGPDV-PYTFGLIGDLG 166</td>	1bP AP 2   Q9 SD 29  /1-465	124 L E Y N T K Y Y Y E V G I G	- NTTRSFWFTTPPEVGPDV-PYTFGLIGDLG 166
ARPAP25 (023244/)/1469       124       L E Y D T K Y Y Y E U G T D	AtP AP 11   Q9 SI 18   / 1-44 1	125 L E Y D	- <u> P</u> SKSRSRCSLHIRYY <mark>SDLG</mark> 147
AHPAP12       Q38924       //1469       128       LEFDTKYYYEIGSG       KWSRRFWFFIPP       KSGPDV-PYTFGLIGDLG       GDLG       170         NHPAP(Q4K23)       1/1455       124       LKYNTKYYWEYGGG       H3RRFWFTPP       VFTPQLG       160 LG       155         OgPAP2(Q85505)       1/1455       122       LEYNTKYYWEYGGG       NTTRQFWFTPP       FLGPDV-PYTFGLIGDLG       164         LAP1(Q830M7)       1/1450       122       LEFDTTYYEYGGG       DSAREFWFETPPAIDPA-SYTFGIG       GDLG       164         LAP2(Q36L1)       1/1457       122       LEFDTTYYEYGGG       DSAREFWFETPP       VDPA-SYFFGIG       GDLG       164         APP2(07661)       1/1457       122       LEYNTKYYWIGGG       DSAREFWFETPP       FLPDVDA-SYFFGIG       GDLG       170         UAP2(Q36L1)       1/458       127       LEYNTKYYWIGGG       DSAREFWFETPP       FLPDVDA-SYFFGIG       GDLG       165         APPAP10(Q35V9)       1/1468       127       LEYNTKYYYEYGGL       NTTRFSFITPP       FLODV-PYTFGLIGDC       164         TAPAP(G30KP1/14761       122       LEYNTKYYYEYGGL       NTTRFSFITPP       FLODV-PYTFGLIGDC       166         APPAP2(Q38K0)       124       LEYNTKYYYEYGGL       NTTRFSFITPP       FLODV-PYTFGLIGDC       160       16	GmP AP 1   Q09 13 1   / 1-4 64	122 L E Y K T K Y Y Y E V G L G	- NTTRQFWFVTPPEIGPDV-PYTFGLIGDLG 164
INP AP   Q84K23//1461       124 L K Y N T K Y Y Y W G G G	AtP AP 25 / 023244 / /1-466	124 LEYDTKYIYEVGTD	- GSVRQFSFTSPPKVGPDV-PYTFGIIGDLG 166
INP AP   Q84K23//1461       124 L K Y N T K Y Y Y W G G G	AtP AP 12/038924//1-469	128 LEEDTKYYYEIGSG	- KWSRREWEELPPKSGPDV-PYTEGLIGDLG 170
MtP AP 1/Q4K U02//1465       123       L E Y N T K Y Y Y E V G L G       N T T R Q FWF T T P P       E I G P D V P Y T F G L G D L G       164         OSP AP 2 (Q85305 //1476       122       L E F D T T Y Y V F V G G G       D S A R E FW F T P P E V G L D V P Y T F G L G D L G       164         P VP AP 2 (Q764C1//1457       128       L E F D T T Y Y V F V G G G       D S S R E FW F T P P E V G L D V P Y T F G L G D L G       170         U AP 2 (Q816L1//1463       124       L E F N T T Y Y V V G G G       N T T R Q FW F T T P P E V G L D V P Y T F G L G D L G       166         APP AP 10 (Q83V9/1/1468       124       L E N T T Y Y V V G G G       N T T R Q FW F T T P P E I G P D V P Y T F G L G D L G       166         AP AP 10 (Q83V9/1/1468       124       L E N T X Y Y V L G V G G       N T T R Q FW I T P P E I G P D V P Y T F G L G D L G       166         AP AP 0 (Q930F0//14650       122       L K N T K Y Y V L G G G       D S A R E FW F T P P A I D T D A - S Y T F G I G D L G       166         AP AP (Q33WP4//1481       128       L E Y D T K Y Y K I G K G       D A A R E FW F T P P A I D T D A - S Y T F G I G D L G       160       160       170         AP AP 2 (Q3WF09//1473       128       L E Y D T K Y Y K I G K G       D A A R F W F T P P V K I D P A - S Y T F G I G D L G       170         S AP AP 2 (Q3WF09//1473       128       L K Y N T K I G K G       D A R E FW F T P P V K I			
0sPAP2/Q8505/1-476       122       LEYNTKYYYKIGSG       DSAREFWFETPPAIDPASYTFGIIGDLG       164         LaP2/Q8505/1-476       122       LEFDTTYYYEVGIG       NTTRQFWFITPPEVGDV-PYTFGIIGDLG       164         PvPAP2/Q764C1/1457       124       LEFNTYYVEGIG       NTTRQFWFITPP       EVGLDV-PYTFGIIGDLG       166         ArP2/Q816L1/1-463       124       LEFNTYYVUGVGG       NTTRQFWFITPP       EVGINV-PYTFGIIGDLG       166         ArP2/Q3056/1-459       122       LEYNTKYYVUGVGG       OTERKFWFFTPP       EIGPDV-PYTFGIIGDLG       164         TAACP(ADS10/1-459       122       LEYNTKYYVUGVGG       NTTRQFWFITPP       EIGPDV-PYTFGIIGDLG       164         TAACP(ADS10/1-459       122       LEYNTKYYVUGVGG       NTTRQFWFITPP       EIGPDV-PYTFGIIGDLG       164         TAACP(ADS10/1-459       122       LEYNTKYYVUGVGG       NTTRQFWFITPP       EIGPDV-PYTFGIIGDLG       164         TAACP(ADS10/1-477       123       LEYNTKYYVEVGLR       NTTRQFWFITPP       NTTRQFWFITPP       164       164         ArPAFGQ92510/1-473       128       LEYNTKYYVEVGLR       NTTRQFWFITPP       164       164       164       164       164       164       164       164       164       164       164       164       164       164       164       164 <td>1 4 10</td> <td></td> <td></td>	1 4 10		
LaAP1/Q33VM7//1460       122       LE F D T T Y Y Y R V G I G       N T T R Q F W F I T P F V G L D V - P Y T F G I I G D L G			
PvPAP2/Q764C1//1457       128       LEYKTKYYYRIGSG       DSSREFWFETPP       KVDPDA-SYKFGII       GDLG       170         LIAP2/Q8L5L1//1458       124       LEFNTTYFYVGIG       NTTRQPWFITPP       EVGINV-PYTFGII       GDLG       166         ARPAP1Q9S9V9/1458       127       LEYDTKYYVGIG       OTERKEWFFTPP       EVGINV-PYTFGII       GDLG       169         PvPAP1/P80366//1459       122       LKYNTKYYVEVGLR       NTTRRFSFITPP       QTGLDV-PYTFGII       GDLG       164         TaACP/C4PKL1//1477       123       LEYNTKYYVEVGLR       NTTRRFSFITPP       QTGLDV-PYTFGII       GDLG       164         ARPAP(090510/1476       124       LEYDTKYYVEVGLR       DSAREFWFTPP       AIDTDA-SYTFGII       GDLG       166         ARPAP(090510/1474       128       LEYDTKYYVEVGLG       DAAREFWFHTPP       EVGPDV-PYTFGII       GDLG       170         APAP3(0650M8/1-477       121       LQYDTKYYVEVGLG       DAARKFWFETPP       EVGPDV-PYTFGII       GDLG       170         ARPAP26(0949Y3/1-475       122       LEYDTKYYVEGGG       DAKRGWFYTPP       EVGPDV-PYTFGII       GDLG       170         ARPAP26(0949Y3/1-475       122       LEYDTKYYVEIGGG       DASREFWFTPP       IVPDA-SYKFGII       GDLG       170         MAP2/102500/1-473       <			
UAP2/Q8L6L1//1-463       124       LEFNTTYFYVVGIG			
AtPAP 10 / Q9SV9 // 1468       127       L E Y D T K Y Y Y V L G V G N T T R F S F I T P P I G L G P U P Y T F G L I G D L G			
PvPAP1/P80366//1459       122       LKYNTKYYYEVGLR       NTTRRFSFITPP       QTGLDV-PYTFGLIGDLG       164         TaACP(CAPKL1/1477       123       LEYNTKYYYKIGTG       DSAREFWFQTPPAIDTDA-SYTFGIIGDLG       165         AtPAP6(Q9C510/1466       124       LEYDTKYYKIGTG       SXREFWFQTPPAIDTDA-SYTFGIIGDLG       166         AtPAP6(Q9C50/14766       124       LEYDTKYYKIGTG       DSAREFWFQTPP       NTTRFFFTPPK       STFGIIGDLG       166         AtPAP3(Q9St09/1/470       128       LEYDTKYYKIGTG       DAAREFWFHTPP       PVFTFGIIGDLG       160       170         AcPAP32(Q9XF09/1/470       128       LKHNTKYHYEGGG       DAAREFWFHTPPKVDPA-SYKFGIIGDLG       160       170         SFPAP3(GD5M8/1/477       121       LQYDTKYYYKIGFG       DSAREFWFHTPPKVDPA-SYKFGIIGDLG       161         AtPA22(Q9XF09/1/473       132       LEYDTKYYKIGFG       DSAREFWFTPPKVDPA-SYKFGIIGDLG       164         RCPAP3(B9SXP6/1/488       128       LEYDTKYYKIGFG       DSSREFWFTPPHVPKVPFKFGIVGDV-PYKFGIIGDLG       164         RCPAP3(Q9X24/1/458       124       LEYDTKYYKIGFG       DSSREFWFTPPKVVPPKVFFKGIVGDV-PYKFGIIGDLG       164         RCPAP3(Q4YZ4/1/458       124       LEYDTKYYKIGSG       DSSREFWFTPPKVVPPKVPKVFGIIGDLG       200         LAP2(Q9X24/1/458       124       LEYTKYYKIGSG			
To ACP / C4PKL1/1477       123       LEYNTKYYYKIGTG			
AtP AP 6 [ 09 C5 10 ] / 1-466       124       L E Y D T K Y I Y E V G T D C A A R E FW FH T P P (I H P D A - S Y T F G I G D L G 170         AcP AP 32 [ 09 XF09 ] / 1-470       128       L E Y D T K Y Y K I G K G D A A R E FW FH T P P (I H P D A - S Y T F G I G D L G 170         AcP AP 32 [ 09 XF09 ] / 1-470       128       L K H N T K Y H Y E V G I G D A A R E FW FH T P P (I H P D A - S Y T F G I G D L G 170         StP AP 32 [ 04 XF09 ] / 1-470       128       L K H N T K Y H Y E V G I G D S A R K FW FE T P F K V D P D A - S Y K F G I I G D L G 171         JbP AP 1] (29 SE00 ] / 1-473       132       L E Y D T K Y Y K I G S G D A K R G FW FV T P K P G P D V - P Y K F G I I G D L G 174         AtP AP 26 [ Q449 Y3] / 1-475       122       L E H D T K Y Y K I G S G D S S R E FW FV T P P H V H P D A - S Y K F G I I G D L G 170         UAP 1] Q8 L50 I / 1-488       128       L E Y D T K Y Y K I G S G D S S R E FW FV T P P K V E P D V - P Y K F G I I G D L G			
AcP AP [093WP4/1-481       128       L EY D T K Y Y Y K I G K G       D A A R E FWFHTPP       Q I HP D A - S Y T F G I I G D L G       170         AoP AP32 [035M8/1-477       128       L K H N T K Y H Y E V G I G       D S A R K FWF E T P P K V D P D A - S Y K F G I I G D L G       160 L G       170         SrP AP3 [045M8/1-477       121       L Q Y D T K Y Y Y E L G K G       D S A R K FWF E T P P K V D P D A - S Y K F G I I G D L G       163         IbP AP1 [095B0/1-473       132       L EY D T K Y Y Y E L G F G       D S A R K P WF E T P P K V D P D A - S Y K F G I I G D L G	Ta ACP   C4PKL1 /1-477	123 LEYNTKYYYKIGTG	- DSAREFWFQTPPAIDTDA - SYTFGII <mark>GDLG</mark> 165
AoP AP 32 (0)       (0)       128       LKHNTKYHYEVGIG       HTVRSFWFMTPP       EVGPDV-PYTFGLIGDLG       170         StPAP3 (Q)       (0)       5M8 (1)       121       LQYDTKYYYEIGKG       DSARKFWFETPP       FVDDA-SYKFGIIGDLG       163         IbPAP1 (0)       120       LYDTKYYYELGFG       DAKRGWEVTPP       FVDDA-SYKFGIIGDLG       164         AtPAP26 (0)       124       122       LENDTKYYYELGFG       DAKRGWEVTPP       FVPP VYFGLIGDG       164         AtPAP26 (0)       148       LEYDTKYYYELGFG       DSSREFWFVTPP       FVPP DT-PYVFGLIGDG       164         RcPAP3 (0)       128       LEYDTKYYYELGFG       DSSREFWFVTPP       FVPP TYFFGLIGDLG       164         UPP1 (0)       128       LEYDTKYYER (0)       DSSREFWFKTPP       KVDPDS-PYKFGIIGDLG       166         GmPAP3 (0)       129       LEYTKYYER (0)       DSSREFWFKTPP       KVDPDS-PYKFGIIGDLG       164         UPP04 (0)       128       LEYDTKYYER (0)       SSWESSW       NTTRHFWVYER (0)       SSWESSW       164         UPP04 (0)       10       VXIIIFGD       101       LKYTTKYER (0)       SWESSW       NTTRHFWVENFF       104       105       102       106       100       106       100       100       100       100	AtP AP 6   Q9 C5 10   / 1-4 66	124 L E Y D T K Y I Y E V G T D	- KSVRQFSFTTPPKIGPDV-PYTFGIIGDLG 166
StP AP3 / Q6J5M8 / 1-477       121       L Q Y D T K Y Y Y E I G K G       D S A R K FW F E T P P       K V D P D A - S Y K F G I I       G D L G       163         IbP AP 1/Q95E00 / 1-473       132       L E Y D T K Y Y Y R L G F G       D A K R Q FW F V T P P       K P Q P D V - P Y V F G L I       G D L G       164         ArP AP26 (Q949Y3 / 1-475       122       L E H D T K Y Y Y K I E S G       D S S R E FW F V T P P       H V H P D A - S Y K F G I I       G D L G       164         RcP AP3 / Q95(51 / 1-488       128       L E Y D T K Y Y K I G D G       D S S R E FW F V T P P       H V H P D A - S Y K F G I I       G D L G       164         MAP 1 Q8 L52 L / 1-477       124       L E Y K T K Y Y K I G D G       D S S R E FW F V T P P       H V P D Y - P Y K F G I I       G D L G       166         Gm PA3 / Q6VGT3 / / 1-477       124       L E Y K T K Y Y R I G S G	AcP AP   Q93WP4   /1-481	128 LEYDTKYYYKIGKG	- DAAREFWFHTPPQIHPDA - SYTFGIIGDLG 170
StP AP3 / Q6/5M8 / 1-477       121       L Q Y D T K Y Y Y E I G K G       D S A R K FW F E T P P K V D P D A - S Y K F G I I G D L G       163         IbP AP1 / Q95E00 / 1-473       132       L E Y D T K Y Y Y R L G F G       D A K R Q FW F V T P P K P G P D V - P Y V F G L I G D L G       174         AP AP26 (Q949 Y3 / 1-475       122       L E H D T K Y Y Y K I E S G       E S S R E FW F V T P H V H P D A - S Y K F G I I G D L G	App Ap 32   Q9XF09   /1-470	128 LKHNTKYHYEVGIG	- HTVRSFWFMTPPEVGPDV-PYTFGLIGDLG 170
IbP AP 1 (095E00)/1-473       132       L EY D T K Y Y Y R LG F G D A K R Q FW F V T P P       K P G P D V - P Y V F G L I       G D I G	StP AP310615M81/1-477	121 LOYDTKYYYEIGKG	- DSARKEWEETPPKVDPDA-SYKEGILIGDIG 163
AtP AP26 j Q949Y3 / 1-475       122       L EH D T K Y Y Y K I ES G ES S R E FW F V T P H V H P D A . S Y K F G I I G D L G 164       RcP AP3 j 895XP 6 / 1-488       128       L E Y D T K Y Y Y K I G D G D S S R E FY F Q T P P I I N P D T - P Y K F G I I G D L G 170       IJAP 1 Q8 L5E1 / 1-477       124       L E Y K T K Y Y Y R I G S G D A S R E FW F E T P P K V D P D Y - P Y K F G I I G D L G	1 4 10		
RcPAP3 (B5XP6//1-488       128       L E Y D T K Y Y Y K I G D G D S S R E F Y F Q T P P I I N P D T - P Y K F G I I G D L G 170       149 1 / Q8L5E1 / 1-477       124       L E Y K T K Y Y Y R I G S G D A S R E FW F E T P P K V E P D V - P Y K F G I I G D L G 166       166         GmPAP3 / Q6YGT9 / / 1-512       160       L E Y E T K Y Y Y R I G S G D S S R E FW F K T P P K V D P D S - P Y K F G I I G D L G			
UAP 1/Q8L5E1/1-477       124       LEYKTKYYYRIGSG       DASREFWFETPP       KVEPDV-PYKFGII       GDLG       166         GmPAP3/Q6YGT9//1-512       160       LEYETKYYYRIGSG       DSSREFWFKTPP       KVDPDS-PYKFGII       GDLG       202         LaAP2/Q9XJ24//1-638       121       LKYTTKYHYEVGSW       NTTRHEWYYNFP       IQFGLDVPCTFGLIGDLG       164         UPP04/Q8VXF4//1-629       265       LWPNQRYTYRLGHILSNGSY       VKSKKYSFKGAP       YPGQSS-VQRVVIFGDMG       313         UPP01/Q8VX11//1-612       248       LWPNREYTYKLGHRLKNGSY       VKSKKYSFKGAP       YPGQSS-VQRVVIFGDMG       299         UPP02/Q8VX56//1-612       248       LWPNREYTYKLGHRLKNNGTYIWSQNYQFRAAP       FPGQKS-UQRVAIFGDMG       296         TnPAP1/Q4RL44//1-378       97       LRPAATY       500       GWSRRFRFRALK       SARFGDMG       296         MmPAP7/Q68X37//1-438       101       LLP GVQYVYRCGSAQ       GWSRFRFRFALK       SARFGDMG       132         MmPAP7/Q8X37//1-438       101       LP GAQVYYRCGSSQ       AMSSIFHFRQ       PD PSQ       PLRAAIFGDMG       143         DmPAP1/Q9V256//1-458       107       LEP GAQVYYRCGSSQ       GWSRFFRFTALK       SAVDWSP-SLAYFGDMG       143         DmPAP2/Q9V258//1458       117       LP PATYSYCGSPL       GWSAVFNFKTPPA       GEKW	· · · · · · · · · · · · · · · · · · ·		
GmPAP3/Q6YGT9//1-512       160       LEYETKYYYRIGSG       DSSREFWFKTPP       KVDPDS-PYKFGII       GDLG       202         LaAP2/Q9XJ24//1-638       121       LKYTTKYHYEVGSW       NTTRHFWVYNFP       IQFGLDVPCTFGLI       GDLG       164         UPPD4/Q8VXF4//1-629       265       LWPNQRYTYRLGHILSNGSYVKSKKYSFKGAP       YPGQNS-LQRVIFGDMG       313         UPPD1/Q8VX11/1-615       215       LWPNREYTYKLGHRLFNGTTIWSKEYHFKASP       YPGQNS-LQRVAIFGDMG       299         UPPD2/Q8VXF6//1-612       248       LWPNRIYEYKIGHRLFNGTTIWSKEYHFKASP       YPGQNS-LQRVAIFGDMG       296         TnPAP1/Q4RLR4//1-378       97       LRPAATY			
La AP 2 / Q9XJ24 // 1-638       121       LK Y T T K Y H Y EV G S W N T T R H FWV Y N F P I Q F G L D V P C T F G L I G D L G			
UPP D4 \ Q8 VXF4 \ / 1-629       265       LWP NQRYTYRLGHILSNGSYVKSKKYSFKGAP       YP GQNS-LQRVIFF       GDMG       313         UPP D1 \ Q8 VXF4 \ / 1-615       251       LWP NR EYTYKLGHRLFNGTTIWSKEYHFKASP       YP GQNS-LQRVIFF       GDMG       299         UPP D2 \ Q8 VXF6 \ / 1-612       248       LWP NR LY EYKLGHRLNNGTYIWS QNYQFRAAP FP GQKS-LQRVAIFGDMG       296         TnP AP1 \ Q4RLR4 \ / 1-378       97       LRP AATY       103         HsP AP7 \ (Q6L)F0 \ / 1-438       101       LP GQ VY VY RCGS AQ       GWS RR FR FRALK N-GAHWSP-RLAV FGD LG       143         CeP AP3 \ Q91 \ AMM \ / 1-18       92       LVP GQ VY YY QV GS SQ       AMS SI FH FR QL       PD P SQ - P LRAAIF GD LG       143         DmP AP7 \ Q82X37 \ / 1-438       101       LQP GAQ YV YR CGS SQ       GWS RR FR FTALK N-GV HWSP - R LAV F GD MG       143         DmP AP 1 \ Q9VZ56 \ / 1-458       117       LEP NATY SY HC GS DF GWS AV FN FK TP PA - G EKWSP - SLAIF GD MG       160         DmP AP2 \ Q9VZ58 \ / 1-450       108       LEP D TR Y EY SC GS P L GWS AV FN FK TP PA - G EKWSP - SLAIF GD MG       150         AmP AP \ / 0A0872W E4 \ / 1-438       92       LTP NTKY I Y HC GS K Y GWS NI FY LK TIP       EST KWS P - SLAIF GD MG       135         CeP AP1 \ (001320 \ / 1-438       92       LTP NTKY I Y HC GS EL GWS AV FN FK TP PA - G EKWSP - SLAIF GD MG       135     <	1		
UPP DI Q8VX11/1-615       251       LWP NR EYTYKLGHRLFNGTT IWSKEYHFKASPYP GQSS-VQRVVIF GDMG       299         UPP D2 Q8VXF6/1-612       248       LWP NR IYEYKIGHRLNNGTYIWSQNYQFRAAP FP GQKS-LQRVAIF GDMG       296         TnPAP1 Q4RLR4/1-378       97       LRPAATY       103         HsPAP7 Q6ZNF0/1-438       101       LLP GV QYVYRCGSAQ       GWS RF FR FRALK N-GAHWSP-RLAVF GD LG       103         MmP AP7 Q88X37/1-438       101       LLP GV QYVYRCGSSQ       AMS SIFHFR Q       PP DS Q-P LRAAIF GD LS       132         MmP AP7 Q88X37/1-438       101       LQP GAQYVYRCGSSQ       GWS RF FR FTALK N-GV HWSP - RLAVF GD LG       143         DmP AP1 Q9V256/1-458       101       LQP GAQYVYRCGSSQ       GWS RF FR FTALK N-GV HWSP - RLAVF GD LG       143         DmP AP1 Q9V256/1-458       101       LQP GAQYVYRCGSSQ       GWS RF FR FTALK N - GV HWSP - RLAVF GD MG       143         DmP AP1 Q9V256/1-458       101       LQP GAQYVYRCGSSQ       GWS AI FQ FR TVP SASVDWSP - SLAIF GD MG       160         DmP AP2 Q9V258/1-450       108       LEP D T RY EY SCGSP L       GWS AI FQ FR TVP SASVDWSP - SLAIF GD MG       150         AmP AP1 [A0A0872WE4]/1-438       92       LTP N T Y IY CG S K Y       GWS AV FN FK TP PA - GEK WSP - HI VIF G DMG       135         CaP AP1 [001320]/1-419       57       ISS SEDVP LYNGN       GWS AI FY KT I'' R			
UPP D2   Q8VXF6 /1-612       248       LWP NR I Y EYK I GHR LNNGTY I WS QNY QFRAAP       FP GQK S - LQRVA I F GDMG       296         TnP AP1   Q4RLR4   /1-378       97       LRP AATY       103         HsP AP7   Q6ZNF0   /1-438       101       LLP GV QYVYR CGS AQ       GWS RR FR FRALK N - GAHWS P - R LAV F GD L G       103         MsP AP7   Q6ZNF0   /1-438       101       LLP GV QYVYR CGS SQ       AMS S I FH FR Q       P D P S Q - P LRAAIF GD L S       132         MmP AP7   Q8X37   /1-438       101       LQP GA QYVYR CGS SQ       GWS RR FR FTALK N - GV HWS P - R LAV F GD MG       143         DmP AP1   Q9V256   /1-438       101       LQP GA QYVYR CGS SQ       GWS AI F Q FR TVP SASV DWS P - S LA I Y G DMG       143         DmP AP1   Q9V256   /1-438       101       LQP GA QYVYR CGS SQ       GWS AI F Q FR TVP SASV DWS P - S LA I Y G DMG       143         DmP AP1   Q9V256   /1-438       101       LQP GA QYVYR CGS SQ       GWS AI F Q FR TVP SASV DWS P - S LA I Y G DMG       143         DmP AP2   Q9V258   /1-438       101       LQP GA CGS P GWS AV F N FK TVP SASV DWS P - S LA I Y G DMG       160         DmP AP1   Q0 /0320 //1-438       102       LTP N T KY I Y H CG S K Y GWS AV F N FK TVP SASV DWS P - S LA I Y G DMG       135         CaP AP1   (00 1320 //1-419       57       IS S ED V P LY N G N			
TnPAP1/Q4RLR4//1-378       97       L R P A A T Y       103         HsPAP7/Q6ZVF0//1-438       101       L L P G V Q Y V R C G S A Q       GWS R R F R F R A L K N - G A HWS P - R L A V F G D L G       143         CeP AP3/Q9IVAM9//1-418       92       L V P G Q V Y Y Q V G S S Q       AMS S I F H F R Q       P D P S Q - P L R A A I F G D L S       132         MmP AP7/Q88X37//1-438       101       L Q P G Q Q V Y R C G S S Q       GWS R R F R F T A L K N - G V HWS P - R L A V F G D M G       143         DmP AP1/Q9V256//1-458       101       L Q P G A Q Y V Y R C G S D F       GWS A I F Q F R T V P S A S V D WS P - R L A V F G D M G       143         DmP AP1/Q9V256//1-458       107       L E P N A T Y S Y H C G S D F       GWS A V F N F K T V P S A S V D WS P - S L A I Y G D M G       160         DmP AP2/Q9V258//1-450       108       L E P D T R Y E Y S C G S P L       GWS A V F N F K T P P A G E K WS P - S L A I Y G D M G       150         AmP AP /A0A0872W E4//1-438       92       L T P N T K Y I Y H C G S K Y       GWS N I F Y L K T I P E ES T K WS P - H I V I F G D M G       135         CaP AP1/001320//1-419       57       I S S E D V P L Y N G N       I Y D P E R D S K S F R I L L V G D T G G I P I L E       95         DmP AP3/Q9V257//1-453       107       L K P N S T Y L Y H C G S E L       GWS A T Y W F R T R F D H A D WS P - S L A I Y G D M G       149			
HsPAP7/Q621/F0//1438       101       LLP GV QY VYR CGSAQ       GWS RR FR FRALK N-GAHWSP-RLAVF GD LG       143         CePAP3/Q9I/AM9//1418       92       LVP GQV YYQ QGSSQ       AMSSIFHFRQ       PDPSQ-PLRAAIFGDLS       132         MmPAP7/Q88X37//1438       101       LQP GAQYVYR CGSSQ       GWS RR FR FTALK N-GVHWSP-RLAVFGDMG       143         DmPAP1/Q9V256//1458       101       LQP GAQYVYR CGSSQ       GWS RR FR FTALK N-GVHWSP-RLAVFGDMG       143         DmPAP1/Q9V258//1458       101       LPP NATYSYHCGSDF       GWS AV FN FK TPPA-GEKWSP-SLAIFGDMG       160         DmPAP2/Q9V258//1450       108       LPP DTRY EYSCGSPL       GWS AV FN FK TPPA-GEKWSP-SLAIFGDMG       150         AmPAP(A0A0872WE4//1438       92       LTP NTKY I YHCGSKY       GWS NIFYLKT I PESTKWSP-HIVIFGDMG       135         CePAP1(001320//1419       57       ISS SEDVPLYNGN       GWS ATYWFRT       R FDHADWSP-SLAIFGDMG       149         DmPAP3/Q9V257//1453       107       LKPNSTYLYHCGSEL       GWS ATYWFRT       R FDHADWSP-SLAIFGDMG       149	UPP D2   Q8VXF6 /1-612	248 LWPNRIYEYKIGHRLNNGT	Y IWS QNY Q FRAAP FP G Q K S - L Q R V A I F G D M G 296
HsPAP7/Q621/F0//1438       101       LLP GV QY VYR CGSAQ       GWS RR FR FRALK N-GAHWSP-RLAVF GD LG       143         CePAP3/Q9I/AM9//1418       92       LVP GQV YYQ QGSSQ       AMSSIFHFRQ       PDPSQ-PLRAAIFGDLS       132         MmPAP7/Q88X37//1438       101       LQP GAQYVYR CGSSQ       GWS RR FR FTALK N-GVHWSP-RLAVFGDMG       143         DmPAP1/Q9V256//1458       101       LQP GAQYVYR CGSSQ       GWS RR FR FTALK N-GVHWSP-RLAVFGDMG       143         DmPAP1/Q9V258//1458       101       LPP NATYSYHCGSDF       GWS AV FN FK TPPA-GEKWSP-SLAIFGDMG       160         DmPAP2/Q9V258//1450       108       LPP DTRY EYSCGSPL       GWS AV FN FK TPPA-GEKWSP-SLAIFGDMG       150         AmPAP(A0A0872WE4//1438       92       LTP NTKY I YHCGSKY       GWS NIFYLKT I PESTKWSP-HIVIFGDMG       135         CePAP1(001320//1419       57       ISS SEDVPLYNGN       GWS ATYWFRT       R FDHADWSP-SLAIFGDMG       149         DmPAP3/Q9V257//1453       107       LKPNSTYLYHCGSEL       GWS ATYWFRT       R FDHADWSP-SLAIFGDMG       149	TnP AP 1   Q4R LR 4   / 1-378	97 L R P A A T Y	103
CaP AP3/Q9I/AM9//1-418         92         LVP GQV Y Y QV GS SQ AMS SI FH FR Q P DP SQ - P LRAAIF GD LS         132           MmP AP7/Q88X37//1-438         101         LQP GAQ YV YR CGS SQ GWS RR FR FTALK N - GV HWS P - R LAV F GD MG         143           DmP AP1/Q9V256//1-458         117         LEP NATY SYH CGS DF GWS AIF Q FR TV P SAS VD WS P - SLAIY GD MG         160           DmP AP2/Q9V258//1-450         108         LEP D TR Y EY SCGS P L GWS AV FN FK TP PA - GEKWS P - SLAIY GD MG         150           AmP AP /A0A0872W E4//1-438         92         LTP N TK YI YH CGS K Y GWS AV FN FK TP PA - GEKWS P - SLAIY GD MG         150           CaP AP1/001320//1-419         57         IS SEDVP LY NG N GWS AV FN FK TP PA - GEKWS P - HIV IF GD MG         135           DmP AP3/Q9V257//1-453         107         LKP NS TY LY HCGS EL GWS AT YWFR T R FD HA DWS P - SLAIY GD MG         149			
MmPAP7/Q88X37//1438       101       LQP GAQYVYR CGSSQ       GWS R F R F T ALK N - GV HWSP - R LAV F G DMG 143         DmPAP1/Q9V256//1458       117       LEP NATYSYH CGSDF       GWS AI F Q F R T V P S A S V DWSP - S LAI Y G DMG 160         DmPAP2/Q9V258//1450       108       LEP D T R Y E Y S C G S P L GWS AV F N F K T P P A - G E K WSP - S LAI F G DMG 150         AmPAP/A0A0872WE4//1438       92       LTP N T K Y I Y H C G S K Y GWS N I F Y LK T I P E E S T K WSP - H I V I F G DMG 135         CeP AP1/001320//1419       57       I S S S E D V P L Y N G N I Y D P E R D S K S F R I L L V G D T G G I P I LE       95         DmP AP3/Q9V257//1453       107       LK P N S T Y L Y H C G S E L GWS AT YWFR T R F D H A D WS P - S LAI Y G DMG 140       149			
DmPAP1/Q9VZ56//1458       117       LEPNATYSYHCGSDFGWSAIFQFRTVPSASVDWSP-SLAIYGDMG160         DmPAP2/Q9VZ58//1450       108       LEPDTRYEYSCGSPLGWSAVFNFKTPPA-GEKWSP-SLAIFGDMG150         AmPAP/A0A0872WE4//1438       92       LTPNTKYIYHCGSKYGWSNIFYLKTIPEESTKWSP-HIVIFGDMG150         CmPAP1/001320//1419       57       ISSEDVPLYNGN	1 4 10		
DmP AP 2 / Q9 VZ58 / / 1-450 108 LEPDTRYEYSCGSPLGWSAVFNFKTPPA-GEKWSP-SLAIFGDMG150 AmP AP   A0 A0872WE4 / / 1-438 92 LTPNTKYIYHCGSKYGWSNIFYLKTIPEESTKWSP-HIVIFGDMG135 CeP AP 1 / 00 1320 / / 1-419 57 ISSSEDVPLYNGN			
AmP AP   AO A087ZW E4 /1-438 92 LTP N T K Y I Y H C G S K Y <mark>G W S N I F Y L K T I P</mark> E E S T K W S P - H I V I F <mark>G D M G</mark> 135 CeP AP 1/001320//1-419 57 I S S S E D V P L Y N G N I Y D P E R D S K S F R I L L V G D T G G I P I L E 95 DmP AP 3/Q9 VZ57//1-453 107 L K P N S T Y L Y H C G S E L <mark>G W S A T Y W F R T -</mark> R F D H A D W S P - S L A I Y G D M G 149			
CeP AP 1/00 1320 // 1-419 57 ISSSED VPLYNGN IVDPERDSKSFRILL VGD TGGIPILE 95 DmP AP 3/Q9 VZ57 // 1-453 107 LKPNSTYLYHCGSEL GWSA TYWFRT <mark>-</mark> RFD HAD WSP-SLAIYGD MG 149	1		
DmP AP 3   Q9 VZ57   / 1-453 107   LK P N S T Y L Y H C G S E L <mark>GWS A T Y W F R T - R</mark> F D H A D W S P - S L A I Y G D M G 149			
hyrr fyrronal/1405 55 Lyraan teth coan weeen ows Activent MA-GIDWSP-SLAIPGDWG 141	1 4 10		
	Agr Ar   U/F 01/0   / 1463	JJ <u>LUFSSKIETHCUSKW</u>	141

HvPAPhy a/C4PKL2//1-544	202	LTYNTTSTVDHMTSNRPDLVVLVGDVSYANMYLTN-GTGT 240
TaP APhy a 11C4PKK71/1-550	199	LTYNTTSTVDHMASNRPDLVLLVGDVCYANMYLTN-GTGA 237
		LTYNTTSTVEHMASNQPDLVLLLGDVSYANLYLTN-GTGT 236
· _ · · · ·		LTY NTTS TV EHMASN - QP DLV LLLGDV S YANLY LTN - GTGT 235
·= · · · ·		
		LTYNTTSTVEHMASNQPDLVLLVGDVSYANLYLTN-GTGT 235
		LTYNTTSTVEHMASNQPDLVLLVGDVSYANLYLTN-GTGT 235
OsP AP hy_b   D6QSX9   /1-539	197	LTYNTTSTVEHMVSNQPDLVLLLGDVSYANLYLTN-GTGT 235
ZmP APhy_b C4PKL6 /1-544	202	LTYNTTSTVDHLVRNRPDLVLLLGDVCYANLYLTN-GTGA 240
MtP APhv   Q3ZFI 1   /1-543	204	LTYNTTSTVNHMISNHPDLILLVGDASYANMYLTN-GTGS 242
		LTYNTTSTVSHMISNRPDLILLVGGVTYANLYLTN-GTGS 257
1 17		LTYNTTSTVSHLMGNDPNLVLLVGDVTYANLYLSN-GTGS 241
		LTYNTTATINHLTSNKPDLLLLIGDVTYANLYLTN-GTGS 239
71 17		LTYNTTTTIGHLTSNEPDLLLLIGDVTYANLYLTN-GTGS 243
		LTYNTTDTISHLIHN-SPDLILLIGDVSYANLYLTN-GTSS 235
		LTYNTTSTVDHMASNRPDLVLLV <mark>GDVCY</mark> ANMYLTN-GTGA 236
·= · · · ·		LTYNTTSTVDHMMSNRP-DLVVLVGDVSYANLYLTN-GTGA 239
TmP APhy_a 1   F6MIW8   / 1-545	194	LTYNTTSTVDHMVSNRPDLVLLVGDVCYANMYLTN-GTGA 232
TaP AP hy_a3 (F6MI W2 (/1-539	197	LTYNTTSTVDHMASNRPDLVLLLGDVSYANLYLTN-GTGA 235
TaP AP hy_a2   C4P KK8   /1-549	198	LTYNTTSTVDHMASNRPDLVLLVGDVCYANMYLTN-GTGA 236
ScP APhy a 1/F6MIX2 //1-541	197	L T Y N T T S T V D H M V S N R P D L V V L V G D V S Y A N L Y L T N - G T G A 235
		LTYNTTSTVEHMASNQPDLVLLLGDVSYANLYLTN-GTGT 234
		LTY NTTS TV EHMASK QP DLV LLL GDV S YANLY LTN - GTGT 237
		LTY NTTS TV EHMASN QP DLV LLL GDVS TANLYLTN - GTGT 236
/ //		
		LTY NTTS TV EHMASN LP DLV LLL GDV S YANLYLTN - GT GT 236
		LTYNTTSTVDHLISNNPDLILLVGDATYANLYLTN-GTGA 263
		LTYNSTATIDHLISNKPDLVLLVGDVTYANQYLTN-GTGS 236
		LTYNTTTIGHLTNNEPDLILLIGDVTYANLYLTN-GTGS 243
VrP APhy   B5 AR Z7   / 1-547	206	LTR NSTSTIDHLIHN - DP SMILMV GDLTY ANQYLTTGGKGV 245
		LTYNTTDTISHLIHNSPDLVLLI <mark>GDVSY</mark> ANLYLTN-GTSS 235
1 11		LTSNTTTTIDHLMENDPSLVIIVGDLTYANQYRTIGGKGV 236
		QTGWTKSTLAHIDQCKYDVYLLPGDLSYADCMQHL 190
		LTGNPTATVDHLARNDPSLVLMVGDMTYANQYLTTGGKGV 261
/		
		L T G N S T A T V D H L A H N D P S L V L M V G D M T Y A N Q Y L T T G G K G V 261
<b>—</b> · · · ·		LTGNSTSTVDHLARNDPSMILMVGDMTYANQYLTTGGRGV 259
1 1 17		LTHNSSTTLDHIIQNDPSLLLMI <mark>GDLSY</mark> ANQYLTT-GESA 244
OsP AP 3   Q6ZCX8   /1-622	225	LTGNSTSTVEHLARNDPSLVVVVGDMTYANQYRTTGGRGV 264
OsP AP 4   B8 B909   /1-622	225	LTGNSTSTVEHLARNDPSLVVVVGDMTVANQYRTTGGRGV 264
AtP AP 5   Q9 C9 27   /1-39 6	128	Q T Y A S N Q T L Y N Y MS N P - K G Q A V L F A G D L S Y A D D H P N H 163
AtP AP 20   Q9 LXI 7   /1-427	150	TSE
AtP AP 22   085340   /1-434	151	Q T E
		QTY DSNTTLTHYELNPVKG QSLLFVGDLSYADRYPNH 165
		QTD
1 4 10		QTFDSNVTLTHYESNPGGQAVLYVGDLSYADVYPDH 198
1 1 1 1		
		Q T Y N S L S T L R H F M Q S R G Q A V I F L G D L S Y A D K H S F N 177
		Q S F D S N R T L T H Y E R N P I K G Q A V L F V G D L S Y A D N Y P N H 203
		Q T Y A S N Q T L Y N Y M S N P - K G Q A V L F V GD L S Y A D D H P N H 183
GmP AP 1   Q09 13 1   / 1-4 64	165	QSFDSNKTLSHYELNPRKGQTVLFVGDLSYADNYPNH 201
AtP AP 25   023244   / 1-466	167	Q T L A S N E T L Y H Y M S N P - K G Q A V L F P G D L S Y A D D H P N H 202
AtP AP 12   Q38924   /1-469	171	Q T Y D S N S T L S H Y EMN P G K G Q A V L F V G D L S Y A D R Y P N H 207
NtP AP   Q84KZ3   /1-461	167	Q T Y D P NMT L T H Y EMN P T Q G Q T V L F V G D L S Y A D K Y P N H 203
MtP AP 1 / Q4KU02 / /1-465	166	Q S Y
		QTFNSLSTLQHYEKSEGQTVLFVGDLSYADRYQHN 199
		QTFDSNTTLTHYQNSNGTALLYVGDLSYADDYPYH 199
		QTFNSLSTLEHY   QSGAETVLFV   GDLCYADRYEYN 205
		QTFDSNTTLTHYQNSKGNTLLYVGDLSYADNYPNH 201
		Q S Y D S N I T L T H Y EN NP T K G Q A V L F V G D I S Y A D T Y P D H 206
1 12		Q S F D S N T T L S H Y E L S P K K G Q T V L F V G D L S Y A D R Y P N H 201
		Q T F N S L S T L Q H Y L K S G G E S V L F V G D L S Y A D R Y Q H N 200
		Q T Y A S N E T L Y H Y MS N P - K G Q A V L F A G D L S Y A D D H P N H 202
1		Q T Y N S L S T L E H Y M K S K G Q T V L F V G D L S Y A D R Y S C N 205
		Q S Y D S N S T L T H Y E F N P T K G Q A V L F V G D L S Y A D T Y P N H 207
StP AP 3   Q6J5M8   /1-477	164	Q T Y N S L S T L Q H Y MA S G A K S V L F V G D L S Y A D R Y Q Y N 198
16P AP 1   Q9 SB00   / 1-473	175	QTH DSNTTLTHYEQNSAKG QAVLFMGDLSYSNRWPNH 211
AtP AP 26   Q949 Y3   /1-475	165	Q T F N S L S T L E H Y M E S G A Q A V L F L G D L S Y A D R Y Q Y N 199
		0 T Y N S L S T L E H F I Q S K A Q A V L F V G D L S Y A D R Y Q Y N 205
RcP AP 3   B9 5XP 6   / 1-488	171	Q T Y N S L S T L E H F I Q S K A Q A V L F V G D L S Y A D R Y Q Y N 205 Q T F N S L S T L E H Y L Q S G A Q T V L F V G D L S Y A D R Y K Y N 201
RcP AP 3   B95XP 6   / 1-488 U AP 1   Q8 L5 E1   / 1-477	171 167	Q T F N S L S T L E H Y L Q S G A Q T V L F V <mark>G D L S Y</mark> A D R Y K Y N 201
RcP AP 3   B95XP 6   / 1-488 U AP 1   Q8L5E1   / 1-477 GmP AP 3   Q6YGT9   / 1-512	171 167 203	Q T F N S L S T L E H Y L Q S G A Q T V L F V <mark>G D L S Y</mark> A D R Y K Y N 201 Q T F N S L S T L E H Y I Q S G A Q T V L F <mark>V</mark> G D L S Y A D R Y Q Y N 237
R.cP AP 3   B95XP 6  /1-488 U AP 1   Q8 L5 E1  /1-477 GmP AP 3   Q6 YG T9  /1-512 La AP 2   Q9XJ24  /1-638	171 167 203 165	Q T F N S L S T L E H Y L Q S G A Q T V L F V <mark>G D L S Y</mark> A D R Y K Y N 201 Q T F N S L S T L E H Y I Q S G A Q T V L F V G D L S Y A D R Y Q Y N 237 Q T F D S N Q T L T H Y Q H N P R K G Q A V L Y <mark>V G D L S Y</mark> A D N Y P N H 201
R.cP AP 3   B95XP 6  /1-488 U AP 1   Q8 L5 E1  /1-477 GmP AP 3   Q6 YG T9  /1-512 La AP 2   Q9XU24  /1-638 UPP D4   Q8 VXF4  /1-629	171 167 203 165 314	Q T F N S L S T L E H Y L Q S G A Q T V L F V <mark>G D L S Y</mark> A D R Y K Y N 201 Q T F N S L S T L E H Y I Q S G A Q T V L F V G D L S Y Q T F D S N Q T L T H Y Q H N P R K G Q A V L Y V G D L S Y A D N Y P N H 201 K A E R D G S N E Y A N Y Q P G S L N T T D Q L I K D L D N Y D I V F H I <mark>G D L P Y</mark> A N G Y I S Q 362
RcP AP 3   B95XP 6  /1-488 U AP 1   Q8L5 E1  /1-477 GmP AP 3   Q6YGT9  /1-512 La AP 2   Q9XU24  /1-638 UPP D4   Q8VXF4  /1-629 UPP D1   Q8VX11  /1-615	171 167 203 165 314 300	Q T F NS L S T L E H Y L Q S G A Q T V L F V <mark>G D L S Y</mark> A D R Y K Y N 201 Q T F NS L S T L E H Y I Q S G A Q T V L F V G D L S Y A D R Y Q Y N 237 Q T F D S N Q T L T H Y Q H N P R K G Q A V L Y V G D L S Y A D N Y P N H 201 K A E R D G S N E Y A N Y Q P G S L N T T D Q L I K D L D N Y D I V F H I G D L P Y A N G Y I S Q 362 K A E A D G S N E Y N N F Q P G S L N T T K Q I I Q D L E D I D I V F H I G D L C Y A N G Y I S Q 348
RCP AP 3   895XP 6   / 1-488 U AP 1   Q8L5 E1   / 1-477 GmP AP 3   Q6YGT9   / 1-512 La AP 2   Q9XU24   / 1-638 UPP D4   Q8VXF4   / 1-629 UPP D1   Q8VXF4   / 1-615 UPP D2   Q8VXF6   / 1-612	171 167 203 165 314 300 297	Q T F N S L S T L E H Y L Q S G A Q T V L F V G D L S Y A D R Y K Y N 201 Q T F N S L S T L E H Y I Q S G A Q T V L F V G D L S Y A D R Y Q Y N 237 Q T F D S N Q T L T H Y Q H N P R K G Q A V L Y V G D L S Y A D N Y P N H 201 K A E R D G S N E Y A N Y Q P G S L N T T D Q L I K D L D N Y D I V F H I G D L P Y A N G Y I S Q 362 K A E A D G S N E Y N N F Q P G S L N T T Q Q L I Q D L E D I D I V F H I G D L C Y A N G Y I S Q 348 K D E V D G S N E Y N N F Q R G S L N T T Q Q L I Q D L E D I D I V F H I G D L C Y A N G Y I S Q 348
RCP AP 3  B95XP 6 /1-488 U AP 1  Q8L5 E1 /1-477 GmP AP 3  Q6YGT9  /1-512 La AP 2  Q9X124  /1-638 UPP D4   Q8VXF4 /1-615 UPP D1   Q8VX11 /1-615 UPP D2   Q8VXF6 /1-612 TnP AP 1  Q4R LR4  /1-378	171 167 203 165 314 300 297 104	Q T F NS L S T L E H Y L Q S G A Q T V L F V G D L S Y A D R Y K Y N 201 Q T F NS L S T L E H Y I Q S G A Q T V L F V G D L S Y A D R Y Q Y N 237 Q T F D S N Q T L T H Y Q H N P R K G Q A V L Y V G D L S Y A D N Y P N H 201 K A E R D G S N E Y A N Y Q P G S L N T T D Q L I K D L D N Y D I V F H I G D L P Y A N G Y I S Q 362 K A E A D G S N E Y N N F Q P G S L N T T Q L I Q D L E D I D I V F H I G D L C Y A N G Y I S Q 348 K D E V D G S N E Y N N F Q R G S L N T T Q L I Q D L E N I D M V F H I G D L S Y A N G Y L S Q 348 R D F A Y - D M H E D N A R I G - 118
RCP AP 3   B95XP 6  /1-488 U AP 1   Q8L5 E1  /1-477 GmP AP 3   Q6YGT9  /1-512 La AP 2   Q9XJ24  /1-638 U PP D4   Q8VXF4  /1-639 U PP D1   Q8VX11  /1-615 U PP D2   Q8VXF6  /1-612 TnP AP 1   Q4R LR4  /1-378 H SP AP 7   Q6ZI \F0  /1-438	171 167 203 165 314 300 297 104 144	Q T F NS L S T L E H Y L Q S G A Q T V L F V G D L S Y A D R Y K Y N 201 Q T F NS L S T L E H Y I Q S G A Q T V L F V G D L S Y A D R Y Q Y N 237 Q T F D S N Q T L T H Y Q H N P R K G Q A V L Y V G D L S Y A D N Y P N H 201 K A E R D G S N E Y A N Y Q P G S L N T T D Q L I K D L D N Y - D I V F H I G D L P Y A N G Y I S Q 348 K A E A D G S N E Y N N F Q R G S L N T T Q L I Q D L E D I D I V F H I G D L C Y A N G Y I S Q 348 K D E V D G S N E Y N N F Q R G S L N T T Q L I Q D L E D I D I V F H I G D L S Y A N G Y I S Q 348 K D E V D G S N E Y N N F Q R G S L N T T Q L I Q D L E N I D NV F H I G D L S Y A N G Y L S Q 345 
RCP AP 3   B95XP 6  /1-488 U AP 1   Q8L5 E1  /1-477 GmP AP 3   Q6YGT9  /1-512 La AP 2   Q9X124  /1-638 U PP D4   Q8VXF4  /1-629 U PP D1   Q8VX11  /1-615 U PP D2   Q8VXF6  /1-612 TnP AP 1   Q4R LR4  /1-378 H SP AP 7   Q6ZI NF0  /1-438 CeP AP 3   Q9I IAM9  /1-418	171 167 203 165 314 300 297 104 144 133	QTFNSLSTLEHYLQSGAQTVLFV       GDLSY       ADRYKYN201         QTF
RCP AP 3   B95XP 6  /1-488 U AP 1   Q8L5 E1  /1-477 GmP AP 3   Q6YGT9  /1-512 La AP 2   Q9X124  /1-638 U PP D4   Q8VXF4  /1-629 U PP D1   Q8VX11  /1-615 U PP D2   Q8VXF6  /1-612 TnP AP 1   Q4R LR4  /1-378 H SP AP 7   Q6ZI NF0  /1-438 CeP AP 3   Q9I IAM9  /1-418	171 167 203 165 314 300 297 104 144 133	Q T F NS L S T L E H Y L Q S G A Q T V L F V G D L S Y Q T F NS L S T L E H Y I Q S G A Q T V L F V G D L S Y A D R Y Q Y N 237 Q T F D S N Q T L T H Y Q H N P R K G Q A V L Y Y G D L S Y A D N Y P N H 201 K A E R D G S N E Y A N Y Q P G S L N T T D Q L I K D L D N Y D I V F H I G D L P Y A N G Y I S Q 362 K A E A D G S N E Y N N F Q P G S L N T T K Q I I Q D L E D I D I V F H I G D L S Y A N G Y I S Q 348 K D E V D G S N E Y N N F Q R G S L N T T Q L I Q D L E D I D I V F H I G D L S Y A N G Y I S Q 348 K D E V D G S N E Y N N F Q R G S L N T T Q L I Q D L E N I D NV F H I G D I S Y A N G Y I S Q 345 
RcP AP 3   895XP 6  /1-488 UAP 1   Q8L5 E1  /1-477 GmP AP 3   Q6YGT9  /1-512 La AP 2   Q9XU24  /1-638 UPP D4   Q8VX14  /1-639 UPP D2   Q8VXF6  /1-615 UPP D2   Q8VXF6  /1-612 TnP AP 1   Q4RLR4  /1-378 HsP AP 7   Q62 VF6  /1-438 CeP AP 3   Q9VIAM9  /1-418 MmP AP 7   Q8 BX37  /1-438 DmP AP 1   Q9VZ56  /1-458	171 167 203 165 314 300 297 104 144 133 144 161	QTFNSLSTLEHYLQSGAQTVLFV       GDLSY       ADRYKYN201         QTF
RcP AP 3   895XP 6  /1-488 UAP 1   Q8L5 E1  /1-477 GmP AP 3   Q6YGT9  /1-512 La AP 2   Q9XU24  /1-638 UPP D4   Q8VX14  /1-639 UPP D2   Q8VXF6  /1-615 UPP D2   Q8VXF6  /1-612 TnP AP 1   Q4RLR4  /1-378 HsP AP 7   Q62 VF6  /1-438 CeP AP 3   Q9VIAM9  /1-418 MmP AP 7   Q8 BX37  /1-438 DmP AP 1   Q9VZ56  /1-458	171 167 203 165 314 300 297 104 144 133 144 161	QTFNSLSTLEHYLQSGAQTVLFV       GDLSY       ADRYKYN201         QTF
RcP AP 3   895XP 6  /1-488 UAP 1   Q8L5E1  /1-477 GmP AP 3   Q6YGT9  /1-512 La AP 2   Q9XU24  /1-638 UPP D4   Q8VXF4  /1-629 UPP D1   Q8VXF1  /1-615 UPP D2   Q8VXF6  /1-612 TnP AP 1   Q4RLR4  /1-378 HsP AP 7   Q6ZWF0  /1-438 CeP AP 3   Q91IAM9  /1-418 MmP AP 7   Q8 BX37  /1-438 DmP AP 1   Q9VZ56  /1-458 DmP AP 2   Q9VZ58  /1-450	171 167 203 165 314 300 297 104 144 133 144 161 151	QTFNSLSTLEHYLQSGAQTVLFV       GDLSY       ADRYKYN201         QTF
R CP AP 3   89 SXP 6  /1-488 U AP 1   Q8 L5 E1  /1-477 GmP AP 3   Q6 YG T9  /1-512 La AP 2   Q9 X124  /1-638 UPP D4   Q8 VXF4  /1-629 UPP D1   Q8 VX 11  /1-615 UPP D2   Q8 VXF6  /1-612 TnP AP 1   Q4R LR4  /1-378 HsP AP 7   Q6Z NF0  /1-438 CeP AP 3   Q9 I AM9  /1-418 MmP AP 7   Q8 X37  /1-438 DmP AP 1 (Q9 VZ56  /1-458 DmP AP 2   Q9 VZ58  /1-450 AmP AP   40 A087ZW E4  /1-438	171 167 203 165 314 300 297 104 144 133 144 161 151 136	QTF
R CP AP 3   B95XP 6  /1-488 U AP 1   Q8L5 E1  /1-477 GmP AP 3   Q6YGT9  /1-512 La AP 2   Q9X124  /1-638 UPP D4   Q8VXF4  /1-629 UPP D1   Q8VX11  /1-615 UPP D2   Q8VXF6  /1-612 TnP AP 1   Q4R LR4  /1-378 HsP AP 7   Q6ZIVF0  /1-438 CeP AP 3   Q91AM9  /1-418 MmP AP 7   Q8X37  /1-438 DmP AP 1   Q9VZ56  /1-458 DmP AP 1   Q9VZ58  /1-450 AmP AP   A0A87ZWE4  /1-438 CeP AP 1   001320  /1-419	171 167 203 165 314 300 297 104 144 133 144 161 151 136 96	Q T F NS L S T L E H Y L Q S G A - Q T V L F Y       G D L S Y       A D R Y K Y N 201         Q T F NS L S T L E H Y I Q S G A - Q T V L F Y       G D L S Y A D R Y Q Y N 237       237         Q T F D S N Q T L T H Y Q H N P R K G - Q A V L Y Y G D L S Y A D N Y P N H 201       2362         K A E R D G S N E Y A N Y Q P G S L N T T D Q L I K D L D N Y - D I V F H I G D L P Y A N G Y I S Q 348       362         K A E A D G S N E Y N N F Q P G S L N T T Q Q I I Q D L E D I - D I V F H I G D L S Y A N G Y L S Q 348       348         K D E V D G S N E Y N N F Q R G S L N T T Q Q I Q D L E N I - D M V F H I G D L S Y A N G Y L S Q 348       348         K D E V D G S N E Y N N F Q R G S L N T T Q Q I Q D L Q L E N I - D M V F H I G D L S Y A N G Y L S Q 345       348         K D E V D G S N E Y N N F Q R G S L N T T Q Q I Q D L Q D L N I - D M V F H I G D L S Y A N G Y L S Q 345       348         K D E V D G S N E Y N N F Q R G S L N T T Q Q I Q D L Q D N Y F M O D N A R Y G - 118       - R D F A Y - D M H E D N A R I G - 118         A
R CP AP 3   B95XP 6  /1-488 U AP 1   Q8L5 E1  /1-477 GmP AP 3   Q6YGT9  /1-512 La AP 2   Q9X124  /1-638 U PP D4   Q8VX11  /1-665 U PP D2   Q8VXF4  /1-675 U PP D2   Q8VXF6  /1-612 TnP AP 1   Q4R LR4  /1-378 H SP AP 7   Q6Z VF0  /1-438 CeP AP 3   Q9I/AM9  /1-418 MmP AP 7   Q8 BX37  /1-438 DmP AP 7   Q8 BX37  /1-438 DmP AP 1   Q9VZ56  /1-458 DmP AP 2   Q9VZ58  /1-453 CeP AP 1   00 1320  /1-419 DmP AP 3   Q9VZ57  /1-453	171 167 203 165 314 300 297 104 144 133 144 161 151 136 96 150	Q T F NS L S T L E H Y L Q S G A - Q T V L F V       G D L S Y       A D R Y K Y N 201         Q T F NS L S T L E H Y I Q S G A - Q T V L F V       G D L S Y A D R Y Q Y N 237       Q T F

HvP APhy_a   C4PKL2   /1-544 TaP APhy_a 1   C4PKK7   /1-550		
	241	DCYSCSFGKSTPIHETYOPRWDY-WGRYMEPVTSSTPMMVVEGNHEIEEOIGN 292
		D C Y S C A F G K S T P I H E T Y Q P R W D Y - W G R Y M E A V T S G T P M M V V E G N H E I E E Q I G N 289
TaP APhy b1/C4PKK9//1-538		D C Y S C S F A K S T P I H E T Y Q P R W D Y - W G R Y M E P V T S S T P M M V V E G N H E I E Q Q I G N 288
TaP APhy b2   C4PKL0   /1-537		DCYSCSFAKSTPIHETYQPRWDY-WGRYMEPVTSSTPMMVVEGNHEIEQQIGN 287
HvP APhy_b2   C4PKL4   /1-537		D C Y S C S F A K S T P I H E T Y Q P R W D Y - W G R Y M E P V T S S T P M W V E G N H E I E Q Q I G N 287
HvP APhy_b1/C4PKL3//1-536		D C Y S C S F A K S T P I H E T Y Q P R WD Y - WG R Y M E P V T S S T P MMV V E G N H E I E Q Q I G N 287
OsP APhy b/D6Q5X9//1-539	236	D C Y S C S F A N S T P I H E T Y Q P R WD Y - WG R Y M E P V T S R I P MMV V E G N H E I E E Q I D N 287
ZmP APhy_b   C4PKL6   /1-544		D C Y S C A F A K S T P I H E T Y Q P R WD Y - WG R Y M E P V T S S I P MMV V E G N H E I E Q Q I H N 292
MtP APhy/Q3ZFI1//1-543		D C Y S C S F S N T P I H E T Y Q P R WD Y - WG R Y MEP L I S S V P V MV V E G N H E I E E Q A V N 293
P tP AP 3 / V9 LXK5 / / 1-564	258	D C Y S C S F A N <mark>- S P I H</mark> E T Y Q P R WD Y - WG R Y MQ P V L S K V P I L V V E <mark>G N H E</mark> Y E E Q A E N 308
11tP APhy   A5YB111   /1-551		D C Y S C S F N D - T P I H E T Y Q P R WD Y - WG R Y MQ P L V S K I P I M V V E G N H E I E E Q A E N 292
LaP APhy   D2 YZL4   / 1-543	240	D C Y S C S F P H - T P I H E T Y Q P R WD Y - WG R F M Q N L V S K V P MMV V E G N H E I E K Q A E D 290
GmP APhy_b   Q93XG4   / 1-547	244	DCYSCSFPL - TPIHETYQPRWDY-WGRFMQNLVSNVPIMVVEGNHEIEKQ A EN 294
AtP AP 15   Q95FU3   /1-532	236	DCYSCSFPE <mark>-TPIHETYQPRWDY-WGRFMENLTSKVPLMVIE</mark> GNHEIELQAEN 286
AtaP APhy_a1/F6MIX0//1-549	237	DCYSCAFGKSTPIHETYQPRWDY-WGRYMEAVTSGTPMMVVEGNHEIEEQIGN 288
ScP APhy a2 (F6MIX4)/1-543		D C Y S C A F G K S T P I H E T Y Q P R WD Y - WG R Y M E A V T S G T P MMV V E G N H E I E E Q I G K 291
TmP APhy_a1/F6MIW8//1-545	233	D C Y S C A F G K S T P I H E T Y Q P R WD Y - WG R Y M E A V T S G T P MMV V E G N H E I E E Q I R N 284
TaP APhy_a3   F6MIW2   / 1-539		D C Y S C A F G K S T P I H E T Y Q P R WD Y - WG R Y M E A V T S G T P M V V E G N H E I E E Q I G N 287
TaP APhy_a2   C4PKK8   / 1-549	237	D C Y S C A F G K S T P I H E T Y Q P R WD Y - WG R Y M E A V T S G T P MMV V E G N H E I E E Q I G N 288
ScP APhy_a1/F6MIX2//1-541	236	D C Y S C A F G K S T P I H E T Y Q P R WD Y - WG R Y M E A V T S G T P MMV V E G N H E I E E Q I G K 287
TaP APhy_b3   F6MIW6   / 1-536	235	D C Y S C S F A K S T P I H E T Y Q P R WD Y - WG R Y M E S V T S T T P MMV V E G N H E I E Q Q I G N 286
TmP APhy_b1   F6MIW9   /1-539	238	D C Y S C S F A K S T P I H E T Y Q P R WD Y - WG R Y M E P V T S T T P MMV V E G N H E I E Q Q I G N 289
AtaP APhy_b1/F6MIX1//1-538	237	D C Y S C S F A K S T P I H E T Y Q P R WD Y - WG R Y M E P V T S S T P MMV V E G N H E I E Q Q I G N 288
ScP APhy_b1/F6MIX5//1-538	237	D C Y S C S F A N <u>S</u> T P I H E T Y Q P R WD Y - WG R Y M E P V T S S T P MMV V E <mark>G N H E</mark> I E Q Q I G N 288
RcP AP 1   B9R W G6   / 1-566	264	DCYKCAFPQ <mark>-TPIH</mark> ETYQPRWDY-WGRYMQPLISRIPIMVVE <mark>GNHE</mark> IEQQAQN 314
VvP AP   A5 BGI 6   /1-540	237	D C Y S C S F P Q <mark>- T P I H</mark> E T Y Q P R W D Y - W G R F M Q N L V S K V P M M V I E <mark>G N H E</mark> I E E Q A E K 287
PvPAPhy/V7B3Z4//1-546	244	DCYKCSFPQ- <mark>SPIH</mark> ETYQPRWDY-WGRFMQNLVAEVPIMVVE <mark>GNHE</mark> TEEQADN 294
VrP APhy   B5 AR Z7   / 1-547	246	S C Y S C A F P D <mark>- A P I R</mark> E T Y - P R W D G - W G R F M Q N L I S K V P I M V V E <mark>G N H E</mark> T E E Q A D N 295
AIP AP 15   D7L636   /1-532	236	DCYSCSFPE <mark>TPIH</mark> ETYQPRWDY-WGRFMENLTSKVPLMVIE <mark>GNHE</mark> IELQAEN 286
AtP AP 23   Q6TPH 1   / 1-458	237	PCFSCSFPD <mark>-APIR</mark> ETYQPRWDA-WGRFMEPLTSKVPTMVIE <mark>GNHE</mark> IEPQASG 287
GmP AP4   V9HXG4   /1-442	191	
ZmP AP_c   C4PKL7   /1-566	262	PCFSCSFPK - APIR ESYQPRWDG - WGRFMEPITSKIPLMVIE <mark>GNHE</mark> IEPQGH - GGE 314
SbP AP   A0 A1Z5R9 T8  /1-566	262	PCFSCSFPN - APIR ESYQPRWDG - WGRFMEPITSKIPLMVIE <mark>GNHE</mark> IEPQGH - GGE 314
HvPAP_c C4PKL5 /1-564	260	PCFSCSFPD - APIR ESYQPRWDG - WGRFMEPLTSK VPMMVTEGNHE I EPQGH - GGA 312
		PCYSCAFPD - SPTRETYQPHWDD-WGRFMQPLISKVPMMVIE <mark>GNHE</mark> IEPQAGG 295
0sP AP 3   Q6ZCX8  /1-622	265	PCFSCSFPD-APLRESYQPRWDG-WGRFMEPLTSRIPMMVIE <mark>GNHE</mark> IEPQGQ-GGA 317
0sP AP 4   B8 B909  /1-622		PCFSCSFPD - APLR ESYQPRWDG - WGRFMEPLTSR I PMMV I EGNHD I EPQGQ - GGA 317
AtP AP 5   Q9 C927   / 1-39 6	164	DQSKWDS - YGR FVEPSAAYQPWIWAA <mark>GNHE</mark> IDYAQSIGET 202
AtP AP 20   Q9 LXI 7   / 1-42 7		QPLWDT-FGRLVQPLASQRPWMVTHGNHELEKIPI-LHS 218
		THQPLWDS-FGRLVEPLASKRPWMVTEGNHEIEFFPI-IEH 219
		DNNRWDT-WGRFVERSTAYQPWIWTAGNHEIDFVPDIGET 204
		THQPLWDS-FGRLLETLASTRPWMVTEGNHEIESFPT-NDH 223
		DNVRWDT-WGRFVERSTAYQPWIWTTGNHEIDYAPEIGEY 237
1 11		DVGIRWDS-WGRLVENSTAYLPWFWSVGNHEIEYLAYMGEI 217
16P AP 2   Q9 5D Z9   /1-465		DNVRWDT-WGRFVERSTAYQPWIWTAGNHEIDFAPEIGET 242
1 - 11		DQR KWDS - YGR FV EP SAAY QP WS WAA GN Y E I D YAQS I S ET 222
GmP AP 1   Q09 131   /1-464		DNIRWDS-WGRFTERSVAYQPWIWTAGNHENHFAPEIGET 240
AtP AP 25   023244   /1-466		DQRKWDS-WGRFVEPCAAYQTFIYAAGNHEIDFVPNIGEP 241
AtP AP 12   Q38924   / 1-469	208	
the second second is a second		
1. 17		DNNGWDT-WGRFVERSNAYQPWIWTAGNHDVDFAPEIGEP 242
MtP AP 1   Q4KU02   / 1-465	203	DNN GWD T - WGR F V ER S NA Y Q P W I W T A <mark>G N H D</mark> V D F A P E I G E P 242 DNV R WD T - WGR F A E R S V A Y Q P W I W T V G N H E L D F A P E I G E T 241
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476	203 200	
MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q8S505  /1-476 La AP 1   Q93 VM7  /1-460	203 200 200	
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q8S505   /1-476 La AP 1   Q93VM7   /1-460 P vP AP 2   Q764 C1   /1-457	203 200 200 206	
MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 U AP 2   Q8L6L1  /1-463	203 200 200 206 202	
MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 U AP 2   Q8L6L1  /1-463 AtP AP 10   Q95IV9  /1-468	203 200 200 206 202 207	
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476 La AP 1   Q93VM7 / /1-460 P vP AP 2   Q764 C1   /1-457 UAP 2   Q8L6L1   /1-463 AtP AP 10   Q9SIV9   /1-468 P vP AP 1   P80366   /1-459	203 200 200 206 202 207 207	-         242         -         -         -         -         -         -         -         241         -         -         -         -         -         -         241         -         -         -         -         -         -         241         -         -         -         -         -         -         241         -         -         -         -         -         -         -         241         -         -         -         -         -         -         -         241         -
MtP AP 1   Q4KU02  /1-465 Os <sup>p</sup> AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-463 LI AP 2   Q8L6L1  /1-463 AtP AP 10   Q95I V9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP   C4PKL1  /1-477	203 200 206 202 207 207 202 201	-       -       -       DNN GWDT - WGR FV ER SNAY QP WIWTA GNH D       V D FAP EI GEP       242         -       -       DNV RWDT - WGR FA ER SVAY QP WIWTV GNH E       L D FAP EI GET       241         -       -       D GV RWDS - WGR LV ER STAY QP WIWTV GNH E       L D FAP EI GET       238         -       -       D NV RWDT - WGR FT ER SAAY QP WIWTA GNH E       I D FD L QI GET       238         -       -       D NV RWDT - WGR FT ER SAAY QP WIWTA GNH E       I D FD L QI GET       238         -       -       D V RWDT - WGR FV ER STAY HP WIWAA GNH E       I D FD P QI GET       245         -       -       D NV RWDT - WGR FI ER SAAY QP WIWTA GNH E       I D FD P QI GET       240         -       -       D NV RWDT - WGR FA ER STAY QP WIWTA GNH E       L D FAP EI GEN       245         -       -       D NV RWDT - WGR FT ER SVAY QP WIWTA GNH E       L D FAP EI GEN       240         -       -       D NV RWDT - WGR FT ER SVAY QP WIWTA GNH E       L D FAP EI GEN       240         -       -       D NV RWDT - WGR FT ER SVAY QP WIWTA GNH E       L D FAP EI GEN       240         -       -       -       D N RWDS - WGR FV ER STAY QP WIWTA GNH E       L D FAP EI GEN       240         -       -       -       D N RWDS - WGR FV ER S
MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 U AP 2   Q8 L6L1  /1-463 AtP AP 10   Q9S V9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP (C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466	203 200 206 202 207 202 207 202 201 203	- DNN GWDT - WGR FV ER S NA Y QP WI WTA G NH D V D FAP E I G EP 242 - DNV RWDT - WGR FA ER S VA Y QP WI WTV G NH E L D FAP E I G ET 241 - D GV RWDS - WGR LV ER S TA Y QP WI WTA G NH E I D FD L Q I G ET 238 - D V G LR WDT - WGR FT ER S AA Y QP WI WTA G NH E I D FD L Q I G ET 240 - D V R WDT - WGR FI ER S AA Y QP WI WTA G NH E I D FD P Q I G ET 240 - D NV RWDT - WGR FI ER S AA Y QP WI WTA G NH E I D FD P Q I G ET 240 - D N R RWDS - WGR FA ER S TA Y QP WI WTA G NH E I D FAP E I G EN 245 - D N V RWDT - WGR FT ER S VA Y QP WI WTA G NH E - D N V RWDT - WGR FT ER S VA Y QP WI WTA G NH E - D N R RWDS - WGR FT ER S VA Y QP WI WTA G NH E - D N R RWDS - WGR FT ER S TA Y QP WI WTA G NH E - FAP E I N ET 240 - D R RWDS - WGR FT ER S TA Y QP WI WN S G NH E - D R RWDS - WGR FT ER S TA Y QP WI WN S G NH E - E FAP E I N ET 240 - D Q R KWDT - WGR FMEP CAA Y QP FI FAA G NH E - D FV P N I G EP 241
MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 U AP 2   Q8 L6L1  /1-463 AtP AP 10   Q95 V9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP / C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP   Q93WP 4  /1-481	203 200 206 202 207 202 207 202 201 203 206	-       -       DNN GWDT - WGR FV ER SNAYQP WIWTA GNH D       V D FAP E I G E P       242         -       -       DNV RWDT - WGR FA ER SVAYQP WIWTV GNH E       L D FAP E I G E T       241         -       -       D GV RWDS - WGR LV ER STAYQP WIWTV GNH E       L D FAP E I G E T       238         -       -       D OV RWDT - WGR FT ER SAAYQP WIWTA GNH E       I D FD L Q I G E T       238         -       -       D NV RWDT - WGR FT ER SAAYQP WIWTA GNH E       I D FD L Q I G E T       242         -       -       D V C L RWDT - WGR FT ER SAAYQP WIWTA GNH E       I D FDP Q I G E T       245         -       -       D NV RWDT - WGR FI ER SAAYQP WIWTA GNH E       I D FDP Q I G E T       240         -       -       D N R RWD S - WGR FA ER STAYQP WIWTA GNH E       L D FAP E I G EN       245         -       -       D N R RWD S - WGR FT ER SVAYQP WIWT G NH E       L D FAP E I G EN       245         -       -       D N R RWD S - WGR FT ER SVAYQP WIWT G NH E       L D FAP E I G EN       245         -       -       D N R WD S - WGR FT ER SVAYQP WIWT G NH E       L D FAP E I G EN       245         -       -       D N R WD S - WGR FT ER SVAYQP WIWT G NH E       L D FAP E I D E I D E       240         -       -       D G I RWD S - WGR FT ER SVAYQP WIWNT G
MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 U AP 2   Q816L1  /1-463 AtP AP 10   Q95I V9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP (AP KL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP   Q93WP4  /1-481 AoP AP 32   Q9XF09  /1-470	203 200 206 202 207 202 207 202 201 203 206 208	-       -       DNN GWDT - WGR FV ER SNAY QP WIWTA GNHD       VD FAP EIGEP       242         -       -       DNV RWDT - WGR FA ER SVAY QP WIWTY       GNHE       LD FAP EIGET       241         -       -       DOV RWDS - WGR FA ER SVAY QP WIWTY       GNHE       LD FAP EIGET       241         -       -       DOV RWDS - WGR LV ER STAY QP WIWTA GNHE       L EYRP DLGET       238         -       -       DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE       I D FDL QI GET       245         -       -       DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE       L D FAP EIGEN       245         -       -       DNV RWDT - WGR FT ER SAAY QP WIWTA GNHE       L D FAP EIGEN       245         -       -       DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE       L D FAP EIGEN       245         -       -       DN R WDS - WGR FT ER SVAY QP WIWT GNHE       L D FAP EIGEN       245         -       -       DN R WDS - WGR FT ER SVAY QP WIWT GNHE       L D FAP EIGEN       245         -       -       DN R WDS - WGR FT ER SYAY QP WIWT GNHE       L D FAP EIGEN       245         -       -       DN R WDS - WGR FV ER SYAY QP WIWT A GNHE       L EYRP D LGET       233         -       -       D Q R KWDT - WGR FMEP CAAY QP WIWTY GNHE       L D FVP N I GEP
MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7 //1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 ArP AP 10   Q9SV9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9510  /1-466 AcP AP 2   Q93WP4  /1-481 AoP AP 3   Q9JKP03  /1-470 StP AP 3   Q6J5M8  /1-477	203 200 206 202 207 202 201 203 206 208 199	-       -       -       DNN GWDT - WGR FV ER SNAY QP WIWTA GNHD       VD FAP EIGEP       242         -       -       DNV RWDT - WGR FA ER SVAY QP WIWTY       GNHE       LD FAP EIGET       241         -       -       DGV RWDS - WGR LV ER STAY QP WIWTA GNHE       L V FAP EIGET       238         -       -       DNV RWDT - WGR FT ER SAAY QP WIWTA GNHE       I D FDL QI GET       238         -       -       DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE       I D FDL QI GET       245         -       -       DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE       L D FAP EI GEN       245         -       -       DN R WDT - WGR FT ER SAAY QP WIWTA GNHE       L D FAP EI GEN       245         -       -       DN R WDT - WGR FT ER SVAY QP WIWTA GNHE       L D FAP EI GEN       245         -       -       DN R WDT - WGR FT ER SVAY QP WIWT GNHE       L D FAP EI GEN       245         -       -       DN R WDT - WGR FT ER SVAY QP WIWT GNHE       L D FAP EI GEN       245         -       -       DN R WDT - WGR FT ER SVAY QP WIWT GNHE       L D FAP EI GEN       240         -       -       D N R WDT - WGR FT ER SVAY QP WIWT GNHE       L FAP EI N ET       240         -       -       D R KWDT - WGR FV ER SVAY QP WIWT GNHE       I E Y RP D L G E
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476 La AP 1   Q93VM7   /1-460 P vP AP 2   Q764C1   /1-457 UAP 2   Q8L6L1   /1-463 AtP AP 10   Q9SV9   /1-468 P vP AP 1   P80366   /1-459 Ta ACP / C4PKL1   /1-477 AtP AP 6   Q9C5 10   /1-466 AcP AP 2   Q9ST09   /1-470 StP AP 3   Q6J5M8   /1-477 IbP AP 1   Q9SE00   /1-473	203 200 206 202 207 202 201 203 206 208 199 212	-       -       DNN GWDT - WGR FV ER SNAY QP WIWTA GNHD       VD FAP EIGEP       242         -       -       DNV RWDT - WGR FA ER SVAY QP WIWTY       GNHE       LD FAP EIGET       241         -       -       DOV RWDS - WGR FA ER SVAY QP WIWTY       GNHE       LD FAP EIGET       241         -       -       DOV RWDS - WGR LV ER STAY QP WIWTA GNHE       L EYRP DLGET       238         -       -       DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE       I D FDL QI GET       245         -       -       DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE       L D FAP EIGEN       245         -       -       DNV RWDT - WGR FT ER SAAY QP WIWTA GNHE       L D FAP EIGEN       245         -       -       DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE       L D FAP EIGEN       245         -       -       DN R WDS - WGR FT ER SVAY QP WIWT GNHE       L D FAP EIGEN       245         -       -       DN R WDS - WGR FT ER SVAY QP WIWT GNHE       L D FAP EIGEN       245         -       -       DN R WDS - WGR FT ER SYAY QP WIWT GNHE       L D FAP EIGEN       245         -       -       DN R WDS - WGR FV ER SYAY QP WIWT A GNHE       L EYRP D LGET       233         -       -       D Q R KWDT - WGR FMEP CAAY QP WIWTY GNHE       L D FVP N I GEP
MtP AP 1   Q4KU02  /1-465 OgP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8 L6L1  /1-457 UAP 2   Q8 L6L1  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C510  /1-466 AcP AP 1 (Q93WP4  /1-481 AoP AP 32   Q9XF09  /1-470 StP AP 3   Q6J50M 8  /1-477 IbP AP 1   Q95200  /1-473 AtP AP 26   Q949Y3  /1-475	203 200 206 202 207 202 201 203 206 208 199 212 200	<ul> <li>DNN GWDT - WGR FV ER SNAY QP WIWTA GNHD</li> <li>VD FAP E I G EP</li> <li>DNV RWDT - WGR FA ER SVAY QP WIWTY GNHE</li> <li>D FAP E I G ET</li> <li>D GV RWDS - WGR LV ER STAY QP WIWTA GNHE</li> <li>I D FD L QI GET</li> <li>D V G LRWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD L QI GET</li> <li>DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD L QI GET</li> <li>DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD L QI GET</li> <li>DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD L QI GET</li> <li>DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD P QI GET</li> <li>DNV RWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD P QI GET</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE</li> <li>I E FAP E I N ET</li> <li>240</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE</li> <li>I E FAP E I N ET</li> <li>240</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE</li> <li>I E FAP E I N ET</li> <li>241</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE</li> <li>I E FAP E I N ET</li> <li>242</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE</li> <li>I E FAP E I N ET</li> <li>240</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET</li> <li>241</li> <li>NG T RWDS - WGR FV ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET</li> <li>242</li> <li>DNV RWDT - WGR FV ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET</li> <li>244</li> <li>DNV RWDT - WGR FV ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET</li> <li>245</li> <li>DNV RWDT - WGR FV ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET</li> <li>246</li> <li>DNV RWDT - FG R LV EQ STAY QP WIWTA GNHE</li> <li>I E YRP D L G ET</li> <li>246</li> <li>DNN RWDT - WGR FS ER SVAY QP WIWTA GNHE</li> <li>I E YRP D L G ET</li> <li>250</li> </ul>
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476 La AP 1   Q93VM7   /1-460 P VP AP 2   Q764 C1   /1-457 U AP 2   Q164 C1   /1-457 AtP AP 10   Q93V9   /1-468 P VP AP 1   P80366   /1-459 Ta ACP   C4PKL1   /1-477 AtP AP 6   Q9C510   /1-466 AcP AP 2 0   Q5500   /1-470 StP AP 3   Q650M8   /1-477 I bP AP 1   Q9500   /1-473 AtP AP 2 6   Q949 Y3   /1-475 RcP AP 3   B95XP 6   /1-488	203 200 206 202 207 202 201 203 206 208 199 212 200 206	<ul> <li>DNN GWDT - WGR FV ER SNAY QP WIWTA GNHD</li> <li>VD FAP EIGEP 242</li> <li>DNV RWDT - WGR FA ER SVAY QP WIWTV GNHE</li> <li>D FAP EIGET 241</li> <li>D GV RWDS - WGR LV ER STAY QP WIWTA GNHE</li> <li>I D FD L QIGET 238</li> <li>DV G L RWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD L QIGET 245</li> <li>DV G L RWDT - WGR FI ER SAAY QP WIWTA GNHE</li> <li>I D FD P QIGET 240</li> <li>DN R RWDS - WGR FA ER STAY QP WIWTA GNHE</li> <li>I D FD P QIGET 240</li> <li>DN R RWDS - WGR FA ER STAY QP WIWTA GNHE</li> <li>I D FD P QIGET 240</li> <li>DN R RWDS - WGR FA ER STAY QP WIWTA GNHE</li> <li>I D FD P QIGET 240</li> <li>DN R RWDS - WGR FA ER STAY QP WIWTA GNHE</li> <li>I E FAP EIN ET 240</li> <li>DN R RWDS - WGR FA ER STAY QP WIWTA GNHE</li> <li>I E FAP EIN ET 240</li> <li>DN R RWDS - WGR FY ER STAY QP WIWTA GNHE</li> <li>I E FAP EIN ET 240</li> <li>DN RWDT - WGR FY ER STAY QP WIWTA GNHE</li> <li>I E FAP EIN ET 240</li> <li>DN RWDT - WGR FY ER STAY QP WIWTA GNHE</li> <li>I E FAP EIN ET 240</li> <li>DN RWDT - WGR FY ER STAY QP WIWTY GNHE</li> <li>I E YRP D L G ET 241</li> <li>NG TRWDS - WGR FV ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET 244</li> <li>DN V RWDT - WGR FY ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET 246</li> <li>DV G V RWDT - WGR FY ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET 246</li> <li>DV G V RWDT - WGR FY ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET 246</li> <li>DV G V RWDT - WGR FY ER SVAY QP WIWTY GNHE</li> <li>I E YRP D L G ET 246</li> <li>DV G V RWDT - WGR FY ER SVAY QP WIWTY A GNHE</li> <li>I D YAP D I G ET 246</li> <li>DV G V RWDT - WGR FY ER STAY QP WIWTY A GNHE</li> <li>I D YAP D I G ET 246</li> <li>DV G V RWDS - WGR FY ER STAY QP WIWTY A GNHE</li> <li>I D YAP D I G ET 246</li> <li>DV G V RWDS - WGR FY ER STAY QP WIWTY A GNHE</li> <li>I D YAP D I G ET 250</li> <li>DV G V RWDS - WGR FY ER STAY QP WIWTY A GNHE</li> </ul>
MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 U AP 2   Q8 L6L1  /1-463 AtP AP 10   Q95 V9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP (C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP 3 2   Q9XF09  /1-470 StP AP 3 2   Q9XF09  /1-470 StP AP 3   Q655M8  /1-477 I bP AP 1   Q9500  /1-473 AtP AP 26   Q949 Y3  /1-475 RcP AP 3   B55XP 6  /1-488 U AP 1   Q8 L5 11  /1-477	203 200 206 202 207 202 207 202 201 203 206 208 199 212 200 206 202	<ul> <li>DNN GWDT - WGR FV ER SNAY QP WIWTA GNHD</li> <li>VD FAP EIGEP 242</li> <li>DNV RWDT - WGR FA ER SVAY QP WIWTV GNHE</li> <li>D FAP EIGET 241</li> <li>D GV RWDS - WGR LV ER STAY QP WIWTA GNHE</li> <li>I D FD L QIGET 238</li> <li>DV G LRWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD L QIGET 246</li> <li>DNV RWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD P QIGET 240</li> <li>DNV RWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD P QIGET 240</li> <li>DNV RWDT - WGR FT ER SAAY QP WIWTA GNHE</li> <li>I D FD P QIGET 240</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE</li> <li>I D FD P QIGET 240</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE</li> <li>I D FAP EIGEN 245</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE</li> <li>I E FAP EIN ET 240</li> <li>DNV RWDT - WGR FT ER SVAY QP WIWTA GNHE</li> <li>I E FAP EIN ET 240</li> <li>DN R RWDS - WGR FV ER STAY QP WIWTA GNHE</li> <li>I E YR P D L G ET 241</li> <li>N G T RWDS - WGR FV ER STAY QP WIWTY GNHE</li> <li>I E YR P D L G ET 244</li> <li>N G T RWDS - WGR FV ER SVAY QP WIWTY GNHE</li> <li>I E YR P D L G ET 244</li> <li>D N V RWDT - WGR FF V ER SVAY QP WIWTY GNHE</li> <li>I E YR P D L G ET 244</li> <li>D N V RWDT - WGR FV ER SVAY QP WIWTY GNHE</li> <li>I E YR P D L G ET 246</li> <li>DV G V RWDT - FGR LV EQ STAY QP WIWTY GNHE</li> <li>I D F P D I G ET 248</li> <li>DV G V RWDT - WGR FS ER SVAY QP WIWTA GNHE</li> <li>I D F P D I G ET 246</li> <li>DV G V RWDT - WGR FV ER STAY QP WIWTA GNHE</li> <li>I D F P D I G ET 246</li> <li>DV G V RWDT - WGR FS ER SVAY QP WIWTA GNHE</li> <li>I D F P D I G ET 246</li> <li>DV G V RWDT - WGR FV ER STAY QP WIWTA GNHE</li> <li>I D F P D I G ET 246</li> <li>DV G V RWDT - WGR FV ER STAY QP WIWTA GNHE</li> <li>I D Y P D I G EY 250</li> <li>DV G V RWDT SWGR FV ER STAY QP WIWTA GNHE</li> <li>I D Y AP D I G EY 250</li> <li>DV G I RWDS SWGR FV EK STAY LP WLWS A GNHE</li> <li>I E YMP YMG EV 245</li> </ul>
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476 La AP 1   Q93VM7   /1-460 P vP AP 2   Q764C1   /1-457 UAP 2   Q8L6L1   /1-463 ArP AP 10   Q9SV9   /1-468 P vP AP 1   P80366   /1-459 Ta ACP   C4FKL1   /1-477 AtP AP 6   Q9C510   /1-468 AcP AP 3   Q9SWP4   /1-481 AoP AP 3   Q9SWP4   /1-473 StP AP 3   Q9SWP6   /1-473 AtP AP 2 6   Q949Y3   /1-475 R cP AP 3   B9SXP6   /1-488 UAP 1   Q8L5E1   /1-477 GmP AP 3   Q6YGT9   /1-512	203 200 200 202 207 202 207 202 203 206 208 199 212 200 206 202 202	<ul> <li>DNN GWD T - WGR FV ER S NA Y QP WI WTA G NH D</li> <li>V D FAP E I G EP</li> <li>Q42</li> <li>DNV RWD T - WGR FA ER S VA Y QP WI WTY</li> <li>G N H E</li> <li>L D FAP E I G ET</li> <li>Q41</li> <li>D G V RWD S - WGR LV ER S TA Y QP WI WTA G NH E</li> <li>I D FD L Q I G ET</li> <li>Q42</li> <li>DNV RWD T - WGR FT ER S AA Y QP WI WTA G NH E</li> <li>I D FD L Q I G ET</li> <li>Q42</li> <li>DNV RWD T - WGR FY ER S TA Y QP WI WTA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q42</li> <li>D NV RWD T - WGR FT ER S AA Y QP WI WTA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q44</li> <li>DNV RWD T - WGR FT ER S AA Y QP WI WTA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q44</li> <li>DNV RWD T - WGR FT ER S AA Y QP WI WTA G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>D NV RWD T - WGR FT ER S VA Y QP WI WTA G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>D NV RWD T - WGR FT ER S VA Y QP WI WTA G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>D N R WD S - WGR FV ER S TA Y QP WI WTA G NH E</li> <li>I E Y RP D L G ET</li> <li>Q41</li> <li>D G I RWD S - WGR FV ER S VA Y QP WI WT G NH E</li> <li>I E Y RP D L G EY</li> <li>Q44</li> <li>D N R WD T - WGR FV ER S VA Y QP WI WT Y G NH E</li> <li>I D FV P N I G EP</li> <li>Q41</li> <li>D N W WD T - WGR FV ER S VA Y QP WI WT Y G NH E</li> <li>I D FP D I G ET</li> <li>Q46</li> <li>D V G V RWD T - FG R LV EQ S TA Y QP WI WT A G NH E</li> <li>I D F P D I G ET</li> <li>Q46</li> <li>D V G V RWD S - WGR FV ER S VA Y QP WI WT A G NH E</li> <li>I D F P D I G ET</li> <li>Q46</li> <li>D V G V RWD S - WGR FV ER S TA Y QP WI WT A G NH E</li> <li>I D F P D I G EY</li> <li>Q46</li> <li>D V G V RWD S - WGR FV ER S TA Y QP WI WT A G NH E</li> <li>V D Y MP Y MG EV</li> <li>Q39</li> <li>D V G V RWD S - WGR FV ER S TA Y QP WI WT A G NH E</li> <li>V D Y MP Y MG EV</li> <li>Q39</li> <li>D V G I RWD S - WGR FV ER S TA Y QP WI WS A G NH E</li> <li>V D Y MP Y MG EV</li> <li>Q44</li> </ul>
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476 La AP 1   Q93VM7   /1-460 P vP AP 2   Q764C1   /1-457 UAP 2   Q8L6L1   /1-463 ArP AP 10   Q9SV 9   /1-468 P vP AP 1   P80366   /1-459 Ta ACP   C4PKL1   /1-477 ArP AP 6   Q9C3 10   /1-466 AcP AP 3   Q9SVP 4   /1-481 AoP AP 32   Q9XF09   /1-470 StP AP 3   Q6JSM 8   /1-477 IbP AP 1   Q95E00   /1-473 AtP AP 2 6   Q949 Y3   /1-475 RcP AP 3   B5SYP 6   /1-488 UAP 1   Q8L5E1   /1-477 GmP AP 3   Q6VGT3   /1-512 La AP 2   Q9XJ24   /1-538	203 200 206 202 207 202 207 202 203 206 208 199 212 200 206 202 202 238 202	<ul> <li>DNN GWD T - WGR FV ER S NA Y QP WIWTA G NH D</li> <li>V D FAP E I G EP</li> <li>Q V RWD T - WGR FA ER S VA Y QP WIWTY G NH E</li> <li>D FAP E I G ET</li> <li>Q V RWD S - WGR LV ER S TA Y QP WIWTA G NH E</li> <li>I D FD L Q I G ET</li> <li>D V G LRWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD L Q I G ET</li> <li>D V G LRWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>D N V RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>D N V RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>D N V RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>D N V RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>245</li> <li>D N R RWD S - WGR FA ER S TA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>246</li> <li>D N R WD S - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I E FAP E I N ET</li> <li>D Q R KWD T - WGR FT ER S VA Y QP WIWNS G NH E</li> <li>I E FAP E I N ET</li> <li>D Q R KWD T - WGR FT ER S VA Y QP WIWNS G NH E</li> <li>I E Y RP D L G ET</li> <li>D Q R KWD T - WGR FY ER S VA Y QP WIWTY G NH E</li> <li>I D FV P N I G EP</li> <li>D V G V RWD S - WGR FV ER S VA Y QP WIWTY G NH E</li> <li>I D FV P N I G EP</li> <li>D V G V RWD T - WGR FS ER S VA Y QP WIWTY G NH E</li> <li>I D Y P D L G EY</li> <li>D V G V RWD T - WGR FY ER S TA Y QP WIWTY G NH E</li> <li>I D Y P D I G EY</li> <li>D V G V RWD T - WGR FY ER S TA Y QP WIWTA G NH E</li> <li>I D Y P D I G EY</li> <li>D V G V RWD S - WGR FY ER S TA Y QP WIWTA G NH E</li> <li>V D Y MP YMG EY</li> <li>D V G L RWD T - WGR FY ER S TA Y QP WIWTA G NH E</li> <li>V D YMP YMG EY</li> <li>D V G L RWD T - WGR FY ER S TA Y QP WIWS A G NH E</li> <li>V D YMP YMG EY</li> <li>D V G L RWD T - WGR FY ER S TA Y QP WIWS A G NH E</li> <li>V D YMP YMG EY</li> <li>D V G L RWD T - WGR FA ER S TA Y QP WIWS A G NH E</li> <li>V D YMP YMG EY</li> <li>D V G L RWD T - WGR FY ER S TA Y QP WIWS A G NH E</li> <li>V D YMP YMG EY</li> <li>D V G L RWD T - WGR FA ER S</li></ul>
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476 La AP 1   Q93VM7   /1-460 P vP AP 2   Q764 C1   /1-457 UAP 2   Q8 (6L1   /1-463 AtP AP 10   Q95 V9   /1-468 P vP AP 1   P80366   /1-459 Ta ACP / C4PKL1   /1-477 AtP AP 6   Q9 C5 10   /1-466 AcP AP 2   Q93 WP 4   /1-481 AoP AP 32   Q9XF09   /1-470 StP AP 3   Q6J50M8   /1-477 IbP AP 1   Q95E00   /1-473 AtP AP 2 6   Q949 Y3   /1-475 RcP AP 3   B95XP 6   /1-488 UAP 1   Q8 US 5 6   /1-488 UAP 1   Q8 US 5 6   /1-638 UPP D4   Q8 VXF4   /1-629	203 200 206 202 207 202 207 202 203 206 208 199 212 200 206 202 238 202 238	<ul> <li>DNN GWD T - WGR FV ER S NA Y QP WIWTA G NH D</li> <li>V D FAP E I G EP</li> <li>DNV RWD T - WGR FA ER S VA Y QP WIWTY G NH E</li> <li>L D FAP E I G ET</li> <li>D G V RWD S - WGR LV ER S TA Y QP WIWS A G NH E</li> <li>I D FD L Q I G ET</li> <li>D V G L RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD L Q I G ET</li> <li>D V G L RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>D V G L RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>D N V RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>D N V RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>D N V RWD T - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>242</li> <li>D N V RWD T - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>D N V RWD T - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I E FAP E I N ET</li> <li>D N V RWD T - WGR FT ER S VA Y QP WIWT G NH E</li> <li>I E FAP E I N ET</li> <li>D N V RWD T - WGR FT ER S VA Y QP WIWN S G NH E</li> <li>I E Y RP D L G ET</li> <li>D N V RWD T - WGR FV ER S VA Y QP WIWT G NH E</li> <li>I D FVP N I G EP</li> <li>241</li> <li>D V G V RWD T - WGR FV ER S VA Y QP WIWT G NH E</li> <li>I D Y P D L G ET</li> <li>D V G V RWD T - WGR FF V ER S VA Y QP WIWT G NH E</li> <li>I E Y FP S MG E E</li> <li>D V G V RWD T - WGR FF V ER S VA Y QP WIWT A G NH E</li> <li>I E Y FP S MG EE</li> <li>D V G V RWD T - WGR FF V ER S TA Y QP WIWT A G NH E</li> <li>I D Y AP D I G EY</li> <li>D V G V RWD S - WGR FV ER S TA Y QP WIWT A G NH E</li> <li>V D Y MP Y MG EV</li> <li>D V G U RWD S - WGR FV ER S TA Y QP WIWT A G NH E</li> <li>V D Y MP Y MG EV</li> <li>D V G L RWD T - WGR FF V ER S TA Y QP WIWT A G NH E</li> <li>V D Y MP Y MG EV</li> <li>D V G L RWD T - WGR FF V ER S TA Y QP WIWS A G NH E</li> <li>V D Y MP Y MG EV</li> <li>D V G L RWD T - WGR FF V ER S TA Y QP WIWS A G NH E</li> <li>V D Y MP Y MG EV</li> <li>D V G L RWD T - WGR FF V ER S TA Y QP WIWS A G NH E</li> <li>V D Y MP Y MG EV<!--</td--></li></ul>
MtP AP 1/Q4KU02//1465 OsP AP 2/Q85505/1476 La AP 1/Q93VM7//1460 P vP AP 2/Q764C1//1457 UAP 2/Q8L6L1//1453 AtP AP 10/Q9SV9/1468 P vP AP 1/P80366/1459 Ta ACP / C4PKL1//1477 AtP AP 6/Q9C510//1476 AcP AP 1093WP4//1481 AoP AP 32/Q9ST69/1470 StP AP 3/Q6J5M8/1477 IbP AP 1/Q8500/1473 AtP AP 26/Q949Y3/1475 RcP AP 3/B95XP 6//1488 UAP 1/Q8L5E1/1477 GmP AP 3/Q6YE19/1-512 La AP 2/Q9XU24/1638 UPP D4/Q8VX11/1615	203 200 206 202 207 202 207 202 208 199 212 208 206 202 208 202 208 202 206 303 206 202 208 202 208 202 208 200 200 200 200	<ul> <li>DNN GWDT - WGR FV ER S NA Y QP WIWTA G NH D</li> <li>VD FAP E I G EP</li> <li>DNV RWDT - WGR FA ER S VA Y QP WIWTY G NH E</li> <li>LD FAP E I G ET</li> <li>DV G WDS - WGR LV ER S TA Y QP WIWS A G NH E</li> <li>I D FD L Q I G ET</li> <li>DV G LRWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD L Q I G ET</li> <li>DV G LRWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD L Q I G ET</li> <li>DNV RWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>DNV RWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>DNV RWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>DNV RWDT - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>245</li> <li>DNV RWDT - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>246</li> <li>DNV RWDT - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I E FAP E I N ET</li> <li>DNV RWDT - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I E FAP E I N ET</li> <li>DN R WDS - WGR FV ER S TA Y QP WIWNS G NH E</li> <li>I E FAP E I N ET</li> <li>DN R WDS - WGR FV ER S VA Y QP WIWNS G NH E</li> <li>I E YR P D L G ET</li> <li>AG R WDS - WGR FV ER S VA Y QP WI WT Y G NH E</li> <li>I D FVP N I G EP</li> <li>AG R WDS - WGR FV ER S VA Y QP WI WT Y G NH E</li> <li>I D FVP D L G ET</li> <li>DV G V RWDT - WGR FS ER S VA Y QP WI WT Y G NH E</li> <li>I D YAP D L G ET</li> <li>DV G V RWD T - WGR FF V ER S TA Y QP WI WT A G NH E</li> <li>I D YAP D L G EY</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WI WS A G NH E</li> <li>I D YAP D L G EY</li> <li>DV G L RWD T - WGR FF V ER S TA Y QP WI WS A G NH E</li> <li>V D YMP YMG EV</li> <li>239</li> <li>DV G L RWD T - WGR FF V ER S TA Y QP WI WS A G NH E</li> <li>I D YAP D I G EY</li> <li>DV G L RWD T - WGR FF V ER S TA Y QP WI WS A G NH E</li> <li>I D YAP D I G EY</li> <li>DV G L RWD T - WGR FF V ER S TA Y QP WI WS A G NH E</li> <li>I D YAP YMG EV</li> <li>241</li> <li>DV G L RWD T - WGR FF V ER S TA Y QP WI WS A G NH E</li> <li>I D YMP YMG EV</li> <li>242</li> <li>DV G L RW</li></ul>
MtP AP 1   Q4KU02  /1-465 Os <sup>P</sup> AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9SV9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 Ac P AP 1 (Q9 SWP 4  /1-481 AoP AP 32   Q9XF09  /1-473 StP AP 3   Q6J5M8  /1-477 IbP AP 1   Q9SWD 4  /1-475 RcP AP 3   Q6VGT9  /1-512 La AP 2   Q9XV24  /1-612 UPP D1   Q8VXF4  /1-612	203 200 206 202 207 202 207 202 208 199 212 208 206 202 208 202 208 206 302 206 349 346	<ul> <li>DNN GWDT - WGR FV ER SNAYQP WIWTA GNH D</li> <li>VD FAP EIGEP 242</li> <li>DNV RWDT - WGR FA ER SVAYQP WIWTV GNH E</li> <li>DFAP EIGET 241</li> <li>DVG LRWDT - WGR FT ER SAAYQP WIWTA GNH E</li> <li>ID FDL QIGET 238</li> <li>DVG LRWDT - WGR FT ER SAAYQP WIWTA GNH E</li> <li>ID FDL QIGET 245</li> <li>DVG LRWDT - WGR FI ER SAAYQP WIWTA GNH E</li> <li>ID FDP QIGET 240</li> <li>DN R RWDS - WGR FA ER STAYQP WIWTA GNH E</li> <li>ID FDP QIGET 240</li> <li>DN R RWDS - WGR FA ER STAYQP WIWTA GNH E</li> <li>ID FDP QIGET 240</li> <li>DN R RWDS - WGR FA ER STAYQP WIWTA GNH E</li> <li>ID FAP EIGEN 245</li> <li>DN R RWDS - WGR FA ER STAYQP WIWTA GNH E</li> <li>IE FAP EIN ET 240</li> <li>DN R RWDS - WGR FA ER STAYQP WIWTA GNH E</li> <li>IE FAP EIN ET 240</li> <li>DN RWDT - WGR FT ER SVAYQP WIWTA GNH E</li> <li>IE FAP EIN ET 240</li> <li>DN RWDT - WGR FY ER STAYQP WIWTA GNH E</li> <li>IE FAP EIN ET 240</li> <li>DN RWDT - WGR FY ER STAYQP WIWTA GNH E</li> <li>IE FAP EIN ET 240</li> <li>DN RWDT WGR FY ER SYAYQP WIWTS GNH E</li> <li>IE YRP DL GET 241</li> <li>NG TRWDS - WGR FV ER SVAYQP WIWTY GNH E</li> <li>IE YRP DL GET 244</li> <li>DN V RWDT - WGR FY ER SVAYQP WIWTY GNH E</li> <li>IE YRP DL GET 245</li> <li>DV GV RWDT - FGR LV EQ STAYQP WIWTY GNH E</li> <li>IE YRP DL GET 246</li> <li>DV GV RWDT - FGR LV EQ STAYQP WIWTA GNH E</li> <li>IE YRP DL GET 245</li> <li>DV GV RWDS - WGR FY ER STAYQP WIWTA GNH E</li> <li>IE YRP DL GET 246</li> <li>DV GV RWDS - WGR FY ER STAYQP WIWTA GNH E</li> <li>IE YRP DL GET 246</li> <li>DV GV RWDS - WGR FY ER STAYQP WIWTA GNH E</li> <li>V YMP YMGEY 245</li> <li>DV GV RWDS - WGR FY ER STAYQP WIWTA GNH E</li> <li>V YMP YMGEY 245</li> <li>DV GV RWDS - WGR FY ER STAYQP WIWTA GNH E</li> <li>V YMP YMGEY 245</li> <li>DV GL RWDT - WGR FA ER STAYQP WIWS A GNH E</li> <li>V YMP YMGEY 245</li> <li>DV GL RWDT - WGR FT ER VAYQP WIWS A GNH E</li> <li>V YMP YMGEY 245</li> <li>DV GL RWDT - WGR FT ER VAYQP WIWTA GNH E</li> <li>V YMP YMGEY 245</li> <li>DV GL RWDT WGR FT ER VAYQP WIWS A GNH E</li> <li>V YMP YMGEY</li></ul>
MtP AP 1   Q4KU02  /1-465 Os <sup>p</sup> AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9SV9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C510  /1-466 AcP AP 3 Q (Q5500 )/1-470 StP AP 3   Q6J508  /1-477 IbP AP 1   Q95E00  /1-473 AtP AP 2 6   Q949 Y3  /1-475 RcP AP 3   Q6VGT9  /1-470 GmP AP 3   Q6VGT9  /1-512 La AP 2   Q9XL74  /1-629 UPP D1   Q8VXF6  /1-612 UPP D2   Q8VXF6  /1-612	203 200 202 207 202 207 202 203 206 208 208 208 202 200 202 202 202 202 202	<ul> <li>DNN GWD T - WGR FV ER S NA Y QP WIWTA G NH D</li> <li>VD FAP E I G EP</li> <li>Q42</li> <li>DNV RWD T - WGR FA ER S VA Y QP WIWTY G NH E</li> <li>DFAP E I G ET</li> <li>Q41</li> <li>DV RWD T - WGR FA ER S TA Y QP WIWTY G NH E</li> <li>I D FD L Q I G ET</li> <li>DV G L RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FDP Q I G ET</li> <li>DNV RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FDP Q I G ET</li> <li>DNV RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FDP Q I G ET</li> <li>DNV RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FDP Q I G ET</li> <li>DNV RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>DNV RWD T - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>DNV RWD T - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>DNV RWD T - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I E FAP E I N ET</li> <li>DN R WD S - WGR FV ER S TA Y QP WIWTA G NH E</li> <li>I E YR P D L G ET</li> <li>DN R WD S - WGR FV ER S VA Y QP WIWTA G NH E</li> <li>I D FV P N I G EP</li> <li>DN R WD T - WGR FT ER S VA Y QP WIWTY G NH E</li> <li>I D FV P N I G EP</li> <li>DN R WD T - WGR FV ER S VA Y QP WIWTY G NH E</li> <li>I D FV P N I G EP</li> <li>DN R WD T - WGR FV ER S VA Y QP WIWTY G NH E</li> <li>I D FV P D L G ET</li> <li>DV G V RWD T - FG R LV EQ S TA Y QP WIWTY G NH E</li> <li>I D FP D L G ET</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WIWTA G NH E</li> <li>I D YAP D I G EY</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WIWTA G NH E</li> <li>V D YMP YMG EV</li> <li>DV G L RWD T - WGR FA ER S TA Y QP WIWTA G NH E</li> <li>V D YMP YMG EV</li> <li>DV G L RWD T - WGR FY ER S TA Y QP WIWTA G NH E</li> <li>V D YMP YMG EV</li> <li>DV G L RWD T - WGR FY ER S TA Y QP WIWTA G NH E</li> <li>V D YMP YMG EV</li> <li>DV G L RWD T - WGR FY ER S TA Y QP WIWTA G NH E</li> <li>V D YMP YMG EV</li> <li>DV G L RWD T - WGR FY ER S TA Y QP WIWS A G NH E</li> <li>V D YMP YMG EV</li> <li>DV G L RWD T - WGR FY ER S TA Y QP WIWS A G NH E</li> <li>V D YMP YMG EV<!--</td--></li></ul>
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476 La AP 1   Q93VM7 / /1-460 P vP AP 2   Q764 C1   /1-457 UAP 2   Q8 L6L1   /1-463 AtP AP 10   Q95 V9   /1-468 P vP AP 1   P80366   /1-459 Ta ACP   C4FKL1   /1-477 AtP AP 6   Q9 C5 10   /1-466 AcP AP 2   Q9KD9   /1-470 StP AP3   Q9SKP0   /1-470 StP AP3   Q9SKP0   /1-473 AAP AP 2 6   Q949 Y3   /1-475 RCP AP3   B9SXP 6   /1-488 UAP 1   Q8 L5E1   /1-477 GmP AP3   Q9SXP6   /1-512 La AP2   Q9XVF4   /1-629 UPP D1   Q8VXF4   /1-629 UPP D1   Q8VXF6   /1-612 TnP AP 1   Q4RUR4   /1-378 HSP AP7   Q6Z1 F0   /1-438	203 200 202 207 202 207 202 203 206 208 208 208 208 202 200 206 202 200 202 238 202 238 363 349 346 119 184	<ul> <li>DNN GWD T - WGR FV ER S NA Y QP WIWTA G NH D</li> <li>VD FAP E I G EP</li> <li>Q42</li> <li>DNV RWD T - WGR FA ER S VA Y QP WIWTY</li> <li>GN HE</li> <li>LD FAP E I G ET</li> <li>Q41</li> <li>DV G V RWD S - WGR LV ER S TA Y QP WIWTY</li> <li>GN HE</li> <li>I D FD L Q I G ET</li> <li>Q43</li> <li>DV G LRWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD L Q I G ET</li> <li>Q44</li> <li>DV G LRWD T - WGR FY ER S TA Y HP WI WAA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q45</li> <li>DNV RWD T - WGR FF I ER S AA Y QP WI WT A G NH E</li> <li>I D FD P Q I G ET</li> <li>Q46</li> <li>DNV RWD T - WGR FF I ER S AA Y QP WI WT A G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>DNV RWD T - WGR FF I ER S AA Y QP WI WT A G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>DNV RWD T - WGR FF I ER S AA Y QP WI WT A G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>DNV RWD T - WGR FF I ER S AA Y QP WI WT A G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>DNV RWD T - WGR FF I ER S XA Y QP WI WT A G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>DNV RWD T - WGR FF V ER S TA Y QP WI WT A G NH E</li> <li>I E Y RP D L G ET</li> <li>Q48</li> <li>D Q R KWD T - WGR FF V ER S VA Y QP WI WT Y G NH E</li> <li>I D FV P N I G EP</li> <li>Q41</li> <li>DV G V RWD S - WGR FV ER S VA Y QP WI WT Y G NH E</li> <li>I D F VP N I G EP</li> <li>Q41</li> <li>DV G V RWD T - WGR FF V ER S TA Y QP WI WT A G NH E</li> <li>I D Y AP D I G EY</li> <li>Q46</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WI WT A G NH E</li> <li>I D Y AP D I G EY</li> <li>Q46</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WI WT A G NH E</li> <li>V D Y MP YMG EV</li> <li>Q38</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WI WT A G NH E</li> <li>V D Y MP YMG EV</li> <li>Q39</li> <li>DV G L RWD T - WGR FA ER S TA Y QP WI WS A G NH E</li> <li>V D Y MP YMG EV</li> <li>Q41</li> <li>DV G L RWD T - WGR FA ER S TA Y QP WI WS A G NH E</li> <li>V D Y MP YMG EV</li> <li>Q41</li> <li>DV G L RWD T - WGR FA ER S TA Y Q PWI WS A G NH E</li> <li>V D Y MP YMG EV</li></ul>
MttP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8 L6L1  /1-463 AtP AP 10   Q95V 9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP   C93WP4  /1-481 AoP AP 32   Q95C0  /1-476 AcP AP   Q93WP4  /1-481 AoP AP 32   Q95C0  /1-473 AtP AP 26   Q949 Y3  /1-475 RcP AP 3   B95XP 6  /1-488 UAP 1   Q8 L5E1  /1-477 GmP AP 3   Q67G79  /1-512 La AP 2   Q9XZ4  /1-638 UPP D4   Q8 VXF4  /1-638 UPP D4   Q8 VXF4  /1-638 UPP D2   Q8VXF6  /1-418 HSP AP 7   Q62 IF0  /1-418 CeP AP 3   Q91 IAN  /1-418 MmP AP 7   Q8X37  /1-418	203 200 206 202 207 202 207 208 208 208 208 208 208 208 208 208 208	<ul> <li>DNN GWDT - WGR FV ER S NA Y QP WIWTA G NH D</li> <li>VD FAP E I G EP</li> <li>Q42</li> <li>DNV RWDT - WGR FA ER S VA Y QP WIWTV</li> <li>GN HE</li> <li>LD FAP E I G ET</li> <li>Q41</li> <li>DGV RWDS - WGR LV ER S TA Y QP WIWS A G NH E</li> <li>I D FD L Q I G ET</li> <li>Q38</li> <li>DV G LRWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD L Q I G ET</li> <li>Q45</li> <li>DNV RWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q46</li> <li>DNV RWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q47</li> <li>DNV RWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q40</li> <li>DNV RWDT - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q40</li> <li>DNV RWDT - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>DNV RWDT - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FVP D L G ET</li> <li>Q40</li> <li>DNV RWDT - WGR FT ER S VA Y QP WIWTY G NH E</li> <li>I E FAP E I N ET</li> <li>Q40</li> <li>DN R WDS - WGR FV ER S TA Y QP WI WTY G NH E</li> <li>I E YR P D L G ET</li> <li>Q41</li> <li>NG T RWDS - WGR FV ER S VA Y QP WI WTY G NH E</li> <li>I E YR P D L G ET</li> <li>Q44</li> <li>DN V RWDT - WGR FF V ER S VA Y QP WI WTY G NH E</li> <li>I E YR P D L G ET</li> <li>Q44</li> <li>DN V RWDT - WGR FF V ER S TA Y QP WI WTY G NH E</li> <li>I E YR P D L G ET</li> <li>Q44</li> <li>DN V RWDT - WGR FF V ER S TA Y QP WI WTY G NH E</li> <li>I D YAP D I G EY</li> <li>Q50</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WI WTA G NH E</li> <li>I D YAP D I G EY</li> <li>Q50</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WI WTA G NH E</li> <li>I D YAP D I G EY</li> <li>Q51</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WI WTA G NH E</li> <li>I D YAP D I G EY</li> <li>Q50</li> <li>DV G L RWD T - WGR FF ER S TA Y QP WI WTA G NH E</li> <li>I D YAP D I G EY</li> <li>Q51</li> <li>Q50 G R W D Y MP YMG EY</li> <li>Q50 H E</li> <li>Q51 G R WD T - WGR FF ER S TA Y QP WI WS A G NH E</li> <li>Q50 H E V D YMP YMGEY</li> <li>Q77</li></ul>
MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q85505  /1-476 UAP 2   Q8505  /1-476 AP 2   Q164 L  /1-477 AP 2   Q1695 V9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C93WP4  /1-481 AP P AP 2   Q93WP4  /1-481 AP AP 2   Q93WP4  /1-481 AP AP 3   Q95E00  /1-473 AtP AP 2   Q94509  /1-473 AtP AP 2   Q949Y3  /1-475 RcP AP 3   B95XP 6  /1-488 UAP 1   Q8 L5E1  /1-477 GmP AP 3   Q6YG79  /1-512 La AP 2   Q9XV24  /1-638 UPP D4   Q8VXF4  /1-638 UPP D4   Q8VXF4  /1-615 UPP D2   Q8VXF6  /1-612 Tn PAP 1   Q4R L44  /1-378 HSP AP 7   Q62 VF0  /1-418 CeP AP 3   Q91AV9  /1-418 MmP AP 7   Q8X37  /1-418	203 200 206 202 207 202 207 208 208 208 208 208 208 208 208 208 208	<ul> <li>DNN GWD T - WGR FV ER S NA Y QP WIWTA G NH D</li> <li>VD FAP E I G EP</li> <li>Q42</li> <li>DNV RWD T - WGR FA ER S VA Y QP WIWTY G NH E</li> <li>LD FAP E I G ET</li> <li>Q41</li> <li>DV G V RWD S - WGR LV ER S TA Y QP WIWS A G NH E</li> <li>I D FD L Q I G ET</li> <li>Q43</li> <li>DV G LRWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD L Q I G ET</li> <li>Q44</li> <li>DV G LRWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q45</li> <li>DNV RWD T - WGR FT I ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>Q46</li> <li>DNV RWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>DNV RWD T - WGR FT ER S VA Y QP WIWT A G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>DNV RWD T - WGR FT ER S VA Y QP WIWT A G NH E</li> <li>I D FAP E I G EN</li> <li>Q45</li> <li>DNV RWD T - WGR FT ER S VA Y QP WIWT A G NH E</li> <li>I E FAP E I N ET</li> <li>Q40</li> <li>D Q R KWD T - WGR FT ER S VA Y QP WIWT G NH E</li> <li>I E Y RP D L G ET</li> <li>Q41</li> <li>D Q R KWD T - WGR FV ER S VA Y QP WIWT G NH E</li> <li>I D FVP N I G EP</li> <li>Q41</li> <li>D V G V RWD T - WGR FV ER S VA Y QP WIWT G NH E</li> <li>I E Y RP D L G ET</li> <li>Q44</li> <li>D V G V RWD T - WGR FV ER S VA Y QP WIWT G NH E</li> <li>I E Y RP D L G ET</li> <li>Q44</li> <li>D V G V RWD T - WGR FY ER S VA Y QP WIWT G NH E</li> <li>I E Y FP SMG EE</li> <li>Q38</li> <li>D V G V RWD T - WGR FY ER S TA Y QP WIWT A G NH E</li> <li>I E Y FP SMG EE</li> <li>Q38</li> <li>D V G V RWD T - WGR FY ER S TA Y QP WIWT A G NH E</li> <li>I E Y PP J L G EY</li> <li>Q44</li> <li>D V G V RWD T - WGR FY ER S TA Y QP WIWT A G NH E</li> <li>V P MP YMG EV</li> <li>Q45</li> <li>D V G V RWD S - WGR FY ER S TA Y QP WIWT A G NH E</li> <li>I E Y PP SMG EE</li> <li>Q38</li> <li>D V G L RWD T - WGR FY ER S TA Y QP WIWT A G NH E</li> <li>V D YMP YMG EV</li> <li>Q44</li> <li>D V G L RWD T - WGR FY ER S TA Y QP WIWT A G NH E</li> <li>V D YMP YMG EV</li> <li>Q45</li> <li>D V G L RWD T - WGR FY ER S TA Y Q</li></ul>
MtP AP 1/Q4KU02//1465 OsP AP 2/Q85505/1476 La AP 1/Q93VM7//1460 PvP AP 2/Q764C1//1457 UAP 2/Q8L6L1//1463 AtP AP 10/Q9SIV9//1468 PvP AP 1/P80366//1459 Ta ACP / C4PKL1//1477 AtP AP 6/Q9C510//1476 AcP AP 1/Q9SWP4//1481 AoP AP 32/Q9XF03//1470 StP AP 3/Q6J5M8//1477 IbP AP 1/Q9SE01/1473 AtP AP 26/Q949Y3//1475 RcP AP 3/B95XP 6//1488 UAP 1/Q8L5E1/1477 GmP AP 3/Q6YGT9/1512 La AP 2/Q9X24//1638 UPP D1/Q8VXF4//1629 UPP D1/Q8VXF4//1612 TnP AP 1/Q4R LR4//1-378 HsP AP 7/Q88X37//1438 DmP AP 2/Q9V256//1438	203 200 206 202 207 201 203 206 208 208 208 208 208 208 208 208 208 208	<ul> <li>DNN GWD T - WGR FV ER S NA Y QP WIWTA G NH D</li> <li>VD FAP E I G EP</li> <li>242</li> <li>DNV RWD T - WGR FA ER S VA Y QP WIWTY</li> <li>GN HE</li> <li>LD FAP E I G ET</li> <li>241</li> <li>DV G V RWD S - WGR LV ER S TA Y QP WIWTA G NH E</li> <li>I D FD L Q I G ET</li> <li>238</li> <li>DV G LRWD T - WGR FT ER S AA Y QP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>240</li> <li>DNV RWD T - WGR FY ER S TA Y UP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>241</li> <li>DNV RWD T - WGR FY ER S TA Y UP WIWTA G NH E</li> <li>I D FD P Q I G ET</li> <li>245</li> <li>DNV RWD T - WGR FF I ER S AA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>245</li> <li>DNV RWD T - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>245</li> <li>DNV RWD T - WGR FT ER S VA Y QP WIWTA G NH E</li> <li>I D FAP E I G EN</li> <li>246</li> <li>DNV RWD T WGR FY ER S TA Y QP WIWTA G NH E</li> <li>I E YR P D L G ET</li> <li>241</li> <li>D Q I RWD S - WGR FV ER S TA Y QP WIWT G NH E</li> <li>I E YR P D L G ET</li> <li>242</li> <li>DN R WD T - WGR FF V ER S VA Y QP WIWT Y G NH E</li> <li>I E YR P D L G EY</li> <li>244</li> <li>DN R WD T - WGR FF V ER S VA Y QP WIWT Y G NH E</li> <li>I D FV P N I G EP</li> <li>241</li> <li>DV G V RWD T - WGR FV ER S VA Y QP WIWT Y G NH E</li> <li>I D FV P N I G EP</li> <li>242</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WIWT Y G NH E</li> <li>I D Y P D I G EY</li> <li>246</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WIWT A G NH E</li> <li>I D Y P D I G EY</li> <li>250</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WIWT A G NH E</li> <li>V D Y MP YMG EV</li> <li>238</li> <li>DV G I RWD S - WGR FV ER S TA Y QP WIWT A G NH E</li> <li>V D Y MP YMG EV</li> <li>239</li> <li>DV G V RWD S - WGR FV ER S TA Y QP WIWS A G NH E</li> <li>V D Y MP YMG EV</li> <li>244</li> <li>DV G L RWD T - WGR FA ER S TA Y QP WIWS A G NH E</li> <li>V D Y MP YMG EV</li> <li>239</li> <li>DV G L RWD T - WGR FA ER S TA Y QP WIWS A G NH E</li> <li>V D Y MP YMG EV</li> <li>241</li> <li>DV G L RWD T - WGR FA ER S TA</li></ul>
MtP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476 La AP 1   Q93VM7 / /1-460 P vP AP 2   Q764 C1   /1-453 AtP AP 10   Q95V9   /1-468 P vP AP 1   P80366   /1-459 Ta ACP   C4PKL1   /1-477 AtP AP 6   Q9 C5 10   /1-466 AcP AP 6   Q9 C5 10   /1-466 AcP AP 3   Q6J5M8   /1-477 IbP AP 1   Q95E00   /1-473 AtP AP 2 6   Q949 Y3   /1-475 RcP AP 3   Q6J5M8   /1-477 IbP AP 1   Q95E00   /1-473 AtP AP 2 6   Q949 Y3   /1-475 RcP AP 3   Q6YGT9   /1-512 La AP 2   Q9XVF4   /1-638 UPP D4   Q8VXF6   /1-638 UPP D4   Q8VXF6   /1-612 TnP AP 1   Q4RUR4   /1-378 HsP AP 7   Q6ZVF0   /1-418 MmP AP 7   Q8EX37   /1-438 DmP AP 2   Q9VZ56   /1-458 DmP AP 2   Q9VZ56   /1-458	203 200 206 202 207 202 203 202 208 202 208 202 208 202 200 206 202 238 202 238 202 238 202 238 202 238 202 211 201 206 205 207 207 207 207 207 207 207 207 207 207	<ul> <li>DNN GWD T - WGR FV ER SNAY QP WI WTA GNH DVD FAP EIGEP 242</li> <li>DNV RWD T - WGR FA ER SVAY QP WI WTY GNH ELD FAP EIGET 241</li> <li>DGV RWD S - WGR LV ER STAY QP WI WTA GNH ELD FAP EIGET 242</li> <li>DNV RWD T - WGR FT ER SAAY QP WI WTA GNH EID FD LQIGET 238</li> <li>DV GLRWD T - WGR FT ER SAAY QP WI WTA GNH EID FD PQIGET 240</li> <li>DNV RWD T - WGR FI ER SAAY QP WI WTA GNH EID FD PQIGET 240</li> <li>DNV RWD T - WGR FI ER SAAY QP WI WTA GNH EID FD PQIGET 240</li> <li>DNV RWD T - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DNV RWD T - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DNV RWD T - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DN R RWD S - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DN R RWD S - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DN R WD T - WGR FT ER SVAY QP WI WTA GNH EID FVP NIGET 239</li> <li>DG IR WD S - WGR FV ER STAY QP WI WTY GNH EID FVP NIGET 244</li> <li>NG TR WD S - WGR FV ER SVAY QP WI WTY GNH EID FVP NIGET 244</li> <li>DN V RWD T - WGR FV ER SVAY QP WI WTY GNH EID FVP NIGET 244</li> <li>DN V RWD T - WGR FV ER SVAY QP WI WTY GNH EID FVP DLGET 245</li> <li>DN R WD T - WGR FV ER STAY QP WI WTY GNH EID FVP DLGET 246</li> <li>DN R WD T - WGR FV ER STAY QP WI WTY GNH EID FVP DLGET 240</li> <li>DV G V RWD S - WGR FV ER STAY QP WI WTS GNH EID YAP DIGE 238</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WTS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WTS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WTS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WTA GNH EID FVP EIGET 240</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WS GNH END YD YM FA GNH EID FVP ATAG GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WS GNH END YD YM FYMGEV 245</li> <li>DV G L RWD T - WGR FY ER SYAY QP WI WS GNH END YD YM FYMGEV 2</li></ul>
MttP AP 1 [Q4KU02]/1-465 OsP AP 2   Q85505]/1-476 La AP 1   Q93VM7]/1-460 P vP AP 2   Q764C1]/1-457 UAP 2   Q8L6L1]/1-463 AtP AP 10   Q9SV9]/1-468 P vP AP 1   P80366]/1-459 Ta ACP   C4PKL1]/1-477 AtP AP 6   Q9C5 101/1-466 AcP AP 1   Q9S010]/1-470 StP AP 3   Q9SYC9]/1-470 StP AP 3   Q9SYC9]/1-470 StP AP 3   Q9SYC9]/1-475 RCP AP 3   B9SXP 6]/1-488 UAP 1   Q8L5E1/1-477 GmP AP 3   Q9SXP6]/1-478 UAP 1   Q8L5E1/1-477 GmP AP 3   Q9SXP6]/1-512 La AP 2   Q9XVF4]/1-618 UPP D1   Q8VXF4]/1-615 UPP D1   Q8VXF4]/1-615 UPP D1   Q8VXF4]/1-615 UPP D1   Q8VXF4]/1-615 UPP D1   Q8VXF4]/1-438 CeP AP 3   Q9VZ6]/1-438 DmP AP 1   Q9VZ56]/1-438 DmP AP 1   Q9VZ58]/1-438 DmP AP 1   Q9VZ58]/1-438 DmP AP 1   Q9VZ58]/1-438 CeP AP 1   001320]/1-419	203 200 206 202 207 202 207 208 208 208 208 208 208 208 208 208 208	<ul> <li>DNN GWD T - WGR FV ER S NA Y Q PWI WTA G NHD V D FAP E I G EP 242</li> <li>DNV R WD T - WGR FA ER S VA Y Q PWI WTY G NH E L D FAP E I G ET 241</li> <li>DGV RWD S - WGR L V ER S TA Y Q PWI WTA G NH E I D FAP E I G ET 241</li> <li>DNV R WD T - WGR FT ER S AA Y Q PWI WTA G NH E I D FD Q I G ET 238</li> <li>DV G L RWD T - WGR FT ER S AA Y Q PWI WTA G NH E I D FD Q I G ET 240</li> <li>DNV R WD T - WGR FT ER S AA Y Q PWI WTA G NH E I D FD P Q I G ET 240</li> <li>DNV R WD T - WGR FT ER S AA Y Q PWI WTA G NH E I D FD P Q I G ET 240</li> <li>DN V R WD T - WGR FT ER S Y A Y Q PWI WTA G NH E I D FAP E I G EN 245</li> <li>DN V R WD T - WGR FT ER S Y A Y Q PWI WTA G NH E I D FAP E I G EN 245</li> <li>DN V R WD T - WGR FT ER S Y A Y Q PWI WTA G NH E I E Y R P D L G ET 240</li> <li>D Q R K WD T - WGR FT V ER S TA Y Q PWI WTA G NH E I E Y R P D L G ET 241</li> <li>D Q R K WD T - WGR FMEP CAA Y Q P WI WTY G NH E I E Y R P D L G ET 242</li> <li>D Q R K WD T - WGR FMEP CAA Y Q P WI WTY G NH E I E Y R P D L G ET 242</li> <li>D Q R K WD T - WGR FF V ER S VA Y Q PWI WTY G NH E I E Y R P D L G ET 242</li> <li>D V G V R WD T - FG R LV E Q S TA Y Q PWI WTY G NH E I E Y R P D L G ET 243</li> <li>D V G V R WD T - WGR FF V ER S VA Y Q PWI WTY G NH E I E Y FP S MG EE 238</li> <li>D N N R WD T - WGR FF V ER S TA Y Q PWI WTY G NH E I E Y FP S MG EE 238</li> <li>D V G V R WD T - WGR FF V ER S TA Y Q PWI WTY G NH E L D F P D I G ET 245</li> <li>D V G V R WD T - WGR FF V ER S TA Y Q PWI WTA G NH E I E Y FP S MG EE 238</li> <li>D N N R WD T - WGR FF V ER S TA Y Q PWI WTA G NH E I D YAP D I G EY 250</li> <li>D V G L R WD T - WGR FF V ER S TA Y Q PWI WTA G NH E I D YAP D I G EY 250</li> <li>D V G L R WD T - WGR FF V ER S TA Y Q PWI WTA G NH E I D YMP YMG EV 245</li> <li>D V G L R WD T - WGR FF V ER S TA Y Q PWI WTA G NH E I D YMP YMG EV 245</li> <li>D V G L R WD T - WGR FF V ER S TA Y Q PWI WTA G NH E I D YMP YMG EV 245</li> <li>D V G L R WD T - WGR FF V ER S TA Y Q PWI WTA G NH E I D YMP YMG EV 245</li> <li>D V G L R WD T - WGR FF V ER S</li></ul>
MttP AP 1   Q4KU02   /1-465 OsP AP 2   Q85505   /1-476 La AP 1   Q93VM7   /1-460 P vP AP 2   Q76401   /1-475 UAP 2   Q764061   /1-463 AtP AP 10   Q95V9   /1-468 P vP AP 1   P80366   /1-459 Ta ACP   C4PKL1   /1-477 AtP AP 6   Q9C 310   /1-466 AcP AP 1   Q9500   /1-470 StP AP 3   Q6J5M8   /1-477 IbP AP 1   Q9500   /1-473 AtP AP 26   Q949 Y3   /1-475 RcP AP 3   B95XP 6   /1-488 UAP 1   Q85E1   /1-477 GmP AP 3   Q6V5T9   /1-512 La AP 2   Q9XZ4   /1-638 UPP D1   Q8VXF4   /1-638 UPP D1   Q8VXF4   /1-638 UPP D1   Q8VXF4   /1-378 HsP AP 7   Q62 IF0   /1-438 CeP AP 3   Q9VZ6   /1-438 DmP AP 1   Q9VZ56   /1-418 DmP AP 2   Q9VZ55   /1-438 CeP AP 3   Q09VZ6   /1-438 CeP AP 3   Q09VZ6   /1-438 CeP AP 3   Q09VZ57   /1-438	203 200 206 202 207 202 207 203 206 202 208 208 202 208 202 208 202 208 202 208 202 208 202 208 208	<ul> <li>DNN GWD T - WGR FV ER SNAY QP WI WTA GNH DVD FAP EIGEP 242</li> <li>DNV RWD T - WGR FA ER SVAY QP WI WTY GNH ELD FAP EIGET 241</li> <li>DGV RWD S - WGR LV ER STAY QP WI WTA GNH ELD FAP EIGET 242</li> <li>DNV RWD T - WGR FT ER SAAY QP WI WTA GNH EID FD LQIGET 238</li> <li>DV GLRWD T - WGR FT ER SAAY QP WI WTA GNH EID FD PQIGET 240</li> <li>DNV RWD T - WGR FI ER SAAY QP WI WTA GNH EID FD PQIGET 240</li> <li>DNV RWD T - WGR FI ER SAAY QP WI WTA GNH EID FD PQIGET 240</li> <li>DNV RWD T - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DNV RWD T - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DNV RWD T - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DN R RWD S - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DN R RWD S - WGR FT ER SVAY QP WI WTA GNH EID FAP EIGEN 245</li> <li>DN R WD T - WGR FT ER SVAY QP WI WTA GNH EID FVP NIGET 239</li> <li>DG IR WD S - WGR FV ER STAY QP WI WTY GNH EID FVP NIGET 244</li> <li>NG TR WD S - WGR FV ER SVAY QP WI WTY GNH EID FVP NIGET 244</li> <li>DN V RWD T - WGR FV ER SVAY QP WI WTY GNH EID FVP NIGET 244</li> <li>DN V RWD T - WGR FV ER SVAY QP WI WTY GNH EID FVP DLGET 245</li> <li>DN R WD T - WGR FV ER STAY QP WI WTY GNH EID FVP DLGET 246</li> <li>DN R WD T - WGR FV ER STAY QP WI WTY GNH EID FVP DLGET 240</li> <li>DV G V RWD S - WGR FV ER STAY QP WI WTS GNH EID YAP DIGE 238</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WTS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WTS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WTS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WTA GNH EID FVP EIGET 240</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WS GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WS GNH END YD YM FA GNH EID FVP ATAG GNH EV DY MP YMGEV 245</li> <li>DV G L RWD T - WGR FA ER STAY QP WI WS GNH END YD YM FYMGEV 245</li> <li>DV G L RWD T - WGR FY ER SYAY QP WI WS GNH END YD YM FYMGEV 2</li></ul>

HypAPhy alCAPKI21/1.544	293 K T F A A Y R S	222
	290 K T F A A Y R S R F A F P S T E S G S F S P F Y Y S F D A G G I H F L M L G A Y	
TaP AP hy_b1   C4P KK9   /1-538	289 K T F A A Y S A	328
TaP APhy b2/C4PK10//1-537	288 K T F A A Y S A R F A F P S M E S E S F S P F Y Y S F D A G G I H F I M L A A Y	327
·= · · · ·	288 K T F A A Y S A	
2 1 10	288 K T F A A Y S A R F A F P S K E S E S F S P F Y Y S F D V G G I H F I MLA A Y	
OsP APhy_b   D6QSX9   / 1-539	288 K T F A S Y S S R F S F P S T E S G S F S P F Y Y S F D A G G I H F V M L A A Y	327
ZmP APhy b   C4PKL6   /1-544	293 R T F A A Y S S R F A F P S E E S G S S S P F Y Y S F D A G G I H F V M L A S Y	332
MtP APhy/037FI1//1-543	294 K T F V A Y S S R F A F P S E E S G S S S T L Y Y S F N A G G I H F I M L G S Y	333
	309 R T F L A Y T S R F A F P S K E S G S L S K F Y Y S F N A G G I H F I M L G A Y	
1 11		
	293 Q T F A A Y R S R F A F P S K E S G S S S P F Y Y S F N A G G I H F I M L G G Y	
	291 K Q F V A Y S S R F A F P S E E S G S S S T F Y Y S F N A G G I H F I M L G A Y	
GmPAPhy_b Q93XG4 /1-547	295 R T F V A Y S S R F A F P S Q E S G S S S T F Y Y S F N A G G I H F I ML G A Y	334
AtP AP 15   Q95FU3   /1-532	287 K T F E A Y S S	326
AtaP APhy a 1/E6MIX01/1-549	289 K T F A A Y R S R F A F P S T E S G S F S P F Y Y S F D A G G I H F L M L G A Y	328
	292 K T F E A Y R S	
· <b>-</b> · · · ·		
· = · · · · ·	285 R T F A A Y R S R F A F P S T E S G S F S P F Y Y S F D A G G I H F V M L A A Y	
TaP AP hy_a3   F6MI W2   / 1-539	288 K T F A A Y R S R F A F P S T E S G S F S P F Y Y S F D A G G I H F V M L G A Y	327
TaP AP hy_a2   C4P KK8   / 1-549	289 K T F A A Y R S R F A F P S T E S G S F S P F Y Y S F D A G G I H F L M L G A Y	328
ScPAPhy a1/F6MIX2//1-541	288 K T F E A Y R S R F A F P S A E S G S F S P F Y Y S F D A G G I H F I M L A A Y	327
	287 K T F A A Y S A	
	290 K T F A A Y S A	
·= · · · ·		
	289 K T F A A Y S A R F A F P S ME S E S F S P F Y Y S F D A G G I H F I MLA A Y	
ScPAPhy_b1/F6MIX5//1-538	289 K T F A A Y S A R F A F P S K E S E S F S P F Y Y S F D A G G I H F I M L A A Y	328
RcP AP 1   B9R W G6   /1-566	315 Q T F A A Y S S R F A F P S K E S G S P S T F Y Y S F N A G G I H F V M L G A Y	354
VVP AP ( A5BGI6 / 1-540	288 K N F V A Y S S R F A F P S K E S G S A S T F Y Y S F N A G G I H F I M L G A Y	327
	295 R T F V A Y S S	
	296 K T F V A Y S S R F A F P S E E S G S L S T L Y Y S F N A G G I H F I M L G A Y	
AIP AP 15   D7L636   /1-532	287 <u>K T F E A Y S S -  -  -  -  -  -  -  -  R F A F P F K E S G S S S T L Y Y -  -  -  S F N A G G I H F V M L G A -  -  Y</u>	326
AtP AP 23   Q6TP H 1   / 1-458	288   T F K S Y S E R F A V P A S E S G S N S N L Y Y S F D A G G V H F V M L G A Y	327
GmP AP4 (V9HX G4 (/1-442	224 D E F V S Y N S	263
	315 V T F A S Y L A R V A V P S K E S G S N T K F Y Y S F N A G G I H F I M L G A Y	
	315 V T F A S Y L A	
HvP AP_c   C4PKL5   / 1-564	313 V T F A S Y L A R F A V P S E E S G S N T K F Y Y S F N A G G I H F I M L G A Y	352
PpPAP   A9SPI2   /1-557	296 K S F V A Y E S	335
0sP AP 3   Q6ZCX8   /1-622	318 V T F A S Y L A R F A V P S E E S G S N T K F Y Y S F N A G G I H F I M L G A Y	357
	318 V T F A S Y L A R F A V P S E E S G S N T K F Y Y S F N A G G I H F I M L G A Y	
	203 QP FKP YKN	
1 4 10		
	219 N P F T A Y N K R W R M P F E E S G S S S N L Y Y S F N V Y G V H I I M L G S Y	
AtP AP 22   Q85340   / 1-434	220 T T F K S Y N A R W L MP H T E S F S T S N L Y Y S F D V A G V H T V M L G S Y	259
IbP AP 3   Q9ZP 18   / 1-427	205 V P F K P F T H R F F M P F E S S G S T S P L W Y S I K R A S A H I I V M S S Y	244
AtP AP 2 1   09 LXI4   / 1-437	224   S F K S Y N A R W L MP H A E S L S H S N L Y Y S F D V A G V H T V M L G S Y	263
	238 V P F K P F T H	
	218 I P F K N Y V Y R Y P T P Y MA S N S S S P L W Y A I R R A S A H I I V L N S Y	
1 . 10	243 K P F K P F T K R Y H V P Y K A S G S T E T F W Y P I K R A S A Y I I V L S S Y	
AtP AP 11   Q9 SI 18   / 1-44 1	223 Q P F K P Y K N R Y H V P Y K A S Q S T S P L W Y S I K R A S T Y I I V L S S Y	262
GmP AP 1   Q09 13 1   / 1-4 64	241 V P F K P Y T H R Y H V P Y K A S Q S T S P F W Y S I K R A S A H I I V L A S Y	280
AtP AP 25/023244//1-466	242 HAFKPYIH	281
	247 EP FK P FMN	
	243 EP FR P Y T N R Y P V P Y Q A S G S S S P L W Y S I K R A S A Y I I V L S T Y	
	242 K P F K P Y S H R Y R T P Y K A S Q S T S P F W Y S I K R A S A H I I V L A S Y	
0sPAP2 Q85505 /1-476	239 STFKPYLH RCHTPYLASKSSSPMWY AVRRASAH I I VLSS Y	278
La AP 1   Q93 VM7   / 1-460	239 Q P F K P F S T R Y H T P Y E A S Q S T E P F Y Y S I K R G P A H V I V L A T Y	278
PvPAP2/Q764C1//1-457	245 V P F K N F L Y R Y T T P Y L A S N S S N P L W Y A V R R A S A H I I V L S S Y	285
	241 QP FKP FSN	
	246 R P F K P F T H	
	241 EP FK P FS Y R Y H V P Y EAS QS TS P FWY S I K R A S A H I I V L S S Y	
Ta ACP   C4PKL1   / 1-477	240 STFKPYLH	279
AtP AP 6   Q9 C5 10   / 1-4 66	242 HA FK P Y T H R Y P NA Y K A S Q S T S P L W Y S V R R A S A H I I V L S S Y	281
AcP AP   Q93WP4   /1-481	245 FP FRAY LN R Y P T P H LASASSS P LWY S I R RASAH I I V LSS Y	284
ADP AP 32 ( D9 XED 9 / / 1-470	247 K P F K P F S N R Y R T P Y K A S N S T S P F F Y S I K R G P A H I I V L A S Y	286
	239 V P F R S F L S	
	251 Q P F V P F T N R Y P T P H E A S G S G D P L W Y A I K R A S A H I I V L S S Y	
AtP AP 2 6   Q949 Y3   / 1-475	240 TP FR N Y L Q R Y T P Y L A S K S S S P L W Y A V R R A S A H I I V L S S Y	279
RcP AP 3   B9 5XP 6   / 1-488	246 TP FK S Y L H R Y P T P H L A S K S S S P L W Y A I R C A S A H I I V L S S Y	285
UAP 1/08L5E1//1-477	242 TP FK N F L N R Y T T P Y L A S Q S S S P L W Y A I R R A S A H I I V L S S Y	281
	278 V P F K N Y L Y R Y T T P Y L A S N S S S P L W Y A V R R A S A H I I V L S S Y	
1	241 K P F K P F T H	
1. 17	395 S F F D T P D S G G E C G V L A E T M Y Y F P A E N R A K F W Y K A D Y G M F R F C I A D S E	
	381 S F Y G N L D S G G E C G V P A Q T M F F V P A E N R E K F W Y S T D Y G M F R F C I A H T E	
UPP D2   Q8VXF6 /1-612	378 <u>S F Y E NMD S G G E C G V L A Q I M F Y V P A S N R A K F W Y P I D Y G M F R F R I A D T E</u>	424
	146 - N F S N Y R N R F S M P G Q T E S L W Y S W N L G P V H I I S L S T E V Y	
	211 - N F S N Y K A	
	201 - D F N H I K N	
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1 1 11	211 - N F S N Y K A R F S M P G D N E G L W Y S W D L G P A H I I S F S T E V Y	
1	228 - N F S N Y R A R F S M P G G T E N M F Y S F D L G P V H F V G I S T E V Y	
DmP AP 2   Q9 VZ58  /1-450	218 - N F S N Y R A R F N M P G E T D S L W Y S F N L G P V H F V S F S T E V Y	254
AmP AP   A0 A087ZW E4   /1-438	203 - N F S N Y R F R F T M P G D S E G L W Y S F N I G P V H F I G I E T E A Y	239
	174 EYTKHSK	
1 10		
	217 - NESHVIN	252
	217 - N F S H Y I N	
	217 - N F S H Y I N	

HvPAPhy_a C4PKL2 /1-544	333	A D Y G R S G E Q Y R W L E K D L A K V D R	354
TaP APhy_a1 C4PKK7 /1-550	330	A D Y G R S G E Q Y R W L E K D L A K V D R	351
TaP APhy b1/C4PKK9//1-538	329	A D Y S K S G E Q Y R W L E K D L A K V D R	350
TaP APhy b2   C4PKL0   /1-537	328	A D Y S K S G E Q Y R W L E K D L A K V D R	349
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		Y FM N Y G I K Q L V K Q Y EWL K K D L MEA NMP K N R	
		S L C G N T K D I Q N A G F I EMLR N ES H D P R G P V N I T A A E E Q WAWL E N N L E A	
		Y F T	
		YFMNYGLKPLVKQYEWLRRDLEEANRPENR	

11-D 401			
HVPAPhV allaPhL21/1-344	355 SVTPWLV	A GWH	A P W - Y T T Y K A H Y R E V E C M R V A M E E L - L Y S 392
· · · · ·			A P W - Y T T Y K A H Y R E V E C M R V A M E E L - L H S 389
·= · · · ·			
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HvPAPhy_b2 C4PKL4 /1-537	350 SVTPWLV	A G W F	A P W - Y
HvPAPhy_b1/C4PKL3//1-536	349 SVTPWLV	AGWE	A P W - Y
OsP APhy biD6Q5X91/1-539	350 S V T P W V I	AGWH	A P W - Y
/_ / / //			A P W - Y T T Y K A H Y R E A E C M R V E M E E L - L Y A 392
			A P W - Y S T Y K S H Y R E A E C MR V NMED L - L Y K 393
			A P W - Y
NtP AP hy   A5 YBN 1   / 1-55 1	355 TVTPWLV	A T WH	P P W - Y
LaP APhy   D2 YZL4   /1-543	353 SETPWLV	ATWE	P P W - Y
GmP APhy b1093XG41/1-547	357 SITPWLV	<u>у т w н</u>	P P W - Y
			P P W - Y
			A P W - Y T T Y K A H Y R E V E C MR V A ME E L - L Y S 388
			A P W - Y T T Y K A H Y R E V E C M R V A M E E L - L Y S 391
TmP APhy_a1/F6MIW8//1-545	347 AVTPWLV	A G W F	A P W - Y T T Y K A H Y R E V E C M R V A M E E L - L Y S 384
TaP APhy_a3 (F6MIW2 (/1-539	350 SVTPWLV	AGWE	A P W - Y T T Y K A H Y R E V E C M R V A M E E L - L Y S 387
TaP APhy a21C4PKK81/1-549	351 SVTPWLV	AGWE	A P W - Y T T Y K A H Y R E V E C M R V A M E E L - L Y S 388
· · · ·			A P W - Y T T Y K A H Y R E V E C M R V S M E E L - L Y S 387
· · · · ·			A P W - Y
AtaPAPhy_b1/F6MIX1//1-538	351 SVTPWLV	A G W F	A P W - Y
ScPAPhy_b1/F6MIX5//1-538	351 SVTPWLV	A GWH	A P W - Y
RcP AP 1   B9R WG6   / 1-566	377 EVTPWLV	A T WH	P P W - Y N T Y K A H Y R E A E C M R V A M E E L - L Y K 414
			P P W - Y
			P P W - Y
			P P W - Y
			P P W - Y S S Y T A H Y R E A E C MK E A ME E L - L Y S 386
AtP AP 23   Q6TP H 1   / 1-458	350 AVTPWLV	A T MH	P P W - Y N S Y S S H Y Q E F E C MR Q E ME E L - L Y Q 387
GmP AP4 / V9HXG4 / /1-442	286 KRTPWLL	VLEE	V P W - Y N S N K A H Q G A G D D MMA A M E P L - L Y A 323
			P P W - Y N S Y S S H Y Q E F E C MR Q E M E E L - L Y E 414
			P P W - Y N S Y S S H Y Q E F E CMR Q EME E L - L Y E 414
<b>_</b> · · · · ·			S P W - Y N S C S S H Y Q E F E CMR Q EMEG L - L Y Q 412
			P P W - Y N S Y S S H Y R E F E C MR L E ME E L - L Y S 395
OsP AP 3   Q6ZCX8   / 1-622	380 R V T P W V V	AAWH	P P W - Y N S Y S S H Y Q E F E C M R Q A M E G L - L Y Q 417
OsP AP 4   B8 B909   /1-622	380 R V T P WA V	AAWE	P P W - Y N S Y S S H Y Q E F E C M R Q A M E G L - L Y Q 417
			A P W - Y T F E P W - F V E 277
			A P W - Y N S N E A H Q G E K E S V EMK E S M E T L - L Y K 320
			A P W - Y N T N E A H E G E G E S MR E A ME S L - L F N 319
			C P M - Y S S Y V H H Y M E G E T M R V L Y E P W - F V E 304
AtP AP 2 1   Q9 LXI4   / 1-437	286 K K T P W L V	V V MH	TPW-YALESL-LYR 323
LpP AP   Q9MB07 /1-455	300 SETPWLI	V L ME	SPL-Y
RcP AP 2   B9 5XP 8   /1-463	280 EETPWLI	ννтн	V P L - Y N S N E A H Y M E G E S M R A A F E E W - F I E 317
16P AP 21 09 50 79 1 / 1-4 65	305 TETRWI I	V I ME	SPW-V
			SPW-YNSYNYHYMEGETMRVMYEPW-FVQ 342
AtP AP 11/Q95/18//1-441	285 SETSWLI	VLVF	A P W - Y T F E P W - F V E 322
AtP AP 11   Q95 18   / 1-441 GmP AP 1   Q09 13 1   / 1-464	285 SETSWLI 303 TETPWLI	V L V F V L MF	A P W - Y N S N N Y H Y ME G E S MR V T F E P W - F V E 322 S P W - Y N S Y N Y H Y ME G E T MR V MY E P W - F V Q 340
AtP AP 11  Q95I 18 /1-441 GmP AP 1  Q09 131 /1-464 AtP AP 25  O23244 /1-466	285 SETSWLI 303 TETPWLI 304 EETPWLI	V L V F V L M F V M V F	A P W - Y N S N N Y H Y ME G E S MR V T F E P W - F V E 322 S P W - Y N S Y N Y H Y ME G E T MR V MY E P W - F V Q 340 S P W - Y N S N N Y H Y ME G E S MR A MF E S W - F V N 341
AtP AP 11  Q95  18 /1-441 GmP AP 1  Q09 131 /1-464 AtP AP 25  O23244 /1-466 AtP AP 12  Q38924 /1-469	285 SETSWLI 303 TETPWLI 304 EETPWLI 309 TETPWLI	V L V F V L M F V M V F V L V F	A P W - Y N S N N Y H Y ME G E S MR V T F E P W - F V E 322 S P W - Y N S Y N Y H Y ME G E T MR V MY E P W - F V Q 340 S P W - Y N S N N Y H Y ME G E S MR A MF E S W - F V N 341 S P F - Y S S Y V H H Y ME G E T L R V MY E Q W - F V K 346
AtP AP 11  Q95  18 /1-441 GmP AP 1  Q09 131 /1-464 AtP AP 25  O23244 /1-466 AtP AP 12  Q38924 /1-469	285 SETSWLI 303 TETPWLI 304 EETPWLI 309 TETPWLI	V L V F V L M F V M V F V L V F	A P W - Y N S N N Y H Y ME G E S MR V T F E P W - F V E 322 S P W - Y N S Y N Y H Y ME G E T MR V MY E P W - F V Q 340 S P W - Y N S N N Y H Y ME G E S MR A MF E S W - F V N 341
AtP AP 11   Q95  18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 I \tP AP   Q84KZ3  /1-461	285 SETSWLI 303 TETPWLI 304 EETPWLI 309 TETPWLI 305 KETPWLI	V L V F V L M F V M V F V L V F V L M F	A P W - Y T F E P W - F V E 322 S P W - Y N S N N Y H Y ME G E S MR V T F E P W - F V Q 340 S P W - Y N S N N Y H Y ME G E S MR A MF E S W - F V N 341 S P F - Y S S Y V H H Y ME G E T L R V MY E Q W - F V K 346 C P W - Y N S Y G Y H Y ME G E T MR V I Y E P W - F V K 342
AtP AP 11   Q95   18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 NtP AP   Q84KZ3  /1-461 MtP AP 1 (Q4KU02  /1-465	285 SETSWLI 303 TETPWLI 304 EETPWLI 309 TETPWLI 305 KETPWLI 304 TETPWLI	V L V F V L MF V MV F V L V F V L MF V L MF	A P W - Y N S N N Y H Y ME G E S MR V T F E P W - F V E 322 S P W - Y N S Y N Y H Y ME G E T MR V MY E P W - F V Q 340 S P W - Y N S N N Y H Y ME G E S MR A MF E S W - F V N 341 S P F - Y S S Y V H H Y ME G E T L R V MY E Q W - F V K 342 C P W - Y N S Y G Y H Y ME G E S MR V I Y E P W - F V K 342 S P W - Y N S Y N Y H Y ME G E S MR V MY E P W - F V K 341
AtP AP 11   Q95   18  /1-441 GmP AP 1   Q09   13   /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q389244  /1-469 INTP AP   Q84K23  /1-461 MtP AP 1 (Q4KU02  /1-465 OsP AP 2   Q85505  /1-476	285 SETSWLI 303 TETPWLI 304 EETPWLI 309 TETPWLI 305 KETPWLI 304 TETPWLI 301 EKTPWLI	V L V F V L MF V L V F V L V F V L MF V L MF V L MF	A P W - Y N S N N Y H Y ME G E S MR V T F E P W - F V E 322 S P W - Y N S Y N Y H Y ME G E T MR V MY E P W - F V Q 340 S P W - Y S S Y V H H Y ME G E S MR A MF E S W - F V N 341 S P F - Y S S Y V H H Y ME G E T L R V MY E Q W - F V K 342 C P W - Y N S Y G Y H Y ME G E S MR V I Y E P W - F V K 342 S P W - Y N S Y N Y H Y ME G E S MR V MY E P W - F V K 341 S P M - Y N S N E A H Y ME G E S MR A A F E K W - F V K 338
AtP AP 11   Q95/18  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 INTP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 O\$P AP 2   Q85505  /1-476 La AP 1   Q93 VM7  /1-460	285 SETSWLI 303 TETPWLI 304 EETPWLI 305 TETPWLI 305 KETPWLI 304 TETPWLI 304 TETPWLI 301 EKTPWLI 301 SETSWLI	V L V F V L MF V L V F V L V F V L MF V L MF V L MF	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V E       322         S P W - Y N S Y N Y H Y ME G E - T MR V MY E P W - F V Q       340         S P W - Y S S N N Y H Y ME G E - S MR A MY E P W - F V Q       341         S P F - Y S S Y V H H Y ME G E - S MR A MY E Q W - F V K       346         C P W - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       342         S P M - Y N S Y G Y H Y ME G E - T MR V I Y E P W - F V K       342         S P W - Y N S Y G Y H Y ME G E S MR V I Y E P W - F V K       342         S P W - Y N S Y N Y H Y ME G E S MR V MY E P W - F V K       341         A P W - Y N S N N H Y ME G E S MR A A F E K W - F V K       338         A P W - Y N S S N N H Y ME G E P MR V I Y E S L - F L K       338
AtP AP 11   Q95/18  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-466 INTP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 O\$P AP 2   Q85505  /1-476 La AP 1   Q93 VM7  /1-460 P vP AP 2   Q764 C1  /1-457	285 S E T S W L I 303 T E T P W L I 304 E E T P W L I 309 T E T P W L I 305 K E T P W L I 304 T E T P W L I 301 E K T P W L I 301 S E T S W L I 308 E K T P W L I	V L V F V L MF V L V F V L MF V L MF V L MF V L MF V L MF	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V E       322         S P W - Y N S Y N Y H Y ME G E - T MR V MY E P W - F V Q       340         S P W - Y S S Y N H H Y ME G E - S MR A MY E P W - F V Q       341         S P F - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       346         C P W - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       346         S P M - Y N S Y G Y H Y ME G E - T MR V I Y E P W - F V K       342         S P W - Y N S Y G Y H Y ME G E - T MR V I Y E P W - F V K       342         S P W - Y N S N N H Y ME G E - S MR A A F E K W - F V K       343         A P W - Y N S N S N N H Y ME G E - P MR V I Y E S L - F L K       338         V P L - Y N S N G A H Y ME G E - S MR S V F E S W - F I K       345
AtP AP 11   Q95/18  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 INTP AP 1 Q4KZ3  /1-461 MtP AP 1 Q4KU02 //1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764C1  /1-453 UAP 2   Q8L6L1  /1-463	285 S E T S W L I 303 T E T P W L I 304 E E T P W L I 305 T E T P W L I 305 K E T P W L I 304 T E T P W L I 301 S E T S W L I 308 E K T P W L I 308 E K T P W L I 308 T K T S W L I	V L V F V L MF V L V F V L MF V L MF V L MF V L MF V L MF	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V E       322         S P W - Y N S Y N Y H Y ME G E - T MR V MY E P W - F V Q       340         S P W - Y S S Y N H H Y ME G E - S MR A MF E S W - F V N       341         S P F - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       346         C P W - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       342         S P W - Y N S Y G Y H Y ME G E - T MR V I Y E P W - F V K       342         S P W - Y N S Y N Y H Y ME G E S MR V MY E P W - F V K       342         S P M - Y N S N A H Y ME G E - S MR A A F E K W - F V K       338         A P W - Y N S N G A H Y ME G E - S MR S V F E S L - F L K       343         V P L - Y N S N G A H Y ME G E - S MR S V F E S L - F L K       342
AtP AP 11   Q95/18  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 ItP AP 1 Q44K23  /1-461 MtP AP 1 Q44K23  /1-461 OsP AP 2   Q8505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L61 1/1-468	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         T E T P W L I           305         K E T P W L I           306         K E T P W L I           307         K E T P W L I           308         K T P W L I           308         E K T P W L I           308         T K T S W L I           303         T K T S W L I           303         T K T S W L I	V L V H V L MH V L V H V L MH V L MH V L MH V L MH V L MH V L MH	A P W - Y N S N N Y H YME G E - S MR V T F E P W - F V E       322         S P W - Y N S Y N Y H YME G E - T MR V MY E P W - F V Q       340         S P W - Y S S Y N H H YME G E - S MR A MF E S W - F V N       341         S P F - Y S S YV H H YME G E - T L R V MY E Q W - F V K       346         C P W - Y S S YV H H YME G E - T L R V MY E Q W - F V K       342         S P W - Y N S Y G Y H YME G E - T MR V I Y E P W - F V K       342         S P W - Y N S Y G Y H YME G E - S MR V MY E P W - F V K       342         S P M - Y N S N E A H YME G E - S MR A A F E K W - F V K       343         A P W - Y N S N N H YME G E - S MR S V F E S L - F L K       338         A P W - Y N S N G A H YME G E - S MR S V F E S W - F I K       342         S P M - Y N S N G A H YME G E - P MR V V F E S L - F L K       343         S P W - Y N S Y S H YME G E - P MR V V F E S L - F V K       340         S P W - Y N S Y O Y H YME G E - T MR V V F E S L - F V K       345
AtP AP 11   Q95/18  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 ItP AP 1 Q44K23  /1-461 MtP AP 1 Q44K23  /1-461 OsP AP 2   Q8505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L61 1/1-468	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         T E T P W L I           305         K E T P W L I           306         K E T P W L I           307         K E T P W L I           308         K T P W L I           308         E K T P W L I           308         T K T S W L I           303         T K T S W L I           303         T K T S W L I	V L V H V L MH V L V H V L MH V L MH V L MH V L MH V L MH V L MH	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V E       322         S P W - Y N S Y N Y H Y ME G E - T MR V MY E P W - F V Q       340         S P W - Y S S Y N H H Y ME G E - S MR A MF E S W - F V N       341         S P F - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       346         C P W - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       342         S P W - Y N S Y G Y H Y ME G E - T MR V I Y E P W - F V K       342         S P W - Y N S Y N Y H Y ME G E S MR V MY E P W - F V K       342         S P M - Y N S N A H Y ME G E - S MR A A F E K W - F V K       338         A P W - Y N S N G A H Y ME G E - S MR S V F E S L - F L K       343         V P L - Y N S N G A H Y ME G E - S MR S V F E S L - F L K       342
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1 //1-464 AtP AP 25   023244 //1-466 AtP AP 12   Q38924 //1-469 HtP AP   Q84K23  /1-461 MtP AP 1   Q4KU02 //1-465 OSP AP 2   Q85505 //1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1 //1-457 UAP 2   Q85 (1/1-458 AtP AP 10   Q9S V9 //1-468 P vP AP 1  P80366 //1-459	285 S E T S W L I 303 T E T P W L I 304 E E T P W L I 305 K E T P W L I 305 K E T P W L I 304 T E T P W L I 304 T E T P W L I 304 S E K T P W L I 308 T E T P W L I 308 T E T P W L I 308 S E T P W L I	V L V H V L MH V L V H V L MH V L MH V L MH V L MH V L MH V L MH V L MH	A P W - Y N S N N Y H YME G E - S MR V T F E P W - F V E       322         S P W - Y N S Y N Y H YME G E - T MR V MY E P W - F V Q       340         S P W - Y S S Y N H H YME G E - S MR A MF E S W - F V N       341         S P F - Y S S YV H H YME G E - T L R V MY E Q W - F V K       346         C P W - Y S S YV H H YME G E - T L R V MY E Q W - F V K       342         S P W - Y N S Y G Y H YME G E - T MR V I Y E P W - F V K       342         S P W - Y N S Y G Y H YME G E - S MR V MY E P W - F V K       342         S P M - Y N S N E A H YME G E - S MR A A F E K W - F V K       343         A P W - Y N S N N H YME G E - S MR S V F E S L - F L K       338         A P W - Y N S N G A H YME G E - S MR S V F E S W - F I K       345         A P W - Y N S Y S H YME G E - S MR S V F E S W - F I K       345         A P W - Y N S Y S H YME G E - P MR V V F E S L - F V K       340         S P W - Y N S Y O Y H YME G E P MR V V F E S L - F V K       345
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q389244  /1-469 INTP AP   Q84K23  /1-461 MtP AP 1 Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93 VM7  /1-460 P VP AP 2   Q764 C1  /1-457 UAP 2   Q8L11/1-463 AtP AP 10   Q95 V9  /1-468 P VP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           305         K E T P W L I           304         T E T P W L I           304         T E T P W L I           301         E K T P W L I           301         S E T S W L I           303         T K T S W L I           303         T E T P W L I           303         S E T P W L I           304         T E T P W L I           305         K T P W L I           306         T E T P W L I           307         K T E T P W L I           308         T E T P W L I           303         S E T P W L I           302         E K T P W L I	V L V H V L MH V L V H V L MH V L MH	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y N S Y N Y H Y ME G E T MR V MY E P W - F V Q       340         S P W - Y S S Y N Y H Y ME G E S MR A MY E P W - F V N       341         S P F - Y S S Y V H H Y ME G E T LR V MY E Q W - F V K       342         S P W - Y S Y V H H Y ME G E T LR V MY E Q W - F V K       342         S P W - Y
AtP AP 11   Q9SI 18  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   Q38924  /1-469 INTP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 Lo AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9SI V9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9C510  /1-466	285 S E T S W L I 303 T E T P W L I 304 E E T P W L I 305 K E T P W L I 305 K E T P W L I 301 S K T P W L I 301 S E T S W L I 303 T K T S W L I 303 T K T S W L I 303 S E T P W L I 303 S E T P W L I 304 E E T P W L I	V L V H V L MH V L V H V L MH V L MH	A P W - Y N S N N Y H YME G E - S MR V T F E P W - F V E       322         S P W - Y N S Y N Y H YME G E T MR V MY E P W - F V Q       340         S P W - Y S S Y N Y H YME G E S MR A MY E S W - F V N       341         S P F - Y S S Y V H H YME G E T L R V MY E Q W - F V K       342         C P W - Y S S Y V H H YME G E T L R V MY E Q W - F V K       342         S P W - Y NS Y G Y H YME G E T MR V I Y E P W - F V K       342         S P W - Y NS Y G Y H YME G E S MR V I Y E P W - F V K       341         S P M - Y NS N N H YME G E S MR A A F E K W - F V K       343         A P W - Y NS N S N N H YME G E S MR S V F E S U - F U K       345         A P W - Y NS N G A H YME G E S MR S V F E S U - F U K       345         S P W - Y NS N Y S H YME G E S MR S V F E S U - F U K       340         S P W - Y NS Y O S H YME G E S MR V V F E S U - F V K       340         S P W - Y NS Y N H H F ME G E MR V V F E S U - F V K       340         S P U - Y NS Y N H H F ME G E S MR A A F E K W - F V K       340         S P U - Y NS N N A H YME G E S MR A A F E K W - F V K       340         S P W - Y
AtP AP 11   Q9SI 18  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 INTP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93 VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q84611  /1-463 AtP AP 10   Q95 V9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6 [ 09 C5 10  /1-461 AcP AP   Q93 WP4  /1-481	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         E T P W L I           305         K E T P W L I           304         E T P W L I           305         K E T P W L I           301         E K T P W L I           301         S E T S W L I           303         T E T P W L I           304         T E T P W L I           305         K T P W L I           306         E T P W L I           307         S E T P W L I           304         E T P W L I           305         S E T P W L I           306         E T P W L I           307         E K T P W L I           304         E T P W L I           307         E K T P W L I	V L V H V L MH V L V H V L MH V L MH	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V E       322         S P W - Y N S Y N Y H Y ME G E - T MR V MY E P W - F V Q       340         S P W - Y S S N N Y H Y ME G E - S MR A MY E S W - F V N       341         S P F - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       346         C P W - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       342         S P W - Y N S Y G Y H Y ME G E - T MR V I Y E P W - F V K       342         S P W - Y N S Y G Y H Y ME G E - S MR A A F E K W - F V K       343         A P W - Y N S N S N H Y ME G E - S MR A A F E K W - F V K       338         A P W - Y N S N G A H Y ME G E - S MR S V F E S U - F U K       345         A P W - Y N S N G A H Y ME G E - S MR S V F E S U - F U K       340         S P W - Y N S Y Y S H Y ME G E - T MR V V F E S U - F V K       340         S P W - Y N S Y N H H F ME G E - T MR V V F E S U - F V K       340         S P U - Y N S Y N H H F ME G E - A MR T K F E AW - F V K       340         S P U - Y N S N N A H Y ME G E - S MR A A F E K W - F V K       340         S P M - Y N S N N A H Y ME G E - S MR A A F E K W - F V K       341         A P M - Y N S N N A H Y ME G E - S MR A A F E K W - F V K
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-466 INTP AP   Q8KC33  /1-461 MtP AP   Q4KU02  /1-465 OSP AP 2   Q8S505  /1-476 La AP 1   Q9S VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9S V9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP   Q9S WP4  /1-481 AoP AP 32   Q9XF09  /1-470	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           306         K E T P W L I           307         K E T P W L I           308         K T P W L I           301         S K T P W L I           301         S K T P W L I           303         T K T S W L I           303         T K T S W L I           303         S E T P W L I           303         S E T P W L I           304         E T P W L I           305         S E T P W L I           306         E K T P W L I           307         E K T P W L I           307         E K T P W L I           307         E K T P W L I	V L V H V L MH V L MH	A P W - Y N S N N Y H YME G E - S MR V T F E P W - F V C       322         S P W - Y N S Y N Y H YME G E - T MR V MY E P W - F V Q       340         S P W - Y S S Y N H H YME G E - S MR A MY E S W - F V N       341         S P F - Y S S Y V H H YME G E - T L R V MY E Q W - F V K       346         C P W - Y S S Y V H H YME G E - T L R V MY E Q W - F V K       342         S P M - Y N S Y G Y H YME G E - T MR V I Y E P W - F V K       342         S P M - Y N S N A H YME G E - S MR A A F E K W - F V K       343         A P W - Y N S N G A H YME G E - S MR S V F E S U - F U K       343         Y P L - Y N S N G A H YME G E - S MR S V F E S U - F U K       344         S P M - Y N S N G A H YME G E P MR V V F E S U - F V K       340         S P W - Y N S N G A H YME G E P MR V V F E S U - F V K       340         S P W - Y N S Y D H YME G E P MR V V F E S U - F V K       340         S P W - Y N S Y N H H F ME G E M R T K F E A W - F V K       345         S P U - Y N S N N A H YME G E S MR A A F E K W - F V K       345         S P W - Y N S N N A H YME G E - S MR V A F E S W - F V K       343         A P M - Y N S N N A H YME G E - S MR V A F E S W - F
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1 //1-464 AtP AP 25   023244 //1-466 AtP AP 12   Q38924 //1-469 ItP AP   Q84K23  /1-461 MtP AP 1   Q4KU02 //1-465 OSP AP 2   Q85505 //1-476 La AP 1   Q93VM7 //1-460 P vP AP 2   Q764 C1 //1-457 UAP 2   Q8L611 //1-463 AtP AP 10   Q9SV9 //1-468 P vP AP 1  P80366 //1-459 Ta ACP   C4PKL1 //1-477 AtP AP 6   Q9C C1 //1-461 AcP AP 2   Q9SKP9 //1-470 StP AP 3   Q6J5M8 //1-477	285 S E T S W L I 303 T E T P W L I 304 E E T P W L I 305 K E T P W L I 305 K E T P W L I 305 K E T P W L I 301 E K T P W L I 303 T K T S W L I 308 T E T P W L I 308 T E T P W L I 308 S E T P W L I 304 S E T P W L I 305 E K T P W L I 307 E K T P W L I 309 T E S P W L I 309 T E S P W L I 301 E K T P W L I	V L V H V L MH V L V H V L MH V L MH	A P W - Y N S N N Y H YME G E - S MR V T F E P W - F V Q       340         S P W - Y N S Y N Y H YME G E T MR V MY E P W - F V Q       340         S P W - Y S S Y N Y H YME G E S MR A MF E S W - F V N       341         S P F - Y S S Y V H YME G E T LR V MY E QW - F V K       342         S P W - Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 131  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   038924  /1-469 INP AP   Q84K23  /1-461 MtP AP 1 (Q4KU02 //1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9SV9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9C510  /1-468 AcP AP 32   Q9XF09  /1-470 StP AP 3   Q9SK09  /1-473 IbP AP 1   Q9SE00  /1-473	285 S E T S W L I 303 T E T P W L I 304 T E T P W L I 305 K E T P W L I 305 K E T P W L I 304 T E T P W L I 304 T E T P W L I 305 S E T P W L I 308 T E T P W L I 308 T E T P W L I 303 S E T P W L I 304 E E T P W L I 305 T E S P W L I 305 S E T P W L I 307 S E T P W L I 308 T E S P W L I 301 E K T P W L I 301 S E T P W L I	V L V H V L MH V L MH	A P W - Y N S N N Y H YME G E - S MR V T F E P W - F V Q       340         S P W - Y S S Y N Y H YME G E T MR V MY E P W - F V Q       340         S P W - Y S S Y N H YME G E - S MR A MY E S W - F V N       341         S P F - Y S S Y V H YME G E T L R V MY E Q W - F V K       342         S P M - Y S S Y V H YME G E T L R V MY E Q W - F V K       342         S P M - Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   038924  /1-469 INTP AP   Q84K23  /1-461 MtP AP 1 Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764C1  /1-457 UAP 2   Q8L11/1-463 AtP AP 10   Q9SV 9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP 2   Q9ST09  /1-470 StP AP 3   Q6J5M8  /1-477 IbP AP 1   Q9500  /1-473 AtP AP 26   Q949 Y3  /1-475	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         S E T S W L I           303         S E T F W L I           303         S E T P W L I           303         S E T P W L I           304         E T P W L I           305         K T P W L I           306         T E T P W L I           307         E K T P W L I           308         T E T P W L I           309         T E T P W L I           300         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E T P W L I           305         S E T P W L I           306         T E S P W L I           307         E K T P W L I           308         T E V L I           309         E K T P W L I           3002         E K T P W L I	V L V H V L V H V L V H V L V H V L M H	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y S S N N Y H Y ME G E T MR V MY E P W - F V Q       340         S P F - Y S S Y V H H Y ME G E S MR A MY E S W - F V N       341         S P F - Y S S Y V H H Y ME G E T L R V MY E Q W - F V K       342         C P W - Y
AtP AP 11   Q9S   18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   Q38924  /1-469 INTP AP   Q84K23  /1-461 MtP AP   Q84K23  /1-461 OsP AP 2   Q85505  /1-476 La AP 1   Q93 VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q95 V9  /1-468 P vP AP 1   P803 66  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP 2   Q3XF09  /1-470 StP AP 3   Q65M8  /1-477 I bP AP 1   Q95800  /1-473 AtP AP 2   Q949 Y3  /1-475	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           301         S E T S W L I           303         T K T S W L I           303         T E T P W L I           303         S E T P W L I           304         E E T P W L I           305         K T P W L I           306         E E T P W L I           307         E K T P W L I           308         E K T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         E K T P W L I           306         E Q T P W L I           307         E K T P W L I	V L V H V L MH V L MH	A P W - Y N S N N Y H YME G E - S MR V T F E P W - F V Q       340         S P W - Y S S N N Y H YME G E T MR V MY E P W - F V Q       340         S P F - Y S S Y V H H YME G E S MR A MY E S W - F V N       341         S P F - Y S S Y V H H YME G E T L R V MY E Q W - F V K       342         C P W - Y
AtP AP 11   Q9S   18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   Q38924  /1-469 INTP AP   Q84K23  /1-461 MtP AP   Q84K23  /1-461 OsP AP 2   Q85505  /1-476 La AP 1   Q93 VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q95 V9  /1-468 P vP AP 1   P803 66  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP 2   Q3XF09  /1-470 StP AP 3   Q65M8  /1-477 I bP AP 1   Q95800  /1-473 AtP AP 2   Q949 Y3  /1-475	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           301         S E T S W L I           303         T K T S W L I           303         T E T P W L I           303         S E T P W L I           304         E E T P W L I           305         K T P W L I           306         E E T P W L I           307         E K T P W L I           308         E K T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         E K T P W L I           306         E Q T P W L I           307         E K T P W L I	V L V H V L MH V L MH	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y S S N N Y H Y ME G E T MR V MY E P W - F V Q       340         S P F - Y S S Y V H H Y ME G E S MR A MY E S W - F V N       341         S P F - Y S S Y V H H Y ME G E T L R V MY E Q W - F V K       342         C P W - Y
AtP AP 11   Q9S   18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   Q38924  /1-469 INTP AP   Q84K23  /1-461 MtP AP   Q4KU02  /1-465 OSP AP 2   Q5505  /1-476 Lo AP 1   Q93 VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9S V9  /1-468 P vP AP 1   P803 66  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9C5 10  /1-466 AcP AP   Q93 WP4  /1-481 AoP AP 32   Q9XF09  /1-470 StP AP 3   Q6J5M8  /1-477 IbP AP 1   Q9500  /1-473 AtP AP 26   Q949 Y3  /1-475 RCP AP3   385XF 6  /1-488 UAP 1   Q8L5E1  /1-477	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         E T P W L I           305         K E T P W L I           304         E T P W L I           304         E T P W L I           301         E K T P W L I           301         S E T S W L I           303         S E T P W L I           304         T E T P W L I           305         S E T P W L I           306         E T P W L I           307         E K T P W L I           308         E T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           304         E C T P W L I           305         S E T P W L I           306         E Q T P W L I           307         E K T P W L I           308         E Q T P W L I           304         E K T P W L I	V L V H V L MH V L MH	A P W - Y N S N N Y H YME G E - S MR V T F E P W - F V Q       340         S P W - Y S S N N Y H YME G E T MR V MY E P W - F V Q       340         S P F - Y S S Y V H H YME G E S MR A MY E S W - F V N       341         S P F - Y S S Y V H H YME G E T L R V MY E Q W - F V K       342         C P W - Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1 //1-464 AtP AP 25   02 3244 //1-466 AtP AP 25   02 3244 //1-469 ItP AP   Q84K23  /1-461 MtP AP 1   Q4KU02 //1-465 OSP AP 2   Q85505 //1-476 La AP 1   Q93VM7 //1-460 P VP AP 2   Q764C1 //1-457 UAP 2   Q8L6L1 //1-453 AtP AP 10   Q9SV9 //1-468 P VP AP 1   P80366 //1-459 Ta ACP   C4PKL1 //1-477 AtP AP 6   Q9 C3U1/1-466 AcP AP 2   Q9SKP0 //1-473 AtP AP 3   Q6J5M8 //1-477 IbP AP 1   Q9SE00 //1-473 AtP AP 2 6   Q949Y3 //1-475 RcP AP 3   Q8L5E1 //1-477 GmP AP 3   Q8L5E1 //1-477	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           304         T E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           303         T K T S W L I           304         T E T P W L I           305         K E T P W L I           306         T E T P W L I           307         E K T P W L I           308         T E T P W L I           309         T E S P W L I           301         K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         S E T P W L I           301         E K T P W L I           302         E K T P W L I           303         E K T P W L I           304         E K T P W L I           304         E K T P W L I	V L V + V L M	A P W - Y N S N N Y H YME G E - S MR V T F E P W - F V Q       340         S P W - Y N S Y N Y H YME G E T MR V MY E P W - F V Q       340         S P W - Y S S Y V H H YME G E S MR A MY E S W - F V N       341         S P F - Y S S Y V H H YME G E T L R V MY E Q W - F V K       342         C P W - Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 131  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   038924  /1-469 INEP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93VW7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9SV9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 ACP AP 32   Q9XF09  /1-473 AtP AP 32   Q9XF09  /1-473 AtP AP 3   G9SE00  /1-473 AtP AP 3   B9SE00  /1-475 RCP AP 3   B9SE0  /1-512 La AP 2   Q9X124  /1-638	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           301         E K T P W L I           302         K T S W L I           303         K T F P W L I           303         S E T P W L I           304         E T P W L I           305         S E T P W L I           306         T E T P W L I           307         E K T P W L I           308         T E T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         E Q T P W L I           304         E K T P W L I           305         K T P W L I           306         E Q T P W L I           307         E K T P W L I           308         E Q T P W L I           304         E K T P W L I	V L V + V L M	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y S S Y N Y H Y ME G E T MR V MY E P W - F V Q       340         S P W - Y S S Y N H Y ME G E S MR A MY E S W - F V N       341         S P F - Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 131  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   038924  /1-466 MtP AP 1 Q84K23  /1-461 MtP AP 1 Q84K23  /1-461 OSP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9SV 9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9C 510  /1-466 AcP AP 2   Q9SD0  /1-473 AtP AP 3   Q9STF09  /1-473 AtP AP 2   Q9L611 //1-475 RcP AP 3   BSSXF 6  /1-488 UAP 1   Q8 SSXF 6  /1-488 UAP 1   Q8 LSE  /1-477 GmP AP 3   Q6VGT9  /1-512 La AP 2   Q9X124  /1-628 UPP D4   Q8VXF4  /1-629	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           302         E K T P W L I           303         K T S W L I           304         E K T P W L I           305         K T S W L I           306         T E T P W L I           307         K T S W L I           308         T E T P W L I           309         T E S P W L I           3007         E K T P W L I           301         E K T P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         K E T P W L I           305         K E T P W L I           305         K E T P W L I	V L V H V L MH V L V V L V V L V V L V V V V V V V V V	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y S S N N Y H Y ME G E - S MR A MY E P W - F V Q       340         S P F - Y S S Y V H H Y ME G E - S MR A MY E S W - F V N       341         S P F - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       342         S P M - Y S S Y V H H Y ME G E T L R V MY E Q W - F V K       342         S P M - Y NS Y G Y H Y ME G E T MR V I Y E P W - F V K       342         S P M - Y NS N G A H Y ME G E S MR A A F E K W - F V K       343         A P W - Y NS N G A H Y ME G E S MR A A F E K W - F V K       343         A P W - Y NS N G A H Y ME G E S MR A A F E K W - F V K       343         S P W - Y NS N G A H Y ME G E S MR S V F E S L - F V K       340         A P W - Y NS Y N H H F ME G E M R V NY E A W - F V K       342         S P W - Y NS N N A H Y ME G E S MR A A F E K W - F V K       343         S P W - Y NS N N A H Y ME G E - S MR A A F E K W - F V K       343         A P M - Y NS N N A H Y ME G E - S MR A A F E K W - F V K       333         A P L - Y NS N E A H F ME G E - S MR A A F E K W - F V K       344
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1 //1-464 AtP AP 25   023244  /1-466 AtP AP 2   038244  /1-466 AtP AP 12   038924  /1-461 MtP AP   Q84K23  /1-461 MtP AP 1 Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764C1  /1-457 U AP 2   Q8L11  /1-463 AtP AP 10   Q9SV 9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP 2   Q9SD9  /1-470 StP AP 3   Q6J5M8  /1-477 IbP AP 1   Q95B00 //1-473 AtP AP 2 6   Q949 Y3  /1-475 RcP AP 3   Q6SYG79  /1-512 La AP 2   Q3VZ4  /1-638 UPP D4   Q8VXE4  /1-629 UPP D1   Q8VX11  /1-615	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T F W L I           303         S E T P W L I           303         S E T P W L I           304         E E T P W L I           305         K T P W L I           306         T E S P W L I           307         E K T P W L I           308         T E S P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E C T P W L I           305         K T P W L I           306         E K T P W L I           307         E K T P W L I           308         E V P W L I           309         E K T P W L I           300         E K T P W L I           305         K T P W L I	V L V H V L MH V L N V L N V L N V L N V L N V L N V L N V L N V V V V	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y S S N N Y H Y ME G E T MR V MY E P W - F V Q       340         S P F - Y S S Y V H H Y ME G E - S MR A MY E S W - F V N       341         S P F - Y S S Y V H H Y ME G E T L R V MY E Q W - F V K       342         C P W - Y S S Y V H H Y ME G E T L R V MY E Q W - F V K       342         S P M - Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1 //1-464 AtP AP 25   023244  /1-466 AtP AP 2   Q38244  /1-466 AtP AP 2   Q384K23  /1-461 MtP AP   Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93 VM7  /1-460 P vP AP 2   Q764 C1  /1-457 U AP 2   Q8 L6L1 //1-457 U AP 2   Q8 L6L1 //1-457 Ta ACP   C4P KL1 //1-477 AtP AP AP 10   Q95 V9 //1-468 A VP AP 1   P803 66  /1-459 Ta ACP   C4P KL1 //1-477 AtP AP 6   Q9 C5 10 //1-466 AcP AP 2   Q9 SWP4  /1-481 AOP AP 32   Q9 ST09 //1-470 StP AP 3   Q6 ST08 //1-473 AtP AP 2 6   Q94 9 Y3 //1-475 RcP AP 3   Q6 ST09 //1-470 MP AP 3   Q6 ST09 //1-470 MP AP 3   Q6 ST09 //1-470 MP AP 3   Q6 ST09 //1-473 ALP AP 2 6   Q94 9 Y3 //1-475 RcP AP 3   Q6 ST09 //1-510 UPP D4   Q8 VXF4 //1-619 UPP D2   Q8 VXF6 //1-612	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           301         S E T S W L I           303         S E T P W L I           303         S E T P W L I           303         S E T P W L I           304         E E T P W L I           305         E T P W L I           306         E K T P W L I           307         E K T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         E Q T P W L I           306         E K T P W L I           307         E K T P W L I           308         E Q T P W L I           309         E K T P W L I           304         E K T P W L I           305         K E T P W L I           305         K E T P W L I <td>V L V H V L MH V V L MH V V V V V V V V V V V V V V V V V V</td> <td>A P W. Y</td>	V L V H V L MH V V L MH V V V V V V V V V V V V V V V V V V	A P W. Y
AtP AP 11   Q9S   18   / 1-441 GmP AP 1   Q09 13   / 1-464 AtP AP 25   023244   / 1-466 AtP AP 25   023244   / 1-469 I \tP AP   Q84K23   / 1-461 MtP AP   Q84K23   / 1-461 MtP AP   Q84K23   / 1-460 P \tP AP 2   Q764C1   / 1-457 UAP 2   Q8503   / 1-476 AtP AP 10   Q9S \tV 9   / 1-468 P \tP AP 2   Q764C1   / 1-457 UAP 2   Q8L611 / 1-457 AtP AP 10   Q9S \tV 9   / 1-468 P \tP AP 2   Q764C1   / 1-457 AtP AP 6   Q9C5 10   / 1-466 AcP AP 2   Q9S \tV 9   / 1-481 AoP AP 32   Q9S \tV 9   / 1-470 StP AP 3   Q65 \tV 9   / 1-477 AtP AP 5   Q95 \tV 9   / 1-475 RcP AP 3   B9S \tV 6   / 1-488 UAP 1   Q8 L5 E1   / 1-477 GmP AP 3   Q6 \tV 17   / 1-615 UPP D1   Q8 \tV 11   / 1-615 UPP D2   Q8 \tV 16   / 1-612 TnP AP 1   Q4 RL84   / 1-378	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           301         S E T S W L I           303         T E T P W L I           303         T E T P W L I           303         S E T P W L I           304         E E T P W L I           305         E T P W L I           306         E E T P W L I           307         E K T P W L I           308         E K T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         E Q T P W L I           306         E Q T P W L I           307         E K T P W L I           308         E Q T P W L I           304         E K T P W L I           305         K E T P W L I           306         K T P W L I	V L V H V L MH V L MH F S L A H F S L A H F S L A H	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y S S N N Y H Y ME G E - S MR A MY E P W - F V Q       340         S P F - Y S S Y V H H Y ME G E - S MR A MY E S W - F V N       341         S P F - Y S S Y V H H Y ME G E - T L R V MY E Q W - F V K       342         C P W - Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 ItP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93VW7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q84C 11/1-457 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q95 XV9  /1-468 AvP AP 1   Q93WP4  /1-481 AoP AP 32   Q95 KD0  /1-473 AtP AP 3   Q65 M8  /1-477 IbP AP 1   Q95 ED0  /1-473 AtP AP 26 (Q94 9Y3 )/1-475 RCP AP 3   Q6 VGT9  /1-512 La AP 2   Q9X V24  /1-638 UPP D4   Q8 VXF4  /1-629 UPP D1   Q8VXF6  /1-612 TnP AP 1   Q4 RL4 1/1-378 HSP AP 7   Q6 ZWF0  /1-438	285         S E T S W L I           303         T E T P W L I           304         T E T P W L I           305         K E T P W L I           304         T E T P W L I           301         E K T P W L I           303         K T S W L I           303         S E T P W L I           303         S E T P W L I           304         E E T P W L I           305         E T P W L I           306         T E T P W L I           307         E K T P W L I           308         T E T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         K E T P W L I           304         E K T P W L I           304         E K T P W L I           305         K E T P W L I           304         E K T P W L I           305         K E T P W L I           306         K E T P W L I	V L V H V L MH V L MH V L MH V L MH V L MH V L MH V L M V V L M V L M V V L M V V L M V V L M V V L M V V L M V V V V	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y S S Y N Y H Y ME G E T MR V MY E P W - F V Q       340         S P F - Y S S Y V H Y ME G E S MR A MY E S W - F V N       341         S P F - Y
AtP AP 11   Q9S   18   / 1-441 GmP AP 1   Q09   13   / 1-464 AtP AP 25   023244 / / 1-466 AtP AP 20   02824 / 1-469 INP AP   Q84K23   / 1-461 MtP AP 1   Q4KU02 / / 1-465 OSP AP 2   Q85505 / 1-476 La AP 1   Q93VW7   / 1-460 P vP AP 2   Q764C1 / / 1-457 UAP 2   Q8L6L1 / 1-463 AtP AP 10   Q9SV9 / / 1-468 P vP AP 1   P80366 / 1-459 Ta ACP   C4PKL1 / 1-477 AtP AP 6 [ Q9C510 / 1-466 AcP AP 32   Q9XF09 / 1-470 StP AP 3   Q9SXP0 / 1-473 AtP AP 3   Q9XF09 / 1-473 AtP AP 3   Q9SXP0 / 1-473 AtP AP 3   S9SXP 6   / 1-488 UAP 1   Q8L5E1 / 1-477 GmP AP 3   Q8VXF1 / 1-512 La AP 2   Q8VXF4 / 1-629 UPP D1   Q8VXF4 / 1-615 UPP D2   Q8VXF6 / 1-438 HSP AP 7   Q6Z #0 / 1-438 CeP AP 3   Q9I / AM9 / 1-418	285         S E T S W L I           303         T E T P W L I           304         T E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           302         E K T P W L I           303         K T S W L I           304         T E T P W L I           305         E T P W L I           306         T E T P W L I           307         E K T P W L I           308         E T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E Q T P W L I           305         K T P W L I           306         E Q T P W L I           307         K K T P W L I           308         E Q T P W L I           304         E K T P W L I           305         K T P W L I	V L V H V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V V L M V L M V V L M V V L M V V L M V V L M V V V V	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y S S Y N Y H Y ME G E T MR V MY E P W - F V Q       340         S P F - Y S S Y V H Y ME G E - S MR A MY E S W - F V N       341         S P F - Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1 //1-464 AtP AP 25   023244 //1-466 AtP AP 2   Q382924 //1-469 INTP AP   Q84K23 //1-461 MtP AP 1 Q4KU02 //1-465 OSP AP 2   Q85505 //1-476 La AP 1   Q93VM7 //1-460 P vP AP 2   Q764C1 //1-457 UAP 2   Q8L6L1 //1-463 AtP AP 10   Q95V 9 //1-468 P vP AP 1   R80366 //1-459 Ta ACP   C4PKL1 //1-477 AtP AP 6 [ Q9C5 10 //1-466 AcP AP 2   Q9StF09 //1-473 IBP AP 1   Q95E00 //1-473 AtP AP 2 6 [ Q949 Y3 //1-475 RcP AP 3   B8SXF 6 //1-488 UAP 1   Q85XF 6 //1-618 UPP D4   Q8VXF4 //1-629 UPP D1   Q8VXF4 //1-638 UPP D2   Q8VXF4 //1-638 UPP D2   Q8VXF4 //1-638 CP AP 3   Q91AM9 //1-418 AmP AP 7   Q8EX37 //1-438	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T S W L I           303         S E T P W L I           303         S E T P W L I           304         E E T P W L I           305         K T P W L I           306         E K T P W L I           307         E K T P W L I           308         E T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         K E T P W L I           450         Q K Q P W L I           447         Q K Q P W L I           447         Q R Q P W L I	V L V H V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L M V L M V L MH V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V V L M V V V V	A P W. Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1 //1-464 AtP AP 25   023244 //1-466 AtP AP 2   Q382924 //1-469 INTP AP   Q84K23 //1-461 MtP AP 1 Q4KU02 //1-465 OSP AP 2   Q85505 //1-476 La AP 1   Q93VM7 //1-460 P vP AP 2   Q764C1 //1-457 UAP 2   Q8L6L1 //1-463 AtP AP 10   Q95V 9 //1-468 P vP AP 1   R80366 //1-459 Ta ACP   C4PKL1 //1-477 AtP AP 6 [ Q9C5 10 //1-466 AcP AP 2   Q9StF09 //1-473 IBP AP 1   Q95E00 //1-473 AtP AP 2 6 [ Q949 Y3 //1-475 RcP AP 3   B8SXF 6 //1-488 UAP 1   Q85XF 6 //1-618 UPP D4   Q8VXF4 //1-629 UPP D1   Q8VXF4 //1-638 UPP D2   Q8VXF4 //1-638 UPP D2   Q8VXF4 //1-638 CP AP 3   Q91AM9 //1-418 AmP AP 7   Q8EX37 //1-438	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T S W L I           303         S E T P W L I           303         S E T P W L I           304         E E T P W L I           305         K T P W L I           306         E K T P W L I           307         E K T P W L I           308         E T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         K E T P W L I           450         Q K Q P W L I           447         Q K Q P W L I           447         Q R Q P W L I	V L V H V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L MH V L M V L M V L MH V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V L M V V L M V V V V	A P W - Y N S N N Y H Y ME G E - S MR V T F E P W - F V Q       340         S P W - Y S S Y N Y H Y ME G E T MR V MY E P W - F V Q       340         S P F - Y S S Y V H Y ME G E - S MR A MY E S W - F V N       341         S P F - Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1 //1-464 AtP AP 25   O23244  /1-466 AtP AP 2   O38244  /1-466 AtP AP 12   O38924  /1-465 OSP AP 2   Q8S505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q8505  /1-476 AtP AP 0   O95V 9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP 2   Q9SD709  /1-470 StP AP 3   Q9ST09  /1-470 StP AP 3   Q9ST09  /1-473 AtP AP 2 6   Q949 Y3  /1-475 RcP AP 3   B95XP 6  /1-488 UAP 1   Q8 L5E1  /1-477 GmP AP 3   Q6 YGT9  /1-512 UPP D1   Q8VX11  /1-615 UPP D2   Q8VXF6  /1-638 CeP AP 3   Q9IIAM9  /1-418 MmP AP 7   Q8 B37  /1-438 MmP AP 1   Q8 B37  /1-438 MmP AP 1   Q8 B37  /1-438 MmP AP 1   Q8 B37  /1-438	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           303         S E T S W L I           303         S E T P W L I           303         S E T P W L I           303         S E T P W L I           304         E E T P W L I           305         K T P W L I           306         T E T P W L I           307         E K T P W L I           308         T E S P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         K T P W L I           304         E K T P W L I           305         K E T P W L I	V L V H V L MH V L MH V L MH V L L MH V L V L MH V L MH V L MH V L MH V L MH V L MH V L M V V L M V V L M V V V L M V V V V	A P W. Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1 //1-464 AtP AP 25   023244  /1-466 AtP AP 2   Q38924  /1-469 INTP AP   Q84K23  /1-461 MtP AP 1 Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93 VM7  /1-460 P vP AP 2   Q764 C1  /1-457 UAP 2   Q8 L611 //1-463 AtP AP 10   Q95 V9  /1-468 P vP AP 1   P803 66  /1-459 Ta ACP   C4PKL1 //1-477 AtP AP 6   Q9 C5 10 //1-466 AcP AP 2   Q93 WP4  /1-481 AoP AP 32   Q9XF09 //1-470 StP AP 3   Q65 M8 //-477 IbP AP 1   Q95 E00 //1-473 AtP AP 26   Q94 Y93 //1-475 RcP AP 3   Q5 E00 //1-473 AtP AP 26   Q94 Y93 //1-475 RcP AP 3   Q5 VG79 //1-512 La AP 2   Q8 VXF6 //1-612 ThP AP 1   Q4R L84 //1-378 HSP AP 7   Q62 W6 //1-418 MmP AP 7   Q8 VX76 //1-438 DmP AP 2   Q9 V258 //1-458 DmP AP 2   Q9 V258 //1-458	285         S E T S W L I           303         T E T P W L I           304         E E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           301         S E T S W L I           303         S E T P W L I           303         K T F T W L I           303         S E T P W L I           304         E E T P W L I           305         E K T P W L I           306         E K T P W L I           307         E K T P W L I           308         E K T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         E Q T P W L I           306         E Q T P W L I           307         E K T P W L I           308         E Q T P W L I           309         E K T P W L I           304         E K T P W L I           305         K E T P W L I<	V L V H V L MH V L V L MH V L V V L MH V L V V L V V V V V V V V V V V V V V V	A P W. Y
AtP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 ItP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93VW7  /1-460 P vP AP 2   Q764611/1-453 AtP AP 10   Q9SV9  /1-468 P vP AP 1   P80366 /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9C 101/1-466 AtP AP 10   Q9SW94  /1-481 AOP AP 32   Q3KF09  /1-473 StP AP 3   Q6J5M8  /1-477 IbP AP 1   Q85E0  /1-473 AtP AP 26   Q949Y3 //1-475 RCP AP 3   Q8551  /1-477 GmP AP 3   Q85E1  /1-477 GmP AP 3   Q85E1  /1-477 GmP AP 3   Q85E1  /1-477 GmP AP 3   Q85E1  /1-473 AtP AP 26   Q949Y3  /1-475 RCP AP 3   Q8VXF4  /1-638 UPP D4   Q8VXF4  /1-638 UPP D4   Q8VXF4  /1-638 UPP D4   Q8VXF6  /1-612 TnP AP 1   Q4RL84  /1-378 HSP AP 7   Q62WF0  /1-418 MmP AP 7   Q8V258  /1-450 DmP AP 2   Q9V258  /1-450 AmP AP   Q9V258  /1-450	285         S E T S W L I           303         T E T P W L I           304         T E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           304         T E T P W L I           304         T E T P W L I           301         E K T P W L I           303         K T S W L I           304         T E T P W L I           305         K T P W L I           306         T E T P W L I           307         K T P W L I           308         T E T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         E Q T P W L I           304         E K T P W L I	V L V H V L MH V L MH V L MH V L V L V L V L V L V L V L V L V L V V L V	A P W. Y
AtP AP 11   Q9S 18 / 1-441 GmP AP 1   Q09 131 / 1-464 AtP AP 25   023244 / 1-466 AtP AP 20   Q3824 / 1-469 ItP AP   Q84K23 / 1-461 MtP AP 1   Q4KU02 / 1-465 OSP AP 2   Q85505 / 1-476 La AP 1   Q93VW7 / 1-460 P vP AP 2   Q764 C1 / 1-457 UAP 2   Q764 C1 / 1-457 Ta ACP   C4PKL1 / 1-477 AtP AP 6   Q9 C5 10 / 1-468 AvP AP 1   Q93006 / 1-459 Ta ACP   C4PKL1 / 1-477 AtP AP 6 (Q9 C5 10 / 1-466 AvP AP 3   Q93VW9 / 1-481 AoP AP 3 2   Q9XF09 / 1-473 AtP AP 3   G05M8 / 1-477 IbP AP 1   Q95E00 / 1-473 AtP AP 3   G95W79 / 1-475 RcP AP 3   B95XP 6 / 1-488 UAP 1   Q8L5 E1 / 1-477 GmP AP 3   Q8VXF4 / 1-629 UPP D1   Q8VXF4 / 1-629 UPP D2   Q8VXF6 / 1-512 La AP 2   Q8VXF4 / 1-629 UPP D2   Q8VXF6 / 1-418 MmP AP 7   Q8 EX37 / 1-438 DmP AP 1   Q9 Z58 / 1-438 DmP AP 1   Q9VZ8 / 1-438	285         S E T S W L I           303         T E T P W L I           304         T E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           303         K T S W L I           303         K T F P W L I           303         K T F P W L I           303         S E T P W L I           304         E T P W L I           305         E T P W L I           306         T E T P W L I           307         E K T P W L I           308         T E T P W L I           309         T E S P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         K E T P W L I           306         E Q T P W L I           307         E X P W L I           308         K E T P W L I           305         K E T P W L I           305         K E T P W L I           305         K E T P W L I	V L V H V L MH H V L MH H V L L M H V L M H V L L M H V L M H H H V L M H H H H V L M H H H H H V L M H H H H H H H H H H H H H H H H H H	A P W - Y
AtP AP 11   Q9S   18   / 1-441 GmP AP 1   Q09   13   / 1-464 AtP AP 25   023244 / / 1-466 AtP AP 2   03924 / 1-469 INTP AP   Q84K23 / 1-461 MtP AP 1 Q84K23 / 1-461 MtP AP 1 Q84K23 / 1-461 OSP AP 2   Q85505 / 1-476 La AP 1   Q93VW7 / 1-460 P vP AP 2   Q764C1 / 1-457 UAP 2   Q8L6L1 / 1-463 AtP AP 10   Q93VV9 / 1-468 P vP AP 1   P80366 / 1-459 Ta ACP   C4PKL1 / 1-477 AtP AP 6 [ Q9C510 / 1-466 AcP AP 2   Q9SD0 / 1-473 AtP AP 3   Q9ST09 / 1-473 AtP AP 3   G8J5M8 / 1-477 IbP AP 1   Q95E00 / 1-473 AtP AP 26 [ Q949 Y3 / 1-475 RcP AP 3   B8SXF 6 / 1-488 UAP 1   Q8L5E1 / 1-473 AtP AP 26   Q94Y3 / 1-638 UPP D4   Q8VXF4 / 1-638 UPP D1   Q8VXF4 / 1-638 UPP D1   Q8VXF4 / 1-638 UPP D1   Q8VXF4 / 1-638 BAP AP 7   Q62 VF0 / 1-438 CeP AP 3   Q9VZ55 / 1-438 DmP AP 1   Q9VZ56 / 1-438 DmP AP 2   Q9VZ58 / 1-438 DmP AP 2   Q9VZ58 / 1-438 DmP AP 3   Q9VZ57 / 1-438 CeP AP 3   Q9VZ57 / 1-435	285         S E T S W L I           303         T E T P W L I           304         T E T P W L I           305         K E T P W L I           304         T E T P W L I           305         K E T P W L I           301         E K T P W L I           301         E K T P W L I           302         E K T P W L I           303         E K T P W L I           304         T E T P W L I           305         K T F W L I           306         T E T P W L I           307         T K T S W L I           308         T E T P W L I           309         T E S P W L I           3007         E K T P W L I           301         E K T P W L I           302         E K T P W L I           303         S E T P W L I           304         E K T P W L I           305         K E T P W L I           306         E K T P W L I           307         E K T P W L I           308         E K T P W L I           309         K K H Q P W L I           440         E K T P W L I           305         K E T P W L I           305         K K R P W I I	V L V H V L MH H V L MH H V L L M H V L L MH H V L M H V L L MH H V L L MH H V L M H V L V L M H V L V L V L V L V L V L V L V L V L V L	A P W - Y N S N N Y H Y ME G E S MR V T F E P W - F V Q       340         S P W - Y N S Y N Y H Y ME G E S MR A MY E P W - F V Q       340         S P F - Y

HvPAPhv a/C4PKL2//1-544	393 HGLDIAFTGHVH	A Y E R S N R V F N Y T L D P C G A V Y I S V G D G G 431
		A Y E R
		A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 427
		A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 426
		A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 426
/_ / //		A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 425
OsP APhy_b   D6QSX9   /1-539	388 YAVDVVFTGHVH	A Y E R S N R V F N Y T L D P C G P V H I S V G D G G 426
ZmP APhy_b   C4PKL6   /1-544	393 YGVDVVFTGHVH	A Y E R S N R V F N Y T L D A C G P V H I S V G D G G 431
MtP APhy/Q32FI1//1-543	394 YGVDIVFNGHVH	A Y E R S N R V Y N Y T L D P C G P V Y I T V G D G G 432
		A Y E R S N R V Y N Y T L D P C G P V H I T V G D G G 447
		A Y E R S N R V Y N Y T L D P C G P V Y I T V G D G G 431
		A Y E R S N R V Y N Y N L D P C G P V H I T I G D G G 429
		A Y E R S N R V Y N Y N L D P C G P V Y I T V G D G G 433
		A Y E R S N R V Y N Y E L D P C G P V Y I V I G D G G 425
AtaP APhy_a 1   F6MIX0   /1-549	389 HGLDIAFTGHVH	A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 427
ScPAPhy a2/F6MIX4//1-543	392 HGLDIAFTGHVH	A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 430
TmP APhy a 1 (EGMIW81/1-545	385 HOLDLAFT GHVH	A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 423
		A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 426
<i>i</i>		
·= · · · ·		A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 427
		A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 426
TaP AP hy_b3 (F6MIW6   /1-536	387 YGLDIVFTGHVH	A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 425
TmP APhy_b1/F6MIW9//1-539	390 YGLDIVFTGHVH	A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 428
AtaP APhy b1/F6MIX1//1-538	389 YGLDIVFTGHVH	A Y E R S N R V F N Y T L D P C G A V H I S V G D G G 427
· _ · · · · ·		A Y E R S Y R V F N Y T L D P C G A V H I S V G D G G 427
		A Y E R S N R V Y N Y T L D P C G P V H I T V G D G G 453
1 17		
		A Y E R S N R V Y N Y T L D P C G P V H I MV G D G G 426
		A Y E R S N R V Y N Y S L D P C G P V H I A V G D G G 433
VrP APhy  B5 AR Z7   /1-547	396 YGVDIVFN <mark>GH</mark> VH	A Y E R S N R V Y N Y S L D P C G P V H I A V G D G G 434
AIP AP 15   D7L636   /1-532	387 YGIDIVFNGHVH	A Y E R S N R V Y N Y E L D P C G P V Y I V V G D G G 425
		A Y E R
		A Y E R
<b>_</b> · · · ·		A Y E R MN R V F N Y T L D P C G P I Y I G I G D G G 453
		A Y E R M N R V F N Y T L D P C G P V Y I G I G D G G 453
		A Y E R MN R V F N Y T L D S C G P V Y I T I G D G G 451
PpP AP   A9 SP12   /1-557	396 YKVNIVFS GHVH	A Y E R T N Q V Y N Y T L N P C G P V Y V T V G D G G 434
0sP AP 3   Q6ZCX8   /1-622	418 HGVDIVFSGHVH	A Y E R M N R V F N Y T L D P C G P V Y I T I G D G G 456
OsP AP 4   B8 B909   /1-622	418 HGVDIVFSGHVH	A Y E R
		AYER SERVSNIQYNITDGMSTPVKDQNAPVYITIGDGG 327
		A Y E R F S R V Y Q D K F D K C G P V Y I N I G D G G 359
1		
		A Y E R F K R V Y N N K A D P C G P I H I T I G D G G 358
		S Y E R T E R V S N V A Y N I V N G L C S P K N D S S A P V Y I T I G D G G 354
AtP AP 2 1   Q9 LX14   / 1-437	324 A Q V D V V F A G H V H	T Y E R F K P I Y N K K A D P C G P M Y I T I G D G G 362
АtP AP 2 1   Q9 LXI4   / 1-437 LpP AP   Q9 MB0 7   / 1-455	324 A Q V D V V F A G H V H 338 Y K V D V I F A G H V H	T Y E R F K P I Y N K K A D P C G P M Y I T I G D G G 362 A Y E R S Y R I S N V A Y N I T D G K C T P T S D L S A P V Y I T V G D G G 387
AtP AP 2 1   Q9 LXI4   / 1-437 LpP AP   Q9MB0 7   / 1-455 RcP AP 2   B95XP8   / 1-463	324 A Q V D V V F A G H V H 338 Y K V D V I F A G H V H 318 Y K V D V I F S G H V H	T Y E R F K P I Y N K K A D P C G P M Y I T I G D G G 362 A Y E R S Y R I S N V A Y N I T D G K C T P T S D L S A P V Y I T V G D G G 387 A Y E R S Y R F S N V R S S V S S P N C Y P V A N E S A P M Y I T V G D G G 367
AtP AP 2 1   Q9 LXI4   / 1-437 LpP AP   Q9MB0 7   / 1-455 RcP AP 2   B95XP8   / 1-463	324 A Q V D V V F A G H V H 338 Y K V D V I F A G H V H 318 Y K V D V I F S G H V H	T Y E R F K P I Y N K K A D P C G P M Y I T I G D G G 362 A Y E R S Y R I S N V A Y N I T D G K C T P T S D L S A P V Y I T V G D G G 387
AtP AP 2 1   Q9 LXI4 //1-437 LpP AP   Q9 MB07  /1-455 RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465	324 A Q V D V V F A G H V H 338 Y K V D V I F A G H V H 318 Y K V D V I F S G H V H 343 H K V D L V F A G H V H	T Y E R F K P I Y N K K A D P C G P M Y I T I G D G G 362 A Y E R S Y R I S N V A Y N I T D G K C T P T S D L S A P V Y I T V G D G G 387 A Y E R S Y R F S N V R S S V S S P N C Y P V A N E S A P M Y I T V G D G G 367
AtP AP 2 1   Q9 LXI4   /1-437 LpP AP   Q9MB07  /1-455 RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 AtP AP 11   Q95I 18  /1-441	324 A Q V D V V F A G H V H 338 Y K V D V I F A G H V H 318 Y K V D V I F S G H V H 343 H K V D L V F A G H V H 323 N K V D I V F A G H V H	T Y E R F K P I Y N K K A D P C G P M Y I T I G D G G 362 A Y E R S Y R I S N V A Y N I T D G K C T P T S D L S A P V Y I T V G D G G 387 A Y E R S Y R F S N V R S S V S S P N C Y P V A N E S A P M Y I T V G D G G 367 A Y E R S E R V S N V A Y D I V N G K C T P V R D Q S A P V Y I T I G D G G 392
AtP AP 2 1   Q9 LXI4   /1-437 LpP AP   Q9MB07  /1-455 RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 AtP AP 11   Q95I 18  /1-441 GmP AP 1   Q09 131  /1-464	324 A QV DVV FAGHVH 338 YKVDVI FAGHVH 318 YKVDVI FSGHVH 343 HKVDLVFAGHVH 323 NKVDLVFAGHVH 341 YKVDVVFAGHVH	T Y E R F K P I Y N K K A D P C G P M Y I T I G D G G 362 A Y E R S Y R I S N V A Y N I T D G K C T P T S D L S A P V Y I T V G D G G 387 A Y E R S Y R F S N V R S S V S S P N C Y P V A N E S A P M Y I T V G D G G 367 A Y E R S E R V S N V A Y D I V N G K C T P V R D Q S A P V Y I T I G D G G 392 A Y E R S K R I S N I H Y N I T D G MS T P V K D Q N A P I Y I T I G D G G 372
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   B9SXP8 //1-463 IbP AP 2   09SD29  /1-463 AtP AP 11   09S1 18 //1-441 GmP AP 1   009 13 1 //1-464 AtP AP 25   023244  /1-466	324         A QV DVV FAGHVH           338         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           323         N KV D LV FAGHVH           323         N KV D LV FAGHVH           341         Y KV DVV FAGHVH           342         S KV D LV LS GHVH	T Y E R F K P I Y N K K A D P C G P M Y I T I G D G G 362 A Y E R S Y R I S N V A Y N I T D G K C T P T S D L S A P V Y I T V G D G G 387 A Y E R S Y R F S N V R S S V S S P N C Y P V A N E S A P M Y I T V G D G G 367 A Y E R S E R V S N V A Y D I V N G K C T P V R D Q S A P V Y I T I G D G 392 A Y E R S E R V S N I H Y N I T D G MS T P V K D Q N A P I Y I T I G D G 372 A Y E R S E R V S N V A Y D I V N G L C A P V N D K S A P V Y I T I G D G 391 S Y E R S E R V S N I K Y N I T N G L S Y P V K D P S A P I Y I T I G D G 391
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   B95XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   09518  /1-411 GmP AP 1   009 131  /1-464 AtP AP 22   023244  /1-469	324         A QV DVV FAGHVH           338         Y KV DV I FAGHVH           318         Y KV DV I FSGHVH           318         Y KV DV I FSGHVH           324         A KV D LV FAGHVH           323         N KV D LV FAGHVH           324         A KV D LV FAGHVH           324         S KV D LV LS GHVH           342         S KV D LV LS GHVH           347         Y KV DVV FAGHVH	TY ER FKP I YNKKA DP C GP MY I T I GD G G       362         A Y ER S YR I S NVA YN I TD GK C TP TS D LS AP VY I TV GD G G       387         A Y ER S YR FS NVR S SVS SP N C YP VAN ES AP MY I TV GD G G       367         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G G       392         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G G       372         A Y ER S ER VS NVA YD I VN GL CAP VN DK SAP VY I T I GD G G       390         S Y ER S ER VS NVA YN I VN GL CAP VN DK SAP VY I T I GD G G       391         A Y ER S ER VS NI K YN I TN GL S YP VK DP SAP I YI T I GD G G       392         A Y ER S ER VS NI K YN I VN GL CEP I S D ES AP I YI T I GD G G       395
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   09518  /1-441 GmP AP 12   099131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 I\tP AP (084K23  /1-461	324         A QV DVV FAGHVH           338         Y KV DV I FAGHVH           318         Y KV DV I FSGHVH           343         H KV D LV FAGHVH           343         H KV D LV FAGHVH           341         Y KV D VV FAGHVH           342         S KV D LV LS GHVH           343         Y KV D VV FAGHVH           344         Y KV D VV FAGHVH	TY ER FKP I YNKKA DP C GP MY I T I GD G G       362         A Y ER S YR I S NVA YN I TD GK C TP TS D LS AP VY I TV GD G G       387         A Y ER S YR FS NVR S VS S P N C YP VAN ES AP MY I TV GD G G       367         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G G       392         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G G       372         A Y ER S ER VS NVA YD I VN GL C AP VN DK S AP VY I T I GD G G       390         S Y ER S ER VS NVA YN I VN G L C AP VN DK S AP VY I T I GD G G       391         A Y ER S ER VS N I A YN I VN GL C EP IS DE S AP I Y I T I GD G G       391         A Y ER S ER VS N I A YN I VN GL C EP IS D ES AP I Y I T I GD G G       392         A Y ER S ER VS N I A YN I VN GL C EP IS D ES AP I Y I T I GD G G       391         A Y ER S ER VS N I A YN I VN GL C EP IS D ES AP I Y I T I GD G G       392
AtP AP 2 1   Q9 LX 4  /1-437 LpP AP   Q9MB07  /1-455 RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 AtP AP 11   Q95 18  /1-441 GmP AP 1   Q09 13 1/1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 IttP AP   Q84K23  /1-461 MtP AP 1 [Q4KU02  /1-465	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F S G H V H           343         H K V D L V F A G H V H           343         H K V D L V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V F A G H V H           342         S K V D L V L S G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V A G H V H	TY ER FKP I YNKKA DP C GP MY I T I GD G 362         A Y ER S YR I S NVA YN I TD GK C TP TS D LS AP VY I TV GD G 387         A Y ER S YR FS NVR S S VS S P N C YP VAN ES AP MY I TV GD G 367         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G 322         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G 372         A Y ER S ER VS NVA YN I TD GMS TP VK D QNAP I Y I T I GD G 372         A Y ER S ER VS NVA YN I VN G L C AP VN DK S AP VY I T I GD G 390         S Y ER S ER VS N I A YN I VN G L C AP VN DK S AP VY I T I GD G 391         A Y ER S ER VS N I A YN I VN G L C EP I S D ES AP I Y I T I GD G 392         A Y ER S KR I S N I D YK I VS G E C TP AS NP S AP VY I T VG D G 322         A Y ER S KR I S N I D YK I VS G C TP I K D QS AP VY I T I GD G 391
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   B95XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   095 I 18  /1-441 GmP AP 1   009 13 I/1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 ItP AP 1084tZ3  /1-461 MtP AP 12   04KU02  /1-465 OSP AP 2   085555  /1-476	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F S G H V H           343         H K V D L V F A G H V H           343         H K V D L V F A G H V H           343         H K V D L V F A G H V H           344         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D L V L S G H V H           346         Y K V D V V F A G H V H           347         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           342         Y K V D V V Y A G H V H           343         Y K V D V V Y A G H V H           343         Y K V D V V Y A G H V H           343         Y K V D V V Y A G H V H           343         Y K V D V V Y A G H V H	TY ER FKP I YNKKA DP C GP MY I T I GD G 362         A Y ER S YR I S NVA YN I TD GK C TP TS D LS AP VY I TV GD G 387         A Y ER S YR FS NVR S VS S P N C YP VAN ES AP MY I TV GD G 367         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G 392         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G 372         A Y ER S ER VS NVA YN I TD GMS TP VK D QNAP I Y I T I GD G 390         S Y ER S ER VS NVA YN I VN G L C AP VN DK S AP VY I T I GD G 391         A Y ER S ER VS N I A YN I VN G L C P V K DP S AP I Y I T I GD G 391         A Y ER S KR I S N I A YN I VN G L C P I S D ES AP I Y I T I GD G 392         A Y ER S KR I S N I D YK I VS G EC TP AS NP S AP VY I T VG D G 392         A Y ER S KR I S N I N YN VN G I C TP I K D QS AP VY I T I GD G 391         A Y ER S KR I S N I N YN VN S G I C TP I K D QS AP VY I T VG D G 392         A Y ER S KR I S N I N YN VN S G I C TP I K D QS AP VY I T VG D G 391         A Y ER S KR I S N I N YN VN S G I C TP I K D QS AP VY I T VG D G 391
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 1   095I38  /1-461 GmP AP 1   09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 IVEP AP   084K23  /1-461 MtP AP 1   04KU02  /1-465 OSP AP 2   08505  /1-476 La AP 1   093VM7  /1-460	324         A QV DVV FAGHVH           338         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           341         Y KV D VV FAGHVH           342         S KV D LV FAGHVH           344         Y KV D VV FAGHVH           347         Y KV D VV FAGHVH           343         Y KV D VV FAGHVH           344         Y KV D VV FAGHVH           345         Y KV D VV FAGHVH           346         Y KV D VV FAGHVH           347         Y KV D DVV FAGHVH           348         Y KV D DVV FAGHVH           349         Y KV D DVV FAGHVH           349         Y KV D DVV FAGHVH           339         Y KV D DVV FAGHVH	TY ER FKP I YNKKA DP C G PMY I T I GD G G       362         AY ER SYR FS NVAYN I TD GK C TP TS D LS AP VY I TV GD G G       387         AY ER SYR FS NVA SSYS SP NCYPVAN ES AP MY I TV GD G G       367         AY ER SKR IS NVA YD I VN GK C TP VR D QS AP VY I TI GD G G       392         AY ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I TI GD G G       372         AY ER S ER VS NVA YN I VN GL CAP VNDK SAP VY I TI GD G G       391         SY ER S ER VS NVA YN I VN GL CAP VNDK SAP VY I TI GD G G       391         AY ER S ER VS NI KYN I TN GL S YP VK DP SAP I YI TI GD G G       392         AY ER S ER VS NI KYN I TN GL C EP I SD ES AP I YI TI GD G G       391         AY ER S ER VS NI AYN VN GL C PI SD ES AP I YI TI GD G G       392         AY ER S ER VS NI AYN VN GL C PI SD ES AP VY I TV GD G G       392         AY ER S ER VS NI AYN VN GL C PI SD ES AP VY I TV GD G G       392         AY ER S KR I S NI DYK I VS GE C TP AS NP SAP VY I TV GD G G       391         AY ER S YR I S NI NYN I TS GNR YP VP DK SAP VY I TV GD G 388       388         AY ER S S RV S NNK YN I TN G I C TP VE D I TAP I YI TN GD G 388       388
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 1   095I38  /1-461 GmP AP 1   09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 IVEP AP   084K23  /1-461 MtP AP 1   04KU02  /1-465 OSP AP 2   08505  /1-476 La AP 1   093VM7  /1-460	324         A QV DVV FAGHVH           338         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           341         Y KV D VV FAGHVH           342         S KV D LV FAGHVH           344         Y KV D VV FAGHVH           347         Y KV D VV FAGHVH           343         Y KV D VV FAGHVH           344         Y KV D VV FAGHVH           345         Y KV D VV FAGHVH           346         Y KV D VV FAGHVH           347         Y KV D DVV FAGHVH           348         Y KV D DVV FAGHVH           349         Y KV D DVV FAGHVH           349         Y KV D DVV FAGHVH           339         Y KV D DVV FAGHVH	TY ER FKP I YNKKA DP C GP MY I T I GD G 362         A Y ER S YR I S NVA YN I TD GK C TP TS D LS AP VY I TV GD G 387         A Y ER S YR FS NVR S VS S P N C YP VAN ES AP MY I TV GD G 367         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G 392         A Y ER S ER VS NVA YD I VN GK C TP VR D QS AP VY I T I GD G 372         A Y ER S ER VS NVA YN I TD GMS TP VK D QNAP I Y I T I GD G 390         S Y ER S ER VS NVA YN I VN G L C AP VN DK S AP VY I T I GD G 391         A Y ER S ER VS N I A YN I VN G L C P V K DP S AP I Y I T I GD G 391         A Y ER S KR I S N I A YN I VN G L C P I S D ES AP I Y I T I GD G 392         A Y ER S KR I S N I D YK I VS G EC TP AS NP S AP VY I T VG D G 392         A Y ER S KR I S N I N YN VN G I C TP I K D QS AP VY I T I GD G 391         A Y ER S KR I S N I N YN VN S G I C TP I K D QS AP VY I T VG D G 392         A Y ER S KR I S N I N YN VN S G I C TP I K D QS AP VY I T VG D G 391         A Y ER S KR I S N I N YN VN S G I C TP I K D QS AP VY I T VG D G 391
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   89SXP8  /1-463 IbP AP 2   09SD29  /1-465 AtP AP 11   095 18  /1-411 GmP AP 1   009 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 INTP AP 1   04KU23  /1-461 MtP AP 1   04KU23  /1-461 DtP AP 2   08505  /1-476 La AP 1   03VM7  /1-460 P vP AP 2   0764 C1  /1-457	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           347         Y K V D V V F A G H V H           348         Y K V D V V F A G H V H           349         Y K V D V V F A G H V H           349         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H	TY ER FKP I YNKKA DP C G PMY I T I GD G G       362         AY ER SYR FS NVAYN I TD GK C TP TS D LS AP VY I TV GD G G       387         AY ER SYR FS NVAYN I TD GK C TP TS D LS AP VY I TV GD G G       367         AY ER SKR IS NVA YD I VN GK C TP VR D QS AP VY I TI GD G G       392         AY ER SER VS NVA YD I VN GK C TP VR D QS AP VY I TI GD G G       392         AY ER SER VS NVA YN I VN GL CAP VNDK SAP VY I TI GD G G       392         AY ER SER VS NVA YN I VN GL CAP VNDK SAP VY I TI GD G G       391         AY ER SER VS NI KYN I TN GL SYP VK DP SAP I YI TI GD G G       391         AY ER SER VS NI KYN I VN GL CEP I SD ESAP I YI TI GD G G       392         AY ER SER VS NI AYN VN GL CEP I SD ESAP I YI TI GD G G       392         AY ER SER VS NI AYN VN GL CEP I SD ESAP VY I TV GD G G       392         AY ER SER VS NI AYN VN GL CEP I SD ESAP VY I TV GD G G       392         AY ER SKR I SN I DYK I VS GE CTP AS NP SAP VY I TV GD G G       391         AY ER SKR I SN I NYN I TS GNR YP VP DK SAP VY I TV GD G 381       391         AY ER SYR I SN I NYN I TS GNR YP VP DK SAP VY I TV GD G 388       388
AtP AP 2 1   09 LX 4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   89SXP8  /1-463 IbP AP 2   09SD29  /1-465 AtP AP 1   09S18  /1-411 GmP AP 1   009131  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   084K23 //1-461 MtP AP 1   04KU02  /1-465 OSP AP 2   08505  /1-476 La AP 1   093VM7  /1-460 P vP AP 2   0764C1  /1-453	324         A QV DVV FAGHVH           338         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           318         Y KV DV I FAGHVH           341         Y KV DV Y FAGHVH           342         S KV D LV LS GHVH           344         Y KV DVV FAGHVH           344         Y KV DVV FAGHVH           344         Y KV DVV FAGHVH           345         Y KV DVV FAGHVH           346         Y KV DVV FAGHVH           346         Y KV DVV FAGHVH           341         Y K Q DVV FAGHVH	TY ER FKP I YNKKA DP C G PMY I T I GD G 362         AY ER SYR I SNVAYN I TD GK C TP TS D LS AP VY I TV GD G 387         AY ER SYR FS NVR SSVS SP NCYP VAN ES AP MY I TV GD G 367         AY ER S ER VS NVA YD I VNGK C TP VR DQS AP VY I TV GD G 392         AY ER S ER VS NVA YD I VNGK C TP VR DQS AP VY I T I GD G 372         AY ER S ER VS NVA YD I VNGL CAP VNDK SAP VY I T I GD G 372         AY ER S ER VS NVA YN I VNGL CAP VNDKS AP VY I T I GD G 391         AY ER S ER VS NVA YN I VNGL CAP VNDKS AP VY I T I GD G 391         AY ER S ER VS NI KYN I TNGLS YP VK DP SAP I YI T I GD G 392         AY ER S ER VS NI KYN I VNGL CEP I SD ES AP I YI T I GD G 392         AY ER S ER VS NI AYN VNGL CEP I SD ES AP I YI T I GD G 392         AY ER S ER VS NNA YN VNGL CEP I SD ES AP I YI T I GD G 392         AY ER S ER VS NNA YN VNGL G CTP I K DQ SAP VY I TV GD G 392         AY ER S ER VS NNA YN VNGL G TP I K DQ SAP VY I TV GD G 391         AY ER S ER VS NNK YN TNG I CTP V PD KS AP VY I TV GD G 388         AY ER S ER VS NNK YN I TNG I CTP VED I TAP I YI TNG DG 388         AY ER S ER VS NNK YN I TNG I CTP VED KS AP VY I TV GD G 388         AY ER S ER VS NNK YN I TNG I CTP VED I TAP I YI TNG DG 388         AY ER S ER VS NNK YN I TNG I CTP VED I TAP I YI TNG DG 388         AY ER S ER VS NNK YN I TNG NR YP LPD KS AP VY I TV GD G 385    <
AttP AP 2 1   09 LX 4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   B9 SXP 8  /1-463 IbP AP 2   09 SD29  /1-465 AttP AP 11   09 S1 8  /1-441 GmP AP 1   00 9 131  /1-464 AttP AP 2 2   038924  /1-469 INTP AP 1 04K U02  /1-465 OS AP 2   08 S503  /1-476 La AP 1   09 SVM7  /1-460 P VP AP 2   07 64 C1  /1-457 UAP 2   08 L6L1  /1-463 AttP AP 10   09 SV9  /1-468	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F S G H V H           318         Y K V D V I F S G H V H           343         H K V D L V F A G H V H           343         H K V D L V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V L S G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K G D V V F A G H V H           342         Y K V D V V F A G H V H           344         Y K G D V V F A G H V H           346         Y K V D V V F A G H V H	TY ER FKP I YNKKA DP C GP MY I T I GD G 362         AY ER SYR I SNVAYN I TD GK CTP TS DLS AP VY I TV GD G 387         AY ER SYR FS NVR SSVS SP N CYP VAN ES AP MY I TV GD G 367         AY ER SERVS NVAYD I VN GK CTP VR DQS AP VY I T I GD G 392         AY ER SERVS NVAYD I VN GK CTP VR DQS AP VY I T I GD G 372         AY ER SERVS NVAYD I VN GL CAP VN DKS AP VY I T I GD G 393         AY ER SERVS NVAYN I VN GL CAP VN DKS AP VY I T I GD G 393         SY ER SERVS NVAYN I VN GL CAP VN DKS AP VY I T I GD G 391         AY ER SERVS N I AYN I VN GL CEP I SD ES AP I Y I T I GD G 392         AY ER SERVS N VAYN VN GI CTP I KD QSAP VY I T VG DG G 392         AY ER SERVS N I AYN I VN GL CEP I SD ES AP I Y I T I GD G 391         AY ER SERVS N NAYN VN GI CTP I KD QSAP VY I T VG DG G 382         AY ER SERVS NNAYN VN N I TS GNR YP VP D KSAP VY I T VG DG G 388         AY ER SYR FS N I D YN I TN G I CTP VK D I SAP VY I T N GD G 388         AY ER SYR FS N D KYN TN GI CTP VK D SAP VY I T N GD G 355         AY ER SRR VS N KYN I TN GI CTP VK D SAP VY I T N GD G 355         AY ER SRR VS N KYN I N GI CTP VK D SAP VY I T N GD G 355         AY ER SRR VS N KYN T N GI CTP VK D SAP VY I T N GD G 355         AY ER SRR VS N KYN N N N GI CTP VK D SAP VY I T N GD G 355         AY ER SRR VS N KYN N YN VN GI CTP VK D SAP VY I T I GD G 355
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   B95XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   095181  /1-441 GmP AP 12   0389241  /1-466 AtP AP 22   0389241  /1-469 INTP AP   084K23  /1-461 MtP AP 1   04KU02  /1-465 OSP AP 2   08505  /1-476 La AP   029 VM7  /1-460 P vP AP 2   0764 C1  /1-453 AtP AP 10   0951 V9  /1-468 P vP AP 10   0951 V9  /1-468 P vP AP 10   0951 V9  /1-468	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V I F A G H V H           343         H K V D L V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V L S G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V F A G H V H           341         Y K O D V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H	TY ER FKP I YNKKA
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 1   09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 NtP AP 1   04KC32  /1-461 MtP AP 1   04KC32  /1-465 OSP AP 2   08505  /1-476 La AP 1   093VM7  /1-460 P vP AP 2   0764 C1  /1-457 UAP 2   08L6L1  /1-463 AtP AP 10   093V9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           344         Y K V D V V F A G H V H           347         Y K V D V V F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           345         Y K V D VV F A G H V H           346         Y K V D VV F A G H V H           347         Y K Q D VV F A G H V H           348         Y K V D VV F A G H V H           349         Y K V D VV F A G H V H           341         Y K Q D VV F A G H V H           341         Y K V D VV F A G H V H           340         Y K V D L V F A G H V H	TY ER FKP I YNKKA DP C G PMY I T I GD G 362         AY ER SYR I SNVAYNITD GK CTPTSDLSAPVYITVGDG 387         AY ER SYR FSNVR SSVS SPNCYPVANESAPMY I TVGDG 372         AY ER SERVSNVAYD I VNGK CTPVRDQSAPVYITIGD G 392         AY ER SERVSNVAYD I VNGK CTPVKDQ APIYITIGD G 372         AY ER SERVSNVAYN I VNGL CAPVNDKSAPVYITIGD G 372         AY ER SERVSNVAYN I VNGL CAPVNDKSAPVYITIGD G 391         AY ER SERVSNI KYNITNGLSYPVKDPSAPIYITIGD G 392         AY ER SERVSNI KYNITNGL CEPISDESAPIYITIGD G 392         AY ER SERVSNI KYNITNGL G PISDESAPIYITIGD G 391         AY ER SERVSNI AYNIVNGL CEPISDESAPIYITIGD G 392         AY ER SERVSNI AYNIVNG G CTPASNPSAPVYITVGD G 392         AY ER SERVSNI AYNIVNG G I CTPIKDQSAPVYITVGD G 392         AY ER SYR I SNI NYNITSGNRYPVPDKSAPVYITVGD G 388         AY ER SYR FSNI OYNITNG I CTPVED I TAPIYITNGD G 391         AY ER SERVSNKYN YNTNG G CTPVED I TAPIYITNGD G 388         AY ER SYR FSNI DYNITNG I CTPVED I TAPIYITNGD G 395         AY ER SERVSN KYN TYNTNG G CTPVKD QSAPVYITVGD G 395         AY ER SERVSN AYNVNG G I CTPVKD QSAPVYITNG G G 395         AY ER SERVSN AYNVNG G CTPVKD QSAPVYITIGD G 395         AY ER SERVSN AYNVNG G CTPVKD QSAPVYITIGD G 395         AY ER SERVSN AYN YNVNG G CTPVKD QSAPVYITIGD G 395         AY ER
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09MB07  /1-455 RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 1   09518  /1-411 GmP AP 1   09518  /1-414 GmP AP 1   09318  /1-466 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 IItP AP   084K23  /1-461 MtP AP 1   084K23  /1-461 MtP AP 1   093VM7  /1-460 P vP AP 2   0764 C1  /1-457 UAP 2   08561  /1-463 AtP AP 10   0951V9  /1-468 P vP AP 1   08366  /1-459 Ta ACP (04FKL1  /1-477 AtP AP 6   09 C5 10  /1-466	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           344         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K O D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           342         Y K V D L V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           342         Y K V D L V F A G H V H           340         Y K V D L V F A G H V H           342         Y K V D L V F A G H V H	TY ER FKP I YNKKA DP C G PMY I T I GD G G       362         AY ER SYR I SNVAYNITD GK CTP TSDLSAPVYITVGD G       387         AY ER SYR FSNVR SSVS SPNCYPVANESAPMYITVGD G G       367         AY ER SERVSNVAYD I VNGK CTP VRD QSAPVYIT GD G G       392         AY ER SERVSNVAYD I VNGK CTP VRD QSAPVYIT I GD G G       392         AY ER SERVSNVAYD I VNGL CAPVNDKSAPVYIT I GD G G       392         AY ER SERVSNVAYN I VNGL CAPVNDKSAPVYIT I GD G G       391         AY ER SERVSNVAYN I VNGL CEP I SD ESAPIYIT I GD G G       391         AY ER SERVSNNAYN VNGL CEP I SD ESAPIYIT I GD G G       392         AY ER SERVSNNAYN VNGL CEP I SD ESAPIYIT I GD G G       392         AY ER SERVSNNAYN VNG G I CTP I KD QSAPVYIT VG D G G       391         AY ER SERVSNN VAYNVNG I CTP I KD QSAPVYIT VG D G 388       391         AY ER SERVSNNKYN I TNG I CTP VED I TAPIYITNG D G 388       392         AY ER SERVSNNKYN TNG I CTP VED I TAPIYITNG D G 395       395         AY ER SERVSNNKYN TNG I CTP VED I SAPVYITVG D G 395       392         AY ER SERVSNNKYN TNG I CTP VKD QSAPVYIT NG D G 395       395         AY ER SERVSNNKYN TNG I CTP VKD QSAPVYIT GD G 395       395         AY ER SERVSN A YNVNG G I CTP VKD QSAPVYIT GD G 395       395         AY ER
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   89 SXP8  /1-463 IbP AP 2   09 5D29  /1-465 AtP AP 1   09 91 8  /1-411 GmP AP 1   09 13 1  /1-464 AtP AP 2 2   0232244  /1-466 AtP AP 1 2   038924  /1-469 INTP AP 1 084K23  /1-461 MtP AP 1 04KU02  /1-465 08P AP 2   08505  /1-476 LaAP 1   093VM7  /1-460 P vP AP 2   07 64 C1  /1-457 UAP 2   08 L611  /1-463 AtP AP 10   09 SIV9  /1-468 P vP AP 1   18066  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP [ 09 C3 10 ]/1-461	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           339         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V L S G H V H	TY ER FKP I YNKKA
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   89 SXP8  /1-463 IbP AP 2   09 SD23  /1-465 AtP AP 11   09 S18  /1-411 GmP AP 1   00 S13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 2   084K23  /1-461 MtP AP 1 04KU02  /1-465 OSP AP 2   075405  /1-476 La AP 1   09 SVM7  /1-460 P vP AP 2   076401  /1-453 AtP AP 10   09 SV9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP   09 SVP 4  /1-461 AcP AP 0 09 S10  /1-466 AcP AP 0 09 S10  /1-461 AcP AP 0 09 S10  /1-461 AcP AP 0 09 S10  /1-461 AcP AP 09 S10  /1-461	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F S G H V H           318         Y K V D V I F S G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           342         S K V D L V L S G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           343         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H	TY ER FKP I YNKKA
AttP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   B9 SXP8  /1-463 IbP AP 2   09 SD29  /1-465 AttP AP 11   09 SI 18  /1-411 GmP AP 1   00 9 I 31  /1-464 AttP AP 2 2   0232244  /1-466 AttP AP 1 2   038924  /1-465 OSP AP 2   08505  /1-476 La AP 1   09 3 VM7  /1-460 P vP AP 2   08 L6L1  /1-463 AttP AP 10   09 SI V9  /1-468 P vP AP 1  P80 366  /1-459 Ta ACP   09 SI V9  /1-466 ActP AP 0   09 SI V9  /1-466 AttP AP 0   09 SI V9  /1-468 P vP AP 1  P80 366  /1-459 Ta ACP   09 SI V9  /1-468 AttP AP 0   09 SI V9  /1-468 P vP AP 3   00 SI V9  /1-470 StP AP 3   00 SI V8  /1-477	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F S G H V H           318         Y K V D V I F S G H V H           343         H K V D L V F A G H V H           323         N K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V L S G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         Y K V D L V F A G H V H           343         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H <t< td=""><td>TY ER FKP I YNKKA</td></t<>	TY ER FKP I YNKKA
AttP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   B9 SXP8  /1-463 IbP AP 2   09 SD29  /1-465 AttP AP 11   09 SI 18  /1-411 GmP AP 1   00 9 I 31  /1-464 AttP AP 2 2   0232244  /1-466 AttP AP 1 2   038924  /1-465 OSP AP 2   08505  /1-476 La AP 1   09 3 VM7  /1-460 P vP AP 2   08 L6L1  /1-463 AttP AP 10   09 SI V9  /1-468 P vP AP 1  P80 366  /1-459 Ta ACP   09 SI V9  /1-466 ActP AP 0   09 SI V9  /1-466 AttP AP 0   09 SI V9  /1-468 P vP AP 1  P80 366  /1-459 Ta ACP   09 SI V9  /1-468 AttP AP 0   09 SI V9  /1-468 P vP AP 3   00 SI V9  /1-470 StP AP 3   00 SI V8  /1-477	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F S G H V H           318         Y K V D V I F S G H V H           343         H K V D L V F A G H V H           323         N K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V L S G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         Y K V D L V F A G H V H           343         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H <t< td=""><td>TY ER FKP I YNKKA</td></t<>	TY ER FKP I YNKKA
AtP AP 2 1   09 LXI4  /1-437 LPP AP   09 MB07  /1-455 RcP AP 2   89 SXP8  /1-463 IbP AP 2   09 SD29  /1-465 ArP AP 1   09 131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 NtP AP 1   04 KC32  /1-461 MtP AP 1   04 KC32  /1-465 OS P AP 2   08505  /1-476 La AP 1   09 SV07  /1-460 P vP AP 2   07 64 C1  /1-457 UAP 2   08 L6L1  /1-463 AtP AP 10   09 SV9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4P KL1  /1-477 AtP AP 6   09 C5 10  /1-466 AcP AP 10 9 SVF09  /1-470 StP AP 3   06 St00  /1-473	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           343         H K V D L V F A G H V H           343         H K V D L V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V L S G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           347         Y K O D V V F A G H V H           348         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V F A G H V H           343         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           351         Y K V D L V F S G H V H	TY ER FKP I YNKKA
AtP AP 2 1   09 LXI4  /1-437 LPP AP   09 MB07  /1-455 RcP AP 2   89 SXP8  /1-463 IbP AP 2   09 SD29  /1-465 AtP AP 1   09 SI29  /1-465 AtP AP 1   09 SI29  /1-464 AtP AP 25   023244  /1-466 AtP AP 1   04 KL23  /1-461 MtP AP 1   04 KL02  /1-465 OSP AP 2   08 S505  /1-476 La AP 1   09 SIV9 //1-468 P vP AP 2   07 64 C1  /1-457 UAP 2   08 L5L1  /1-463 AtP AP 10   09 SIV9  /1-468 P vP AP 10   09 SIV9  /1-468 P vP AP 10   09 SIV9  /1-468 P vP AP 10   09 SIV9  /1-468 AcP AP 00 Q0 S 10  /1-475 AtP AP 6   09 C5 10  /1-466 AcP AP 10 Q9 SWP4  /1-481 AOP AP 32   09 ST09  /1-470 StP AP 3   06 J5580  /1-475 IbP AP 1 (09 SE00  /1-473 AtP AP 26   09 49 Y3  /1-475	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           341         Y K V D VV F A G H V H           342         S K V D I V F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           342         Y K V D VV F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           345         Y K V D VV F A G H V H           346         Y K V D VV F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342 <td>TY ER FKP I YNKKA DP C G PMY I T I GD G G       362         AY ER S YR I S NVA YN I T D GK C TP T S D L S AP VY I T V GD G G       387         AY ER S YR FS NVR S SVS S P N CYP VAN ES AP MY I T V GD G G       387         AY ER S R VS NVA YD I V N GK C TP V R D QS AP VY I T V GD G G       392         AY ER S ER VS NVA YD I V N GK C TP V R D QS AP VY I T I GD G G       392         AY ER S ER VS NVA YD I V N GL CAP V ND K S AP VY I T I GD G G       391         AY ER S ER VS N V AYN I V N GL C AP V ND K S AP VY I T I GD G G       391         AY ER S ER VS N N AYN I V N GL C EP I S D ES AP I YI T I GD G G       392         AY ER S ER VS N N AYN V N GI C TP I K D QS AP VY I T V GD G G       392         AY ER S ER VS N N Y YN V N GI C TP I K D QS AP VY I T V GD G G       392         AY ER S YR I S N I N YN I T S GNR YP VP D KS AP VY I T V GD G G       392         AY ER S YR IS N N K YN I T NG I C TP V K D QS AP VY I T N GD G G       388         AY ER S ER VS N N K YN I T NG I C TP V K D QS AP VY I T N GD G G       395         AY ER S YR IS N I AYKN VN G I C TP V K D QS AP VY I T N GD G G       395         AY ER S YR IS N N YN VN S G NR YP VP D KS AP VY I T N GD G G       395         AY ER S YR IS N I N YN VN S G NR YP VP D KS AP VY I T N GD G G</td>	TY ER FKP I YNKKA DP C G PMY I T I GD G G       362         AY ER S YR I S NVA YN I T D GK C TP T S D L S AP VY I T V GD G G       387         AY ER S YR FS NVR S SVS S P N CYP VAN ES AP MY I T V GD G G       387         AY ER S R VS NVA YD I V N GK C TP V R D QS AP VY I T V GD G G       392         AY ER S ER VS NVA YD I V N GK C TP V R D QS AP VY I T I GD G G       392         AY ER S ER VS NVA YD I V N GL CAP V ND K S AP VY I T I GD G G       391         AY ER S ER VS N V AYN I V N GL C AP V ND K S AP VY I T I GD G G       391         AY ER S ER VS N N AYN I V N GL C EP I S D ES AP I YI T I GD G G       392         AY ER S ER VS N N AYN V N GI C TP I K D QS AP VY I T V GD G G       392         AY ER S ER VS N N Y YN V N GI C TP I K D QS AP VY I T V GD G G       392         AY ER S YR I S N I N YN I T S GNR YP VP D KS AP VY I T V GD G G       392         AY ER S YR IS N N K YN I T NG I C TP V K D QS AP VY I T N GD G G       388         AY ER S ER VS N N K YN I T NG I C TP V K D QS AP VY I T N GD G G       395         AY ER S YR IS N I AYKN VN G I C TP V K D QS AP VY I T N GD G G       395         AY ER S YR IS N N YN VN S G NR YP VP D KS AP VY I T N GD G G       395         AY ER S YR IS N I N YN VN S G NR YP VP D KS AP VY I T N GD G G
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   89 SXP8  /1-463 IbP AP 2   09 5D29  /1-465 AtP AP 1   09 518  /1-411 GmP AP 1   00 513 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 II:tP AP   0484C23  /1-461 MtP AP 1   0484C23  /1-461 MtP AP 1   0484C23  /1-465 05P AP 2   085505  /1-476 La AP 1   093VM7  /1-460 P vP AP 2   0764 C1  /1-457 UAP 2   08560  /1-459 Ta ACP (04P KL1  /1-477 AtP AP 6   09 C5 10  /1-466 AcP AP   093WP4  /1-481 AoP AP 32   095K09  /1-470 StP AP 3   06500  /1-473 ArP AP 2   095K0  /1-473 ArP AP 2   095K0  /1-478	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           344         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           342         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340         Y K V D L V F A G H V H <t< td=""><td>TY ER FKP I YNKKA</td></t<>	TY ER FKP I YNKKA
AtP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   89 SXP8  /1-463 IbP AP 2   09 5D29  /1-465 AtP AP 1   09 518  /1-411 GmP AP 1   09 131  /1-464 AtP AP 2   028924  /1-466 AtP AP 1 2   038924  /1-466 ItP AP 1 04 KU23  /1-461 MtP AP 1 04 KU23  /1-461 MtP AP 1 04 KU23  /1-460 P vP AP 2   0764 C1  /1-457 UAP 2   08 L6L1  /1-463 AtP AP 10   09 SV9  /1-468 P vP AP 1   10806  /1-459 Ta ACP (AP KL11  /1-477 AtP AP 6 (09 C5 10 )/1-476 AcP AP 3 (05 L5M8 )/1-477 IbP AP 3 (05 St00 //1-473 AtP AP 6 (09 AP 3)  /1-456 AcP AP 1 (09 SE00 )/1-473 AtP AP 2 (09 SE00 )/1-475 RcP AP 3 (85 StP 6 )/1-488 UAP 1 (08 L5E1 )/1-477	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           347         Y K V D V V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D V V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H <t< td=""><td>TY ER FKP I YNKKA</td></t<>	TY ER FKP I YNKKA
AttP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   89 SXP8  /1-463 IbP AP 2   09 SD23  /1-465 AttP AP 11   09 S18  /1-411 GmP AP 1   00 S13 1  /1-464 AttP AP 2 2   023244  /1-466 AttP AP 2   084K23  /1-461 MttP AP 1   04KU23  /1-461 MtP AP 1   04KU23  /1-461 MtP AP 2   0764C1  /1-457 UAP 2   0764C1  /1-457 UAP 2   0764C1  /1-463 AttP AP 10   09 SIV9  /1-468 P vP AP 2   09 SVP3  /1-468 P vP AP 2   09 SUV9  /1-468 P vP AP 2   09 SUV9  /1-468 AcP AP 10   09 SIV9  /1-468 AcP AP 10   09 SIV9  /1-475 AttP AP 6   09 SUV9  /1-475 AcP AP 3   09 SWP4  /1-481 AoP AP 32   09 XF09  /1-473 AttP AP 26   09 49 Y3  /1-475 RcP AP 3   08 L5 E1  /1-477 GmP AP 3   06 YGT9  /1-512	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           347         Y K V D V V F A G H V H           348         Y K V D V V F A G H V H           349         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           344         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H <t< td=""><td>TY ER FKP I YNKKA</td></t<>	TY ER FKP I YNKKA
AttP AP 2 1   09 LX 4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   B9 SXP8  /1-463 IbP AP 2   09 SD29  /1-465 AttP AP 1   09 S18  /1-411 GmP AP 1   00 S131  /1-464 AttP AP 2 2   023244  /1-466 AttP AP 1 2   028924  /1-466 MttP AP 1 0 R4K23  /1-461 MttP AP 1 0 R4K23  /1-461 MttP AP 1 0 R4K23  /1-461 D P VP AP 2   0764C1  /1-457 UAP 2   0764C1  /1-457 UAP 2   0764C1  /1-463 AttP AP 10   09 SI V9  /1-468 P VP AP 1  P80366  /1-459 Ta ACP   09 SI V9  /1-468 P VP AP 1  P80366  /1-475 StP AP 3   06 J510  /1-477 StP AP 3   06 J510  /1-473 AtP AP 26   09 - 93 VP 3  /1-473 AtP AP 26   09 - 93 VP 3  /1-473 AtP AP 26   09 - 93 VP 3  /1-473 AtP AP 3   08 L511  /1-477 GmP AP 3   06 J510  /1-512 La AP 2   09 X124  /1-638	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           323         N K V D I V F A G H V H           323         N K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D I V F A G H V H           346         Y K V D I V F A G H V H           341         Y K V D I V F A G H V H           344         Y K V D I V F A G H V H           345         Y K V D I V F A G H V H           346         Y K V D I V F A G H V H           341         Y K V D I V F A G H V H           342         Y K V D I V F A G H V H           344         Y K V D I V F A G H V H           345         Y K V D I V F A G H V H           346         Y K V D I V F A G H V H           347         Y K V D I V F A G H V H           348         Y K V D I V F A G H V H           349         Y K V D I V F A G H V H <t< td=""><td>TY ER FKP I YNKKA</td></t<>	TY ER FKP I YNKKA
AttP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   89 SXP8  /1-463 IbP AP 2   09 SD29  /1-465 AttP AP 1   09 SI31  /1-464 AttP AP 2   09 SD29  /1-466 AttP AP 12   038924  /1-466 AttP AP 12   038924  /1-469 IttP AP   084K23  /1-461 MttP AP 1   04KU02  /1-465 OSP AP 2   085505  /1-476 La AP 1   09 SIV9 //1-468 P vP AP 2   07 64 C1  /1-457 UAP 2   08 LSL1  /1-463 AttP AP 10   09 SIV9  /1-468 P vP AP 10   09 SIV9  /1-468 P vP AP 10   09 SIV9  /1-468 AcP AP 6   09 C5 10  /1-466 AcP AP 10 09 SIV9  /1-473 AttP AP 6   09 SD0  /1-473 AttP AP 2   09 JSD0  /1-473 A	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           345         Y K V D VV F A G H V H           346         Y K V D VV F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340         Y K V D L V F A G H V H           341 <td>TY ER</td>	TY ER
AttP AP 2 1   09 LXI4  /1-437 LpP AP   09 MB07  /1-455 RcP AP 2   89 SXP8  /1-463 IbP AP 2   09 SD29  /1-465 AttP AP 1   09 SI31  /1-464 AttP AP 2   09 SD29  /1-466 AttP AP 12   038924  /1-466 AttP AP 12   038924  /1-469 IttP AP   084K23  /1-461 MttP AP 1   04KU02  /1-465 OSP AP 2   085505  /1-476 La AP 1   09 SIV9 //1-468 P vP AP 2   07 64 C1  /1-457 UAP 2   08 LSL1  /1-463 AttP AP 10   09 SIV9  /1-468 P vP AP 10   09 SIV9  /1-468 P vP AP 10   09 SIV9  /1-468 AcP AP 6   09 C5 10  /1-466 AcP AP 10 09 SIV9  /1-473 AttP AP 6   09 SD0  /1-473 AttP AP 2   09 JSD0  /1-473 A	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           345         Y K V D VV F A G H V H           346         Y K V D VV F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340         Y K V D L V F A G H V H           341 <td>TY ER FKP I YNKKA</td>	TY ER FKP I YNKKA
AttP AP 2 1   09 LXI4   / 1-437 LpP AP   09MB07   / 1-455 RcP AP 2   895XP8   / 1-463 IbP AP 2   095D29   / 1-465 AttP AP 1   09518   / 1-411 Gm PA P 1 (09131 / 1-464 AttP AP 25   023244   / 1-466 AttP AP 12   038924   / 1-469 IttP AP   084K23 / 1-461 MttP AP 1   04KK02   / 1-465 OSP AP 2   085505   / 1-476 La AP 1   093VM7   / 1-460 P vP AP 2   0764 C1   / 1-457 UAP 2 (0816L1   / 1-463 AttP AP 10   0951 V9   / 1-468 P vP AP 10   0951 V9   / 1-468 AttP AP 6   09 C5 10   / 1-466 AcP AP   093WP4   / 1-481 AoP AP 32   095K09   / 1-470 StP AP 3   06J5M8   / 1-477 IbP AP 1 (095L5E1   / 1-477 Gm PAP 3   06751   / 1-518 UAP 2   09XV74   / 1-638 UPP D4   08VXF4   / 1-638	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           342         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340         H K V D V I F A G H V H           341         Y K V D I V F A G H V H <t< td=""><td>TY ER</td></t<>	TY ER
AttP AP 2 1   09 LXI4   / 1-437 LpP AP   09MB07   / 1-455 RcP AP 2   89SXP8   / 1-463 IbP AP 2   095D29   / 1-465 AttP AP 1   09518   / 1-411 GmP AP 1   09131   / 1-464 AttP AP 2 2   023244   / 1-466 AttP AP 1 2   038924   / 1-469 IttP AP 1 084K23   / 1-461 MttP AP 1 084K23   / 1-461 MttP AP 1 084K23   / 1-461 MtP AP 1 093VM7   / 1-460 P vP AP 2   0764 C1   / 1-457 UAP 2   08505   / 1-476 La AP 1   093VM7   / 1-463 AttP AP 10   095V9   / 1-468 P vP AP 10   095V9   / 1-468 P vP AP 1   093056   / 1-459 Ta ACP ( C4PKL1   / 1-477 AttP AP 6 ( 09 C5 10   / 1-461 AcP AP 2   093WP4   / 1-481 AoP AP 32   095W0   / 1-470 StP AP 3   095W0   / 1-473 RcP AP 3   095W0   / 1-473 RcP AP 3   06VGT9   / 1-512 La AP 2   09XVF4   / 1-619 UPP D 1   08VXF4   / 1-619	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           342         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           345         Y K V D VV F A G H V H           346         Y K V D VV F A G H V H           347         Y K V D VV F A G H V H           348         Y K V D VV F A G H V H           341         Y K V D VV F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           343         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D U V F A G H V H           347         Y K V D V I F A G H V H           348         Y K V D V I F A G H V H           349 </td <td>TY ER FKP I YNKKA</td>	TY ER FKP I YNKKA
AttP AP 2 1   09 LXI4   / 1-437 LpP AP   09 MB07   / 1-455 RcP AP 2   89 SXP8   / 1-463 IbP AP 2   09 5D29   / 1-465 AttP AP 1   09 91 8   / 1-411 GmP AP 1   09 91 8   / 1-414 GmP AP 1   09 03 8   / 1-469 IttP AP 1 2   038924   / 1-469 IttP AP 1 0 (084K23   / 1-461 MttP AP 1 0 (084K23   / 1-461 MttP AP 1 0 (084K23   / 1-461 MtP AP 1 0 (084K23   / 1-461 MtP AP 1 0 (084K23   / 1-463 AttP AP 1 0 (095 V9 / 1-468 P vP AP 2   07 64 C1   / 1-477 AttP AP 0 0 (09 SV9   / 1-468 P vP AP 1   P80366   / 1-459 Ta ACP (AP KL1   / 1-477 AttP AP 6 (09 C5 10   / 1-466 AcP AP 1 0 93 WP 4   / 1-481 AoP AP 32   09 SE00   / 1-473 AttP AP 26 (09 49 Y3   / 1-75 RcP AP 3   B5 SXP 6   / 1-488 UAP 1 (08 L5 E1   / 1-477 GmP AP 3   06 YGT9   / 1-512 La AP 2 (09 X/24   / 1-638 UPP D 1 (08 VX 11   / 1-615 UPP D 1 (08 VX 11   / 1-615	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V I F A G H V H           323         N K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           342         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D U V F A G H V H           340         H K V D U V F A G H V H           341         Y K V D U V F A G H V H <t< td=""><td>TY ER FKP I YNKKA</td></t<>	TY ER FKP I YNKKA
AttP AP 2 1   Q9 LXI4   / I - 437 LpP AP   Q9 MB07   / I - 455 RcP AP 2   B9 SXP8   / I - 463 IbP AP 2   Q9 5D23   / I - 465 AttP AP 1   Q9 5 18   / I - 411 GmP AP 1   Q9 5 18   / I - 414 AttP AP 2   Q3 5 2 - 4 - 4 - 4 - 4 - 4 - 4 - 4 - 4 - 4 -	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           323         N K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V L S G H V H           342         Y K V D VV F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           345         Y K V D VV F A G H V H           346         Y K V D VV F A G H V H           341         Y K V D VV F A G H V H           344         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340         H K V D V I F A G H V H           341<	TY ER FKP I YNKKA
AttP AP 2 1   Q9 LXI4   / I - 437 LpP AP   Q9MB07   / I - 455 RcP AP 2   B9SXP8   / I - 463 IbP AP 2   Q9SD29   / I - 465 AtP AP 1   Q9 I 31   / I - 464 AtP AP 2   Q9SD29   / I - 465 AtP AP 1   Q9 I 31   / I - 464 AtP AP 2 5   Q23244   / I - 469 ItP AP 1 Q84K23   / I - 461 MtP AP 1   Q4KK02   / I - 465 OSP AP 2   Q85505   / I - 76 La AP 1   Q93VM7   / I - 460 P vP AP 2   Q764 C1   / I - 457 UAP 2   Q8L6L1   / I - 457 UAP 2   Q8L6L1   / I - 463 AtP AP 10   Q9SV9   / I - 468 P vP AP 1   P80366   / I - 459 Ta ACP   C9PSV9   / I - 468 P vP AP   Q93WP4   / I - 481 AcP AP 6   Q9 C5 10   / I - 466 AcP AP 0   Q9SVF09   / I - 70 StP AP 3   Q6J5M8   / - 477 IbP AP 1   Q9SE00   / I - 473 AtP AP 26   Q94 9 Y3   / I - 518 UPP D1   Q8VXF1   / I - 638 UPP D1   Q8VXF1   / I - 638 UPP D1   Q8VXF1   / I - 638 HSP AP 1   Q6I F0   / I - 438 CeP AP 3   Q0   AM9   / I - 418 OEP AP 3   Q0   AM9   / I - 418	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D L V L S G H V H           341         Y K V D V V F A G H V H           342         S K V D L V L S G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           345         Y K V D VV F A G H V H           346         Y K V D VV F A G H V H           341         Y K V D VV F A G H V H           342         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340 </td <td>TY ER</td>	TY ER
AttP AP 2 1   Q9 LXI4   / I - 437 LpP AP   Q9MB07   / I - 455 RcP AP 2   B9SXP8   / I - 463 IbP AP 2   Q9SD29   / I - 465 AttP AP 1   Q9S128   / I - 461 GmP AP 1   Q9S131   / I - 464 AttP AP 25   023244   / I - 466 AttP AP 1 2   Q38924   / I - 469 IttP AP   Q84K23   / I - 469 IttP AP   Q84K23   / I - 469 IttP AP   Q84K23   / I - 469 VP AP 2   Q764 C1   / I - 457 UAP 2   Q8505   / I - 76 La AP 1   Q9SV9 / I - 468 P VP AP 2   Q764 C1   / I - 457 UAP 2   Q8505   / I - 468 P VP AP 2   Q764 C1   / I - 457 UAP 2   Q8505   / I - 468 P VP AP 1   0 P 0 9 SV 9   / I - 468 P VP AP 1   0 P 0 9 SV 9   / I - 468 P VP AP 1   0 P 0 9 SV 9   / I - 468 P VP AP 1   0 9 SV 9   / I - 468 A CP AP 3   0 9 ST 9   / I - 473 AttP AP 6   Q9 C5 10   / I - 468 UAP AP 3   Q6 J SM8   / I - 477 IbP AP 1   Q9 SWP 4   / I - 481 AOP AP 3   Q6 J SM8   / I - 477 GmP AP 3   Q6 J SM9   / I - 513 UPP D 1   Q8 VX F4   / I - 629 UPP D 1   Q8 VX F4   / I - 638 UPP D 1   Q8 VX F4   / I - 638 UPP D 1   Q8 VX F4   / I - 438 CEP AP 3   Q9 I LA18 MmP AP 7   Q8 BX 37   / I - 438	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           338         Y K V D V I F A G H V H           341         Y K V D V I F A G H V H           323         N K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           341         Y K V D VV F A G H V H           342         S K V D I V F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           343         Y K V D VV F A G H V H           344         Y K V D VV F A G H V H           345         Y K V D VV F A G H V H           346         Y K V D VV F A G H V H           341         Y K V D L V F A G H V H           342         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           344 </td <td>TY ER FKP I YNKKA</td>	TY ER FKP I YNKKA
AttP AP 2 1   09 LXI4   / 1-437 LpP AP   09 MB07   / 1-455 RcP AP 2   89 SXP8   / 1-463 IbP AP 2   09 5D29   / 1-465 AttP AP 1   09 518   / 1-411 Gm P AP 1   09 131   / 1-464 AttP AP 2 5   023244   / 1-466 AttP AP 12   038924   / 1-469 IttP AP   084K23   / 1-465 OSP AP 2   085505   / 1-476 La AP 1   093 VM7   / 1-460 P vP AP 2   0764 C1   / 1-457 UAP 2   085605   / 1-476 AttP AP 10   095 V9   / 1-468 AttP AP 10   095 V9   / 1-468 AttP AP 6   09 C5 10   / 1-466 AcP AP 2   09 S09   / 1-470 StP AP 3   06 J508   / 1-477 IbP AP 1   093 WP 4   / 1-481 AoP AP 32   09 StD9   / 1-470 StP AP 3   06 J508   / 1-477 RcP AP 3   08 J518   / 1-477 Gm P AP 3   06 J518   / 1-477 Gm P AP 3   08 J511   / 1-615 UPP D 4   08 VXF4   / 1-638 UPP D 4   08 VXF4   / 1-638 UPP D 4   08 VXF4   / 1-637 HSP AP 7   08 LX37   / 1-418 MmP AP 7   08 LX37   / 1-438 Dm P AP 1   09 V256   / 1-438 Dm P AP 1   09 V256   / 1-438	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           338         Y K V D V I F A G H V H           341         Y K V D V I F A G H V H           323         N K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           344         Y K V D V V F A G H V H           342         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           342         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           343         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H <t< td=""><td>TY ER</td></t<>	TY ER
AttP AP 2 1   09 LXI4   / 1-437 LpP AP   09MB07   / 1-455 RcP AP 2   89SXP8   / 1-463 IbP AP 2   09SD29   / 1-465 AttP AP 1   09S18   / 1-411 GmP AP 1   09 131   / 1-464 AttP AP 2 2   023244   / 1-466 AttP AP 1 2   038924   / 1-469 IutP AP 1 084K23   / 1-461 MttP AP 1 084K23   / 1-461 MttP AP 1 084K23   / 1-461 MttP AP 1 093VM7   / 1-460 P vP AP 2   0764 C1   / 1-457 UAP 2   0846L1   / 1-463 AttP AP 10   09SI V9   / 1-468 P vP AP 10   09SI V9   / 1-468 P vP AP 10   09SI V9   / 1-468 AttP AP 10   09SI V9   / 1-468 AttP AP 10   09SI V9   / 1-463 AttP AP 10   09SI V9   / 1-463 AttP AP 2   09SI 00   / 1-477 AttP AP 2   09SI 00   / 1-477 StP AP 3   09SWP4   / 1-481 AoP AP 32   09SWP6   / 1-478 RcP AP 3   09SWP6   / 1-478 UAP 1   08L5E1   / 1-477 GmP AP 3   06VGT9   / 1-512 UAP 2   09XI 24   / 1-638 UAP 1   08VXF4   / 1-639 UPP D 1   08VXF4   / 1-639 UPP D 1   08VXF4   / 1-637 HSP AP 7   08AX37   / 1-438 DmP AP 1   09V256   / 1-438 DmP AP 2   09V258   / 1-450	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           338         Y K V D V I F A G H V H           341         Y K V D V I F A G H V H           323         N K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           342         Y K V D V V F A G H V H           342         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D V I F A G H V H           348         Y K V D V I F A G H V H           349         Y K V D V I F A G H V H <t< td=""><td>TY ER      </td></t<>	TY ER
AttP AP 2 1   Q9 LXI4   / I - 437 LpP AP   Q9MB07   / I - 455 RcP AP 2   B9SXP8   / I - 463 IbP AP 2   Q9SD29   / I - 465 AttP AP 1   Q9S18   / I - 414 GmP AP 1   Q9S18   / I - 414 AttP AP 2 2   Q38924   / I - 469 IttP AP 1 2   Q38924   / I - 469 IttP AP 1 2   Q38924   / I - 469 IttP AP 1   Q4KU23   / I - 461 MttP AP 1   Q4KU22   / I - 463 OSP AP 2   Q8505   / I - 476 La AP 1   Q93VM7   / I - 468 P vP AP 2   Q764 C1   / I - 477 UAP 2   Q8L6L1   / I - 463 AttP AP 1   P8066   / I - 459 Ta ACP   C4PKL1   / I - 477 AttP AP 6 (Q9 C5 10   / I - 468 P vP AP 1   P8066   / I - 459 Ta ACP   C4PKL1   / I - 477 AttP AP 6 (Q9 C5 10   / I - 468 AcP AP 1   Q93WP4   / I - 481 AoP AP 32   Q9XF09   / I - 470 StP AP 3   Q6J5M8   / I - 477 IbP AP 1   Q95E00   / I - 473 AttP AP 26   Q9 49 Y3   / I - 512 La AP 2   Q9XI24   / I - 638 UPP D 1   Q8VXF6   / I - 138 CeP AP 3   Q9IVA   / I - 418 MmP AP 7   Q6ZVF0   / I - 438 CeP AP 3   Q9VZ56   / I - 438 DmP AP 1   Q0VZ56   / I	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F S G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           342         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           342         Y K V D V V F A G H V H           343         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340         H K V D U V F A G H V H <t< td=""><td>TY ER      </td></t<>	TY ER
AttP AP 2 1   Q9 LXI4   / I - 437 LpP AP   Q9MB07   / I - 455 RcP AP 2   B9SXP8   / I - 463 IbP AP 2   Q9SD29   / I - 465 AttP AP 1   Q9S18   / I - 414 GmP AP 1   Q9S18   / I - 414 AttP AP 2 2   Q38924   / I - 469 IttP AP 1 2   Q38924   / I - 469 IttP AP 1 2   Q38924   / I - 469 IttP AP 1   Q4KU23   / I - 461 MttP AP 1   Q4KU22   / I - 463 OSP AP 2   Q8505   / I - 476 La AP 1   Q93VM7   / I - 468 P vP AP 2   Q764 C1   / I - 477 UAP 2   Q8L6L1   / I - 463 AttP AP 1   P8066   / I - 459 Ta ACP   C4PKL1   / I - 477 AttP AP 6 (Q9 C5 10   / I - 468 P vP AP 1   P8066   / I - 459 Ta ACP   C4PKL1   / I - 477 AttP AP 6 (Q9 C5 10   / I - 468 AcP AP 1   Q93WP4   / I - 481 AoP AP 32   Q9XF09   / I - 470 StP AP 3   Q6J5M8   / I - 477 IbP AP 1   Q95E00   / I - 473 AttP AP 26   Q9 49 Y3   / I - 512 La AP 2   Q9XI24   / I - 638 UPP D 1   Q8VXF6   / I - 138 CeP AP 3   Q9IVA   / I - 418 MmP AP 7   Q6ZVF0   / I - 438 CeP AP 3   Q9VZ56   / I - 438 DmP AP 1   Q0VZ56   / I	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F A G H V H           318         Y K V D V I F S G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           342         S K V D I V F A G H V H           342         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           342         Y K V D V V F A G H V H           343         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         S K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340         H K V D U V F A G H V H <t< td=""><td>TY ER      </td></t<>	TY ER
AttP AP 2 1   Q9 LXI4   / I - 437 LpP AP   Q9 MB07   / I - 455 RcP AP 2   B9 SXP8   / I - 463 IbP AP 2   Q9 SD29   / I - 465 AttP AP 1   Q9 S18   / I - 414 GmP AP 1   Q9 S18   / I - 414 GmP AP 1   Q9 S18   / I - 469 IttP AP 1 2   Q38924   / I - 469 IttP AP 1 2   Q38924   / I - 469 IttP AP 1 2   Q38924   / I - 469 IttP AP 1 Q Q84K23   / I - 461 MttP AP 1 Q Q84K23   / I - 469 IttP AP 2   Q764 C1   / I - 477 UAP 2   Q8L6L1   / I - 463 AttP AP 1 0   Q9S V9   / I - 468 P vP AP 1   P80366   / I - 479 Ta ACP   C4PKL1   / I - 477 AttP AP 6   Q9 C5 10   / I - 468 AcP AP 1 0   Q9S WP4   / I - 481 AoP AP 32   Q9XF09   / I - 470 SttP AP 3   Q6J 5M8   / I - 477 IbP AP 1 0   Q9 SE00   / I - 473 AttP AP 26   Q94 9Y3   / I - 75 RcP AP 3   Q6S VF09   / I - 71 GmP AP 3   Q6 VGT9   / I - 512 La AP 2   Q9X V124   / I - 638 UPP D 1   Q8 VXF6   / I - 638 UPP D 1   Q8 VXF6   / I - 438 CeP AP 3   Q9 I - 438 Dm PAP 7   Q8 BX37   / I - 338 Dm PAP 7   Q8 DX37   / I - 338 Dm PAP 7   Q8 DX37   / I - 338 Dm PAP 2   Q9 VZ56   / I - 438 Dm PAP 2   Q9 VZ56   / I - 438	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           318         Y K V D V I F S G H V H           318         Y K V D V I F S G H V H           323         N K V D I V F A G H V H           323         N K V D I V F A G H V H           323         N K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           342         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H           342         Y K V D L V F A G H V H           343         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H <t< td=""><td>TY ER      </td></t<>	TY ER
AttP AP 2 1   09 LXI4 /1437 LpP AP   09 MB07 /1455 RcP AP 2   89 SXP8  /1463 IbP AP 2   09 SD29 /1465 AtP AP 2   09 SD29 /1465 AtP AP 1   09 I31/1464 AtP AP 2   09 SD29 /1466 AtP AP 12   03 89 24  /1466 AtP AP 12   03 89 24  /1466 AtP AP 1   04 KL23 /1461 MtP AP 1   04 KL23 /1461 MtP AP 1   04 KL23 /1461 MtP AP 1   04 SU3505 /1476 La AP 1   09 SV9 //1468 P vP AP 2   07 64 C1  /1457 UAP 2   08 L5L1  /1463 AtP AP 10   09 SV9 //1468 P vP AP 1   09 SV9 //1468 P vP AP 1   09 SV9 //1468 AcP AP 10   09 SV9 //1468 P vP AP 1   09 SU50 //1473 AtP AP 6   09 C5 10  /1466 AcP AP 3   06 J5M8  /1477 IbP AP 1   09 SE00 //1473 AtP AP 26   09 AP 3   04 J5M8  /1477 Gm PAP 3   06 J5M8  /1477 Gm PAP 3   06 J5M8  /1473 BSXP 6  /1488 UAP 1   08 L5E1  /1477 Gm PAP 3   06 J7  /1512 La AP 2   09 X124  /1-638 UPP D1   08 VX 11  /1-615 UPP D2   08 VX F4  /1-629 UPP D1   08 VX 11  /1-615 UPP D2   08 VX F4  /1-638 CeP AP 3   09 UZ58  /1478 MmP AP 7   08 BX37  /1438 Dm PAP 2   09 VZ58  /1478 AmP AP 2   09 VZ58  /1478	324         A Q V D V V F A G H V H           338         Y K V D V I F A G H V H           338         Y K V D V I F A G H V H           341         Y K V D V I F A G H V H           342         S K V D I V F A G H V H           341         Y K V D V V F A G H V H           342         S K V D I V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           343         Y K V D V V F A G H V H           344         Y K V D V V F A G H V H           345         Y K V D V V F A G H V H           346         Y K V D V V F A G H V H           341         Y K V D V V F A G H V H           342         Y K V D L V F A G H V H           344         Y K V D L V F A G H V H           345         Y K V D L V F A G H V H           346         Y K V D L V F A G H V H           347         Y K V D L V F A G H V H           348         Y K V D L V F A G H V H           349         Y K V D L V F A G H V H           340         Y K V D L V F A G H V H           341         Y K V D L V F A G H V H <t< td=""><td>TY ER      </td></t<>	TY ER

GmP AP 1 (Q09 131/) 1-464       391       T       L       G L       A P       AP 25 (223244 /) 1-463       392       N I       E G L       A N S F T D       P Q       P S Y         ARP AP 25 (223244 /) 1-463       393       N I       E G L       A T N M T E       P Q       P S Y         ARP AP 21 (248224 /) 1-461       393       N I       E G L       A T N M T E       P Q       P K Y         MtP AP 1 (Q4KW02 /) 1-465       392       N L       E G L A T N M T E       P Q       P K Y         MtP AP 1 (Q3VM7/) 1-460       389       N L       G L A S K F L D       P Q       P S Y         PVP AP 2 (Q7E4C1 /) 1-457       395       N Q E G L A S K F L D       P Q       P S Y       P S Y         U AP 2 / Q3LGL1 // 1-453       391       N Q E G L A S K F L D       P Q       P S Y       P K Y         Y AP AP 1 (Q9S V/) / 1-463       395       N L E G L A T K M T E       P Q       P S Y       P K Y         Y AP AP 1 (Q9S V/) / 1-463       391       N Y G V I D S N M I O       P Q       P P Y       P Y Y         AP AP 2 (03S L /) / 1-463       391       N Y G C I A S K F K D       P Q       P P Y       P Y Y         ARD AP 32 (QS KD /) / 1-473       390       N E G L A S K F K D       P Q </th <th></th> <th></th> <th></th>			
Tar##p_21(FMR3/P.358       428       N <td>· · · · · ·</td> <th></th> <td></td>	· · · · · ·		
To PPTINAD (ORTHOL/15.37       427       N E K MAT THA DUP 00 CP E CF LST PD E HO       C P L AT HIS 0 F A AS 5 C VVV CP PV         HM #PATNL21 (FKL3)/15.84       428       N E K MAT THA DUP 00 CP F LST PD E HO       C P C AT HIS 10 F A AS 5 C VVV CP PV         DM #PATNL21 (FKL3)/15.84       428       N E K MAT THA DUP 00 CP F LST PD F HO DE HO       C P C AT HIS 10 F A AS 5 C VVV CP PV         DM #PATNL21 (FKL3)/15.84       431       N E K MAT THA DUP 00 CP F LST PD F HO DE HO       C C AT HIS 10 F A AS 5 C VVV CP PV         IM #PATNL21 (FKL3)/15.84       431       N E K MAT THA DUP 10 CP PS T PD F HO DE HO       C C AT HIT 10 F A AS 5 C VVV CP PV         IM #PATNL21 (FKL3)/15.84       431       N E K MAT THA DUP 10 CP PS T PD F HO D HO       C C AT HIT 10 F A AS F C VVV CP PV         IM #PATNL21 (FKL3)/15.84       431       N E K MAT THA DUP 10 CP PLST PV F NO T PV F       C C AT HIT 10 F A AS F C VVV CP PV         IM #PATNL21 (FKL3)/15.84       421       N E K MAT THA DUP 10 CP PLST PV F NA F HA P       C C AT HIT 10 F A AS F C VVV CP PV         IM #PATNL21 (FKL3)/15.84       421       N E K MAT THA DUP 10 CP PLST PV F NA F HA P       C C AT HIT 10 F A AS F C VVV CP PV         IM #PATNL21 (FKL3)/15.84       421       N E K MAT THA DUP 10 CP PLST PV F HA F HA P       C C AT HIT 10 F A AS F C VVV CP PV         IM #PATNL21 (FKL3)/15.84       421       N E K MAT THA DUP 10 CP PLST PV F HA F HA P       C C AT HIT 10 F A AS F C VVV CP PV	/= / //		
HH = APPHy_DL (000000000000000000000000000000000000	· <b>-</b> · · · ·		
HH#P#D_31(PHU3)(J382       H       E       H       E       C	/_ / //		
DP #P#_DIDEQSD(J):543         47         N         E HAN T HA DE P D C P D L ST D F MU G C         C C A H T S G A A G F C WO C         C P Y           MP #Phy(025711/:543         433         N         E HAN T HA DE P G L C P P T S T D F MU G C         C C A H T S G A A G F C WO C         C P Y           MP #Phy(027711/:543         433         N         E HAN T HA DE P G L C P P T S T D F MU G C         C C A H T S G A A G F C WO C         C P Y           ULAP #Phy(027711/:543         433         N         E HAN T HA DE P G L C P P T S T D F F MU G C         C C A T H F I D A A G F C WO C         C P Y           Gm/ P MY_12 (193441/13)         433         N         E HAN T HA DE P G L C P D T T D F F MU F MU G C         C C A H H T S G A A G F C WO C         C P Y           Gm/ P MY_12 (193441/13)         433         N         E HAN T T A DE P G L C P D T T D F F MU F MU G C         C C A H H T S G A A G F C WO C         C P Y           SCAPMY_12 (193441/13)         431         N         E HAN T T A DE P G L C P D T F MU F	/ /		
DmP Pm_1 = 0 (mrk.s)/1.244         412         N         E MA T A H A D E G A D C P D T A T D T D F M D G         C A A H T T O A A D F C VOU C         C P Y           MP Pm/1 (ST 1)/1.544         43         N         E MA V H A D E G A D C P F T T D D F N G         C A C Y F I S G A A D F C VOU C         C P Y           I/P PM/1 (ST 1)/1.543         43         N         E MA V H A D E G A C P P S T D P V N G         C A C Y F I S G A A D F C VOU C         P Y           I/P PM/1 (ST 2)/1.543         433         N         E MA I H A D E G A C P P S T D P V N G         C A C A F I F S G A A C F C VOU C         P Y           I/P PM/1 (ST 2)/1.543         430         N         E M A I H A D E G A C P P C P F T D P V N G         C A C A F I F T O A A C F C VOU C         P Y           I/P PM/1 (ST 2)/1.543         440         N         E M A T H A D E G A C P P C P F T D P V N G         C A C A F I F T O A A C F C VOU C         P Y           I/P PM/1 (ST 2)/1.544         440         N         E M A T H A D E G A C P P C P F F N A F A C         C A C A F I F T O A A C F C VOU C         P Y           I/P PM/1 (ST 2)/1.544         430         N         E M A T H A D E G A C P P C P F F N A F A C         C A C F F F T O A A A C F C VOU C         P Y           I/P PM/1 (ST 2)/1.544         430         N E M A T H A D E G A C P P C S T P D F N A C A C         C A C F F F T O A A A A C F C VOU C         P Y </td <td>· · · ·</td> <th></th> <td></td>	· · · ·		
MPP         MP         M         E         M         T         M         D <thd< th=""> <thd< th=""> <thd< th=""> <thd< th=""></thd<></thd<></thd<></thd<>			
PP.#P.#j.NU.51/J.544         PE         N         PE         PE <td>ZmP APhy_b   C4PKL6   /1-544</td> <th></th> <td></td>	ZmP APhy_b   C4PKL6   /1-544		
NIP #Phy/APW_JI/232         42         N         E A MAIN E A D E PI KO PI K D D P VI GP PY         0         C         C A VI F I S O F A O PI K O VI G A D P VI GP PY D PY         C         C A VI F I S O F A O PI K O VI G A D P VI GP PY D PY         C         C A VI F I S O F A O PI K O VI G A D P VI GP PY D PY         C         C A VI F I S O F A O PI K O VI G A D P VI GP PY D PY         C         C A VI F I S O F A O PI K O VI G A D P VI G A D PY         C A VI F I S O F A O PI K O VI G A D P VI G A D PY         C A VI F I S O F A O PI K O VI G A D PY         C A O PI K O VI G A D PY         C A O PI K O VI G A D PY         C A O PI K O VI G A D PY         C A O PI K O VI G A D PY         C A O PI K O VI G A D PY         C A O PI K O VI G A D PY         C A O PI K O VI G A D PY         C A O PI K O VI G A O PI K O V	MtP APhy   Q3ZFI 1   / 1-543	433 N	IR EKMA I THAD EP GN C PEP L T T P D K FM <mark>-</mark> R G <mark></mark> F C A F N F T S G P A A G K F C W D Q <mark>Q P D Y S 48</mark>
LDP PHylio 202142 (1):243 43         N R E KMA IF FA D E FG HO P D Y N TO P N N TO C - F C A TH FT P D P A ST FC WOD C P D Y           APP PHylio 23560 (1):543 43         N R E KMA IF HA D D FG HO P P FK P M A T I         C - F C A TH FT D P A G F C WO C P D Y           APP PHylio 23 FG WA (1):543 43         N R E KMA TH A D E FG HO P D P FK P M A T I         C - F C A N FT S D P A G F C WO C P D Y           SCP PHYLio 23 FG WA (1):543 43         N R E KMA TH A D E FG HO P P FK P M A T I         C - F C A N FT S D P A G F C WO C P D Y           TDP PHylio 23 FG WA (1):543 43         N R E KMA TH A D E FG HO P P FK P M A T I         C - F C A N FT S D P A G F C WO C P D Y           TDP PHylio 21 FG WA (1):543 43         N R E KMA TH A D E FG HO P P FK P M A T I         C - F C A N FT S D P A G F C WO C P D Y           TDP PHylio 21 FG WA (2):1543 43         N R E KMA TH A D E FG HO P P FK P M A T I         C - F C A N FT S D P A G F C WO C P D Y           TDP PHylio 21 FG WA (2):1543 423         N R E KMA TH A D D F G C P P FK P M A T I         C - F C A N FT S D P A G F C WO C P D Y           TDP PHYLIO 21 FG WA (2):1543 423         N R E KMA TH A D D F G C P P FK P M A T I         C - F C A N FT S D P A G F C WO C P D Y           TDP PHYLIO 21 FG WA (2):1543 423         N R E KMA TH A D D F G C P P S T D D F C O F C A N FT S D P A G F C WO C P D Y           TDP PHYLIO 21 FG WA (2):1543 423         N R E KMA TH A D D F G C P P S T D D F C O F C A N FT S D P A G F C WO C P O Y           M F Z (1):1545 (1):1543 43         N R E KMA T	PtPAP3/V9LXK5//1-564	448 N	IR EKMAVPHADEPGNCPEPSTTPDKIL <mark>-</mark> GG <u>GK</u> FCGFNFTSGPAAGKFCWDR <mark>QPDYS50</mark>
GmP PPU, j0 33XG/1/247         43         N IE EKAN = 1K A DE G OH P P L S T D P V NO         C = 7 A N H F D T K S YE CWOLD Q D Y           AMP A2 10 (20 SV 3/1/33         43         N E KAN T HA D D G G O P P N F N HA F I         C = 7 C A N H T S D P A O G F V C M D Q D Y           SPAPhy, 21 (F6NN3 () 1/34         43         N E KAN T HA D D G G O P P N F N HA F I         C = 7 C A N H T S D P A O G F V C M D Q D Y           Tm <sup>2</sup> APN, 21 (F6NN3 () 1/34         43         N E KAN T HA D D G G O P P N F N HA F I         C = 7 C A H T S D P A O G F V C M D Q D Y           Tm <sup>2</sup> APN, 21 (F6NN3 () 1/34         43         N E KAN T HA D E G G C P D P N F N HA F I         C = 7 C A H T S D P A O G F V C M D Q D Y           Tm <sup>2</sup> APN, 23 (F6NN3 () 1/34         43         N E KAN T HA D E G G C P D P N F N HA F I         C = 7 C A H T S D P A O G F V C M D Q I           Tm <sup>2</sup> APN, 23 (F6NN3 () 1/33         42         N E KAN T HA D D F G C P P T T D F N G A O S C V C M D Y         C = 7 C A H T S D P A O G F V C M O Q P Y           SPAPhy, 21 (F6NN3 () 1/33         42         N E KAN T HA D D F G C P P T T D D F N G A O S C V C M O D Y         C = 7 C A H T S D P A O G F V C M O Q P Y           SPAPhy, 21 (F6NN3 () 1/33         42         N E KAN T HA D D F G C P P T T D D F N G A O S C V C M O D Y           SPAPH, 21 (F6NN3 () 1/33         43         N E KAN T HA D D F G C P F T D D F N G A O S C V C M O D Y           SPAPHy, 21 (F6NN3 () 1/33         43         N E KAN T	NtP APhy A5YBN1 /1-551	432 🛚	IR EKMA I EHAD EPRKCPKPDS TPDK FM <mark>-</mark> GG FCA YN FI S GPAA GN FCWD Q <mark>Q PD Y S</mark> 48
APP #151029513/1233         430         N E K MAT THA OD F GK C P F L T T D P V VE         CC - F C A N H T - F S O F A G F C C VO C D P V           SAP #Pby_21 F KMNA () 1-543         431         N E K MAT THA O E F G H O P P R K P N A F I         CC - F C A N H T S O F A A G F C C VO C D P V           TAP #Pby_21 F KMNA () 1-543         431         N E K KAA T THA O E F G H O P P R K P N A F I         CC - F C A N H T S O F A A G F C C VO C D P V           TAP #Pby_21 F KMNA () 1-543         431         N E K KAA T THA D E F G H O P P R K P N A F I         CC - F C A P N T S O F A A G F C C VO C D P V           TAP #Pby_21 F KMNA () 1-543         431         N E K KAA T THA D E F G H O P P R K P N A F I         CC - F C A P N T S O F A A G F C C VO C D P V           TAP #Pby_21 F KMNA () 1-543         431         N E K KAA T THA D E F G H C P D F N K P A A F I         CC - F C A P N T S O F A A G F C C VO D C P O T           TAP #Pby_21 F KMNA () 1-543         431         N E K KAA T THA D D F G C P F S T D D P C G C - F C A P N T S O P A A G F C C VO D C P O T         C - F C A P N T S O P A A G F C C VO D C P O T           SCM #Pby_21 F KMNA () 1-543         431         N E K KAA T THA D D F G C P F S T D D P C G C - F C A P N T S O P A A G F C C C O C A D P A O F C C C C P A D A O F C C C C C C A P N T S O P A A G F C C C C C C C C A P N T S O P A A G F C C C C C C C C C A P N T S O P A A G F C C C C C C C C P N T S O P A O F C C C C C C C C C C C C C C C C C C	LaP AP hy   D2 YZL4   / 1-543	430 N	R EKMA I K FAD EP GN C P D P S S T P D P YM <mark>-</mark> G G F C A T N F T F G P A V S K F C WD R <mark>Q P N Y S</mark> 48
http://www.setup.org/construction         Note Fire Mart THAD DE Fide P D DE KE MART I         Color         Color         For AN INTS OP A DE KE MOUL OF D D THE KE MART I           fm# APN_p.21/EMAWS (/):543         43         NE E KAAT THAD DE FIGH P D P REKENART I         Color         For A NINTS OP A DE KEY MOUL OF D D THE KE MART I           fm# APN_p.21/EMAWS (/):543         43         NE E KAAT THAD DE FIGH P D P REKENART I         Color         For A NINTS OP A DE FIGURO (D D D THE KE MART I           fm# APN_p.21/EMAWS (/):543         43         NE E KAAT THAD DE FIGH P D P REKENART I         Color         For A NINTS OP A DE FIGURO (D D D THE KE MART I           fm# APN_p.21/EMAWS (/):543         43         NE E KAAT THAD DE FIGURO (D D D THE KE MART I         Color         For A NINTS OP A DE FIGURO (D D D THE KE MART I           fm# APN_p.21/EMAWS (/):533         43         NE E KAAT THAD DE FIGURO (D D D THE KE MART I         Color         For A NINTS OP A DE FIGURO (D D D THE KE MART I           fm# APN_p.21/EMAWS (/):534         43         NE E KAAT THAD DE FIGURO (D D D THE KE MART I         FOR A DE FIGURO (D D D THE KE MART I         FOR A DE FIGURO (D D D THE KE MART I           fm# APN_p.21/EMAXT (/):534         14         NE KE KAAT THAD DE FIGURO (D D THE KE MART I         FOR A DE FIGURO (D D D THE KE MART I         FOR A DE FIGURO (D D D THE KE MART I         FOR A DE FIGURO (D D D D THE KE MART I         FOR A DE FIGURO (D D D D THE KE MART I         FOR A DE FIGURO (D D D D	GmPAPhy_b Q93XG4 /1-547	434 N	R EKMA I K FAD EP GH C P D P L S T P D P YM - G G F C A T N F T F G T K V S K F C WD R Q P D Y S 48
ScP APW, 20 FERMAN (J):434       431       N R E KM AT THA D E F GH C P D F R K PLA I       C       C       C       C C H L T S C P A A G F C VOLD (D P )         ToP APW, 20 FERMAN (J):433       420       N R E KM AT THA D E F G H C P F R K PLA I       C       C C H L T S C P A A G F C VOLD (D P )         ToP APW, 20 FERMAN (J):433       420       N R E KM AT THA D E F G H C P P F K PLA I       C C C C A PLA T S C P A A G F C VOLD (D P )         ScP APW, 21 FERMAN (J):433       420       N R E KM AT THA D D F G C P F L T D D D NC       C C C C A PLA T S C P A A G F C VOLD (D P )         ScP APW, 21 FERMAN (J):533       420       N R E KM AT THA D D F G C P F L S T D D D NC       C C C C A PLA T S C P A A G F C VOLD (D P )         ScP APW, 21 FERMAN (J):533       420       N R E KM AT THA D D F G C P F L S T D D D NC       C C C C A PLA T S C P A A G F C VOLD (P D )         ScP APW, 21 FERMAN (J):533       420       N R E KM AT THA D D F G C P F D T D D F NC       C C C C A PLA T S C P A A G F C VOLD (P D )         ScP APW, 21 FERMAN (J):534       420       N R E KM AT THA D D F G C C P P D T D D F NC       C C C C A PLA T S C P A A G F C VOLD (P O )         ScP APW, 21 FERMAN (J):433       430       N R E KM AT T HA D D F G C C P P D T D D F NC       C C C C A PLA T S C P A A G F C VOLD (P O )         ScP APW, 21 FERMAN (J):433       430       N R E KM AT T HA D D F G C C P P S T D D F NC       C C C F C A N N T F D C P A A G F C VOLD (P O )	AtP AP 15   Q95FU3   /1-532	426	IR EKMA I EHADDP GK CP EP L T T P D P V M - G G F C A W N F T P S D K F C W D R O P D Y S 47
ImP PHU, 2   FEAN W2	AtaPAPhy_a1/F6MIX0//1-549	428	R E K MA T T H A D E P G H C P D P R P K P N A F I - G G F C A S N F T S G P A A G R F C W D R O P D Y S 48
To PPb::g3 (PMW2):1/339       427       N       E KAN T HA DE F GLY PIA Y IA F       G G       C C A F H T S G P A A G F C WD G P D Y         Sc PPb::g3 (PMW2):1/341       427       N       E KAN T HA DE F GLY PIA Y IA F       G G       C C A F H T S G P A A G F C WD G P D Y         Sc PPb::g3 (PMW2):1/341       427       N       E KAN T HA DE F GLY PIA Y IA F       G G       C C A F H T S G P A A G F C WD G P D Y         To PAPb::g3 (PMW2):1/341       431       N       E KAN T HA DD F G C P F L S T P D D FM       G G       C C A F H T S G P A A G F C WD G P D Y         To PAPb::g1 (PMW3):1/338       N       E KAN T HA DD F G C P P L S T P D FM       G G       C C A F H T S G P A A G F C WD G P D Y         Sc P Phy::b1 (PMW3):1/338       N       E KAN T HA D D F G C P P L S T P D FM       G G       C C A F H T S G P A A G F C WD G P D Y         Sc P Phy::b1 (PMW3):1/334       N       E KAN T HA D P G G C P P S T P D F M       G G       C C A T H T T G G A A G F C WD G P D Y         Sc P P A PAD::1/57821/346       N       E KAN T HA D P G G C P P S T P D F M       G G       C C A T H T T G G A A G F C WD G P D Y         V P P A PS :1/57821/346       N       E KAN A H A D P G G C P P S T P D F M       G G C F C A T H T F G G A G F C WD G P D Y         V P A P :1/57821/345       S F K W O Y D F A D F G G C P D Y T D T T I       G G C F C A T H F T G G A A G F C WD G P D Y      <	ScPAPhy a2/F6MIX4//1-543	431 N	R E K MA T T H A D E P G H C P D P R P K P N A F I - G G F C G F N F T S G P A A G R Y C WD R Q P D Y S 48
ToP APPL_p21 (DPRXX)[J-349       48       N       EKAN T HA DE P GIC P P R K F N A F       G0       C C A F H T S G P A G B C Y WO C P D Y         ToP APPL_D1FGAWW(J-1336       45       N       EKAN T HA D P G C C P L S T P D D F K       G0       C C A F H T S G P A G B C Y WO C P D Y         ToP APPL_D1FGAWW(J-1336       N       EKAN T HA D P G C C P L S T P D D F K       G0       C C A F H T S G P A G B C Y WO C P D Y         ToP APPL_D1FGAWX(J-1338       N       EKAN T HA D P G C C P L S T P D D F K       G0       C C A F H T S G P A G S C Y WO C P D Y         SP APPL_D1FGAWX(J-1338       N       EKAN T HA D P G C C P L S T P D T F K       G0       C C A F H T S G P A G S C Y W C P D Y         Y W P APPLSSSGU/J-340       N       EKAN T HA D P G C C P L S T P D T F K       G0       C C A F H T S G P A G S C Y W C P D Y         Y W P APPLSSSGU/J-340       N       EKAN T HA D P G C C P L S D T P D T K       G0       C C A T H T F G P A G F C Y W C P D Y         Y P APPLSSSGU/J-340       N       EKAN T HA D P G C C P L S D T P D T K       G0       C C A T H T F G P A G S C Y W C P D Y         Y P APPLSSGU/J-340       N E K AN I K A D E P G C C P L T D D F K       G0       C C A T H T F G P A G S C Y W C P D Y         Y P APPLSSGU/J-340       N E K A D E P G C P D P M K H       G0       C C A T H T F G P A G S C Y W C P Q P Q Y         Y P APPLSJ G C Y S S V H H D A D P G C	TmP APhy a1/F6MIW8//1-545	424	R E K MA T T H A D E P G H C P D P R P K P N A F I - G G F C A S N F T S G P A A G R F C W D R O P D Y S 47
ToPAPhy_02 (DPNX2)/1349       48       N       EKANT THAO E GIC PPR K Y NAF I       60       C C A FIFTS G PA AG B C YUN C Y D Y         ToPAPhy_D3 (FGNX8)/1349       428       N       EKANT THAO E GIC P PL ST P D D FK       60       C C A FIFTS G PA AG B C YUN C Y D Y         ToPAPhy_D3 (FGNX8)/1338       48       N       EKANT THAO P GIC P FL ST P D D FK       60       C C A FIFTS G PA AG B C YUN C Y D Y         ToPAPhy_D1 (FGNX1)/1338       48       N       EKANT THAO P GIC P FL ST P D D FK       60       C C A FIFTS G PA AG B C YUN C Y D Y         YWPAP (JSBSK)/1340       48       N       EKANT THAO P GIC P FL ST P D FK       60       C C A FIFTS G PA AG B C YUN C Y D Y         YWPAP (JSSS2)/1347       48       N       EKANT THAO P GIC P P ST TP D FK       60       C C A FIFTS G PA AG F C YUN C Y D Y         YWPAP (JSSS2)/1347       43       N       EKANT THAO P GIC P P ST TP D FK       60       C C A TIFT G G PA AG F C YUN C Y D Y         YWPAP (JSSS2)/1347       18       N E KANT THAO P GIC P P L ST D P FK       60       C C A TIFT G G PA AG F C YUN C Y D Y         YWPAP (JSSS2)/1345       18       N E KANT THAO P GIC P P L ST D P FK       60       C C A TIFT G G PA AG F C YUN C Y D Y         YWPAP (JSS2)/1345       18       N E KANT THAO P G G C P P S TO P HY C       60       C C A TIFT TG G PA AG F C YUN C Y      <		427	REKMATTHADEPGHCPEPRAKPNAFI-GG-FCAFNFTSGPAAGRECWDROPDYS 47
SeP Phy_pair (MMX2):334       427       K KMA T H A D G G C C F L ST T D D F M       G G F C A F H T S D P A G S F VVD C P D Y         Tim Phy_bair (FMX3):333       428       K KMA T H H A D D G G C F F L ST T D D F M       G G F C A F H T S D P A G S F VVD C P D Y         SeP Phy_bair (FMX3):333       428       K KMA T H H A D D G G C F F L ST T D D F M       G G F C A F H T S D P A G S F VVD C P D Y         SeP Phy_bair (FMX3):333       428       K KMA T H H A D G G G C F F L ST T D D F M       G G F C A F H T S D P A G S F VVD C P D Y         SeP Phy_bair (FMX3):334       428       K KMA T H H A D F G G C P F S T T D T F M       G G F C A T H T T G P A G S F VVD C P D Y         SeP Phy_bair (FMX3):334       428       K KMA T H A D F G G C P D S T T D E F M       G G F C A T H T T G P A G S F VVD C P D Y         SeP Phy_bair (FMX3):343       427       K KMA T H A D F G G C P D L ST D T F M       G G F C A T H T F D G P A G F VVD C P D Y         VAP Phy bir (SAZZ):347       53       K K M T H A D F G G C P P D L ST D T F M       G G F C A T H T F D G P A G F VVD C P D Y         G M PAP UNG(1:443       54       K K A T H A D F G G C P P D N H P E I       G G F C A T H T F D G P A G F VVD C P D Y         M P PAP PH (MSR):442       54       K K A T H A D P G G C P P D N H P E I       G G F C A T H T F D G P A G F VVD C P D D G C P G N H P E I       G G F C A T H T F D G P A G F VVD C P D D G C P G N H P E I         SP PA (A D A S G F VVD G P A D G G C P	/ /	428	REKMATTHADEPGHCPDPRPKPNAFI-GGFCAFNFTSGPAAGRFCWDROPDYS 48
Tor PAPU_1ESTERNUM_US356       426       N       EXAM TH A D D P G C P F L ST TD D FK       GG       C C A F H FT S G P A AG S F CWD C P D Y         Tor PAPU_1ESTERNUM_US358       438       N       E KAA TH A D D P G C P F L ST TD D FK       GG       C C A F H FT S G P A AG S F CWD C P D Y         RAP PAPU_1ESTERNUM_US358       N       N       E KAA TH A D D P G C P F L ST TD D FK       GG       C C A F H FT S G P A AG S F CWD C P D Y         RAP PAU_1ESTERNUM_US356       AS N       N       E KAA TH A D D P G C P P S TT TD D FK       GG       C C A F H FT S G P A AG S F CWD C P D Y         VAPA       PASSGULJ3-46       AS N       E KAA I H A D P G C C P F S TT TD T FK       GG       C C A T H FT G G P A AG S F CWD C P D Y         VAPAP1SSZULJ3-47       AS N       E KAA I H A D P G C C P F L TT D P KM       GG       C C A T H FT G G P A AG S F CWD C P D Y         VAPAP1SSZULJ3-46       AS N       E K KAA I H A D P G C C P F L TT D P KM       GG       C C A T H FT G G P A AG S F CWD C P D Y         VAPAP1SSZULJ3-46       AS N E F KAA I H A D P G C C P F G L TT D P KM       GG       C C A T H FT G G P A AG S F CWD C P C Y         VAPAP21GENTUJCSSGN H H C F       C F C A H H T S G P A AG S F CWD C P C Y       F K I H H D H A D P G C C P F G L H H F T F D P KM       GG       C C A H H T S G P A AG S F CWD C P C Y         VAPAP21GENTUJCSSGN H H C F       F K I H H A D H A D P G C C P F G L H H F	· · · ·		
Tim PAPU_DIFERMINU/1339       423       N       EKMA THH A D P G CC P E L ST TU D E K       GG - C A F K F TS G P A G S F CWD C P D V         SAP PMU_DIFERMIX/1338       N       EKMA TH A D P G CC P E L ST TU D E K       GG - C A F K F TS G P A G S F CWD C P D V         SKP PMU_DIFERMIX/1338       N       EKMA T H A D P G CC P E L ST TU D E K       GG - C A F K F TS G P A G S F CWD C P D V         SKP PMU_DIFERMIX/1339       430       E KMA T H A D F G CC P E ST TU D E K       GG - C A T K F TS G P A G S F CWD C P D V         SKP PMU_DIFERMIX/1339       431       E KMA T H A D F G CC P D S TT D E K       GG - C A T K F T G F A G F C CWD C P D V         VPAPU/DISAZZ/1347       435       E KKMA T K A D E G CC P D L ST D T M K       GG - C A T K F T G D F A G F C CWD C P D V         GM PAPU/DISAZZ/1347       435       E K KMA T K A D E G CC P D C N T N D F K       GG - C A T K F T D G P A G F C CWD C P D V         GM PAPU/DISAZZ/1347       435       E K K M N A D O G C C P Z O N H P E T       GG - C A T K F T D G P A G F C CWD C P O N H P E T         GM PAPU/DISAZZ/1346       435       E K C M D A D O G C C P Z O N H P E T       GG - C A T K F T F G P A G F C CWD C P O N H P E T         GM PAPU/DISAZZ/1346       54       K C I O D A A D O G C C P Z O N H P E T       GG - C A T K F T G P A G G F C CW D O P O N H P E T         GM PAPU/DISAZZ/1443       55       K C I O D A A D O G C C P Z O N H P E T       GG - C A K G K C CW O O			
Amp Perty _ 1 (FONX.1/1-38       428       N E E MAT THAD D P G NC P E L T P D D F N G G FC A N F T S G P A G S E C WD G D P Y         Sc Perty _ 158W 06(1)-156       454       N E E MA T THAD D P G NC P P E L T P D D F N G G C A N F T S G P A G S E C WD G D P Y         Were P 35806(1)-156       454       N E E MA T THAD D P G NC P P E S T P D T F N G F A G S E C WD G D P Y         Were P 35806(1)-156       434       N E E MA T F A G D F G NC P P E S T P D T F N G F A G S E C WD G D P D Y         Vere P 378372(1)-157       318       N E E M A I E F A G D F G NC P P L S T O P D T N G G G C F C A N F T G D G G C F C F W H D P Y         G G G F C WT/1/1-38       31       N E E M A I E F A G D F G N C P P L S T O P N G N G G C F C F W H D P Y         G G G F P 411/1-48       32       N E E M A I E F A G D P G N C P P S N K F W N P Q P Y         G M P 41/9HXG A 1/-42       33       N E E M A I E F A G D P G N C P P S N K F W N P Q P Y         G M P 41/9HXG A 1/-42       33       N E E M A I E F A G D P G N C P F S N M H P E F = G G - C C H N F T S G A A G K F W N P Q P Y         S P P 41/9AL25293/1/-143       34       N E E M A I A A O P O P O C C P P G D U N H E F = G G - C C H N F T S G A A G K F W F Q Q P Q Y         S P A 1/9 10/1/-143       35       N E E L D D A A O D P G C C P P G D U N H E F = G G - C C H N F T S G A A G K F W F Q P Q Q P Y         S P 1/9 10/1/-143       35       N E G L A N K T N F T C P A A O K F W F Q Q P A A O K K F W P Q P A A O K K F W P Q P A A O K	/ /		
ScPPM_D1[F6NX5]/1-38         420         N E KMAT THAD DP GHC P EP LT P D A FM         G	/ /		
RepPart 1889 W66(1)-1366         454         R E MAA 1 TH AD EP GUC P D S TT PD EF 1         GC         CA T N ET FG A AD K E CWD PD PD PD PP			
wP#p13806()/1-40         427         R E KM AL E HA D A G (C P E P S T P D T E T P D T E T         Cor         c C A T N E T E G R A G (K E C W D G P D C T T P D T E T D T P D T E T P D T			
P+# APhyl/V2822/1/1366       434       N E KMA I K A D E P G LC P P L IST P D Y VL G G _ F C A TH FT G Q E _ S E F C WH (P D Y VL APP 21) (D7L56)(1/32)       435       N E KMA I E H A D E P G LC P E L ITT P D Y VL G G _ F C A TH FT G Q E _ S E F C WH (P D Y VL APP 21) (D7L56)(1/32)       447       N E KMA I E H A D P G LC P E L ITT P D Y VL G G _ F C A TH FT G Q E _ S E F C WH (P D Y VL APP 21) (D7L56)(1/32)       451       N E KMA I E H A D P G LC P E D L ITT P D Y VL G G _ F C A TH FT G Q E _ S E C WH (P D Y VL APP 21) (D7L56)(1/32)       451       N E KMA I E H A D P G LC P E D L ITT P D Y VL G G _ F C A TH FT G Q A K G K C WG R Q E W D APP 21 (D7L51)(1/36)       454       N E K I D D H A D P G C C P S P D D H F E F G G _ V L L H L H TS G P A K G K C WG R Q E W H # P Z (OPKL) (1/36)       454       N E K I D D H A D P G C C P S P D D H E F G G _ V C L L H L H TS G P A K G K C WG R Q E W O P AP3 (0620%) (1/32)       457       N E E K D D H A D P G C C P S P D D H E F G G _ V C H L H FT G Q A K G K C WG R Q E W O P AP3 (0620%) (1/34)       458       N E E K D D H A D P G C C P G O N H E F G G _ V C H L H FT G Q A K G K C WG R Q E W APP 21 (0827) (1/35)       388       N E G L A T K V R D _ P Q _ C C P G O N H E F G G _ V C H L H FT G Q A K G K C WG R Q E W APP 21 (0827) (1/36)       388       N E G L A T K V R D _ P Q _ C C C P G O N H A D S G C P S Q D H A D S G C P S Q D H A D S G C P S Q D H A D S G C P S Q D H A D S G C P S Q D H A D S G C P S Q D H A D S G C P S Q D H A D S G C P S Q D H A D S G C P S Q U H A D S G C P S Q U H A D S G C C P S Q D H A D S G C C P G Q H A D S G C C P G Q H A D S G C C P S Q D H A D S G C C P S Q U H A D S G C C C C C C C C C C C C C C C C C C			
VP:APD/U354827/1/347       455       M E K MA I K F A D E G GLOP DP LIT S D H F M G G G F C A T M F T E D Q E S E F C WOH Q P D Y APP23(GGFH1/L458       427       M E K V D V D F A D D P G C P P D U H F D G G F C A W F F T D Q E A G F C WOH Q P D Y APP23(GGFH1/L458       427       M E K V D V D F A D D P G C P P D O H H E F G G F L C H L H F T G Q A G F C WOH Q P C M P P A M P A 23/28731/1366       448       N E K V D V D F A D D P G C P P D O H H E F G G F L C H L H F T G Q A A G F C WO Q F E W P APA (A ALZAR 78)/1366       A K A V E K I D D H A D D P G C P P D O H H E F G G F L C H L H F T G Q A A G F C W D Q F C M P P A (A ALZAR 78)/1366       A K A V E K I D D H A D D P G C P P D O H H E F G G F L C H L H F T G Q A A G F C W D Q F C M Q P E W P APA (A SK2/24/357)/1357       A K A V E K I D D H A D D P G C P P D O H H E F G G F V C H L H F T G Q A A G F C W D Q F C Q P Q O H Y E Y G G F V C H L H F T G Q A A G K F C W K Q F E W Q P APA (A SK2/24/357)/1427       A K A V I L I F T G Q A A G K F C W K Q F E W Q P APA (A SK2/24/357)/1437       A K A V I L I F T G Q A A G K F C W K Q F Q W Q H A A A S Q G V V H L I F T G Q A A G K F C W K Q F E W Q P APA (A SK2/24/350)/1437       A K A V I L I F T G Q A A G K F C W K Q F E W Q P APA (A SK2/24/350)/1437       A K A V I L I F T G Q A A G K F C W K Q F E W Q P A A (A SK2/24/340)/1434       A R A V I I I D H A D D P G C P Q G O H H E F G G G V V H L I F T G Q A A G K F C W K Q F E W Q P APA (A SK2/24/340)/1434       A K A V I L I F T G Q A A G K F C W K Q F E W Q Q A A A S (C W X A W A S (C W X A W A S N B G G I A T K K R D P M C A C Y C W K A M A S (C W X A W A S (			
AP AP 15 (07L55) (1-522       425       M E K MA 1 E H A D E P G K C P E D L TT P P V M B G L P A M W F T P F K C WOR Q D V Y         Gm AP 4 (V9HXG/1/-1442       313       M E G L A H K Y I N E K K O C P E G D H F E F G G       G L C H L H T S G P A K G K F C WOR Q D P Y         Sp AP (ADL258978) (1-56       454       N E K L D I D H A D D P G K C P S P G D H F E F G G L C H L H T S G P A K G K F C WOR Q P E Y         M P AP 4 (ADL258978) (1-56       454       N E K L D I D H A D D P G K C P S P G D H F E F G G L C H L H T S G P A K G K F C WOR Q P E Y         M P AP 4 (ADL258978) (1-56       454       N E K L D I D H A D D P G K C P C O D H F E F G G L C H L H T S G P A K G K F C W G R P W         M P AP 4 (ADL258978) (1-52       457       N E K L D I D H A D D P G K C P Q G D H F E F G G L C H L H T S G P A K G K F C W G R P W         M P AP 4 (ADL258073) (1-52       457       N E K L D I D H A D D P G K C P Q G D H H E F G G L V C H L H T S G P A G K F C W K G F W         M P AP 2 (ADL30714) (1-37       380       N E G L A L S F K K       P R L       P F L         A H P 2 D (DUST) (1-127       353       N E G L A L S F K K       P R L       P F L       P S Y         A H P 2 D (DUST) (1-127       353       N E G L A L S F K K       P R L       P S Y       P A P A A A A A A A A A A A A A A A A A			
AP AP 33 (0 GTP H1)/L+48       427       IE K V 10 V D F AD D P GL C       P C         Gm AP 44 (VH KG) (1/42)       63       N E GL AH Y 1 N = P C       P C       F K V         SoP AP (IDALZ2K3 T3) (1/56)       454       N E K I G M D H A D D P G K C P C P D O H H P E F       G G       L C H L H F TS G P A G K F C W D G P E W         M + W AP (IDALZ2K3 T3) (1/56)       454       N E K I D H A D D P G C P P G D I H P E F       G G       L C H L H F TS G P A G K F C W G G P E G D H A D P G C C P P G D I H D E F       G G       V H L H F TS G P A G K F C W G R Q E W         P P AP (IASK12) (1/537)       455       N E E V D V A H A D S G L C P G P G D I V E Y       G G       V C H L I F TS G P A G K F C W C R Q E W         O P AP (IASC3) (1/52)       457       N E K I D D H A D D P G C C P G O N H E F       G G       V C H L II F TS G P A G K F C W C R Q F G W         O P AP (IASS0) (1/42)       358       N E G L A T W TR       P P       G G       V H L II F TS G P A G K F C W C R Q F G W         O P AP (IASS0) (1/42)       358       N E G L A T W TR       P R Q       G G       V H L II F TS G P A G K C W C R P G O H P E F       G G       V H L II F TS G P A G K C W C R Q F G W         O P AP (IASS0) (1/22)       358       N E G L A T W TR       P R Q O P A C (IASS0) (1/4)       S R L E G A N F T C R A G K C W C R P G O H P E F       G G C V V H L II F TS G P A G K C W C R P G N R C (IA S K T C W C R P A D (I			
Gm P#4 (V9HXG/1/142       151       IE C L A HK Y II       P C       P C       P C       P C         ShP A (AAL25R3Ta)/1-56       454       IE K I D I D HA D D P GK C P P S D M P E F       G C       C H N FT S G P A K GK F C WD Q P EW         HW AP_C (OPKLS)/1-56       454       IE K I D I D HA D D P GK C P P S D M P E F       G C       C C H N FT S G P A K GK F C WD Q P EW         W PP AP A (BASDS)/1-522       451       IE K I D I D HA D D P GK C P P S D M P E F       G C       V C K S N FT F G A A K GK F C WE R Q E W         0 P AP 3 (B2CX81/1-522       451       IE K I D I D HA D D P GK C P G D M P E F       G C       V C H N FT S G P A K GK F C WE R Q E W         0 P AP 3 (B2CX81/1-522       457       IE K I D I D HA D D P GK C P G D M P E F       G C       V C H N FT S G P A K GK F C WE R Q E W         0 P AP 3 (B2CX81/1-522       457       IE K I D I D HA D D P GK C P G D M P E F       G C       V C H N FT S G P A K GK F C WE R Q E W         AP AP 21 (D2UX1/1-145       380       IE G I A N F T D       P P N       A F A C 2 (B3C3/1/1-62)       P N       P P N         AP AP 21 (D3UX1/1-147       350       IE G I A N F T D       P Q       P P N       P P N       P P N         AP AP 21 (D3UX1/1-453       380       IE G I A N F T D       P Q       P P N       P P N N         AP AP 21 (D3UX1/1-453 <t< td=""><td></td><th></th><td></td></t<>			
ZmP P_c(QPRLS)/1.366       456       IEK IGMUNA DDPGKCP SPSDNHPEF-       GG-       CCHLNFTSGPAKGKFCWDGQFEW         SbPP(ADLSSP38/1.366       450       IEK IDTDHADDPGKCP SPSDNHPEF-       GG-       CCHLNFTSGPAKGKFCWDQQFEW         MPPAF_CQNRLS)/1.367       435       IEK IDTDHADDPGKCP SPGDNHPEF-       GG-       VCRLNFTSGPAKGKFCWDQFFW         DPAP4(B8003)/1.622       457       IEK IDTDHADDPGKCP AGDNHPEF-       GG-       VCRLNFTSGPAKGKFCWDQFFW         DPAP4(B8003)/1.622       457       IEK IDTDHADDPGKCP AGDNHPEF-       GG-       VCRLNFTSGPAKGKFCWDQFKCP         DPAP4(B8003)/1.622       457       IEK IDTDHADDPGKCP AGDNHPEF-       GG-       VCRLNFTSGPAKGKFCWDQFKCP         APAP3(G02371/1932       350       IEGLATNFTD       PO       PO       PO         APAP3(G02371/1942       350       IEGLATSKK       PF       PO       PO         APAP32(G0350/1/1463       358       NEGLALSSKK       PF       PO       PO       PF         APAP32(G0350/1/1463       350       NEGLALSSKK       PF       PO       PF       PO       PF       PF <td>1</td> <th></th> <td></td>	1		
SbPAP (AD125K78)(1)-56       45K       EK 10 1 DH AD DP 4K C P S G D M P E F _ G _ G _ V C H LN FT S G P AK G K F C WD Q P E W         MP AP (S0P12)(1)-57       43S       N T E EV DV A HA D D S G C P S G D G M V P E Y _ G G _ V C H LN FT S G P AK G K F C WE Q P E W         D9 APA (S0S03)(1-622 457 N T EK 1D 1 DH AD D P 6K C P G P G D M V P E Y _ G G _ V C H LN FT S G P AK G K F C WE K Q F E W       AG - V C H LN FT S G P AK G K F C WE K Q F E W         D9 APA (S0S03)(1-622 457 N T EK 1D 1 DH AD D P 6K C P G P G D M V P E Y _ G G _ V C H LN FT S G P AK G K F C WE K Q F E W       AF APA (S0S03)(1-622 457 N T EK 1D 1 DH AD D P 6K C P G P G D M V P E Y _ G G _ V C H LN FT S G P AK G K F C WE K Q F E W         D9 APA (S0S03)(1-622 457 N T EK 1D 1 D H AD D P 6K C P G P G D M P E F _ G G _ V C H LN FT S G P AK G K F C WE R Q F E W       AF APA (S0GV27)(1-395 328 N E G LA LT N K Q F E M _ F P G _ F Q _ V C H LN FT S G P AK G K F C WE R Q F E W         AF APA (S0GV27)(1-395 328 N E G LA LS F K _ P P G _ F Q _ V C H LN FT S G P AK G K F C WE R Q F E W _ AF APA (S0GV27)(1-395 338 N E G LA LS S M T E G LA LS S M	1 17	-	
He <sup>2</sup> Pe _ (I G PK (S) / L564       452       N I E K I D T D H A D D P G C P P G D H O P E T       G G       V C R S N F T F G P A V G K F C WE G P D W         OP PP 39 (062CM (I - 622       457       N I E K I D I D H A D D P G K C P G P G D H P E F       G G       V C R S N F T F G P A V G K F C WE G P D W         OP PP 41 (08309 (I - 622       457       N I E K I D I D H A D D P G K C P G P G D H P E F       G G       V C H L H T S G P A K G K F C WE G P E W         OP PP 41 (08007 (I - 122)       457       N I E K I D I D H A D D P G K C P G P G D H P E F       G G       V C H L H T S G P A K G K F C WE G P E W         OP PP 41 (08007 (I - 122)       358       N I E G L A T S K K       P P       P E I       G G       P S Y         AP P 20 (09107 (I - 123)       358       N E G L A T S K K       P P       P P       P S Y       P S Y         I I P P 30 (09107 (I - 123)       358       N E G L A T S K K       P P       P P       P N Y         I P P 40 (291007 (I - 143)       358       N E G L A T S K K       P Q       P P Y       P N Y         R P P2 (03207 (I - 144)       358       N E G L A T S K K       P Q       P N Y       R P P P 1 (09131 (I - 44)       S N I E G L A T S K K       P Q       P N Y         R P P 2 (03208 (I - 143)       N I E G L A T S K K       P Q       P S Y       R P P 2 (03207 (I -	= · · · ·		
Pp.F.P.       Pp.F.P.       G.G.       VCRLNFTGPAVGKFCWGE       PDW         OPAP3(G2CX8)/1-622       457 NIEKIDIDHADDPGKCPGPGDNHPEF-GG-VCHUFTGPAKGKFCWEG       PEW         OPAP3(G2CX8)/1-622       457 NIEKIDIDHADDPGKCPGPGDNHPEF-GG-VCHUFTGPAKGKFCWEG       PEW         APAP3(G2CX8)/1-622       457 NIEGIANIFTD       PG       GG-VCHUFTSGPAKGKFCWEG       PEW         APAP3(G2CX8)/1-622       457 NIEGIANIFTD       PG       GG-VCHUFTSGPAKGKFCWEG       PEW         APAP3(G2CX8)/1-433       38 NIEGIALTEYK       PP       SEPL       FE         IPAP3(G2D718)/1-473       355 NIEGIALTEKK       PP       SEPL       FE	1 17		
Op <sup>2</sup> #P3 (GGCCG)/L+C22       457 N   EK   D   D   A D D P GK CP G P G D N H P EF       G G       V C H LN FT S G P A K GK F CWEK Q P EW         AP #42 (DSU227/1)-139 G 38 N   E G   A N   F T D       P G       P G       P G         AP #22 (DSU27/1)-127 36 D N   E G   A N   F T D       P G       P G       P S P L         IbP #3 (DSU27/1)-127 36 D N   E G   A N   F T D       P G       P G       P S P L         IbP #3 (DSU27/1)-127 36 D N   E G   A N   F T D       P G       P G       P S P L         IbP #3 (DSU27/1)-127 36 D N   E G   A N   F T D       P G       P A (D N )			
Og P AP   88309/1-622       457       I EK ID DI HAD DP GK CP GP GDI HP EF       G       V CH LN FTS GP AK GK FCWEK Q F EW         AP AP 3 (Q G327/1/347       380       I EG LA NI FT D       P Q       P P         AP AP 3 (Q G327/1/347       380       N EG LA LS FK K       P P       P P         AP AP 22 (Q S3A0/1/443       350       N EG LA LS FK K       P P       P P         AP AP 21 (Q SUM // 1/437       350       N EG LA LS FK K       P Q       P P         Lip AP (Q DM NO7/1/455       380       N EG LA LS FK K       P Q       P N Y         AP AP 21 (Q SUM // 1/437       350       N EG LA S MT FD       P Q       P N Y         R CP AP 2 (Q SOSM // 1/455       380       N EG LA S MT FD       P Q       P P N         Ib P AP 1 (Q SU M // 1/445       373       N EG LA S MT FD       P Q       P S Y         Gm P AP 1 (Q SU M // 1/445       373       N EG LA T NMT E       P Q       P S Y         Gm P AP 1 (Q SU M // 1/445       373       N EG LA T NMT E       P Q       P S Y         Gm P AP 1 (Q SU M // 1/445       373       N EG LA T NMT E       P Q       P K Y         I M P AP 1 (Q SU M // 1/446       374       N EG LA T NMT E       P Q       P K Y         I M P AP 1 (Q SU SO // 1/446			
AP AP3 (09:037/1/1-39       95       N       EG I AN IFT D       P       P         AP AP2 (09:017/1-427       355       N       EG I AN IFT D       P       P         IbP AP3 (09:217/1-437       355       N       EG I AN IFT D       P       P         IbP AP3 (09:218/1/1-427       355       N       SE GI A T EMT Q       P       Q       P       P         IbP AP3 (09:218/1/1-427       355       N       SE GI A T EMT Q       P       Q       P	1		
ARP AP20 (09UXT/1/1427 360 N       L E G L A T K Y E D       P N       P E I         ARP AP22 (082340/1/1434 356 N R E G L A T K K Y E D       P P       P P       P P         I (P AP2 (0807) (1/1473 366 N G G L A T K K Y E D       P Q       P P       P P         I (P AP2 (10807) (1/1473 366 N G G L A S K K K       P P       P Q       P P         I (P AP2 (10807) (1/1473 366 N G G L A S K K K       P Q       P Q       P N Y         R P AP2 (10202) (1/1463 368 N G E G L A S K K T E       P Q       P Q       P N Y         R P AP2 (1020318) (1/1463 338 N G E G L A S K M T E       P Q       P P D H       I         I (P AP2 (102318) (1/1464 337 N E G L A T N M T E       P Q       P S Y       I         ARP AP2 (1023244) (1/1466 337 N E G L T O MMQ       P Q       P K Y       I         ARP AP2 (1032341) (1/1463 337 N E G L T T K M T E       P Q       P K Y       I         M P AP2 (103030/1/1466 337 N E G L A T N M T E       P Q       P K Y       I         M P AP2 (108030/1/1466 338 N E G L A T M M T E       P Q       P K Y       I         M P AP2 (108030/1/1466 338 N E G L A S K F E D       P Q       P K Y       I         M P AP2 (108030/1/1476 388 N E G L A T M K T E       P Q       P K Y       I         M P AP2 (108030/1/1476 388 N L G C L A T M K T E			
ABPAP22 (QS2840/1/1434       355       N E G LA LS F.K.K       P D         IBPAP3 (QS2F18)/1427       355       N E G LA LE F.K.K       P D         IBPAP3 (QS2F18)/1427       355       N E G LA LE F.K.K       P D         LpPAP (QSM07)/1455       388       N G G LA AS SMT E       P D         LpPAP (QSM07)/1455       393       N LE G LA TIMAT D       P O         IBPAP3 (QSD23)/1465       393       N LE G LA TIMAT D       P O         GRP AP1(QQS13)/1464       315       N LE G LA TIMAT D       P O         GRP AP1(QQS13)/1464       315       N LE G LA TIMAT E       P O         GRP AP1(QQS13)/1464       315       N LE G LA TIMAT E       P O         AfP AP23 (QSS24/1/1464       315       N LE G LA TIMAT E       P O         AfP AP23 (QSS24/1/1464       315       N LE G LA TIMAT E       P O         AfP AP23 (QSS25/1/1461       335       N LE G LA TIMAT E       P O         AfP AP23 (QSSS05/1/1463       358       N LE G LA TIMAT E       P O         AFP AP1 (QS4KZ3/1/1461       353       N LE G LA TIMAT E       P O         AFP AP1 (QS4KZ3/1/1461       353       N LE G LA TIMAT E       P O         AFP AP1 (QS4KZ3/1/1461       353       N LE G LA TIMAT E       P O	1		
IbP AP3   092P 18//1-427       355       N E G LA T EMT Q       P Q         APP AP2 11 (QUHA/1/1-47)       353       N R G G LA S IM K       P Q         Lp AP AP2 11 (QUHA/1/1-47)       358       N R G G LA S IM K       P Q         Re PA 22 103 SD23 /1-463       388       N E G LA S IM T E       P Q         APP AP2 103 SD23 /1-463       381       N E G LA S IM T D       P Q         APP AP2 103 SD23 /1-464       311       N E G LA T IM T D       P Q         APP AP1 1009 131 /1-444       313       N E G LA T IM T E       P Q         APP AP1 1009 131 /1-464       311       T LE G LA T IM T E       P Q         APP AP1 1009 131 /1-464       312       N LE G LA T IM T E       P Q         APP AP2 102 03244 /1-469       323       N LE G LA T IM T E       P Q         APP AP2 104 (SQUZ)/1-465       328       N LE G LA T IM T E       P Q         APP AP2 104 (SQUZ)/1-465       328       N LE G LA T IM T E       P Q         APP AP2 104 (SQUZ)/1-465       328       N LE G LA T IM T E       P Q         APP AP2 104 (SQUZ)/1-463       38       N Q E G LA AS R F S D       P Q         APP AP2 104 (SQUZ)/1-463       38       N Q E G LA AS K F L D       P Q       P P Y         APA AP2 104 (SQUZ)/1-463	1		
AP AP21 [QBLN4//1-437       363       N R E G L A L R F K K       P Q       P Q       P N         LpP AP [QBSURP]/1-455       388       N Q E G L A A S M T E       P Q       P N Y         N R P AP2 [QBSURP]/1-465       388       N Q E G L A A I T N N T D       P Q       P P N Y         AP AP2 [QSD2]/1-465       381       N L E G L A T N N T D       P Q       P P Y         AP AP 21 [QG9131/1-464       391       N L E G L A T N N T D       P Q       P P Y         AP AP 21 [QG9131/1-464       391       N L E G L A T N N T E       P Q       P P Y         AP AP21 [QG8302/1-466       392       N L E G L A T N N T E       P Q       P K Y         AP AP21 [QG8302/1-466       393       N L E G L A T N N T E       P Q       P K Y         MP AP21 [QG4123/1-461       393       N L E G L A T N N T E       P Q       P K Y         MP AP1 [QG4123/1-461       393       N L E G L A T N N T E       P Q       P K Y         MP AP1 [QG4123/1-461       393       N L E G L A T N N T E       P Q       P K Y         MP AP1 [QG4123/1-461       393       N L E G L A T N N T E       P Q       P K Y         MP AP1 [QG4123/1-461       393       N L E G L A T N N T E       P Q       P K Y         UBAP1 [QG412/1-46	AtP AP 22   Q85340  /1-434		
L pPAP (	IbP AP 3   Q9ZP 18  /1-427		
R:P:#2': [B95XP8]/1.463       368       N       D       E       IA       N       F       D       P       D	AtP AP 2 1   Q9 LXI4   / 1-437		
IbPAP2[095D29]/1465       333 N L E G L A T NMT D       P Q       P P Y         ARPAP11(09518)/1441       373 N L E G L A NMT E       P Q       P S Y         ARPAP12(09518)/1446       392 N L E G L A NMT E       P Q       P K Y         ARPAP12(035224)/1466       392 N L E G L A NMT E       P Q       P S Y         ARPAP12(03523244)/1466       392 N L E G L A NMT E       P Q       P K Y         ARPAP12(035305)/1476       393 N S E G L T D MMG       P Q       P K Y         MRPAP1(04KU02)/1465       392 N L E G L A T NMT E       P Q       P K Y         OsPA2(085305)/1476       393 N Q E G L A S R F S D       P Q       P P Y         OsPA2(085305)/1476       393 N Q E G L A S R F S D       P Q       P S Y         UAP2(08LGLI)/1463       391 N Q E G L A S R F S D       P Q       P S Y         UAP2(08LGLI)/1463       391 N Q E G L A S R F S D       P Q       P S Y         UAP2(08LGLI)/1463       391 N Q E G L A S R F N D       P Q       P S Y         VARPAP1(093WR/1/1463       391 N Q E G L A S R F N D       P Q       P S Y         VARPAP1(093WR91/1476       391 N Q E G L A S R F N D       P Q       P S Y         VARPAP23(Q3WP09)/1473       391 N Q E G L A S R F N D       P Q       P S Y         VARPAP23(Q65M	LpP AP   Q9MB07 /1-455		
AtPAP 11(Q9S1B)/L441       373       N       I E G I A N S F T D       P Q       P P Q         ArPAP 1(Q0S1S1/L464       391       T L E G I A N S F T D       P Q       P Q       P S Y         ArPAP 12(Q3S24/L/1463       393       N S E G L L T D MMQ       P Q       P S Y       P S Y         ArPAP 12(Q3S252/L/1463       393       N S E G L L T D MMQ       P Q       P K Y       P K Y         MrPAP 1Q4KU02/L1465       392       N L E G L A T NM T E       P Q       P K Y       P K Y         MrPAP 1Q4KU02/L1465       392       N L E G L A T NM T E       P Q       P P Q       P K Y         UAP 1Q9XW7/L460       398       N L E G L A S K F S D       P Q       P Q       P S Y         UAP 1Q05G0/L1475       396       N Q E G L A S K F L D       P Q       P S Y       Y         VP AP2 1Q76AC1/L1457       396       N Q E G L A S K F L D       P Q       P S Y       Y         VP AP2 1Q76AC1/L1477       396       N Q E G L A S K F N D       P Q       P S Y       Y         ArP AP 10 (Q9S V9/L483       396       N I E G I A N S F Y D       P Q       P S Y       Y         ArP AP (Q3GV9/L4743       391       N Y G Y I D S NMI I Q       P Q       P S Y       Y	RcP AP 2   B95XP8   /1-463	368	I <mark>Q E G I A A N F T D</mark> P Q
GmPAP1[Q09131//1464       391       T       L E G L A N MT E       P Q       P K Y         ARP AP25[Q23244//1465       392       N E G L A N S FT D       P Q       P S Y         ARP AP25[Q23244//1465       393       N E G L T N MT E       P Q       P K Y         MRP AP1[Q84K23//1461       393       N E G L A T N MT E       P Q       P K Y         MRP AP1[Q84K23//1461       393       N E G L A T N MT E       P Q       P K Y         MRP AP1[Q84K23//1465       392       N E G L A S K F S D       P Q       P C         OS P V2 A22 (Q3F C C) 1476       385       N E G L A S K F L D       P Q       P S Y         V U AP2 (Q3 SUM7//1460       385       N E G L A S K F L D       P Q       P S Y         V P V A22 (Q3F C C) 1475       395       N E G L A S K F L D       P Q       P S Y         V P V A21 (Q3 SUM7//1460       395       N E G L A S K F L D       P Q       P S Y         M P A P3 (Q3 SUM7//1463       395       N E G L A S K F L D       P Q       P S Y         M P A P4 10 (Q3 SUM/1477       395       N E G L A S K F L D       P Q       P S Y         M APA P3 (Q3 SUM7/1468       395       N E G L A S K F L D       P Q       P S Y         M APA P3 (Q4 SUM7)/1418       395 <td>IbP AP 2   Q9 SD Z9   /1-465</td> <th>393 🖡</th> <td>LEGLATNMTD</td>	IbP AP 2   Q9 SD Z9   /1-465	393 🖡	LEGLATNMTD
AtP AP25 [023244]/1466       392       N E G L T D MMO       P Q       P S Y         AtP AP 12 [038324]/1466       393       N E G L T D MMO       P Q       P K Y         NtP AP 12 [038324]/1465       393       N E G L T T MMT E       P Q       P K Y         MtP AP 12 [04KU02]/1465       393       N E G L A T MMT E       P Q       P K Y         OsP AP2 [085505]/1476       389       N E G L A S R FS D       P Q       P D Y         IsAP 1[039VM7/1460       389       N E G L A S K FS D       P Q       P P Y         UAP2 [078612]/1475       396       N E G L A S K FS D       P Q       P S Y         UAP2 [078612]/1476       391       N E G L A S K FS D       P Q       P S Y         UAP2 [078612]/1476       396       N E G L A S K FS D       P Q       P S Y         AtP AP 10 [039V9/1488       396       N E G L A S K FN D       P Q       P K Y         TaACP [04PKL1]/1477       390       N E G L A S K FN D       P Q       P S Y         AtP AP 6 [03C3 ID /1466       392       N E G L A S K FN D       P Q       P S Y         AtP AP 6 [03C3 ID /1466       392       N E G L A S K FN D       P Q       P S Y         AtP AP 6 [03C3 ID /1466       392       N E G L A S K FN D       <	AtP AP 11   Q95 18   /1-441	373	
AtP AP 12 [ 038924/1/1469       397       N       E G L L T D MMQ       P Q       P V         INP AP [04KU02/1/1465       393       N L E G L T T K MT E       P Q       P K Y         MtP AP [104KU02/1/1465       392       N L E G L T T K MT E       P Q       P V         OSPAP2 (0S505/1/1475       398       N L E G L A T K M Q       P Q       P V         LGAP1 (093VM7/1/1460       389       N L E G L A S K F L D       P Q       P Q       P S Y         PVP AP2 (0764C1/1/1457       396       N L E G L A S K F L D       P Q       P Q       P S Y         ULAP2 (0816L1/1/1457       395       N L E G L A K MT E       P Q       P S Y       P K Y         PVP AP2 (0764C1/1/1457       396       N L E G L A K MT E       P Q       P S Y       P K Y         AtP AP 10 (095VV)/1468       396       N L E G L A K MT E       P Q       P Q       P K Y         AtP AP 10/Q93WP4 //1481       395       N Q E G L A S R F N D       P Q       P Q       P V         AcP AP (093WP4 //1481       395       N Q E G L A S R F R D       P Q       P Q       P S Y         AcP AP3 (02KO9 //1473       398       N E E G L A S R F R D       P Q       P Q       P S Y         AcP AP3 (02KO9 //1473       3	GmP AP 1   009 13 1   / 1-4 64	391 7	
INPAP (Q84K22)/1461       333       N IEGLTTKMTE       PQ       PK         MPAP 1(Q4KU02)/1465       382       N LEGLATMMTE       PQ       PQ         OSPAP 2(Q8505)/1476       383       N LEGLAE       TMK       PQ       PQ         UAP 1(Q3W7/1460       389       N LEGLAE       TMK       PQ       PS         PWPAP2(Q764C1/1457       386       N LEGLAE       TMK       PQ       PS         UAP2(Q8L5L1/1463       381       N LEGLAE       TMK       PQ       PS       PS         AtPAP1(Q9SW7/1468       386       N LEGLATKMTE       PQ       PS       PS       Y         AtPAP1(Q4SU510/1466       391       N GEGLASK FLD       PQ       PS       Y         TaACP (4PKL1/1477       390       N GEGLASK FND       PQ       PS       Y         AtPAP3(Q3KF09/14740       392       N LEGLAE KNTE       PQ       PS       Y         AbPAP3(Q4S050/1448       395       N GEGLAE KNTE       PQ       PS       Y         AbPAP3(Q4S09/14473       395       N GEGLAE KNTE       PQ       PS       Y         AbPAP3(Q5050/148       395       N GEGLAE KNTE       PQ       PS       Y         AbPAP3(Q4S09/1461       <	AtP AP 25   023244   /1-466	392 🖡	I E G I A N S F T D P Q
NHR AP   Q84K23   /1461       393       N       I E G L T T K MT E       P Q       P Q       P K Y         MtP AP I (Q4KU02 / /1463       392       N L E G L A S R F S D       P Q       P Q       P D Y         OsP AP I (Q4KU02 / /1463       383       N L E G L A S R F S D       P Q       P Q       P D Y         UAP 1 (D33WT//1460       383       N L E G L A S K F L D       P Q       P S Y       P S Y         PVP AP 2 (QFGC1 / /1457       395       N L E G L A S K F L D       P Q       P S Y       P S Y         Atr AP 10 (Q35V9 / /1463       391       N Q E G L A S K F L D       P Q       P S Y       P S Y         Atr AP 10 (Q35V9 / /1463       391       N Q E G L A S K F L D       P Q       P C       P K Y         Ta ACP (C4PKL1 / /1477       390       N Q E G L A S K F N D       P Q       P Q       P D Y         Atr AP 10 (Q35VP4 / /1481       395       N Q E G L A S K F N D       P Q       P Q       P S Y         AcAP AP 11 (Q35KD0 / /1478       391       N S E G L A S K F N D       P Q       P Q       P S Y         AcAP AP 31 (Q35KD0 / /1478       395       N Q E G L A S K F N D       P Q       P Q       P S Y         AcAP AP 31 (Q35KD0 / /1478       395       N Q E G L A S K F N D <td>AtP AP 12   038924   /1-469</td> <th>397</th> <td>I<mark>S EGLLTDMMQ</mark>РКҮS 41</td>	AtP AP 12   038924   /1-469	397	I <mark>S EGLLTDMMQ</mark> РКҮS 41
MtP AP 1 [Q4KU02]/1-465       392       N L E G L A T NMT E       P Q       P E Y         OSP AP 2] (Q8505/1/1-76       389       N L E G L A S R F S D       P Q       P D Y         La AP 1 [Q93505/1/1-76       389       N L E G L A S K F L D       P Q       P S Y         La AP 2 [Q754C11/1-457       396       N L E G L A T K M T Q       P Q       P S Y         MLP 2 [Q816L1/1-463       391       N Q E G L S I NMT Q       P Q       P S Y         AtP AP 10 [Q93V9 1/1-468       395       N L E G L A T K M T E       P Q       P S Y         AtP AP 10 [O293V9 1/1-468       395       N L E G L A T K M T E       P Q       P K Y         Ta ACP [C4PKL1]/1-477       390       N Q E G L A W F N D       P Q       P E Y         Ta ACP [C4PKL1]/1-477       390       N Q E G L A E R F S E       - S Q P D Y       AcP AP 2 [Q3WP4 1/1-481       395       N Q E G L A E R F S E       - S Q P D Y         AcP AP 3 [Q3WP69]/1-470       398       N L E G L A K NMT E       P Q       - P S Y       AcP AP 3 [Q3WP69]/1-477       398       N E G L A S R F R D       P Q       - P S Y         AcP AP 3 [Q5W509]/1-473       391       N E G L A S R F R D       P Q       - P S Y       AcP AP 3 [Q5W509]/1-473       390       N E G L A S R F R D       P Q       <		393	I I E G L T T K M T E P Q
OsPAP2/085505//1476       389       N       CGLASRFSD       P <t< td=""><td>MtP AP 1   Q4KU02   /1-465</td><th>392</th><td>ILEGLATNMTE</td></t<>	MtP AP 1   Q4KU02   /1-465	392	ILEGLATNMTE
La AP 1 [Q33UM7]/1-460       383       N L E G L A _ TMK Q       P Q       P Q         PVP AP2 [Q764 C1]/1-457       396       N Q E G L A S K F L D       P Q       P Q         UAP2 [Q816L1]/1-463       391       N Q E G L S I NMT Q       P Q       P Q         AttP AP 10 [Q93V9]/1-468       396       N E G L A T KMT Q       P Q       P Q         PVP AP 11 [P80366]/1-459       391       N Q E G L A K K MT E       P Q       P Q         Ta ACP [C4PKL1]/1-477       390       N Q E G L A WR F N D       P Q       P Q         AttP AP 6 [Q9 C510]/1-466       392       N L E G L A K N F V D       P Q       P Q         AcP AP [Q93WP4]/1-481       395       N Q E G L A & R F N D       P Q       P Q         AcP AP [Q93WP4]/1-481       395       N Q E G L A & R F N D       P Q       P Q         StP AP3 [Q6J5M8]/1-477       389       N E G L A & R F N D       P Q       P Q         StP AP3 [Q6J5M8]/1-473       390       N Q E G L A & R F N D       P Q       P S Y         Ib PAP 1 [Q95D0]/1-473       391       N Q E G L A & R F N D       P Q       P S Y         Ib PAP 1 [Q84Y84]/1-423       396       N Q E G L A & R F N D       P Q       P S Y         Ib PAP 1 [Q84Y37]/1-423       390       <	1		
PvPAP2/Q764C1//1457       396       N Q E G L A S K F L D       P Q       P P Q         UAP2/Q8L6L1//1463       391       N Q E G L A S K F L D       P Q       P S Y         AtP AP 10/Q9SV9//1468       396       N I E G L A T K MT E       P Q       P K Y         PvP AP 11/P80366//1459       391       N Y G V I D S NMI Q       P Q       P K Y         To ACP (04PKL1//1477       390       N Q E G L A WR F N D       P Q       P D Y         AtP AP 60/Q9CS10//1466       392       N I E G I A N S F V D       P Q       P S Y         AcP AP (039WP4//1481       395       N Q E G L A WR F N D       P Q       P S Y         AcP AP (039WP4//1470       398       N L E G L A K NMT E       P Q       P S Y         StP AP 3/Q (05/508//1477       390       N S E G L A S R F R D       P Q       P S Y         StP AP 3/Q (05/508//1477       390       N Q E G L A G R F T E       P Q       P Q         GmP AP 3/Q (04/5508//1477       390       N Q E G L A S R F R D       P Q       P D Y         M LP AP 10/Q S L S P (1/1477       390       N Q E G L A S R F T D       P Q       P D Y         GmP AP 3/Q (04/5508//1477       390       N Q E G L A S R F T D       P Q       P D Y         UP P 0/Q (08/VF4//147       <			
UAP2/Q8L6L1//1463       391       N       Q E G L S I NMT Q       P Q       P S Y         ArP AP 10   Q9S/Y9 / 1468       396       N       E G L A T K MT E       P Q       P K Y         PvP AP 1/P80366/1/459       391       N Y G V I D S NMI Q       P Q       P K Y         Ta ACP (C4PKL1/1/1477       390       N Q E G L A WR FND       P Q       P Q         ArP AP 6 (Q C510 / 1466       392       N I E G L A S R FV D       P Q       P S Y         ArP AP 32 (QSXF09 / 1470       398       N L E G L A K R MT E       P Q       P K Y         SQ P D Y       ArP AP 32 (QSXF09 / 1477       398       N S E G L A S R FR D       P Q       P Q         StP AP 3 (QSISM8 / 1477       390       N Q E G L A S R FR D       P Q       P S Y       P S Y         ArP AP 2 (Q 949 Y3 / 1475       390       N Q E G L A S R FT D       P Q       P Q       P S Y         ArP AP 3 (QSISM5 / 1488       395       N Q E G L A S R FT D       P Q       P Q       P D Y         GmP AP 3 (QSISM5 / 1488       396       N Q E G L A S R FT D       P Q       P D Y       P D Y         GmP AP 3 (QSYG79 / 1-151       428       N Q E G L A S R FT D       P Q       P D Y       P D Y         GmP AP 3 (QSYG79 / 1-153       <			
AttP AP 10 / Q9SIV9 //1468       396       N I E G L A T K MT E       P Q       P P Q       P K Y         P vPAP 1/P80366//1475       391       N Y G V I D S NMI Q       P Q       P Q       P E Y         Ta ACP (C4PKL1/1477       390       N Q E G L A WR F ND       P Q       P Q       P D Y         AttP AP 6/Q9C510 //1466       392       N I E G I A N S F V D       P Q       P Q       P S Y         AcP AP 32 / Q9XF09 //1470       398       N L E G L A K NMT E       P Q       P Q       P V         StP AP3 / Q6J5M8 //1477       398       N S E G L A S R F R D       P Q       P Q       P S Y         AtP AP 26 (Q949 Y3 //1473       401       N S E G L A S R F R D       P Q       P Q       P S Y         AtP AP 3 / Q6J5M8 //1477       390       N Q E G L A A R F R D       P Q       P Q       P D Y         UAP 11 (Q8 L5E1 //1477       392       N Q E G L A S R F T D       P Q       P D Y       U P D Y         GmP AP3 / Q6YG79 //1-512       428       N Q E G L A S R F T D       P Q       P Q       P E Y         La AP2 / Q9XZ41/1-638       393       N I E G L A N M T E       P Q       P E Y       L A AP2 / Q9XZ41/1-633       393       N I E G L A N M T E       P Q       P K Y         UPP			
PvPAP1/P80366//1-459       391       N Y GV I D S NMI Q       P Q       P Q       P P V         Ta ACP / C4PKL1//1-477       390       N Q E G L A WR F N D       P Q       P Q       P D V         AcP AP 6/ Q9 CS 10 //1-466       392       N I E G L A NS F V D       P Q       P Q       P S V         AcP AP 7/Q3WP4 //1-481       395       N Q E G L A E R F S E       P Q       P Q       P S V         AcP AP 3/Q6/D9/D1/1-470       398       N L E G L A K NMT E       P Q       P Q       P K V         StP AP 3/Q6/D9/M8//1-477       390       N S E G L A S R F R D       P Q       P Q       P K V         StP AP 3/Q6/D9/1473       401       N S E G L A S R F R D       P Q       P Q       P C V       P V         AcP AP 26/Q949Y3 //1-475       390       N Q E G L A G R F T E       P Q       P Q       P D V Y         RcP AP 3/B95XP 6//1-488       396       N Q E G L A G R F T E       P Q       P D V Y       P D V Y         GmP AP 3/Q6YG79 //1-512       428       N Q E G L A S R F L D       P Q       P D V Y       P D V Y         UAP 1/08L5E1//1-477       393       N I E G L A N NMT E       P Q       P E V Y         UAP 1/08LVX11//1-615       542       A S L A E F A P I N       P Q       P E	AtP AP 10 109 SI V9 1/1-465	396	
Ta ACP / C4PKL1/1/1-477       330       N Q E G L A WR F N D       P Q       P D Y         AtP AP 6/Q9 C510 / 1-466       392       N I E G I A N S F V D       P Q       P S Y         AcP AP 1/Q93WP4 / 1/-481       355       N Q E G L A E R F S E       P Q       P S Y         AoP AP 32 (Q93K09 / 1-470       388       N L E G L A K NMT E       P Q       P K Y         StP AP 3 (Q6J5M8 / 1-477)       389       N S E G L A S E M T Q       P Q       P Y         IbP AP 1 (Q95E00 / 1-473       401       N S E G L A S E M T Q       P Q       P Y         IbP AP 26 (Q94 Y 3) / 1-473       390       N Q E G L A G R F T E       P Q       P Q       P S Y         ArP AP 26 (Q94 Y 3) / 1-473       390       N Q E G L A A R F R D       P Q       P Q       P D Y         UAP 1/Q8L5E1/1/1-477       392       N Q E G L A S R F T D       P Q       P D Y       U P D Y         GmP AP 3/ Q9/X073 / 1-512       428       N Q E G L A S R F T D       P Q       P Q       P E Y         GmP AP 3/ Q9/XV11/1/-613       393       N I E G L A N NMT E       P Q       P E Y       P E Y         UPP D4 / Q8/XV11/1/-615       542       A S L S T F T S L K       T T W       P E Y       P E Y         UPP D2 / Q8/X71/1/-612       5			
AtP AP 6 j Q9 C5 10 // 1-466       392       N       I E G I A N S F V D       P Q       P P Q         AcP AP j Q93WP4 // 1-481       395       N       Q E G L A E R F S E       S Q P D Y         AoP AP 32 (Q95K09 // 1-470       388       N L E G L A K NMT E       P Q       P K Y         StP AP 3 (Q65M8 // 1-477       389       N S E G L A S E MT Q       P Q       P K Y         IbP AP 1 (Q95B0 // 1-473       401       N S E G L A S E MT Q       P Q       P Q       P S Y         ArP AP 26 (Q94 Y 3) // 1-473       390       N Q E G L A A R F R D       P Q       P Q       P D Y         ArP AP 26 (Q94 Y 3) // 1-473       390       N Q E G L A A R F R D       P Q       P D Y       P D Y         ArP AP 26 (Q94 Y 3) // 1-473       390       N Q E G L A S R F T D       P Q       P D Y       P D Y         UAP 1/ Q8L5E1 // 1-477       392       N Q E G L A S R F T D       P Q       P D Y       P D Y         GmP AP 3 (Q6YGT9 // 1-512       428       N Q E G L A S R F T D       P Q       P Q       P E Y         GmP AP 3 (Q8YX11 // 1-638       333       N I E G L A N NMT E       P Q       P E Y       P E Y         UPP D4 / Q8VXF6 // 1-612       539       A S L S T F T S L K       T T W       P E Y       P E Y<			
AcP AP   Q93WP4/1/1481       395       N       Q       E       L       R       S       Q       P       V       Y         AoP AP32   Q9XF09   /1470       398       N       L       E       L       P       Q       P       V       Y			
AoP AP32 (Q9XF09)/1-470       398       N LEGLAKNMTE       PQ       PK Y         StPAP3 (Q6J5M8)/1-477       389       N SEGLASRFRD       PQ       PEY         IbP AP1 (Q95800)/1-473       401       N SEGLASENTQ       PQ       PEY         AtP AP26 (Q949 Y3 //1-475       390       N GEGLASENTQ       PQ       PEY         AtP AP26 (Q949 Y3 //1-475       390       N GEGLASENTQ       PQ       PO         AtP AP26 (Q949 Y3 //1-475       390       N GEGLASENTQ       PQ       PO         RcP AP3 (B95XP6) //1-488       396       N GEGLASERFD       PQ       PO         MAP1 (Q815E1) //1-477       392       N GEGLASERFD       PQ       PO         GmP AP3 (G6YGT9) //1-512       428       N GEGLASERFLD       PQ       PEY         LaAP2 (Q9XXF4) //1-638       393       N I EGLANNMTE       PQ       PEY         LaAP2 (Q9XXF4) //1-629       556       S H = - LSDYTPSP       PQ       PK Y         UPP D1 (Q8XXF4) //1-629       556       S L A EFAP I N       TTW       TW         UPP D2 (Q8XXF4) //1-615       542       A S L A EFAP I N       TTW       TK         UPP D2 (Q8XXF6) //1-615       539       A S L S T FTS LK       TK       TK         Th AP1 (Q4RLR			
StP AP 3   Q6J5M8   /1-477       389       N S E G L A S R F R D       P Q       P P Y         IbP AP 1   Q9SB00   /1-473       401       N S E G L A S E MT Q       P Q       P Q       P S Y         AtP AP 26   Q949 Y3   /1-475       390       N Q E G L A G R F T E       P Q       P Q       P D Y         RcP AP 3   Q85XP 6 / /1-488       396       N Q E G L A G R F T D       P Q       P Q       P D Y         UAP 1   Q8 L5E1 / 1-477       392       N Q E G L A S R F T D       P Q       P Q       P D Y         GmP AP 3   Q6YG79 / 1-512       428       N Q E G L A S R F L D       P Q       P Q       P E Y         GmP AP 3   Q4Y1/1-639       393       N I E G L A N MT E       P Q       P Q       P E Y         La AP 2   Q8XXF4 / /1-629       556       S H       - L S D Y T P S P       P Q       P E Y         UPP D4   Q8VXF4 / /1-637       313       C R E K T D R FT P N       P Q       P E Y       P E Y         UPP D2   Q8VXF6 / /1-612       539       A S L S T FT S L K       T K W       T K W       T K W         Th PA P1   Q4R LR4 / /1-378       313       C R E K T D R FT P N       P E       P E K E K E K E K E K E K E K E K E K E			
IbP AP 1/Q958D0//1-473       401       N S E G L A S EMT Q       P Q       P Q       P D Y         AtP AP 26/Q949Y3//1-475       390       N Q E G L A G R F T E       P Q       P D Y         RcP AP 3/B95XP 6//1-488       396       N Q E G L A A R F R D       P Q       P D Y         UAP 1/Q8L5E1/1-477       392       N Q E G L A S R F T D       P Q       P D Y         GmP AP 3/Q6YG79 //1-512       428       N Q E G L A S R F L D       P Q       P Q       P E Y         GmP AP 3/Q6YG79 //1-512       428       N Q E G L A S R F L D       P Q       P Q       P E Y         La AP 2/Q9XU24//1-638       393       N I E G L A N NMT E       P Q       P E Y         UPP D4/Q8VXF4//1-638       393       N I E G L A N NMT E       P Q       P K Y         UPP D1/Q8VXF1//1-615       542       A S L A E F AP I N       P Q       P K Y         UPP D2/Q8VXF6//1-612       539       A S L S T F T S L K       T K W       T K W         Th P AP 1/Q4R LR 4//1-378       313       C R E K T D R F T P N       P K D W       P K D W         HsP AP 7/Q6Z IFO //1-418       373       C E E R L T P F AV F       P S D H 1       MQ D F         Mm P AP 7/Q6B X371//1-418       373       C E E L L T P F V R K       P S D H 1 <td< td=""><td>StP AP 31 06 15 M8 1 / 1_477</td><th>389</th><td></td></td<>	StP AP 31 06 15 M8 1 / 1_477	389	
AtP AP 26 (0949 Y3)/1-475       330       N       Q       E       L       P       Q       P       P       Q       P       D       D       P       D			
RcP AP3/B95XP 6//1-488       396       N Q E G L A A R F R D       P Q       P D Y         UAP1/Q8L5E1//1-477       392       N Q E G L A S R F T D       P Q       P E Y         GmP AP3/Q6YG79//1-512       428       N Q E G L A S R F T D       P Q       P E Y         GmP AP3/Q9XU24//1-638       393       N I E G L A N NMT E       P Q       P E Y         La AP2/Q9XU24//1-638       393       N I E G L A N NMT E       P Q       P K Y         UPP D4/Q8VXF1//1-612       556       S H       L I S D Y T P S P       P V W         UPP D1/Q8VX11//1-615       542       A S L A E F A P I N       T T W         UPP D2/Q8VXF6//1-612       539       A S L S T F T S L K       T K W         TnP AP1/Q4RLR4//1-378       313       C R E K T D R F T P N       P K D W         HsP AP7/Q62/IF0//1-438       373       C E E R L T P F A V F       P S D H 1       MQ D F         MmP AP7/Q8BX37//1-438       373       C E E L L T P F V R K       P       R P W         DmP AP2/Q9V256//1-458       394       C K E G R E P F K G K       P       R P W         DmP AP2/Q9V258//1-450       384       C K E G R E P F K G K       I P E W       I P E W			
UAP1/08L5E1/1-477       392       N Q EG LASR FTD       P Q       P P Q         GmPAP3/Q6YGT9/1/-512       428       N Q EG LASR FLD       P Q       P Q         LaAP2/Q9X/24/1/1-638       333       N I EG LANNMTE       P Q       P K Y         UPPD4/Q8VXF4/1/1-629       556       S H       - LSDYTPSP       P Q       P K Y         UPPD2/Q8VXF6/1/1-615       542       A S LA EFAP I N       TTW       TTW         UPPD2/Q8VXF6/1/1-615       533       A LSTFTSLK       TKW       FK W         TnPAP1/Q4RLR4/1/1-378       313       C R EK TDR FTP N       P       P         MBPAP7/Q6270F0/1/1-418       373       C EER LTP FAV F       P       RP W         CaP AP3/Q91/AM9/1/-418       373       C EER LTP FAV F       P       RP W         MmPAP7/Q8BX37/1/1-438       373       C EEL LTP FAV F       P       RP W         DmPAP1/Q9V256/1/4-458       384       C K EG RE P FK GK       P       RP W         DmPAP2/Q9V258/1/-450       384       C K EG RE P FK OK       IP EW V       IP EW V	Rep AD2 1 DOCVD 21/1 A00	300	
GmP AP 3   QEYGT9   /1-512       428       N       Q       E G L A S R F L D       P Q       P E Y         La AP 2   Q9XJ24   /1-638       393       N       I E G L A N MMT E       P Q       P K Y         UPP D4   Q8VXF4   /1-629       556       S       H       L S D Y T P S P       P V W         UPP D1   Q8VXF1   /1-615       542       A S L A E F A P I N       T T W         UPP D2   Q8VXF6   /1-612       539       A S L S T F T S L K       T K W         TnP AP 1   Q4RLR4   /1-378       313       C       R E K T D R F T P N       P K D W         HsP AP 7   Q6ZI F0 / 1-438       373       C E E R L T P F AV F       P -       R P W         CeP AP 3   Q9I NAM9   /1-418       360       C H       S H E D       P S D H I       MQ D F V         MmP AP 7   Q8 BX37 / 1/1-438       373       C E E L L T P F V R K       P -       R P W         DmP AP 1   Q9 V256 / 1/1-458       394       C K E G R E P F K G K       F P W       P -       R P W         DmP AP 2   Q9 V258 / 1/1-450       384       C K E E R E P F S N D       L P I W       L P I W			
La AP2/Q9X/24//1-638       393       N       I E G L A N NMT E       P Q       P K Y         UPP D4/Q8VXF4//1-629       556       S       H       L S D Y T P S P       P V W         UPP D1/Q8VX11//1-615       542       A       L A E F A P I N       T T W         UPP D2/Q8VXF6//1-612       539       A       L S T F T S L K       T K W         TnP AP1/Q4RUR4//1-378       313       C       R E K T D R F T P N       P K D W         HsP AP7/Q6ZIVF0//1-438       373       C       E E R L T P F A V F       P       R P W         CeP AP3/Q9IVAM9//1-418       360       C       H E D       P S D H I       MQ D F X         MmP AP7/Q8X37//1-438       373       C       E E L L T P F V R K       P       R P W         DmP AP1/Q9V256//1-458       384       C K E G R E P F K G K       F P W       R P W         DmP AP2/Q9V258//1-450       384       C K E G R E P F S N D       L P I W       L P I W			
UPPD4/Q8VXF4//1-629       556       S       H       LSDYTPSP       PVW         UPPD1/Q8VX11//1-615       542       A       LAEFAPIN       TTW         UPPD2/Q8VXF6//1-612       539       A       LSTFTSLK       TKW         TnPAP1/Q4RUR4//1-378       313       C       C REKTDRFTPN       PKDW         HsPAP7/Q6Z7W0//1-438       373       C       E ER LTPFAVF       P         CaPAP3/Q9NAM9//1-418       360       C       H ED       P SDH1       MQ DF3         MmPAP7/Q8X37//1-438       373       C       E EL LTPFVRK       P       RPW         DmPAP1(09V256//1-458       394       C K E GR E PFK G K       P       P       RPW         DmPAP2/Q9V258//1-450       384       C K E ER E PFS N D       LP I W       LP I W			
UPP D1/08VX11//1-615       542       A       S L A E F A P I N       T T W         UPP D2/08VXF6//1-612       533       A S L S T F T S L K       T K W         TnP AP 1/04RLR4//1-378       313       C R E K T D R F T P N       P K D W         HsP AP 7/06ZI/F0//1-418       373       C E E R L T P F A V F       P       R P W         CaP AP 3/09/1A418       373       C E E L L T P F A V F       P       R P W         MmP AP 7/08BX37//1438       373       C E E L L T P F V R K       P       R P W         DmP AP 1/09V256//1-458       384       C K E G R E P F K G K       I P E W       I P E W         DmP AP 2/09V258//1-450       384       C K E E R E P F S N D       L P I W       L P I W			
UPPD2/Q8VXF6//1-612         539         ASLSTFTSLK         TKW:           TnPAP1/Q4RLR4//1-378         313         CREKTDRFTPN         PKDW:           HsPAP7/Q6270F0//1-418         373         CERLTPFAVF         P           CaPAP3/Q9/IA91/1-418         360         CH         SHED           MmPAP7/Q88X37//1-418         373         CELLTPFVRK         P           DmPAP1(Q9V256//1-458         394         CKEGREPFKGK         P           DmPAP2/Q9V258//1-450         384         CKEGREPFK0K         LPIWI			
TnP AP 1/Q4RLR4//1-378       313       C       R E K T D R F T P N       P       P K D W         HsP AP 7/Q6ZNF0//1-438       373       C       E E R L T P F A V F       P       R P W         CeP AP 3/Q9NAM9//1-418       360       C H       S H E D       P       MQ D F         MmP AP 7/Q8BX37//1-438       373       C       E E L L T P F V R K       P       R P W         DmP AP 1/Q9VZ56//1-458       394       C K E G R E P F K G K       P       I P E W       I P E W         DmP AP 2/Q9VZ58//1-450       384       C K E E R E P F S N D       L P I W       L P I W			
HsPAP7/Q621/F0//1-438 373 C EERLTPFAVF CePAP3/Q9NAM9//1-418 360 C HSHED			
CeP AP3   Q9NAM9   /1-418 350 C H S H E D P S D H I P S D H I MQ D F S MmP AP7   Q8 BX37   /1-438 373 C E E L L T P F V R K DmP AP1   Q9V256   /1-458 394 C K E G R E P F K G K DmP AP2   Q9V258   /1-450 384 C K E E R E P F S N D			
MmPAP7/Q88X37//1-438 373 C EELLTPFVRK DmPAP1/Q9V256//1-458 394 C KEGREPFKGK DmPAP2/Q9V258//1-450 384 C KEGREPFKGK LPIW			
DmPAP1/09V256//1-458 394 CKEGREPFKGK DmPAP2/09V258//1-450 384 CKEEREPFSND			
DmPAP2 j Q9V258 j / 1-450 384 CKEEREP FSND			
			KEGREKFISH <mark>KPSWS</mark> 38
<i>CeP AP 1   00 1320   / 1-4 19</i> 340 SRDTLK FNYPE			
DmPAP3/Q9V257//1-453 382 NHEGREPFFKRMPPW	1 4 17		
AgPAP   Q7PUII5   / 1-463 374 CKEGREPFINK	AgP AP   Q7P UI\15   /1-463	374	K E G R E P F I N K I P T WS 38

HvPAPhy a/C4PKL2//1-544	485 A Y R E S S F G H G I L E V K N E T H A L W R W H R N Q D L	514
·= · · · ·	482 A Y R E S S F G H G I L E V K N E T H A L WR WH R N Q D H	
· · · · · · · · · · · · · · · · · · ·	481 A Y R E S S F G H G I L E V K N E T Y A L WKWH R N Q D L	
	480 A Y R E S S F G H G I L E V K N E T H A L WK WH R N Q D L	
	480 A Y R E S S F G H G I L E V K N E T H A L W K W H R N Q D L	
	479 A Y R E S S F G H G I L E V K N E T H A L W K W H R N Q D L	
	481 A Y R E S S F G H G I L E V K N E T H A L W R W H R N Q D L	
ZmP APhy_b   C4PKL6   /1-544	486 A Y R E S S F G H G V L E V R N D T H A L W R WH R N Q D L	515
MtP APhy   Q3ZFI 1   / 1-543	486 A FRESSFGHGILEVKNETHALWSWNRNQDY	515
PtPAP3/V9LXK5//1-564	503 A F R E S S F G H G I L E V K N E T H A L WT WH R N Q D F	532
	485 A Y R E S S F G H G I L E V K S E T H A L WT WH R N Q D M	
	483 A FR ESS FGYGILEVKNETWALWSWYRNQDS	
	487 A F R E S S F G Y G I L E V K N E T WA L WS WY R N Q D S	
	476 A L R E S S F G H G I L EMK N E TWA L WTWYR N Q D S	
	481 A Y R E S S F G H G I L E V K N E T H A L WR WH R N Q D H	
	484 A Y R E S S F G H G I L E V K N E T H A L W R W H R N Q D M	
	477 A Y R E S S F G H G I L E V K N E T H A L W R W H R N Q D H	
	480 A Y R E S S F G H G I L E V K N E T H A L W R W H R N Q D M	
TaP AP hy_a2   C4P KK8   / 1-549	481 A Y R E S S F G H G I L E V K N E T H A L WR WH R N Q D M	510
ScPAPhy_a1/F6MIX2//1-541	480 A Y R E S S F G H G I L E V K N E T H A L WR WH R N Q D M	509
TaP APhy b3/F6MIW6//1-536	479 A Y R E S S F G H G I L E V K N E T H A L W K W H R N Q D L	508
TmP APhy b1/F6MIW9//1-539	482 A Y R E S S F G H G I L E V K N E T H A L W K W H R N Q D L	511
	481 A Y R E S S F G H G I L E V K N E T H A L W K W H R N Q D L	
1 1	481 A Y R E S S F G H G I L E V K N E T H A L WKWH R N Q D L	
	507 A Y R E S S F G H G I L E V K N E T H A L WT WH R N Q D L	
1 17	480 A FR ESS FGHG I L EV K N D TWA L WTWYR N Q D S	
	486 A FR ETS F G Y G I L E V K N E T WA L WS WY R N Q D S	
	487 A F R E T S F G Y G I L E V K N E T WA L W S W Y R N Q D S	
	476 AMR ESSFGHGILEMKNETWALWTWYRNQDS	
AtP AP 23   Q6TP H 1   / 1-458	443 H S S Y D L F F F	451
GmP AP 4   V9H X G4   /1-442	380 EFREASFGHGELKIVNSTHAFWSWHRNDDD	409
ZmP AP_c   C4PKL7   /1-566	506 A Y R E S S F G H G I L E V L N S T Y A L W T W H R N Q D A	535
SbP AP   A0 A1Z5R9 T8   /1-566	506 A Y R E S S F G H G I L E V L N S T Y A L W T W H R N Q D A	535
	504 A FR ESS FGHGILEVVNS TYAL WTWHRNQDT	
	487 A FR ESS FGHGV L EV V N S S H A L WT WHR N Q D M	
	509 A FR ESS FGHGILEVVNSTYALWTWHRNQDA	
	509 A FR ESS FGHG I LEVVNS TYAL WTWHRNQDA	
	345 A FR EAS F G HALLE I K N R T HAH Y T WH R N K ED	
	377 L F R E A S F G H G Q L V V E N A T H A R W E W H R N D D D	
	376 E F R E S S F G H G R L K V MD G K R A H WS WH R N N D S	
	372 A Y R E A S F G H G I F D I K N R T H A H F G W H R N Q D G	
	380 E F R E S S F G H G R L R I I D H K R A H WS WH R N N D E	
LoP AP 1 09 MP0 71 /1_455		
μr Ar / αρινίου / / 1455	405 A Y R E A S F G H A I F G I K N R T H A Y Y N W Y R N Q D G	434
	405 A Y R E A S F G H A I F G I K N R T H A Y Y NWY R N Q D G	
RcP AP 2   B9 SXP 8   / 1-463		414
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95DZ9  /1-465	385 A F R E A S Y G H S T L E I MN K T H A F Y Y WH R N D D G	414 439
RcP AP 2   B95XP8  /1-463  bP AP 2   Q95DZ9  /1-465 AtP AP 11   Q95 18  /1-441	385 A F R E A S Y G H S T L E I MN K T H A F Y Y WH R N D D G	414 439 419
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q95I 18  /1-441 GmP AP 1   Q09 13 1  /1-464	385 A FR E A S Y G H S T L E I MN K T H A F Y Y WH R N D D G	414 439 419 437
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95DZ9  /1-465 AtP AP 11   Q95I 18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   023244  /1-466	385       A F R E A S Y G H S T L E I MN K T H A F Y WH R N D D G	414 439 419 437 438
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArP AP 1   Q95 18  /1-441 GmP AP 1   Q09 13 1  /1-464 ArP AP 25   O23244  /1-466 ArP AP 12   Q38924  /1-469	385       A FR EAS Y GHS T L E I MN K THA F Y WHR N D D G	414 439 419 437 438 443
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 ArtP AP 11   095 18  /1-441 GmP AP 1   009 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 IVtP AP   084KZ3  /1-461	385       A FR EAS Y G H S T L E I MN K T HA F Y WH R N D D G	414 439 419 437 438 443 439
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArP AP 11   Q9518  /1-441 GmP AP 12   Q09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 INP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465	385       A FR EAS Y G H S T L E I MN K T HA F Y YWH R N D D G	414 439 419 437 438 443 439 438
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 ArtP AP 25   023244  /1-466 ArtP AP 12   Q38924  /1-469 INTP AP   Q84K23  /1-461 MrtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476	385       A F R E A S Y G H S T L E I MN K T H A F Y WH R N D D G	414 439 419 437 438 443 439 438 435
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   09518  /1-441 GmP AP 1   009131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 INTP AP 1 084KZ3  /1-461 MtP AP 1   04KU02  /1-465 OSP AP 2   085505  /1-476 La AP 1   093VM7  /1-460	385       A FR EAS Y G H S T L E I MN K T HA F Y WHR N D D G	414 439 419 437 438 443 439 438 435 434
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-469 IVP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457	385       A F R E A S Y G H S T L E I MN K T H A F Y Y WH R N D D G	414 439 419 437 438 443 439 438 435 434 442
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   023244  /1-469 IVP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP 2   Q764 C1  /1-457	385       A FR EAS Y G H S T L E I MN K T HA F Y WHR N D D G	414 439 419 437 438 443 439 438 435 434 442
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArtP AP 11   Q95 18  /1-441 GmP AP 1   Q05 18  /1-441 GmP AP 12   Q38924  /1-466 ArtP AP 12   Q38924  /1-466 IVTP AP   Q84K23  /1-461 MrtP AP 1   Q4KU02  /1-465 OS AP 2   Q8505  /1-476 La AP 1   Q95WN7  /1-460 P VP AP 2   Q846L1  /1-453	385       A F R E A S Y G H S T L E I MN K T H A F Y Y WH R N D D G	414 439 419 437 438 443 439 438 435 434 442 437
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArtP AP 11   Q9518  /1-441 GmP AP 10 Q0918  /1-464 ArtP AP 25   023244  /1-466 ArtP AP 12   Q38924  /1-469 INTP AP   Q84KZ3  /1-461 MrtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP2   Q764C1  /1-453 ArtP AP 10   Q9SV9  /1-468 P vP AP 10   Q9SV9  /1-468 P vP AP 1  P80366  /1-459	385       A FR E A S Y G H S T L E I MN K T HA F Y WH R N D D G	414 439 419 437 438 439 438 439 438 435 434 442 437 442 437
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArtP AP 11   Q9518  /1-441 GmP AP 10 Q0918  /1-464 ArtP AP 25   023244  /1-466 ArtP AP 12   Q38924  /1-469 INTP AP   Q84KZ3  /1-461 MrtP AP 1   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P vP AP2   Q764C1  /1-453 ArtP AP 10   Q9SV9  /1-468 P vP AP 10   Q9SV9  /1-468 P vP AP 1  P80366  /1-459	385       A FR E A S Y G H S T L E I MN K T HA F Y WH R N D D G	414 439 419 437 438 439 438 439 438 435 434 442 437 442 437
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 ArtP AP 11   09518  /1-441 GmP AP 11   09518  /1-441 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-465 MtP AP 1084K23 //1-461 MtP AP 1   04KU02  /1-465 OsP AP 2   085505  /1-476 La AP 1   093VM7  /1-460 P vP AP 2   0764C1  /1-457 UAP 2   08L6L1  /1-463 ArtP AP 10   095V9  /1-468 P vP AP 10   095V9  /1-465 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477	385       A FR E A S Y G H S T L E I MN K T HA F Y WH R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 442 437 442 437 436
RcP AP2   B95XP8  /1-463 IbP AP2   Q95D29  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 12   Q09131  /1-464 AtP AP25   023244  /1-466 AtP AP 12   Q38924  /1-469 INP AP 1 Q84K23  /1-461 MtP AP 1 Q4KU02  /1-465 OsP AP2   Q85505  /1-476 La AP 1   Q93VM7  /1-460 P YP AP2   Q764 C1  /1-457 UAP2   Q8L6L1  /1-463 AtP AP 10   Q93V9  /1-468 P YP AP 1   P803566  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466	385       A FR E A S Y G H S T L E I MN K T HA F Y Y WH R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 442 437 442 437 436 438
RcP AP 2   B95XP8   /1-463 IbP AP 2   Q95D29   /1-465 ArtP AP 11   Q95 18   /1-441 GmP AP 1   Q05 18   /1-441 GmP AP 12   Q38924   /1-466 ArtP AP 25   Q38924   /1-466 IVTP AP   Q84K23   /1-461 MrtP AP 1   Q4KU02   /1-465 OSP AP 2   Q8505   /1-476 La AP 1   Q93VM7   /1-460 P VP AP 2   Q764 C1   /1-457 UAP 2   Q8L6L1   /1-463 ArtP AP 10   Q95V9   /1-468 P VP AP 1   P80366   /1-459 Ta ACP   C4PKL1   /1-477 ArtP AP 6   Q9 C5 10   /1-461 AcP AP   Q9 SWP4   /1-481	385       A FR EAS Y G H S T L E I MN K T HA F Y WH R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 442 437 442 437 436 438 441
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArP AP 11   Q9518  /1-441 GmP AP 1   Q0518  /1-441 GmP AP 1   Q0518  /1-464 ArP AP 25   023244  /1-466 IrP AP   Q84K23  /1-461 MrP AP 1 Q4KU02  /1-465 OSP AP 2   Q8505  /1-476 La AP 1   Q93VM7  /1-463 ArP AP 10   Q95V9  /1-468 P vP AP 1  P80366  /1-457 Ta ACP   C4PKL1  /1-477 ArP AP 6   Q9 C5 10  /1-461 AcP AP 2   Q93WP4  /1-481 AoP AP 32   Q9XF09  /1-470	385       A F R E A S Y G H S T L E I MN K T HA F Y Y WH R N D D G	414 439 419 437 438 438 439 438 435 434 442 437 442 437 436 438 441 444
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 ArP AP 11   09518  /1-441 GmP AP 1009131  /1-464 ArP AP 25   023244  /1-466 ArP AP 12   038924  /1-469 IVP AP   084K23  /1-461 MrP AP 1   04KU02  /1-465 OsP AP 2   085505  /1-476 La AP 11 (095V07  /1-460 P vP AP 2   0764C1  /1-457 UAP 2   08L6L1  /1-463 ArP AP 10   095V9  /1-468 P vP AP 1  P80366  /1-459 Ta ACP   C4PKL1  /1-477 ArP AP 6   09 SV9 4  /1-481 AoP AP 32   095V9 9 /1-470 SrP AP3   0615M8  /1-477	385       A F R E A S Y G H S T L E I MN K T HA F Y Y WH R N D D G	414 439 419 437 438 439 438 435 434 442 437 442 437 436 438 441 444 435
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArtP AP 11   Q9518  /1-441 GmP AP 10 Q9518  /1-444 AttP AP 25   023244  /1-466 AttP AP 12   Q38924  /1-466 INTP AP   Q4KU02  /1-465 OsP AP 2   Q85505  /1-476 La AP 11   Q93VM7  /1-460 P vP AP 2   Q764C1  /1-457 UAP 2   Q8L6L1  /1-463 AttP AP 10   Q9SV9  /1-468 P vP AP 10   Q9SV9  /1-468 P vP AP 10   Q9SV9  /1-468 A ttP AP 10   Q9SV9  /1-468 A ttP AP 10   Q9SV9  /1-473 Ta ACP   C4PKL1  /1-477 ArtP AP 6   Q9 C510  /1-476	385       A F R E A S Y G H S T L E I MN K T H A F Y Y WH R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 442 437 436 438 441 444 435 447
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArtP AP 11   Q9518  /1-441 GmP AP 10 Q9513  /1-464 ArtP AP 25   023244  /1-466 ArtP AP 12   Q38924  /1-465 OsP AP 2   Q8505  /1-476 La AP 1   Q95VM7  /1-460 P vP AP 2   Q764C1  /1-457 UAP 2   Q8L6L1  /1-463 ArtP AP 10   Q95V9  /1-468 P vP AP 10   Q95V9  /1-468 A vP AP 6   Q9 C510  /1-466 AcP AP 2   Q9XF09  /1-477 IbP AP 3   Q6J5M8  /1-477 IbP AP 1   Q95E00  /1-473 ArtP AP 26   Q95V9  /1-475	385       A F R E A S Y G H S T L E I MN K T H A F Y Y WH R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 436 437 436 438 441 444 435 447 436
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 ArP AP 11   Q9518  /1-441 GmP AP 11 (Q9131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-466 IntP AP 1 (Q484C23 //1-461 MtP AP 1 (Q484C23 //1-461 MtP AP 1 (Q484C23 //1-466 OsP AP 2   Q85505  /1-476 La AP 1   Q95V9 //1-468 ArP AP 2 (Q8L6L1) //1-463 ArtP AP 10 (Q95V9 //1-468 P vP AP 1   P803666 //1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-466 AcP AP   Q3SWP4 //1-481 AoP AP 32   Q95K90 //1-473 StP AP 3   Q6J5M8  /1-477 IbP AP 1 (Q95W0 //1-473 AtP AP 26   Q949 Y3 //1-475 RcP AP 3   B95XP 6  /1-488	385       A F R E A S Y G H S T L E I MN K T HA F Y Y WH R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 442 437 442 437 442 437 442 437 445 444 445 447 436 442
RcP AP 2   B9SXP8  /1-463 IbP AP 2   Q9SD29  /1-465 ArP AP 11   Q9S 18  /1-441 GmP AP 1   Q0 91 31  /1-464 AtP AP 25   O23244  /1-469 IVP AP   Q84K23  /1-461 MrP AP 1   Q4KU02  /1-465 OSP AP 2   Q8505  /1-476 La AP 1   Q9SVM7  /1-460 P VP AP 2   Q764C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9SV9  /1-468 P VP AP 10   Q9SV9  /1-468 P VP AP 10   Q9SV9  /1-468 ArP AP 0   Q9SV9  /1-468 ArP AP 0   Q9SV9  /1-468 ArP AP 10   Q9SV9  /1-468 ArP AP 10   Q9SV9  /1-468 ArP AP 10   Q9SV9  /1-477 ArP AP 6   Q9C5 10  /1-477 IbP AP 1   Q9SCM8  /1-477 IbP AP 1   Q9SV9  /1-475 RcP AP 3   Q9SY 6  /1-488 UAP 1   Q8L5E1  /1-477	385       A FR E A S Y G H S T L E I MN K T HA F Y Y WH R N D D G	414 439 419 437 438 433 438 435 434 442 437 442 437 436 444 435 444 435 445 445 445 445 445 445
RcP AP 2   B9SXP8  /1-463 IbP AP 2   Q9SD29  /1-465 ArP AP 11   Q9S 18  /1-441 GmP AP 1   Q09 13 1  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469 IVP AP   Q84K23  /1-461 MrP AP 1   Q4KU02  /1-465 OSP AP 2   Q8505  /1-476 La AP 1   Q93VM7  /1-460 P VP AP 1   Q93VM7  /1-463 AtP AP 10   Q9SV9  /1-468 P VP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 AtP AP 6   Q9 C5 10  /1-476 AcP AP 32   Q9XF09  /1-470 StP AP 3   Q655M8  /1-477 IbP AP 1   Q95E00  /1-475 RcP AP3   B95XP 6  /1-488 UAP 108L5E1  /1-477	385       A F R E A S Y G H S T L E I MN K T HA F Y Y WH R N D D G	414 439 419 437 438 433 438 439 438 434 442 437 442 437 442 437 436 441 444 435 441 444 435 447 436 442 438 442
RcP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 ArP AP 11   09518   /1-441 GmP AP 1009131   /1-464 ArP AP 12   028324   /1-466 ArP AP 12   038324   /1-461 MrP AP 1 084K23   /1-461 MrP AP 1 084K23   /1-461 MrP AP 1 084K23   /1-463 OsP AP 2   0764C1   /1-457 UAP 2   0764C1   /1-457 UAP 2   0764C1   /1-457 Ta ACP   C4PKL1   /1-477 ArP AP 6   09 C510   /1-468 ArP AP 10   095W9   /1-468 ArP AP 6   09 C510   /1-470 StP AP 3 2   095K90 / 1-473 ArP AP 26   094503   /1-473 ArP AP 26   094503   /1-473 RcP AP 38   855XP 6   /1-488 UAP 1   08 L561   /1-512 La AP 2   095X92   /1-512 La AP 2   095X92   /1-512	385       A FR E A S Y G H S T L E I MN K T HA F Y Y W H R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 436 437 436 444 435 447 436 442 438 444 445
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 ArtP AP 11   09518  /1-441 GmP AP 10 09131  /1-464 AttP AP 25   023244  /1-466 AttP AP 12   038924  /1-466 INTP AP   084K23  /1-461 MtP AP 1 04KU02  /1-465 OsP AP 2   08505  /1-476 La AP 11 (093VM7 //1-460 P vP AP 2   0764C1  /1-457 UAP 2   08L6L1  /1-463 AttP AP 10   09SV9  /1-468 P vP AP 10   09SV9  /1-468 P vP AP 10   09SV9  /1-468 AttP AP 10   09SV9  /1-468 AttP AP 10   09SV9  /1-473 AttP AP 6   09C510  /1-473 AttP AP 26   0949Y3  /1-475 RcP AP 3   895XP 6  /1-488 UAP 11 08L5E1  /1-477 GmP AP 3   06YGT9  /1-512 LaAP 2   09XV2  /1-638 UPP D4   08VXF4  /1-629	385       A FR E A S Y G H S T L E I MN K T HA F Y Y W H R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 436 437 436 438 441 435 444 435 447 436 442 438 447 436 598
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 ArtP AP 11   09518  /1-441 GmP AP 10 09131  /1-464 AttP AP 25   023244  /1-466 AttP AP 12   038924  /1-466 INTP AP   084K23  /1-461 MtP AP 1 04KU02  /1-465 OsP AP 2   08505  /1-476 La AP 11 (093VM7 //1-460 P vP AP 2   0764C1  /1-457 UAP 2   08L6L1  /1-463 AttP AP 10   09SV9  /1-468 P vP AP 10   09SV9  /1-468 P vP AP 10   09SV9  /1-468 AttP AP 10   09SV9  /1-468 AttP AP 10   09SV9  /1-473 AttP AP 6   09C510  /1-473 AttP AP 26   0949Y3  /1-475 RcP AP 3   895XP 6  /1-488 UAP 11 08L5E1  /1-477 GmP AP 3   06YGT9  /1-512 LaAP 2   09XV2  /1-638 UPP D4   08VXF4  /1-629	385       A FR E A S Y G H S T L E I MN K T HA F Y Y W H R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 436 437 436 438 441 435 444 435 447 436 442 438 447 436 598
RcP AP 2   B9SXP8  /1-463 IbP AP 2   Q9SD29  /1-465 ArP AP 11   Q9S18  /1-441 GmP AP 11   Q9S18  /1-441 GmP AP 12   Q38324  /1-466 ArP AP 25   023244  /1-466 IVP AP 1 Q4KU02  /1-465 OsP AP 2   Q8S505  /1-476 La AP 1   Q4KU02  /1-465 OsP AP 2   Q764C1  /1-457 UAP 2   Q764C1  /1-457 UAP 2   Q8L6L1  /1-463 ArP AP 10   Q9SV9  /1-468 ArP AP 10   Q9SV9  /1-468 ArP AP 10   Q9SV9  /1-468 ArP AP 2   Q9SX07  /1-475 Ta ACP   C4PKL1  /1-477 ArP AP 6   Q9 C510  /1-466 AcP AP 2   Q9SVP6  /1-473 ArP AP 3   Q6J5M8  /1-477 IbP AP 1   Q9SE00  /1-473 ArP AP 3   Q8SXP 6  /1-488 UAP 1   Q8L5E1  /1-477 GmP AP 3   Q9SV7  /1-618 UPP D4   Q8VXF4  /1-638	385       A FR E A S Y G H S T L E I MN K T HA F Y Y W H R N D D G	414 439 419 437 438 443 439 438 435 434 442 437 436 438 442 437 436 442 438 441 445 445 598 598
RcP AP 2   B9SXP8  /1-463 IbP AP 2   Q9SD29  /1-465 ArtP AP 11   Q9S 18  /1-441 GmP AP 1   Q0 9131  /1-464 ArtP AP 25   Q32244  /1-469 IvtP AP   Q38924  /1-469 IvtP AP   Q4KU23  /1-461 MrtP AP 1   Q4KU02  /1-465 OsP AP 2   Q8505  /1-476 La AP 1   Q9SVM7  /1-460 P vP AP 2   Q764C1  /1-457 UAP 2   Q8L6L1  /1-463 ArtP AP 10   Q9SV9  /1-468 P vP AP 1   P80366  /1-459 Ta ACP   C4PKL1  /1-477 ArtP AP 6   Q9 CS 10  /1-466 AcP AP 22   Q9XF09  /1-470 SrtP AP 3   Q655M8  /1-477 IbP AP 1   Q8L5E1  /1-477 GmP AP 3   Q6579  /1-512 La AP 2   Q9XVF6  /1-615 UPP D2   Q8VXF6  /1-612	385       A FR E A S Y G H S T L E I MN K T HA F Y YWH R N D D G	414 439 419 437 438 443 439 438 442 437 442 437 442 437 442 438 441 444 435 444 435 444 438 441 444 435 445 558 5584 5584
RcP AP 2   B9SXP8   /1-463 IbP AP 2   Q9SD29   /1-465 ArP AP 11   Q9S 18   /1-441 GmP AP 1   Q09 13 1   /1-464 AtP AP 25   023244   /1-466 AtP AP 12   Q38924   /1-469 IVP AP   Q84K23   /1-461 MrP AP 1   Q4KU02   /1-465 OSP AP 2   Q8505 /   -476 La AP 1   Q93VM7   /1-460 P VP AP 2   Q764C1   /1-457 UAP 2   Q8L6L1   /1-463 AtP AP 10   Q9SV9   /1-468 P VP AP 10   Q9SV9   /1-468 P VP AP 10   Q9SV9   /1-468 P VP AP 10   Q9SV9   /1-468 AcP AP 0 0 0 55 10   /1-477 AtP AP 6   Q9 C5 10   /1-477 StP AP 3   Q6J5M8   /1-477 IbP AP 1   Q9SED0   /1-478 RcP AP 3   Q6J5M8   /1-477 GmP AP 3   Q6YG79   /1-512 La AP 2   Q9XF6   /1-458 UPP D4   Q8VXF6   /1-612 UPP D2   Q8VXF6   /1-612 TnP AP 1   Q4R UR4   /1-378	385       A F R E A S Y G H S T L E I MN K T H A F Y Y WH R N Q D G	414 439 419 437 438 433 438 433 438 434 442 437 442 437 442 437 436 441 444 435 447 436 442 438 441 444 558 558 558 5581 358
RcP AP 2   B9SXP8   /1-463 IbP AP 2   Q9SD29   /1-465 ArP AP 11   Q9S18   /1-441 GmP AP 1   Q9S18   /1-441 GmP AP 11   Q3S18   /1-441 ArtP AP 25   023244   /1-466 ArtP AP 12   Q38324   /1-461 MrP AP 1   Q4KU22   /1-465 OsP AP 2   Q8S505 / /1-476 La AP 1   Q9SV07   /1-468 P vP AP 10   Q9SV9   /1-468 ArtP AP 10   Q9SV9   /1-468 ArtP AP 10   Q9SV9   /1-468 ArtP AP 10   Q9SV9   /1-468 ArtP AP 10   Q9SV9   /1-475 Ta ACP   C4PKL1   /1-477 ArtP AP 6   Q9 C510   /1-473 ArtP AP 32   Q9SF09   /1-470 SrtP AP 3   Q6J5M8   /1-477 IbP AP 11 ( Q9SE00 / 1-473 ArtP AP 3   Q6YG79   /1-512 La AP 2   Q9X124   /1-638 UPP D1   Q8VXF6   /1-622 ThP AP 1   Q4R LR4 / /1-378 HsP AP 7   Q6Z VF0   /1-438	385       A FR E AS Y G H S T L E I MNK T H A F Y Y WH R N D D G	414 439 419 437 438 433 438 433 434 442 437 442 437 442 437 436 442 437 436 441 444 435 447 436 598 474 465 598 581 358 418
RcP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 ArP AP 11   09518 / 1-441 GmP AP 10 09131   /1-464 AtP AP 25   023244   /1-466 AtP AP 12   038924 / /1-469 IVP AP   084K23   /1-461 MtP AP   084K23   /1-461 MtP AP   084K23   /1-465 OsP AP 2   08505 / /1-476 La AP 11   093VM7   /1-460 P vP AP 2   0764C1   /1-457 UAP 2   0764C1   /1-457 UAP 2   0764C1   /1-457 Ta ACP   C4PKL1 / /1-477 AtP AP 6   09 C510   /1-466 AcP AP   093WP4   /1-481 AoP AP 32   093WP4   /1-481 AoP AP 32   095K00   /1-473 AtP AP 6   095E00   /1-473 AtP AP 26   0949Y3   /1-475 RcP AP 3   895XP6   /1-488 UAP 1   08 L5E1   /1-477 GmP AP 3   08 V514   /1-615 UPP D4   08 V514   /1-615 UPP D4   08 V514   /1-378 HsP AP 7   047 W64   /1-378 HsP AP 7   047 W64   /1-378	385       A F R E A S Y G H S T L E I MN K T H A F Y Y WH R N D D G	414 439 419 437 438 443 439 438 434 442 437 442 437 436 438 444 435 447 436 444 435 447 436 598 584 598 584 581 358 418 405
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 ArP AP 11   09518  /1-441 GmP AP 10 09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-466 INTP AP   084K23  /1-461 MtP AP   084K23  /1-461 MtP AP 10   04505  /1-476 La AP 11 (093VM7 //1-460 P vP AP 2   0764C1  /1-457 UAP 2   08L6L1  /1-463 AtP AP 10   095V9  /1-468 P vP AP 10   095V9 //1-468 P vP AP 10   095V9 //1-468 P vP AP 10   095V9 //1-468 A VP AP 00   095V9 //1-468 A VP AP 00   095V9 //1-473 AtP AP 6   09 C510 //1-473 AtP AP 32   095K709  /1-477 IbP AP 1   095E00  /1-473 AtP AP 26   0949Y3  /1-475 RcP AP 3   895XP 6 //1-488 UAP 1   08 L5E1  /1-477 GmP AP 3   06VGT9  /1-512 La AP 2   09XV74  /1-638 UPP D4   08VXF4  /1-638 UPP D4   08VXF4  /1-638 HSP AP 7   062 VF0  /1-418 MmP AP 7   08 BX37  /1-418	385       A FR EAS YGHST L E IMNKT HAF Y YWHR N D G	414 439 419 437 438 443 439 438 435 434 442 437 436 437 436 437 436 442 437 436 442 437 436 442 437 436 445 598 584 598 584 598 581 598 581 598 598 418 598 598 419
RcP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 ArtP AP 11   095 18   /1-441 GmP AP 1   009 131   /1-464 ArtP AP 25   023244   /1-469 IvtP AP   084K23   /1-461 MrtP AP 1   04KU02   /1-465 OsP AP 2   08505   /1-476 La AP 1   04KU02   /1-463 ArtP AP 10   095V9   /1-468 P vP AP 2   0764C1   /1-457 UAP 2   08L6L1   /1-463 ArtP AP 10   095V9   /1-468 P vA P 10   095V9   /1-468 P vA P 10   095V9   /1-468 ArtP AP 10   095V9   /1-468 ArtP AP 10   095V9   /1-468 ArtP AP 10   095V9   /1-468 ArtP AP 10   095V9   /1-470 SrtP AP 3   0655M8   /1-477 IbP AP 1   09SE00   /1-473 ArtP AP 2 6   0949Y3   /1-475 RcP AP 3   895XP 6   /1-488 UAP 1   08L5E1   /1-477 GmP AP 3   05VG19   /1-512 La AP 2   09XV24   /1-613 UPP D4   08VXF4   /1-615 UPP D4   08VXF4   /1-615 UPP D2   08VXF6   /1-418 Hsp AP 7   062NF6   /1-438 MmP AP 7   028X37   /1-438 MmP AP 7   09V256   /1-438	385       A FR EAS Y GH ST L E I MN K THA F       Y Y WH R N D D G         410       A FR EAS F GHA T L D I K N R THA Y       Y S WH R N Q D G         390       A FR EAS F GHA I L E I K N R THA Y       Y WH R N Q D G         408       A FR EAS F GHA I L E I K N R THA Y       Y WH R N Q D G         409       A YR EAS F GHA I L E I K N R THA Y       Y WH R N Q D G         410       A YR EAS F GHA I L E I K N R THA Y       Y S WH R N Q D G         410       A YR EAS F GHA I L E I K N R THA Y       Y S WH R N Q D G         410       A YR EAS F GHA I L E I K N R THA Y       Y S WH R N Q D G         409       A YR EAS F GHA I F D I K N R THA Y       Y S WH R N Q D G         401       A YR EAS F GHA I F D I K N R THA H       Y S WN R N Q D G         405       A FR EAS Y GHS I L Q L K N R THA H       Y S WN R N Q D G         413       A FR EAS Y GH S I L E I K N R THA H       Y S WN R N Q D G         413       A FR EAS F GHA I F S I K N R THA H       Y G WH R N D G         408       A YR EAS F GH G T L E I K N R THA H       Y G WH R N D G         408       A YR EAS F GH A I L D I K N R THA H       Y G WH R N D G         413       A FR EAS Y G H S T L E I K N R THA H       Y G WH R N D G         406       A FR EAS Y G H S T L E I K N R THA H       Y G WN R N D G	414 439 419 437 438 433 439 438 435 434 442 437 442 437 442 437 442 438 441 444 435 442 438 441 444 435 442 438 442 438 441 445 558 584 558 558 418 358 840 558 418 405 418 438
RcP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 ArtP AP 11   09518   /1-441 GmP AP 1   09518   /1-441 GmP AP 1   09131   /1-464 ArtP AP 25   023244   /1-469 ItP AP   084K23   /1-461 MrtP AP 1   04KU02   /1-465 OsP AP 2   08505   /1-476 La AP 1   093VM7   /1-460 PrP AP 1   095V9   /1-468 PrP AP 10   095V9   /1-468 PrP AP 10   095V9   /1-468 PrP AP 10   095V9   /1-468 ArtP AP 00   095V9   /1-468 ArtP AP 10   095V9   /1-468 ArtP AP 10   095V9   /1-468 ArtP AP 10   095V9   /1-468 ArtP AP 10   095V9   /1-470 SrtP AP 3   065M8   /1-477 IbP AP 11   095E0   /1-477 SrtP AP 3   065M8   /1-477 IbP AP 10   095V9   /1-512 La AP 2   09X124   /1-638 UPP D1   08VX11   /1-615 UPP D2   08VXF4   /1-638 HSP AP 7   0621+F0   /1-438 CeP AP 3   09IX09   /1-438 CeP AP 3   09IX09   /1-438 MmP AP 7   08BX37   /1-438 DmP AP 1   09V256   /1-438 DmP AP 2   09V258   /1-450	385       A FR EAS Y GHS T L E I MN K THA F       Y Y WH R N D D G         410       A FR EAS F GHA T L D I K N R THA Y       Y S WH R N Q D G         390       A FR EAS F GHA I L D I K N R THA Y       Y WH R N Q D G         408       A FR EAS F GHA Y L E I Y N R THA Y       Y WH R N Q D G         409       A YR EAS F GHA Y L E I Y N R THA Y       Y WH R N Q D G         414       A FR EAS Y GH G L L E I K N R THA Y       Y WH R N Q D G         410       A YR EAS F GHA I L E I K N R THA Y       Y WH R N Q D G         410       A YR EAS Y GH S I L Q L K N R THA Y       Y S WH R N Q D G         405       A YR EAS Y GH S I L Q L K N R THA H       Y S WH R N Q D G         405       A YR EAS Y GH S I L E I K N R THA H       Y S WN R N Q D G         405       A YR EAS Y GH S I L E I K N R THA H       Y S WN R N Q D G         406       A FR EAS Y GH S I L E I K N R THA H       Y S WN R N Q D G         413       A FR EAS Y GH S I L E I K N R THA H       Y S WN R N Q D G         413       A FR EAS Y GH S I L E I K N R THA H       Y S WN R N Q D G         413       A FR EAS Y GH S I L E I K N R THA H       Y S WN R N Q D G         413       A FR EAS Y GH S T L E I K N R THA H       Y S WN R N Q D G         413       A FR EAS Y GH S T L E I K N R THA H       Y WW R N D G <td>414 439 419 437 438 433 438 435 434 442 437 442 437 442 437 442 438 441 444 435 444 435 444 438 441 444 435 598 5584 5584 5581 358 418 405 418 442 443 445 598 584 581 358 418 445 445 445 445 445 445 445 445 445 44</td>	414 439 419 437 438 433 438 435 434 442 437 442 437 442 437 442 438 441 444 435 444 435 444 438 441 444 435 598 5584 5584 5581 358 418 405 418 442 443 445 598 584 581 358 418 445 445 445 445 445 445 445 445 445 44
RcP AP 2   89SXP8  /1-463 IbP AP 2   09SD29  /1-465 ArP AP 11   09S18  /1-441 GmP AP 1   09S18  /1-441 GmP AP 1   009131  /1-464 AtP AP 25   023244  /1-466 ItP AP   084K23  /1-461 MtP AP 1 084K23  /1-461 MtP AP 1 084K23  /1-465 OSP AP 2   08S505 //1-476 La AP 1 09SV9  /1-468 P VP AP 1 09SV9  /1-468 AtP AP 10 09SV9  /1-468 AtP AP 6 09 C5 10 //1-475 Ta ACP (C4PKL1)/1-477 AtP AP 6 09 C5 10 //1-478 AcP AP 3 2 09SF09  /1-470 StP AP 3 1 06S5M8  /1-477 IbP AP 1 (09SE00 //1-473 AtP AP 3 06S5M8  /1-477 GmP AP 3 06S79  /1-512 La AP 2 09SV24  /1-638 UPP D4 08VXF6  /1-612 TnP AP 1 04RLR4  /1-378 HSP AP 7 06ZVF0 //1-438 CeP AP 3 09IAM9 //1-418 MmP AP 7 1 08V256  /1-458 DmP AP 1 09V256  /1-458 DmP AP 1 09V256  /1-458 DmP AP 1 09V256  /1-458	385       A FR EAS Y GH ST L E IMNK T HA F       Y YWHR N D D G         410       A FR EAS F GHA I L D I K NR T HA Y       Y SWHR N Q D G         390       A FR EAS F GHA I F D I T NR T HA Y       Y SWHR N Q D G         403       A FR EAS F GHA I F D I T NR T HA Y       Y SWHR N Q D G         404       A FR EAS F GHA I F D I T NR T HA Y       Y SWHR N Q D G         411       A FR EAS F GHA I E I K NR T HA Y       Y SWHR N Q D G         412       A FR EAS Y GH A I E I K NR T HA Y       Y SWHR N Q D G         409       A YR EAS F GHA I F D I K NR T HA Y       Y SWHR N Q D G         400       A YR EAS F GHA I E I K NR T HA Y       Y SWHR N Q D G         401       A YR EAS Y GH S I L E I K NR T HA H       Y SWHR N Q D G         405       A YR KAS F GH G I F A I K NR T HA H       Y SWN R N Q D G         413       A FR EAS Y GH S T L E I K NR T HA H       Y SWN R N Q D G         413       A FR EAS F G GH A I F S I K NR T HA H       Y SWN R N Q D G         413       A FR EAS F G GH A I F S I K NR T HA H       Y SWN R N Q D G         413       A FR EAS F G H A I K S I K NR T HA H       Y G W R N D D G         413       A FR EAS F G H A I K S I K NR T HA H       Y G W R N Q D G         414       A FR EAS F G H A I K S I K NR T HA H       Y G W R N D D G	414 439 419 437 438 433 438 435 434 442 437 442 437 442 437 442 437 436 441 444 435 447 436 442 438 441 445 598 474 465 598 581 358 418 405 418 429 412
RcP AP 2   895XP8   /1-463 IbP AP 2   095D29   /1-465 ArP AP 11   09518 / 1-441 GmP AP 10 09131   /1-464 ArtP AP 12   028324   /1-466 ArtP AP 12   028505 / 1-476 La AP 1 093VW7   /1-465 OsP AP 2   08505 / 1-476 La AP 10 095V9   /1-465 P vP AP 2   0764C1   /1-457 UAP 2 0764C1   /1-457 Ta ACP   C4PKL1 / 1-463 ArtP AP 10   095V9   /1-468 P vP AP 10   095V9   /1-468 P vP AP 10   095V9   /1-468 ArtP AP 10   095V9   /1-468 ArtP AP 10   095V9   /1-468 ArtP AP 10   095V9   /1-468 ArtP AP 20   095V9   /1-470 StP AP 32   095V9   /1-473 ArtP AP 26   0945V3   /1-475 RcP AP 3   065M8   /1-477 IbP AP 11 ( 095K00 / 1-473 ArtP AP 26   0945V3 / 1-475 RcP AP 3   065V79   /1-512 La AP 2   09XU24   /1-638 UPP D4   08VK74   /1-629 UPP D1   08VXF6   /1-438 CeP AP 3   091AM9   / 1-418 MmP AP 7   08BX37 / 1-438 DmP AP 1   09V258   /1-478 AmP AP 2   09V258   /1-438 DmP AP 1   00V258   /1-438 DmP AP 1   00	385       A FR EAS Y GHS T L E IMNK T HA F       Y YWHR N D D G         410       A FR EAS F GHA I L D I K NR T HA Y       Y SWHR N Q D G         390       A FR EAS F GHA I F D I TNR T HA Y       Y SWHR N Q D G         408       A FR EAS F GHA I F D I TNR T HA Y       Y SWHR N Q D G         409       A YR EAS F GHA I L E I K NR T HA Y       Y SWHR N Q D G         414       A FR EAS Y GH G L E I K NR T HA Y       Y SWHR N Q D G         409       A YR EAS F GHA I L E I K NR T HA Y       Y SWHR N Q D G         400       A YR EAS F GH I L E I K NR T HA Y       Y SWHR N Q D G         401       A YR EAS Y GH S I L Q L K NR T HA H       Y SWHR N Q D G         405       A YR KAS F GH G I F A I K K R T HA H       Y SWNR N Q D G         405       A YR KAS F GH G T L E I K NR T HA H       Y SWNR N Q D G         413       A FR EAS Y GH ST L E L K NR T HA H       Y SWNR N Q D G         413       A FR EAS F GH G MF D I K NR T HA H       Y SWNR N Q D G         413       A FR EAS F GH M F D I K NR T HA H       Y SWNR N Q D G         413       A FR EAS F GH G T L E I K NR T HA H       Y SWNR N Q D G         413       A FR EAS F GH A T L D I K NR T HA H       Y SWNR N Q D G         414       A FR EAS F GH A T L D I K NR T HA H       Y SWNR N Q D G         412	414 439 419 437 438 433 438 434 443 437 436 437 436 437 436 438 441 435 447 436 442 438 447 436 598 584 588 588 588 588 418 588 418 405 418 438 429 412 387
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 ArP AP 11   09518  /1-441 GmP AP 10 09131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-465 0sP AP 10   0484K23  /1-461 MtP AP   084K23  /1-461 MtP AP   084K23  /1-465 0sP AP 2   0764C1  /1-457 UAP 2   0764C1  /1-457 UAP 2   0764C1  /1-457 UAP 2   0764C1  /1-457 Ta ACP   C4PKL1  /1-477 AtP AP 6   09 5V 9  /1-468 P vP AP 10   095V 9  /1-468 P vP AP 10   095V 9  /1-468 AtP AP 10   095V 9  /1-473 Ta ACP   C4PKL1  /1-477 AtP AP 6   09 C50 0  /1-470 StP AP 3 2   095K00  /1-473 AtP AP 26   0949 V3  /1-475 RcP AP 3   08560  /1-473 AtP AP 26   0949 V3  /1-475 RcP AP 3   08560  /1-473 AtP AP 26   0949 V3  /1-475 UAP 10   085E0  /1-418 UAP 11 \0815E1  /1-512 UAP 10   08VXF1  /1-615 UPP D4   08VXF1  /1-615 UPP D2   08VXF1  /1-638 CeP AP 3   09IJAM9  /1-418 MmP AP 7   08BX37  /1-438 DmP AP 1   09VZ56  /1-438 DmP AP 1   09VZ56  /1-438 CeP AP 3   09VZ57  /1-438 CeP AP 3   09VZ57  /1-438	385       A FR EAS Y GH ST L E IMNK T HA F       Y YWHR N D D G         410       A FR EAS F GHA I L D I K NR T HA Y       Y SWHR N Q D G         390       A FR EAS F GHA I F D I T NR T HA Y       Y SWHR N Q D G         403       A FR EAS F GHA I F D I T NR T HA Y       Y SWHR N Q D G         404       A FR EAS F GHA I F D I T NR T HA Y       Y SWHR N Q D G         411       A FR EAS F GHA I E I K NR T HA Y       Y SWHR N Q D G         412       A FR EAS Y GH A I E I K NR T HA Y       Y SWHR N Q D G         409       A YR EAS F GHA I F D I K NR T HA Y       Y SWHR N Q D G         400       A YR EAS F GHA I E I K NR T HA Y       Y SWHR N Q D G         401       A YR EAS Y GH S I L E I K NR T HA H       Y SWHR N Q D G         405       A YR KAS F GH G I F A I K NR T HA H       Y SWN R N Q D G         413       A FR EAS Y GH S T L E I K NR T HA H       Y SWN R N Q D G         413       A FR EAS F G GH A I F S I K NR T HA H       Y SWN R N Q D G         413       A FR EAS F G GH A I F S I K NR T HA H       Y SWN R N Q D G         413       A FR EAS F G H A I K S I K NR T HA H       Y G W R N D D G         413       A FR EAS F G H A I K S I K NR T HA H       Y G W R N Q D G         414       A FR EAS F G H A I K S I K NR T HA H       Y G W R N D D G	414 439 419 437 438 443 437 438 434 442 437 442 437 436 438 444 435 447 436 444 435 447 436 598 584 447 438 444 445 598 584 588 584 581 358 418 429 412 387 426

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HvPAPhy_a/C4PKL2//1-544	515	Y - G S A - G D E	1 Y I V R	EPERC	531
TaP APhy a1/C4PKK7//1-550	512	Y - G S A - G D E	1 Y I V R	EPHRC	528
TaP APhy b1/C4PKK9//1-538	511	Y Q G A V - G D E	1 Y I V B	EPERC	528
		YQGAV-GDE			
		YQGAV-GDE			
		YQGAV-GDE			
/= 1 1/		H A A N V A A D E			
		Y - G T A - G D E			
PtPAP3 V9LXK5 /1-564	533	Y - E A A - G D Q	I Y I V R	QPDLC	549
WtP AP hy   A5 YBW1   / 1-551	515	Y - N K A - G D I	IYIVR	QPEKC	531
LaP APhy   D2 YZL4   /1-543	513	Y - N EV - G D Q	I Y I V R	QPHLC	529
GmPAPhy biQ93XG41/1-547	517	Y - K EV - G D Q	1 Y I V R	QPDIC	533
		S-SEV-GDQ			
		Y-GSA-GDE			
· <b>=</b> · · · · ·					
		Y-GSA-GDE			
		Y - G S A - G D E			
		Y Q G G V - G D E			
TmPAPhy_b1/F6MIW9//1-539	512	Y Q G V V - A D E	IYIVR	EPERC	529
AtaP APhy_b1/F6MIX1//1-538	511	Y Q G A V - G D E	I Y I V R	EPERC	528
ScP APhy_b1/F6MIX5//1-538	511	Y Q G A V - G D E	IFIVR	EPERC	528
		Y - S S A - G D Q			
		R-DNA-GDQ			
		Y-KEV-GDQ			
		Y-KEV-GDQ			
					522
AtP AP 23   Q6TPH 1   / 1-458					
		E-PVK-ADD			
		Y A E N S V G D Q			
		Y G E N S V G D Q			
HvP AP_c   C4PKL5   /1-564	534	Y G E H S V G D E	I Y I V R	EPDKC	552
PpPAP   A9SP12   /1-557	517	Y K E A V - G D Q	1 Y I V R	QPDGC	534
		Y G E D S V G D Q			
		YGEDSVGDQ			
		E-AVI-ADS			
		N-SLL-ADE			
1					
1 4 10		L - A V E - G D S			
		N - A V E - A D S			
		E - A V I - A D S			
GmP AP 1   Q09 13 1   / 1-4 64	438	V - A V E - A D S	LWS		447
AtP AP 25   023244   /1-466	439	E - P V A - A D S	IML		448
AtP AP 12   Q38924   /1-469	444	N - A V A - A D S	VWL		453
		F - S A K - A D S			
		Y - S V E - A D S			
		K-HVP-ADN			
		Y-AVE-ADK			
		K-KVP-TDS			
		· · · · · · · · · · · · · · · · · · ·			
		V - A V E - A D S			
		E - P V A - A D S			
		Y - A V E - A D T			
		NNITTDS			
IbP AP 1   Q95E00   /1-473	448	A - S V E - A D S	LWL		457
AtP AP 26/0949 Y3 //1-475	437	K - K V A - T D E	FVL		446
		N - K V A - T D A			
		K-KVP-IDS			
		K-KVP-TDS			
		QAVVATLLF-AVT-GNDSQDTNQNASLLVSARQFVIAMLVIDTW			
		44VVATELF-AVT-GNDSQDTNQNASELVSARQFVTAMEVTDTW			
		GKV-YDS			
		GKV-IDS			
		T-GKF-LDP			
		GKI-VDD			
		N-GAI-IDD			
DmP AP 2   Q9 VZ58   /1-450	430		FWV IK	DKHGA	445
		E-GAV-LDH			
		GKQ			
	388				
DmP AP3109V/5/1/1452					443
	427	K-GEV-IDS	FWV V K	DКНGР	
	427		FWV V K	DКНGР	

HvP APhy_a   C4PKL2   / 1-544	532	- L H K H N S T
TaP APhy_a 1   C4PKK7   / 1-550	529	- L H K H N S S
TaP APhy_b1/C4PKK9//1-538	529	- L L K S S
		- L L K S S
HvP APhy b2/C4PKL4//1-537	528	- L L S S S
		- L L K S S
		- L I K S S R N
		- L
		P P V M P E E - A H N T
		- P V Q P E A Y R L N K P
		- P V K P K V I K P
		- P I N Q K V C R E
		- P I H Q R V N I D
		- P L H H R L V N H
		- L H K H N S S
ScPAPhy a2/F6MIX4//1-543	531	- L H K H N S T
		- L H K H N S T
		- L H K H N S T
		- L H K H N S T
		- L H K H K H N S T
		- L L K S S
		- L L K S S
AtaP APhy b1/F6MIX1//1-538	529	- L L K S S
		- L L K S S
		- P V K P K - G A I N V L
1 17		- P T L S A V T K L
		- P V P Q R V S G D
		DVPRKVCRD
		- P L H H R L V N H
		NSLN455
GmP AP4   V9HXG4   /1-442	428	VDQKTHE 434
ZmP AP_c   C4PKL7   / 1-566	555	L L Q P A S A S S L N
SbP AP   AO A1Z5R9 T8   /1-566	555	L L Q P T N A S S L N
HvP AP_c   C4PKL5   /1-564	553	L L Q P R G
PpPAP   A9SPI2  /1-557	535	- P Y S S MK N Y R D R K
OsP AP 3   Q6ZCX8   /1-622	558	LLQTTSASSE
OsP AP 4   B8 B909   /1-622	558	LLQTTSASSE
AtP AP 5   Q9 C927   /1-396	385	388 X X X X X X X X X X X X X X X X X X
AtP AP 20   Q9 LXI 7   / 1-427	426	K
AtP AP 22   Q85340   /1-434		
1bP AP 3   Q9ZP 18   /1-427	412	415 A A A A A A A A A A A A A A A A A A A
AtP AP 2 1   Q9 LXI4   / 1-437	429	432 H S N R
LpP AP   Q9MB07   /1-455	445	448 F. F. R. V
RcP AP 2   B95XP8   / 1-463	425	HNQY428
IbP AP 2   Q9 SD Z9   / 1-465	450	S N R F 453
		K K R Y 433
		FNRY 451
		LNRF
		FNRY 453
MtP AP 1   Q4K U02   / 1-465	449	FNRF 452
		HNQY449
		FNRY448
		HNQY
		FNRY 451
		YNRF
		FNRH 451
		HNRH 452
		R N Q Y 455
		FNRY 458
		LNRY 461
		HNQY 450
		HNQY 456
		Y N Q Y 452
		MHRYMHHNKFLYKHIHSQHHRLIVPYSFGALYNHPLVGLILDTIGGA 557
		LARV 618
		LACS 604
	598	LACT601
TnP AP 1   Q4R LR4   / 1-378		
HsP AP 7   Q6ZWF0   / 1-438		
		EK L 418
1	456	458
DmP AP 2   Q9 VZ58   / 1-450	497	
		426 I P T D T S T R S T
		410 
	-130	400

U.D ADE.,			
2 1 12			
TaP APhy_b1 C4PKK9 /1-538	534	I AAY F 5	38
TaP APhy b2/C4PKL0//1-537	533	I A A Y F 5	537
HvP APhy_b2   C4PKL4   / 1-537	533	I AA Y F 5	537
HvP APhy b1/C4PKL3//1-536	532	I AAY F 5	36
OsP APhy b/D6Q5X9//1-539	535	RIAYY5	539
ZmP APhy biC4PKL6I/1-544	540	RLLAY	544
MtP APhy/Q3ZFI1//1-543			
	562	KPQ5	564
		YFAAI5	
		CIASI5	
		C	
AtaP APhy a 1/F6MIX0 //1-549	535		549
		R P A H G R 5	
		RPAHGRQNTTRESGG	
		RPTHGR5	
		RPAHGRQNTTRESGG 5	
ScPAPhy a1/F6MIX2//1-541	536	R P A H G R 5	541
		I A A Y F 5	
		I A A Y F 5	
		I A A Y F 5	
		V A 5	
21 12		FTASI 5	
// //			
		LSN 4	
GmP AP4   V9HXG4   /1-442	435	LR STLLTP	442
		W	
HVPAP c/C4PKL5//1-564	559		564
<b>_</b> · · · ·		LP V GP E Y Q Q H T 5	
0sP AP 3   Q6ZCX8   /1-622	568	- NN C P S E G C P S L V S N S G Y G A Q K D I I R S G H L I WN A S L V I WM I L I S T V F M K G N L C S R F 6	522
OsP AP 4   B8 B909   /1-622	568	- NN C P S E G C P S L V S N S G Y G A Q K D I I R S G H L I WN A F L V I WM I L I S T V F M K G N L C S R F 6	522
AtP AP 5   Q9 C9 27   /1-39 6	389		396
AtP AP 20   Q9 LXI7   /1-427	427		427
AtP AP 22   Q85340   /1-434	425		434
IbP AP 3   Q9 ZP 18   /1-427	416	4	427
AtP AP 2 1   Q9 LXI 4   / 1-437	433	YRGEI4	437
1-0.40.000400.71/4.455			
LDP AP   USIVIBU /   / 1-455	449	WNPREES 4	455
RcP AP 2   B95XP8   /1-463	429	WASNLRQQNLQKHHRRSLGDETASN 4	
RcP AP 2   B9 5XP 8  /1-463 16P AP 2   Q9 5D 29  /1-465	429 454		453
RcP AP 2   B95XP 8  /1-463 IbP AP 2   Q95D 29  /1-465 AtP AP 11   Q95 I 18  /1-441	429 454 434		453 465 438
R CP AP 2   B9 SXP 8   / 1-463 I bP AP 2   Q9 SD 29   / 1-465 AtP AP 11   Q9 SI 18   / 1-441 GmP AP 1   Q0 9 13 1   / 1-464	429 454 434 452		453 465 438
R CP AP 2   B9 SXP 8   / 1-463 I bP AP 2   Q9 SD 29   / 1-465 AtP AP 11   Q9 SI 18   / 1-441 GmP AP 1   Q0 9 13 1   / 1-464	429 454 434 452 453		453 465 438 464 457
RcP AP 2   895XP8  /1-463  bP AP 2   Q95D29  /1-465 AtP AP 11   Q951 18  /1-441 GmP AP 1   Q09 131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   Q38924  /1-469	429 454 434 452 453 458		453 465 438 464 457 466
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11   Q9518 /1-441 GmP AP 1  Q09131 /1-464 ArP AP 25   O23244 /1-466 ArP AP 12   Q38924 /1-469 IVP AP   Q84K23 /1-461	429 454 434 452 453 458 458		453 465 438 464 457 466 461
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 AtP AP 11   Q95 I8  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   Q38924  /1-465 NtP AP 1   Q4KU02  /1-465	429 454 434 452 453 458 454 453		453 465 438 464 457 466 461 465
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 25   Q23244  /1-466 AtP AP 12   Q38924  /1-469 IVTP AP   Q84KZ3  /1-461 MtP AP 1   Q4KU02  /1-465 OsP AP 2   Q8505  /1-476 La AP 1   Q93VM7  /1-460	429 454 452 453 458 454 453 450 449		453 465 438 464 457 466 461 465 474 460
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   09518  /1-441 GmP AP 1   009131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   028924  /1-469 IVTP AP   084KZ3  /1-461 MtP AP 1   04KU02  /1-465 OsP AP 2   085505  /1-476 La AP 1   093VM7  /1-460	429 454 452 453 458 454 453 450 449		453 465 438 464 457 466 461 465 474 460
RcP AP 2   895XP8  /1-463 IbP AP 2   095D29  /1-465 AtP AP 11   09518  /1-441 GmP AP 1   009131  /1-464 AtP AP 25   023244  /1-466 AtP AP 12   038924  /1-469 INTP AP 10 084K23  /1-461 MtP AP 1   04KU02  /1-465 OsP AP 2   08505  /1-476 La AP 1   093VM7  /1-460 P vP AP 2   0764 C1  /1-457	429 454 452 453 458 454 453 450 449 457		453 465 438 464 457 466 461 465 474 460
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11   Q9518 /1-465 ArP AP 11   Q9313 /1-464 ArP AP 25   O23244 /1-466 ArP AP 12   Q38924 /1-469 INP AP 1   Q4KU02 /1-465 OsP AP 2   Q85505 /1-476 La AP 1   Q93VM7/1-460 P vP AP 2   Q764C1 /1-457 UAP 2   Q85L511/1-468 ArP AP 10   Q95V9 /1-468	429 454 452 453 458 454 453 450 449 457 452 457		453 465 438 464 457 466 461 465 474 460 457 463
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 AtP AP 11   Q95129 /1-465 AtP AP 11   Q9131]/1-464 AtP AP 25   O23244 /1-466 AtP AP 12   Q3894/1-469 ItP AP 1   Q4KU02 /1-465 OSP AP 2   Q85505 /1-476 La AP 1   Q93VM7//1-460 P vP AP 2   Q764C1 /1-457 UAP 2   Q8L1 /1-463 AtP AP 10   Q9SV9 /1-468 P vP AP 1 P80366 /1-459	429 454 452 453 458 454 453 450 457 457 452 457		453 465 438 464 457 465 474 465 474 465 457 468 459
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 AtP AP 11  Q9518 /1-441 GmP AP 1   Q09131 /1-464 AtP AP 2   Q09131 /1-464 AtP AP 2   Q38924 /1-469 ItP AP 12   Q38924 /1-469 ItP AP 10   Q4KU02 /1-465 OSP AP 2   Q85505 /1-476 La AP 11   Q93VM7 /1-460 P vP AP 2   Q764C1 /1-457 LIAP 2   Q764C1 /1-457 LIAP 2   Q951V9 /1-468 AtP AP 10   Q951V9 /1-465 P vP AP 1 P80366 /1-459 Ta ACP (C4PKL1 /1-477	429 454 452 453 458 454 453 450 457 457 457 452 451		453 465 438 464 457 466 461 465 474 460 457 463 468 459 475
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 AtP AP 11  Q9518 /1-441 GmP AP 1 Q09131 /1-464 AtP AP 2   Q03224 /1-466 AtP AP 12   Q38924 /1-466 INTP AP   Q84X23 /1-461 MtP AP 1 Q4KU02 /1-465 OSP AP 2   Q85505 /1-476 La AP 1   Q93VM7 /1-460 P vP AP 2   Q764C1 /1-457 UAP 2   Q8L6L1 /1-463 AtP AP 10   Q95IV9 /1-468 P vP AP 1 P80366 /1-459 Ta ACP (C4FKL1]/1-477 AtP AP 6  Q9 C510 /1-466	429 454 452 453 458 454 453 450 449 457 452 457 452 451 453		453 465 438 464 457 465 474 465 474 465 457 468 459
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 AtP AP 11  Q9518 /1-441 GmP AP 1   Q09131 /1-464 AtP AP 2   Q03224 /1-466 AtP AP 12   Q38924 /1-469 INP AP   Q84X23 /1-461 MtP AP 1   Q4KU02 /1-465 OsP AP 2   Q85505 /1-476 La AP 1   Q93VM7 /1-460 P vP AP 2   Q764C1 /1-457 UAP 2   Q8L6L1 /1-457 UAP 2   Q8L6L1 /1-468 P vP AP 1   P80366 /1-459 Ta ACP (C4FKL1]/1-477 AtP AP 6  Q95XVP4 /1-461	429 454 452 453 458 454 453 450 449 457 452 457 452 451 453 456		453 465 438 464 457 466 467 465 465 465 468 459 468 459 466 480
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11(Q9518 /1-441 GmP AP 1 Q09131 /1-464 AtP AP 25  023244 /1-466 AtP AP 12   Q38924 /1-469 INTP AP 1   Q4KU02 /1-465 Os <sup>2</sup> AP 2   Q8505 /1-476 La AP 1 Q93VM7//1-460 P vP AP 2   Q764C1 /1-457 UAP 2   Q8L6L1]/1-463 AtP AP 10   Q93V9 /1-468 P vP AP 10 R0366 /1-459 Ta ACP   C4PKL1 /1-477 AtP AP 6   Q9 C510 /1-466 AcP AP   Q93VP4 /1-470	429 454 434 452 453 458 454 453 450 457 452 457 452 451 453 456 459		453 465 438 464 457 466 457 465 474 460 457 468 459 468 459 475 466 480 470
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11 (Q918)  1-465 ArP AP 11 (Q9131)/1-464 AtP AP 25   O23244  /1-466 AtP AP 12 (Q38924  /1-469 INP AP 1 (Q84K23)/1-461 MtP AP 1 (Q4KU02  /1-465 OSP AP 2 (Q85505)/1-476 La AP 1 (Q93VM7)/1-460 P vP AP 2   Q86L11/1-463 AtP AP 10   Q93VV9  /1-468 P vP AP 1 P80366 /1-459 Ta ACP (C4PKL1)/1-463 AtP AP 6   Q9 C510 //1-466 AcP AP 2 Q93WP4  /1-481 AoP AP 32 (Q35K09)/1-470 StP AP3   Q6J5M8  /1-477	429 454 434 452 453 458 454 453 450 457 457 457 457 455 455 455 455		453 465 438 464 457 466 457 465 474 460 457 468 459 468 459 475 466 480 470
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11(Q9518 /1-441 GmP AP 1 Q09131 /1-464 AtP AP 25  023244 /1-466 AtP AP 12   Q38924 /1-469 INTP AP 1   Q4KU02 /1-465 Os <sup>2</sup> AP 2   Q8505 /1-476 La AP 1 Q93VM7//1-460 P vP AP 2   Q764C1 /1-457 UAP 2   Q8L6L1]/1-463 AtP AP 10   Q93V9 /1-468 P vP AP 10 R0366 /1-459 Ta ACP   C4PKL1 /1-477 AtP AP 6   Q9 C510 /1-466 AcP AP   Q93VP4 /1-470	429 454 434 452 453 458 454 453 457 452 457 452 457 452 453 455 453 455 453 455 452		453 465 438 464 457 466 457 465 474 460 457 468 459 468 459 475 466 480 470
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 AtP AP 11   Q9518 /1-441 GmP AP 11   Q9518 /1-441 GmP AP 11   Q93924 /1-466 AtP AP 2 2   Q38924 /1-466 MtP AP 12   Q38924 /1-461 MtP AP 10 Q4KU02 /1-465 OSP AP 2   Q85505 /1-476 La AP 11   Q93VW7 /1-460 P vP AP 2   Q764C1 /1-457 UAP 2   Q8L6L1 /1-463 AtP AP 10   Q95V9 /1-468 P vP AP 1   P80366 /1-459 Ta ACP   C4PKL1 /1-477 AtP AP 6   Q9 C510   /1-466 AcP AP 6   Q93VW74 /1-481 AoP AP 32   Q9XF09   /1-470 StP AP 3   Q6J5M8 /1-477 IbP AP 1   Q95D0   /1-473 AtP AP 26   Q9493   /1-475	429 454 434 452 453 458 454 453 457 452 457 452 457 452 451 453 455 453 455 453 455 453		453 465 438 465 465 465 466 457 466 457 468 9 470 473 473 475
RcP AP 2   B95XP8  /1-463 IbP AP 2   Q95D29  /1-465 AtP AP 11   Q9518  /1-441 GmP AP 1   Q09131  /1-464 AtP AP 2   Q03121 //1-464 AtP AP 2   Q38924  /1-469 ItP AP 12   Q38924  /1-461 MtP AP 10 Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 11   Q93VM7  /1-460 P vP AP 2   Q764C1  /1-457 UAP 2   Q8L6L1  /1-463 AtP AP 10   Q9510  /1-463 AtP AP 6   Q9 C510  /1-466 AcP AP (Q93WP4  /1-481 AoP AP 3   Q93K09  /1-473 StP AP 3   Q05XD0  /1-473 AtP AP 2 (Q949Y3  /1-455 RcP AP 3   B95XP 6  /1-488	429 454 434 452 453 458 454 453 457 452 457 452 457 452 451 455 452 455 455 452		453 465 434 457 466 457 466 457 466 457 468 457 468 470 473 473 473 481
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11(Q9518]/1-465 ArP AP 11(Q9518]/1-464 ArP AP 25  O23244 /1-466 INP AP 12   Q38924 /1-469 INP AP 1Q84K23 /1-461 MrP AP 1Q94KU02 /1-465 OSP AP 2   Q764C1 /1-463 ArP AP 10  Q93VN7/1/1-66 P vP AP 2   Q764C1 /1-457 UAP 2   Q8L6L1/1/1-463 ArP AP 00   Q93VN9 /1-468 P vP AP 10  Q93VN9 /1-468 P vP AP 10  Q93VN71/1-460 ArP AP 10   Q93VN71/1-460 ArP AP 10   Q93VN71/1-463 ArP AP 10   Q93VN71/1-463 ArP AP 10   Q93VN71/1-477 IBP AP 10   Q93VN701/1-477 IBP AP 10   Q93VN701/1-473 ArP AP 2   Q93VN701/1-473 ArP AP 2   Q949Y31/1-475 RcP AP 3   B95XP 6/11-488 UAP 10   Q815211/1-477	429 454 434 452 453 458 454 453 457 452 457 452 457 452 455 455 455 455 452 455 452 455 452 455		453 4658 4657 4661 4766 4767 4667 4669 4774 473 4751 4751 477
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11 (Q95138]/1-441 GmP AP 11 (Q95138]/1-441 GmP AP 12 (Q38924]/1-469 ArP AP 12   Q38924]/1-469 INTP AP 1 Q4KU02  /1-465 OSP AP 2   Q8505]/1-476 La AP 1/Q93VM7/1/1-460 P vP AP 2   Q764 C1/1-457 UAP 2   Q816L1]/1-463 ArP AP 10   Q93VM7/1-468 P vP AP 10   Q93VM7/1-468 P vP AP 10   Q95V9  /1-468 P vP AP 10   Q951V9  /1-468 P vP AP 10   Q951V9  /1-463 ArP AP 6   Q9 C510  /1-466 AcP AP 6   Q9 C510  /1-466 AcP AP 3   Q6J5M8  /1-477 IbP AP 1 (Q95E00  /1-473 ArP AP 26   Q949 Y3  /1-475 RcP AP 3   B95XP 6  /1-488 UAP 11 (Q815E1]/1-477 GmP AP 3   Q6YGT9  /1-512	429 454 434 452 453 458 454 453 457 457 457 452 457 452 452 452 452 452 452 452 452 452 452		453 4658 467 465 4661 4657 4667 4667 4669 477 473 477 477 477 477 477 477
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11   Q9131 /1-464 ArP AP 11   Q9131 /1-464 ArP AP 25   O23244 /1-466 ArP AP 12   Q38924 /1-469 INP AP 1   Q4KU02 /1-465 OsP AP 2   Q85505 /1-476 La AP 1   Q93VM7 /1-460 P vP AP 2   Q86L11 /1-463 ArP AP 10   Q93VV9 /1-468 P vP AP 1   P80366 /1-459 Ta ACP (C4PKL1]/1-463 ArP AP 6   Q9 C510 /1-466 AcP AP 3 Q Q93VP4 /1-481 AoP AP 3 Q Q9XF09 /1-470 StP AP 3   Q6J5M8 /1-477 IbP AP 1   Q95D0 /1-473 ArP AP 2   Q95D0 /1-473 ArP AP 2   Q95D0 /1-473 ArP AP 2   Q95D0 /1-473 ArP AP 3   Q6J5E1 /1-477 GmP AP 3   Q6YG79 /1-512 La AP 2   Q9XJ24 /1-638	429 454 434 452 453 458 454 453 457 452 457 452 457 451 453 456 459 451 453 455 455 455 558	WASNLRQQNLQKHHRRSLGDETASN 4         WHP V DDSTTTKL         YLPEE         WHP V D         FFPVE         WRAQK         WHP V DESY         WHP V DSTTHVSH         WHP V DDSTTHVSH         WHP V DDSTTHVSH         WHP V DDSTTHVSH         WHP V DDSTTHVSH         WASNTRRRLKKKHFHLDQIEDLIS 4         WHP V DDSTTHVSH         WASNTRRRRLKKKHFHLDQIEDLIS 4         WHP V DDSTTHYSH         WASNTRRRRLKKKHFHLDQIEDLIS 4         WHP V DDSTTHYSH         WASNTRRRRLKKKHFHLDQIEDLIS 4         WHP V DDSTTHYSH         WASNTRRRRLKKKHFHLDQIEDLIS 4         WHP V DSTTHYSH         WHP V DSTHYSH         WHP V DSTHYSH <td>453 4658 46766 4665 4667 4667 4667 4677 4680 4774 4773 4775 4772 313</td>	453 4658 46766 4665 4667 4667 4667 4677 4680 4774 4773 4775 4772 313
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11   Q9318 /1-441 GmP AP 11   Q9318 /1-441 GmP AP 11   Q93244 /1-466 AtP AP 25   O23244 /1-466 AtP AP 12   Q38242 /1-461 MtP AP 1   Q4KU02 /1-465 OSP AP 2   Q85505 /1-476 La AP 1   Q93VM7)/1-460 P vP AP 2   Q86L511/1-463 AtP AP 10   Q93VV3 /1-468 P vP AP 10   Q93VV3 /1-468 P vP AP 1P80366 /1-459 Ta ACP (C4PKL11/1-477 AtP AP 6   Q93VF03 /1-477 StP AP 3   Q6J5M8 /1-477 IbP AP 1   Q93WP4 /1-483 LI AP 1   Q93E00  /1-473 AtP AP 2   Q94500  /1-473 AtP AP 2   Q95200  /1-477 GmP AP 3   Q6VGT3  /1-518 LI AP 2   Q9421/1-638 UPP D4   Q8VXF4 /1-629	429 454 434 452 453 458 454 457 452 457 452 457 452 453 456 459 459 459 459 459 459 459 459 459 459	WASNLRQQNLQKHHRRSLGDETASN 4         WHP V DDSTTTKL         YLPEE         WHP VD         FFPVE         WRAQK         WHP VDESY         WHP VDSTTHVSH         WHP VDSTTHVSH         WRAQK         WHP VDDSTTHVSH         WRAQK         WHP VDDSTTHVSH         WHP VDDSTTHVSH         WHP VDDSTTHVSH         WASNTRRRLKKKHFHLDQIEDLIS 4         WNPLNDSTIHIP         WHP VDDSPSCNS         WHP VDDSPSCNS         WHP VDDSSTRRRLKKKHLRYESLQSLMS 4         FFP VEIVSSNIRA         WNP VDSSTAA         WASNTRRRLKKKHLRYESLQSLMS 4         WNP VDSSTSATA         WASNTRRRLKKKHLRYSQAVERLISS 4         WASNTRRRLKKKHLRYSQUAVERLISS 4         WASNTRRRLKKKHLRYSQUAVERLISS 4         WASNTRRRLKKKHVIRSVVGGWIAT 4         WASNPRRRKLKKHVIRSVVGGWIAT 4         WASNPRRRKLKKHVIRSVVGWIAST 4         WASNPRRRKLKKHVIRSVVGWIAST 4         WASNPRRRKLKKHLLTUVDEAVSM 4         WASNPRRRKLKKHFLLVVIDEVASM 5         SFLISGMSPRISIFFFSFATIKTVDDHCGLWLPGNLFHIFSTTILLTMMFTISFS 6	453 4658 46766 4665 4667 4667 4667 4667 4677 4680 4773 4775 4775 4775 4775 4775 4775 4775
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 AtP AP 11   Q9318 /1-441 GmP AP 11   Q9318 /1-441 GmP AP 12   Q38924 /1-466 AtP AP 12   Q38924 /1-466 AtP AP 12   Q38924 /1-465 OSP AP 2   Q85505 /1-476 La AP 1   Q93VW7//1-460 P vP AP 2   Q764C1 /1-457 UAP 2   Q8L6L1 /1-463 AtP AP 10   Q93V9 //1-468 ArP AP 10   Q93V9 //1-468 ArP AP 10   Q93V9 //1-468 ArP AP 10   Q93V9 //1-467 AtP AP 6   Q9C510 //1-467 AtP AP 6   Q9C510 //1-466 AcP AP   Q93WP4 //1-481 AoP AP 32   Q9XF09 //1-477 StP AP 3   Q6505M8 //1-477 IbP AP 1   Q95E00 //1-473 AtP AP 26   Q949 Y3 //1-475 RcP AP 3   B95XP 6 //1-488 UAP 1   Q8L521 //1-712 La AP 2   Q9XI24 //1-638 UAP 0   Q8VXF4 //1-629 UPP D4   Q8VX11 //1-615	429 454 434 452 453 454 457 452 457 452 457 452 457 452 457 452 457 453 456 459 450 455 450 450 450 450 450 455 450 450	WASNLRQQNLQKHHRRSLGDETASN 4         WHP V DDSTTTKL         YLPEE         WHP VD         WHP VD         WRQK         WHP VDESY         WHP VDSTTHVSH         WHP VDSTTHVSH         WHP VDSTTHVSH         WHP VDSSY         WHP VDSSY         WHP VDDSTHVSH         WHP VDDSTHVSH         WHP VDDSTTHVSH         WASNTRRRLKKKHLDQIEDLIS         WHP VDDSTHVSH         WHP VDDSTTHVSH         WHP VDDSTTHVSH         WHP VDDSTTHVSH         WHP VDDSTTHVSH         WHP VDSTSTHVSH         WHP VDSTSTHVSH         WHP VDSTSTHVSH <t< td=""><td>453 465 465 465 465 465 465 465 465 465 465</td></t<>	453 465 465 465 465 465 465 465 465 465 465
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11 (Q9131]/1-464 ArP AP 2   Q93D29 /1-465 ArP AP 12   Q3924 /1-469 IVP AP 12   Q3924 /1-469 IVP AP 1 Q84K23 /1-461 MrP AP 1 Q94KU02 /1-465 OSP AP 2   Q764C1 /1-457 UAP 2   Q8L6L1/1-463 ArP AP 10   Q93VW7 /1-468 P vP AP 10   Q93VW7 /1-468 P vP AP 10   Q93VW7 /1-468 P vP AP 10   Q93VW7 /1-468 ArP AP 00   Q93VW74 /1-417 TaACP   C4PKL1/1-477 ArP AP 6   Q9C510 /1-466 AcP AP 10 Q93VW74 /1-481 AoP AP 32   Q9XF09 /1-473 SrP AP 3   Q6VGT9 /1-512 La AP 2   Q9XL24 /1-638 UAP 10   Q8VXT6 /1-612 UPP D2   Q8VXT6 /1-612	429 454 434 452 453 454 453 454 457 452 457 452 457 453 459 453 459 453 453 453 453 455 619 558 619 605 602	WASNLRQQNLQKHHRRSLGDETASN4         WHPVDDSTTTKL         YLPEE         WHPVDDSTTKV         WHPVD         WHPVDSTHVSH         WHPVDDSTHVSH         WHPVDDSTHVSH         WHPVDDSTHVSH         WNPLNDSTHHVSH         WNPLNDSTHVSH         WNPLNDSTHVSH         WNPLNDSTHNSH         WNPLNDSTHHVSH         WNPLNDSTHNSH         WHPVDSSCNS         WNPLNDSTHNSKKKHLSKKHLSKKKHLSKK         WNPVDSSCNS         WHPVDDSPSCNS         WNPVDSSNSNS         WNPVDSSNSNSNSNS         WHPVDSSNSNSNSNSNS         WNPVDESTSNER         WSSNERRKLKKHVNNHNSVISER         WSSNERNRRKLKKHVNSVOGWIAST         WGS	453 465 465 465 465 465 465 465 465 465 465
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11(Q9518]/1-441 GmP AP 11(Q9518]/1-441 GmP AP 12   Q3924 /1-469 ArP AP 12   Q38924 /1-469 INTP AP 1 Q4KU02 /1-465 OSP AP 2   Q85505 /1-476 La AP 11 Q4KU02 /1-465 OSP AP 2   Q93VM7/1/1-460 P vP AP 2   Q764C1 /1-457 UAP 2   Q8L6L1]/1-463 ArP AP 10   Q93VM7 /1-468 P vP AP 10   Q95V9 /1-466 AcP AP 6   Q9C510 /1-466 AcP AP 6   Q9C510 /1-466 AcP AP 3   Q6J5M8 /1-477 IbP AP 3   Q6J5M8 /1-477 IbP AP 3   Q95E00 /1-475 RcP AP 3   B95XP 6/1-488 UAP 10   Q95V74/1-638 UAP 10   Q8VXF4/1-638 UPP D4   Q8VXF6/1-612 TnP AP 10   Q8VXF6/1-612 TnP AP 10   Q4RUR4 /1-378	429 454 434 452 453 454 453 454 457 452 457 452 457 452 451 453 459 450 452 451 456 459 450 452 451 455 455 455 455 455 455 455 455 455	WASNLRQQNLQKHHRRSLGDETASN 4         WHP V DDSTTTKL         Y LP EE         WHP VD         FFP VE         WR AQK         WHP V DDS TTHVSH         WN NP V DDS TTHVSH         WN NP V DDS TTHVSH         WW         WNP V DDS TTHVSH         WW         WNP V DDS TTHVSH         WAS N TRRRRLKKKHFHLDQIEDLIS 4         WHP V DDS TSHNSH         WW PV D         WN NP R DDS TIHIP         WHP V DSPS CNS         WHP V DSPS CNS         WHP V DSSN IRA         WHP V DSSN IRA         WY P V D         WSS GLRRRKLKK HLRYSLQSLMS 4         WY P V D         WSS GLRRRK LKK HLRYSLQSLMS 4         WY P V D         WSS GLRRRK LKK HLRYSLQSLMS 4         WSS GLRRRK LKK HLRYSLQSLMS 4         WGS GLRRRK LKK HLRYSLQSLMS 4         WGS GLRRRK LKK HLRYSV GWIAST 4         WSS GLRRRK LKK HLRSV Y GWIAST 4         WGS NR RR KLKK HLRSV Y GWIAST 4         WAS NP RRRRK LKK HLRSV GWIAST 4	453 465 465 465 465 465 465 465 465 465 465
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11   Q91 13 /1-464 AtP AP 11   Q91 13 /1-464 AtP AP 25   O23244  /1-466 AtP AP 12   Q38924  /1-469 INTP AP   Q84K23  /1-461 MtP AP 1   Q4KU02  /1-465 OSP AP 2   Q85505  /1-476 La AP 1   Q93VM7 //1-460 P vP AP 2   Q64 C1  /1-457 UAP 2   Q84 L1  /1-463 AtP AP 10   Q93VV9 //1-468 P vP AP 1   P80366  /1-459 Ta ACP (C4PKL1  /1-473 AtP AP 6   Q9 C510  /1-466 AcP AP 6   Q9 C510  /1-466 AcP AP 3   Q6J5M8  /1-477 IbP AP 1 (Q95D0 )/1-473 AtP AP 3   Q6J5M8  /1-477 GmP AP 3   Q6J5M8  /1-512 La AP 2   Q9XVF6  /1-613 UPP D4   Q8VXF6  /1-612 UPP D4   Q8VXF6  /1-612 Tn AP 1   Q4ELR4  /1-378 HSP AP 7   Q6Z1VF0  /1-438	429 454 434 452 453 454 453 454 453 454 457 452 457 452 457 452 455 455 455 455 455 455 455 455 455	WASNLRQQNLQKHHRRSLGDETASN 4         WHP V DDSTTTKL         YLPEE         WHP VD         FFP VE         WRAQK         WHP VDDSTTHVSH         WHP VDESY         WHP VDSTHVSH         WHP VDSTHVSH         WHP VDSTHVSH         WHP VDSTHVSH         WHP VDSTHVSH         WNP LNDSTIHVSH         WNP LNDSTIHVSH         WNP VDSTKKKKHFHLDQIEDLIS         WNP VDSTSINSH         WNP VDSTIHVSH         WNP VDSTIHVSH         WNP VDSTIHVSH         WNP VDSTIHVSH         WASNTRRRLKKKHFHLDQIEDLIS         WNP VDSTIHVSH         WYP VD         WNP VDSTIHVSH         WYP VD         WYP VD         WYP VD         WYP VD         WYP VD         WSNSN RERRLKKKHERSVOGNIST         WYP VD         WSSN RERRKLKKHLRSVVGWIAST         WGSNRRRRKLKKKHLKKNHLNSVVGWIAST         WGSNRR	453 465 465 465 465 465 465 465 465 465 465
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11 (Q9131)/1-464 ArP AP 25   Q23244 /1-466 ArP AP 12   Q38924 /1-469 INP AP 1 Q84K23 /1-461 MrP AP 1 Q4KU02 /1-465 OSP AP 2   Q85505 /1-476 La AP 1   Q4KU02 /1-465 OSP AP 2   Q85C1/1-476 UAP 2   Q86L11/1-463 ArP AP 10   Q93VV7/1-468 P vP AP 1   P80366 /1-459 Ta ACP (Q9C510)/1-468 ArP AP 6   Q9C510)/1-468 ArP AP 6   Q9C510)/1-468 ArP AP 6   Q9SV9/1-468 ArP AP 6   Q9SV9/1-468 ArP AP 3   Q615M8/1-477 IbP AP 1   Q95E00  /1-473 ArP AP 2 6 (Q949YS)/1-475 RcP AP 3   Q615M8/1-477 IbP AP 1   Q95E00  /1-473 ArP AP 2 6 (Q949YS)/1-475 RcP AP 3   Q616GT3)/1-512 La AP 2   Q9XV24 /1-638 UPP D1   Q8VXF4 /1-629 UPP D1   Q8VXF4 /1-615 UPP D2   Q8VXF6/1-612 TnP AP 1   Q4R,R4 /1-378 HSP AP 3   Q61/IN9/1/-418	429 454 434 452 453 454 453 454 457 452 457 452 457 452 457 452 457 453 456 459 450 455 455 455 455 455 455 602 374 434	<ul> <li>WA S N L R QQ N L QK HHRR S L GD ET A S N 4</li> <li>WH P V D D S T T T K L</li> <li>Y L P E E</li> <li>WH P V D</li> <li>D S T A HV S H</li> <li>WR A QK</li> <li>WH P V D E S Y</li> <li>WH P V D D S T T H V S H</li> <li>WH P V D D S T T HV S H</li> <li>WA S N T R R R L KK K H F H L D Q I E D L I S 4</li> <li>WN P L N D S T I H I P</li> <li>WH P V D S P S C N S</li> <li>WH P V D S P S C N S</li> <li>WY P V D</li> <li>WN P R D D S T I H I P</li> <li>WA S N T R R R L KK K H L R Y ES L Q S L MS 4</li> <li>WN P K D S P S C N S</li> <li>WY P V D</li> <li>WA S N T R R R R L KK K H L R Y ES L Q S L MS 4</li> <li>WN P V D S T S A T A</li> <li>WA S N T R R R L KK K H L R Y ES L Q S L MS 4</li> <li>WN P V D E S T S A T A</li> <li>WA S N R R R K L KK N H L NS V I S E R P F S 4</li> <li>WA S N R R R K L KK N H L NS V I S E R P F S 4</li> <li>WA S N R R R K L KK N H L NS V Y G G W I A T 4</li> <li>WG S N R R R K L KK N H L NS V Y G G W I A T 4</li> <li>WG S N R R R K L KK N F LMT L V D E A Y S M M</li> <li>WG H N R R R K L KK N F LMT L V D E A Y S M M</li> <li>WG H N R R R K L KK N F LMT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F LMT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F LMT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F L MT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F L MT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F L MT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F L MT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F L MT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F L MT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F L MT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F L MT L V D E A Y S M M</li> <li>WG S N R R R K L KK N F L MT L V D E A Y S M M</li> <li>WG S N R R R K L K K N F L M T Y D E A Y S M M</li> <li>WG S N R R R K L K K N F L M T Y G W A Y A Y A Y A Y A Y A Y A Y A Y A Y A</li></ul>	453 4455 4455 4457 4457 4457 4457 4457 4
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11   Q9318 /1-441 GmP AP 11   Q9318 /1-441 GmP AP 11   Q93241/1-466 AtP AP 25   O23244 /1-466 AtP AP 12   Q382924 /1-461 MtP AP 1   Q4KU02 /1-465 OSP AP 2   Q8505 /1-476 La AP 1   Q93VV7/1-460 P vP AP 2   Q64C1/1-457 UAP 2   Q86L11/1-463 AtP AP 10   Q93VV9/1-468 P vP AP 10   Q93VV9/1-468 P vP AP 10   Q93VV9/1-468 P vP AP 10   Q93VV9/1-468 P vP AP 10   Q93VV9/1-468 AtP AP 6   Q9 C510/1-466 AcP AP 2   Q93VF09/1-477 StP AP 3   Q6J5M8 /1-477 IbP AP 1   Q93E00  /1-473 AtP AP 26   Q94YY3 /1-458 UAP 1   Q85E1/1-477 GmP AP 3   Q6VGT9  /1-515 UPP D1   Q8VXF6/1-612 TnP AP 1   Q4RL41/1-378 HSP AP 7   Q68X37 /1-438 CAP AP 3   Q91AM9]/1-418 MmP AP 7   Q88X37 /1-438	429 454 434 452 453 454 453 454 457 452 457 452 451 452 451 452 451 452 453 456 459 452 451 453 459 459 459 459 459 453 459 453 459 453 459 453 459 453 459 453 459 453 459 453 459 453 459 453 459 457 453 455 455 455 455 455 455 455 455 455	<ul> <li>WA S N L R QQ N L QK HHR R S L GD E T A S N 4</li> <li>WH P V D D S T T T K L</li> <li>Y L P E E</li> <li>WH P V D - D S T A HV S H</li> <li>WR A QK</li> <li>WH P V D E S Y</li> <li>WH P V D S T T H V S H</li> <li>WH P V D S T T HV S H</li> <li>WA S N T R R R L K K K H F H L D Q I E D L I S 4</li> <li>WN P L N D S T I H I P</li> <li>WN P K D D S T I H I P</li> <li>WN P K D D S T I H I P</li> <li>WN P K D D S T I H I P</li> <li>WN P V D S T S N I R A</li> <li>WN P V D S T S N I R A</li> <li>WN P V D S T S N I R A</li> <li>WN P V D S T S N I R A</li> <li>WN P V D S T S N I R A</li> <li>WN P V D S T S A T A</li> <li>WA S N T R R R L K K K H F L I S S Q W E R L I S S</li> <li>WA S N R R R K L K K H H L S V V G WI A S T</li> <li>WA S N R R R K L K K H H L S V V G WI A S T</li> <li>WA S N R R R K L K K H H L S V V G WI A S T</li> <li>WA S N R R R K L K K H H L S V V G WI A S T</li> <li>WA S N R R R K L K K H H L S V V G WI A S T</li> <li>WA S N R R R K L K K H H L S V V G WI A S T</li> <li>WG S N R R R K L K K H H L S V V G WI A S T</li> <li>WG S N R R R K L K K H H L S V V G WI A S T</li> <li>WG S N R R R K L K K H H L S V V G WI A S T</li> <li>WG S N R R R K L K K H H L S V V G WI A S T</li> <li>WG S N R R R K L K K H H L S V V G WI A S T</li> <li>WG S N R R R K L K K H H L S V V G WI A S T</li> <li>WG S N R R R K L K K H H L S V V G WI A S T</li> <li>WG S N R R R K L K K N F LMT L V D E A S M S</li> <li>WG S N R R R K L K K N F LMT L V D E A S M S</li> <li>WG S N R R R K L K K N F LMT L V D E A S M S</li> <li>WG S N R R R K L K K N F LMT L V D E A S M S</li> <li>WG S N R R R K L K K N F LMT L V D E A S M S</li> <li>WG S N R R R K L K K H F L K V I D E Y S M S</li> <li>WG S N R R R K L K K N F L M T V D E A S M S</li> <li>WG S N R R R K L K K N F L M T V D E A S M S</li> <li>WG S N R R R K L K K N F L M T Y D H G L W D S T S T L A S S M S M</li></ul>	453 4455 4455 4457 4457 4457 4457 4457 4
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 AtP AP 11   Q9131/1-464 AtP AP 12   Q09131/1-464 AtP AP 25   O23244 /1-466 AtP AP 12   Q38924 /1-469 ItP AP 10 Q4K/23/1-461 MtP AP 10 Q4K/23/1-461 D8 PAP 2   Q85505 /1-476 La AP 1   Q93W97/1-460 P vP AP 2   Q8505 /1-476 UAP 2   Q8LC1 /1-463 AtP AP 10   Q93W9/1-468 P vP AP 10   Q93W9/1-468 P vP AP 10   Q93W9/1-468 P vP AP 10   Q93W9/1-468 AtP AP 20 Q6210/1-457 Ta ACP   C4PKL1 /1-477 AtP AP 6   Q93W9/1-468 AcP AP 2   Q95V09/1-470 StP AP 3   Q655M8 /1-477 IbP AP 1   Q95E00/1-473 AtP AP 26   Q949Y3 /1-475 RcP AP 3   B95XP 6/1-488 UAP 1   Q8L5E1/1-477 GmP AP 3   Q6YG79  /1-512 La AP 2   Q9XL24/1-638 UAP 10   Q8VXF6/1-612 TnP AP 1   Q4RUR41/1-378 HSP AP 7   Q6ZUF0/1-4138 C6P AP 3   Q8X371/1-438 DmP AP 1   Q9V256/1-458	429 454 434 452 453 454 457 452 457 452 457 452 457 453 459 450 453 459 450 453 453 453 453 453 453 453 453 453 453	WASNLRQQNLQKHHRRSLGDETASN         WHP V DDSTTTKL         YLP EE         WHP VD         WHP VD ST THVSH         WHP VD DS TT HVSH         WHP VD DS THVSH         WAS NTR RR LKK KHFHLDQIEDLIS         WHP VD DS TS ALW         WHP VD DS TS ALW         WHP VD DS THVSH         WHP VD DS THVSH         WHP VD DS THVSH         WHP VD DS TS ALW         WHP VD DS TS ALW         WHP VD DS THVSH         WHP VD DS THVSH         WHP VD S THVSH         WHP VD S TS ALW         WHP VD S TS ALW         WHP VD S THVS S ALW         WHP VD S S CNS         WHP VD S S S CNS         WHP VD S S S CNS         WHP VD S S S NTR R R LKK KHL RY S LQS LMS ALW	453584766154465738956004477351723951288
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11 (Q9131)/1-464 ArP AP 21 (Q93131/1-464 ArP AP 25   O23244 /1-466 ArP AP 12   Q38924 /1-469 INTP AP 1 Q84K23 /1-461 MrtP AP 1 Q4KU02 /1-465 OSP AP 2   Q8505 /1-476 La AP 1 (Q93VM7/1-460 P vP AP 2   Q764 C1 /1-457 UAP 2   Q8L6L1 /1-463 ArP AP 10   Q93VM7 /1-468 P vP AP 10   Q93VM7 /1-468 ArP AP 00   Q93VM7 /1-468 ArP AP 00   Q93VM7 /1-477 ArtP AP 6   Q9510 /1-468 AcP AP 10   Q93VM7 /1-481 AoP AP 32   Q9XF09 /1-477 SrtP AP 3   Q6J5M8 /1-477 IbP AP 1   Q95E00 /1-473 ArtP AP 26   Q949Y3 /1-475 RcP AP 3   B5SXP 6/1-488 UAP 1 (Q812511/1-638 UPP D4   Q8VXF6 /1-612 TnP AP 1   Q4RLR4 /1-378 HsP AP 7   Q8X37 /1-438 DmP AP 1 (Q9VZ56 /1-450	429 454 434 452 453 454 453 454 457 452 457 452 457 452 457 453 459 450 451 453 459 450 452 451 453 489 558 619 558 619 605 602 374 434 436 434 436 436 436 437 436 437 437 457 457 457 457 457 457 457 457 457 45	WASNLRQQNLQKHHRRSLGDETASN4         WHPVDDSTTTKL         YLPEE         WHPVDDSTTTKL         WHPVDDSTTTKL         WHPVDDSTTTKL         WHPVDDSTTKL         WHPVDSST         WRAQK         WHPVDSSY         WHPVDDSSTTHVSH         WHPVDDSTTHVSH         WHPVDDSTTHVSH         WHPVDDSSTHVSH         WHPVDDSSTSATA         WGSGLRRKLINNHLNSVISERFFS         WSSNRRRKLIKKHTPSQQVERLISS         WSSNRRRKLIKKHTLSVQWIASTA	453 44658 4457 466154 4677 46738 47751723 5128 4 45532 4 45552 4 455552 4 45552 4 45552 4 45552 4 45552 4 45552 4 45552 4 45552 4 55552 4 55552 4 55552 4 55552 55552 55552 55552 55552 55552 55552 55552 55552 55552 555552 555555
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11 (Q9131]/1-464 AtP AP 21 (Q9131]/1-464 AtP AP 25   Q23244 /1-466 AtP AP 12   Q38924 /1-469 INTP AP 1 Q4KU02  /1-465 OSP AP 2   Q8505 /1-476 La AP 1 (Q93VM7/1/1-460 P vP AP 2   Q764 C1/1/-457 UAP 2   Q816L1]/1-463 AtP AP 10   Q93VM7/1/-468 P vP AP 10   Q93VM7/1-468 P vP AP 10   Q93VM7/1-468 P vP AP 10   Q93VM7/1-468 P vP AP 10   Q93VM7/1-468 AtP AP 6   Q9 C510 /1-466 AcP AP 6   Q9 C510 /1-466 AcP AP 6   Q9 C510 /1-473 AtP AP 6   Q9500/1-473 AtP AP 2   Q95XD0/1-473 AtP AP 2   Q95XD0/1-473 AtP AP 2   Q95XD0/1-475 RcP AP 3   Q615M8 /1-477 IbP AP 1 (Q95SD0/1-473 AtP AP 2   Q9XVF6/1-638 UPP D4 \Q8VXF6/1-615 UPP D2   Q8VXF6/1-615 UPP D2   Q8VXF6/1-615 UPP D2   Q8VXF6/1-615 UPP D2   Q8VXF6/1-615 UPP D2   Q8VXF6/1-615 DPP AP 3   Q9IZ58/1-438 DmP AP 7   Q8Z37/1-438 DmP AP 2   Q9VZ58/1-450 AmP AP   A0A0872W E4 /1-438	429 454 434 452 453 450 454 457 452 457 452 457 452 457 452 457 452 451 453 459 450 452 451 453 459 450 452 451 453 459 455 453 459 453 453 453 453 453 453 453 453 453 453	WASNLRQQNLQKHHRRSLGDETASN4           WHP VDDSTTTKL           YLP EE           WHP VDDSTTKL           WHP VDDSTTKL           WRQK           WRAQK           WHP VDEST           WHP VDEST           WHP VDEST           WHP VDEST           WHP VDEST           WHP VDEST           WHP VDDSTTHVSH           WASNTRRRLKKKHFHLDQIEDLIS           WNP LNDSTIHIP           WNP LNDSTSHIP           WNP KDDSTSCNS           WNP VDDSPSCNS           WNP VDDSSTSATA           WNP VDDSSTSATA           WNP VDESTSATA           WASNTRRRLKKKTPSQAVERLISS           WNP VDESTSATA           WAS NTRRRLKLKKHVIRSVISERPFS           WAS NPRRKLKKHVIRSVUGGWIAT           WGSNRRRRKLKKHVIRSVUGGWIAT           WGSNRRRKLKKHVIRSVUGGWIAT           WGSNRRRKLKKHVIRSVUGWIAST           WGSNRRRKLLKKHVIRSVUGWIAST           WGSNRRRKLKKNVIRSVUGWIAST           WGSNRRRKLLKKNVIRSVUGWIAST           WGSNRRRKLLKKNVIRSVUGWIAST           WGSNRRRKLLKKNVIRSVUGWIAST           WGSNRRRKLLKKNVIRSVUGWIAST           WGSNRRRKLLKKNVIRSVUGWIAST           WGSNRRRKLLKKNVIRSVUGWIAST           WGSNRRRKLLKKNVIRSVUGWIAST	453 44658 447 46654 447 44657 44657 44657 44657 44657 4477 4772 55578 43 43 43 45 45 45 45 45 45 45 45 45 45 45 45 45
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11   Q918 /1-465 ArP AP 11   Q918 /1-464 AtP AP 25   O23244 /1-466 AtP AP 12   Q38924 /1-469 INP AP 1   Q4KU02 /1-465 OSP AP 2   Q85505 /1-476 La AP 1   Q93VM7/1-460 P vP AP 2   Q86L11/1-463 AtP AP 10   Q93VM7/1-460 P vP AP 2   Q64L11/1-463 AtP AP 10   Q93VW7/1-468 P vP AP 1   P80366 /1-459 Ta ACP (C4PKL11/1-477 AtP AP 6   Q9 C510/1-466 AcP AP 32   Q9XF09/1-470 StP AP 3   Q6J5M8 /1-477 IbP AP 1 (Q95D0)/1-473 AtP AP 6   Q9 S100/1-473 AtP AP 2   Q9XF09/1-475 RcP AP 3   Q6J5M8/1-477 IbP AP 1 (Q95D0)/1-473 AtP AP 2   Q9XF09/1-475 RcP AP 3   Q6J5M8/1-477 IbP AP 1 (Q95D0)/1-473 AtP AP 2   Q9XVF0/1-1512 La AP 2   Q9XVF4 /1-638 UPP D4   Q8VXF4 /1-638 UPP D4   Q8VXF4 /1-638 HSP AP 3   Q6HRLR4 /1-378 HSP AP 3   Q6HRLR4 /1-378 HSP AP 3   Q9HAM9 /1-418 MmP AP 7   Q8X37/1/1-488 DmP AP 1   Q9VZ56/1-458 DmP AP 1   Q9VZ58/1/1-450 AmP AP   A0A087ZW E4 /1-438 CeP AP 1   01320 /1-419	429 454 434 452 453 450 454 453 457 452 457 452 457 452 457 452 457 452 457 452 457 453 455 455 455 455 455 455 455 455 455	WASNLRQQNLQKHHRRSLGDETASN 4         WHP VD DSTTTKL         YLP EE         WHP VD         WHP VD         WRAQK         WHP VD DSTTHVSH         WRAQK         WHP VD DSTTHVSH         WNP ND STTHVSH         WASNTRRRLKKKHFHLDQIEDLIS         WNP ND STIHIP         WASNTRRRLKKKHFHLDQIEDLIS         WNP ND STIHIP         WASNTRRRLKKKHLRYESLQSLMS         WNP ND STSTA         WASNTRRRLKKKHLRYESLQSLMS         WR SOLRRRKLKKHLRYESLQSLMS         WASNTRRRLKKKHLYSSLQAVERLISS         WASNTRRRLKKKHLYSSLQAVERLISS         WASNTRRRLKKKHLYVSQAVERLISS         WASSED         WASSEN         WASNTRRRKLKKHLSVSGWIAT         WASNTRRRKLKKNFLMTLVDEAVSM         WASNTRRRKLKKNFLMTLVDEAVSM         WASNTRRRKLKKNFLMTLVDEAVSM         WASNTRRRKLKKNFLMTLVDEAVSM         WASNTRRRKLKKNFLMTLVDEAVSM         WASNTRRRKLKKNFLMTLVDEAVSM         WASNTRRRKLKKNFLMTLVDEAVSM         WASNTRRRKLKKNFLMTLVDEAVSM         WASNTRRRRKLKKNFL         WASNTRRR	453 4455 44457 44677 44677 44677 44677 44677 44677 447755 4778 477557 4778 477557 4778 47755777 47757777777777
RcP AP 2   B95XP8 /1-463 IbP AP 2   Q95D29 /1-465 ArP AP 11   Q9131 /1-464 ArP AP 11   Q9131 /1-464 ArP AP 25   Q23244 /1-466 ArP AP 12   Q38924 /1-469 INP AP 1   Q4KU02 /1-465 OSP AP 2   Q85505 /1-476 La AP 1   Q4KU02 /1-465 OSP AP 2   Q8505 /1-476 La AP 1   Q93WM7 /1-460 P vP AP 1   Q846L1 /1-463 ArP AP 10   Q93VV9 /1-468 P vP AP 1   P80366 /1-459 Ta ACP (C4PKL1 /1-477 ArP AP 6   Q9 C510 /1-468 AcP AP 10   Q93WF09 /1-470 StP AP3   Q6J5M8 /1-477 IbP AP 1   Q93WF09 /1-470 StP AP3   Q6J5M8 /1-477 IbP AP 1   Q93WF09 /1-473 ArP AP 26   Q94Y93 /1-458 UAP 1   Q85E1 /1-477 GmP AP3   Q6VGT9 /1-515 UPP D1   Q8VXF6 /1-612 TnP AP 1   Q9VZ6 /1-438 CeP AP3   Q9VZ8 /1-438 DmP AP 1   Q9VZ56 /1-418 MmP AP 7   Q88X37 /1-438 DmP AP 1   Q9VZ56 /1-418 MmP AP 1   Q9VZ56 /1-418 MmP AP 1   Q9VZ56 /1-418 CeP AP 1   Q9VZ58 /1-450 DmP AP 1   Q9VZ58 /1-458 DmP AP 2   Q9VZ58 /1-458 DmP AP 3   Q9VZ57 /1-453	429 454 434 452 453 458 454 453 454 452 457 452 457 452 457 452 457 452 457 452 457 452 457 452 455 450 452 457 453 456 459 450 452 451 459 450 452 453 456 459 450 452 457 457 452 457 457 457 457 457 457 457 457 457 457	WASNLRQQNLQKHHRRSLGDETASN4           WHP VDDSTTTKL           YLP EE           WHP VDDSTTKL           WHP VDDSTTKL           WRQK           WRAQK           WHP VDEST           WHP VDEST           WHP VDEST           WHP VDEST           WHP VDEST           WHP VDEST           WHP VDDSTTHVSH           WASNTRRRLKKKHFHLDQIEDLIS           WNP LNDSTIHIP           WNP LNDSTSHIP           WNP VDDSPSCNS           WNP VDDSPSCNS           WNP VDDSSTSATA           WNP VDDSSTSATA           WNP VDESTSATA           WASNTRRRLKKKTPSQAVERLISS           WNP VDESTSATA           WAS NTRRRLKLKKHVIRSVISERPFS           WAS NPRRKLKKHVIRSVVGGWIAT           WASNPRRKLKKHVIRSVVGGWIAT           WGSNRRRRKLKKHVIRSVVGGWIAT           WGSNRRRKLKKHVIRSVVGGWIAT           WGSNRRRKLKKHVIRSVVGGWIAT           WGSNRRRKLLKKNFLMT VDEAVSM           WGSNRRRKLLKKNFLMT SVVGWIAST <td>453 44658 447661 4467 4467 44657 447755 477555 477555 477555 477555 477555 477555 47755557 4775557 4775557757577577577777777</td>	453 44658 447661 4467 4467 44657 447755 477555 477555 477555 477555 477555 477555 47755557 4775557 4775557757577577577777777

HvPAPhy_a C4PKL2 /1-544	
TaP APhy_a 1   C4PKK7   /1-550	
TaP APhy_b1 C4PKK9 /1-538	
TaP APhy_b2   C4PKL0   /1-537	
HvP APhy_b2   C4PKL4   /1-537	
HvP APhy_b1 C4PKL3 /1-536 OsP APhy_b D6QSX9 /1-539	
ZmP APhy_b   C4PKL6   / 1-544	
MtP APhy/Q3ZFI1//1-543	
PtPAP3/V9LXK5//1-564	
INTP APhy   A5YBW1   / 1-551	
LaP APhy   D2 YZL4   /1-543	
GmPAPhy_b Q93XG4 /1-547	
AtP AP 15   Q95FU3   /1-532	
AtaPAPhy_a1/F6MIX0//1-549	
ScPAPhy_a2 F6MIX4 /1-543	
TmPAPhy_a1 F6MIW8 /1-545	
TaP APhy_a3   F6MIW2   /1-539	
TaP APhy_a2   C4PKK8   /1-549	
ScPAPhy_a1/F6MIX2//1-541	
TaP APhy_b3   F6MIW6   /1-536	
TmP APhy_b1/F6MIW9//1-539	
AtaP APhy_b1 F6MIX1 /1-538 ScP APhy_b1 F6MIX5 /1-538	
RcP AP 1/B9RWG6//1-566	
VvP AP   A5 BGI 6   / 1-540	
PvP APhy/V7B3Z4//1-546	
VrP APhy   B5 AR Z7   / 1-547	
AIP AP 15   D7L636   /1-532	
AtP AP 23   Q6TPH 1   / 1-458	
GmP AP 4   V9H X G4   /1-442	
ZmP AP_c   C4PKL7   /1-566	
SbP AP   A0 A1Z5R 9 T8   /1-566	
HvP AP_c   C4PKL5   /1-564	
PpPAP   A9SP12  /1-557	
OsP AP 3   Q6ZCX8   /1-622	
OsP AP 4   B8 B909   / 1-622	
AtP AP 5   Q9 C927   / 1-396	
AtP AP 20   Q9 LXI 7   / 1-427 AtP AP 22   Q85340   / 1-434	
IbP AP3   Q9ZP 18   /1-427	
AtP AP 2 1   Q9 LX 14   / 1-437	
LpP AP   Q9MB07   /1-455	
RcP AP 2   B9 5XP 8   / 1-463	454
IbP AP 2   Q9 SD Z9  /1-465	
AtP AP 11   Q95 18   / 1-44 1	439
GmP AP 1   Q09 13 1   /1-4 64	
AtP AP 25   023244   /1-466	458
AtP AP 12   Q38924  /1-469	467
NtP AP   Q84KZ3   /1-461	
MtP AP 1   Q4KU02   / 1-465	475
OsP AP 2   Q85505   / 1-476 La AP 1   Q93 VM7   / 1-460	4/5
PvPAP2/Q764C1//1-457	
UAP2/Q8L6L1//1-463	
AtP AP 10   Q9 SI V9   / 1-468	
PvPAP1/P80366//1-459	
Ta ACP   C4PKL1 /1-477	476
AtP AP 6   Q9 C5 10   / 1-4 66	
AcPAP Q93WP4 /1-481	481
AoP AP 32   Q9 XF0 9  /1-470	
StP AP 3   Q6J5M8   /1-477	475
IbP AP 1   Q95E00   /1-473	
AtP AP 2 6   Q949 Y3   / 1-475 RcP AP 3   B95XP 6   / 1-488	482
UAP1/Q8L5E1//1-477	402
GmP AP3   Q6YGT9   /1-512	
La AP 2   Q9 XJ24  /1-638	
UPP D4   Q8VXF4  /1-629	614
	614
UPP D1/Q8VX11//1-615	614
	614
UPP D1  Q8VX11 /1-615 UPP D2   Q8VXF6 /1-612 TnP AP 1  Q4R LR4  /1-378	614
UPP D1  Q8 VX11 /1-615 UPP D2   Q8 VXF6 /1-612 TnP AP 1  Q4R LR4  /1-378 HsP AP 7  Q621 \F0  /1-438	614
UPP D1  Q8VX11 /1-615 UPP D2  Q8VXF6 /1-612 TnP AP 1  Q4R LR4 /1-378 HsP AP 7  Q621\F0 /1-438 CeP AP 3  Q9I\AM9 /1-418	614
UPP D1  Q8VX11 /1-615 UPP D2  Q8VXF6 /1-612 TnP AP 1  Q4R LR4 /1-378 HsP AP 7  Q621\F0 /1-438 CeP AP 3  Q91\AM9 /1-418 MmP AP 7  Q8 BX37 /1-438	614
UPP D1  Q8VX11 /1-615 UPP D2  Q8VXF6 /1-612 TnP AP 1  Q4R LR4  /1-378 HsP AP 7  Q62\\F0  /1-438 CeP AP 3  Q9!VAM9  /1-418 MmP AP 7  Q8 BX37  /1-438 DmP AP 1  Q9VZ56 /1-458	614
UPP D1  Q8VX11 /1-615 UPP D2  Q8VXF6 /1-612 TnP AP 1  Q4RLR4 /1-378 HSP AP 7  Q6ZIVF0 /1-438 QeP AP 3  Q9IVAM9 /1-418 MmP AP 7  Q8 BX37 /1-438 DmP AP 1  Q9VZ56 /1-456 DmP AP 2  Q9VZ58 /1-450	614
UPP D1  Q8VX11 /1-615 UPP D2  Q8VXF6 /1-612 TnP AP 1  Q4RLR4 /1-378 HsP AP 7  Q6ZIVF0 /1-438 QeP AP 3  Q9IVAM9 /1-418 MmP AP 7  Q8 BX37 /1-438 DmP AP 1  Q9VZ56 /1-458 DmP AP 2  Q9VZ58//1-450 AmP AP   A0 A087ZWE4 /1-438	614
UPP D1  Q8VX11//1-615 UPP D2  Q8VXF6//1-612 TnP AP 1  Q4RLR4 /1-378 HsP AP 7  Q62\F0/1-438 QeP AP 3  Q9I\AM9/1-418 MmP AP 7  Q8 BX37//1-438 DmP AP 1  Q9VZ56//1-458 DmP AP 2  Q9VZ58//1-450 AmP AP   40 A087ZW E4/1-438 CeP AP 1  001320 //1-419	614
UPP D1  Q8VX11 /1-615 UPP D2  Q8VXF6 /1-612 TnP AP 1  Q4RLR4 /1-378 HsP AP 7  Q6ZIVF0 /1-438 QeP AP 3  Q9IVAM9 /1-418 MmP AP 7  Q8 BX37 /1-438 DmP AP 1  Q9VZ56 /1-458 DmP AP 2  Q9VZ58//1-450 AmP AP   A0 A087ZWE4 /1-438	614

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h	2	0
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# Figure A3. PAPhy vs LMW PAPs MSA (See Figure A1 for key)

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HvP APhy_a   C4PKL2   /1-544	1 MPSNNINMWWGS - LLLLAAAV - AVAAA E PPSTLAGPSRPVTVTPREN - RGHAVDLP DTDPRVQRR - ATGWAPEQVAVALSAAPTSAWVSW 8	36
TaP APhy_a1 C4PKK7 /1-550	1	33
TaP APhy_b1/C4PKK9//1-538	1	32
TaP APhy_b2   C4PKL0   /1-537	1 MWMWR GSMP LLLLAPAA AVA E PASTLEGPSR PVTVP LR ED - <mark>R GHAV DLP - DT DP R V QR R</mark> - V T GWAP EQ I AVA LSA AP T S AWV SW 8	31
HvP APhy_b2   C4PKL4   /1-537	1	31
HvP APhy b1/C4PKL3//1-536	1 MWMWR GS LP LF LL LLAA A TA E PASM LEGPS GPV TV LLQED - R GHAV DLP DT PRV QR VT GWAP EQ I AVA LSAAPTS AWVSW 8	31
OsP APhy_b   D6Q5X9   /1-539	1	31
ZmP APhy_b   C4PKL6   /1-544	1	36
MtP APhy   Q3ZFI 1   / 1-543	1	39
PtPAP3/V9LXK5//1-564	1 MASSSLPSISLPVNVFELNNILSLVLKLTIT - LILLANGAMAMAIPTTLDGPFKPVTIPLDESF <mark>RGNTIDLP</mark> DTDPRVQRT - VEGFKPEQISVSLSSTHDSVWISW 10	14
INTP APhy   A5YBIV11   /1-551	1	38
LaP APhy   D2 YZL4   /1-543	1	36
GmP APhy b   Q93XG4   /1-547	1	30
AtP AP 15   Q95FU3   /1-532	1	32
AtaP APhy_a1   F6MIX0   /1-549	1 MWW WGSLLLLLLLLAAA - VAAAA E PASTLTGPSRPVTVALRED - RGHAVDLP DTDPRVQRR - ATGWAPEQIAVALSAAPTSAWVSW 8	32
ScP APhy_a2   F6MIX4   /1-543	1 MPSNMWLGSLRLLLLLAAA - VTAAAE PASTLMGPSRPVTVALRED-RGHAVDLP DTDPRVQRR - ANGWAPEQIAVALSAAPTSAWVSW 8	35
TmP APhy_a 1   F6MIW8   / 1-545	1	78
TaP APhy_a3   F6MIW2   /1-539	1	31
TaP APhy_a2   C4PKK8   /1-549	1	32
ScP APhy_a1/F6MIX2 //1-541	1 PGSTLMGPSRPVTVALRED - RGHAVDLP - DTDPRVQRR - ANGWAPEQIAVALSAAPTSAWVSW 8	31
TaP APhy_b3   F6MIW6   /1-536	1 MG I WR GS L P L L L L A A A A A A E P A S T L E G P S WP V T V P L R E D - <mark>R G H A V D L P -</mark> D T D P R V Q R R - V T G WA P E Q I A V A L S A A P T S A WV S W 8	30
TmP APhy_b1   F6MIW9   /1-539	1 MWIWRGSLPLLLLAAAA - AAAAA E PASTLEGPSRPVTVPLRED - RGHAVDLP - DTDPRVQRR - VTGWAPEQIAVALSAAPTSAWVSW 8	33
AtaP APhy_b1/F6MIX1//1-538	1	32
ScP APhy_b1/F6MIX5//1-538	1	32
RcP AP 1   B9R WG6   / 1-566	1 MNP LFLDS CS FMQGLQ YNR CNMGLLS VP V FALS FY VLLS SATL - AAAHGH I P TTLEGP FK PR TV PLDQS F <mark>R GHAIDLP - DS DPR VQRT</mark> - VR DF EP EQIS VS LS STHDS VWI SW 11	0
VvP AP   A5 BGI 6   / 1-540	1	33
PvPAPhy/V7B3Z4//1-546	1	30
VrP APhy   B5 AR Z7   / 1-547	1	1
AIP AP 15   D7L636   /1-532	1 IPSTLDGP FVPVTVPLDTSL <mark>R GKAIDLP DTPRVRRR</mark> -VTGFEPEQISLSLSSDHDSIWVSW 8	32
AtP AP 23   Q6TPH 1   / 1-458	1 IPTTLDGPFKPLTRRFEPSL <mark>RRGSDDLP</mark> MDHPRLRKR <mark>NVSSDFPEQIALALST-PTSMWVSW</mark> 8	32
GmP AP 4   V9H X G4   /1-442	1 RKTLTTIPWDSISKAHSSYPQQVHISL-AGDKHMRVTW 6	9
1bP AP4   Q9 LL8 1   / 1-3 12	1	7
AtP AP 3   Q8H 129   /1-366	1	
AtP AP 8   Q8 VYZ2  /1-335	1	
PvPAP3 D2D4J4 /1-330		17
StP AP 1   Q6J5M7   /1-328	1 MASMKILNIFISFLLLLLFPAAM	
PvPAP4/Q9LL79//1-331	1	
AtP AP 7   Q85341   / 1-328	1	8
AtP AP 17   Q95CX8   / 1-338	······································	
BrP AP 17_1   D6MW88   /1-337		9
OsP AP 1 Q7XH73 /1-335	1 1 1	
GmP AP 2   Q9 LL80  /1-332	1	
UACP3/Q707M7//1-330		5
P vP AP 5   E2 D740  /1-32 6	1 MSISFLLTLFITSS - LSSLSA 2	
MmPAP5/Q05117//1-327	1 1 1	
RnPAP5/P29288//1-327	1 1	
HsP AP 5   P 13686   /1-325	1 IP	
SsP AP 5   P09889   /1-340	1	
DrP AP 2   Q75XT1   /1-339	1	
TnP AP 2   Q4S755  /1-331	1	
XtP AP 5   Q66  G6   /1-326		
XIP AP 1   Q6GI\G2   /1-325		6
XIP AP 2   Q6IP 56   /1-326		
DrP AP 1   Q6DHF5   /1-327	1 MAKKLAFLLI 1	. 0

HvP APhy_a   C4PKL2  /1-544	87 I T G E F QMG G T V K P L D P R T V G <mark>S V V R Y G</mark> L A A D S L V R E A T G D A L V Y S Q L Y P F E - G L H N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P A I P G <mark>A M S A V H A F R T MP</mark> A A G P R S Y P G R I A V V <mark>G D L G L</mark>	
TaP APhy_a1 C4PKK7 /1-550	84 IT GEFQMGGTVKPLDPGTVG <mark>SVVRYG</mark> LAADSLVRQASGDALVYSQLYPFE-GLQN-YTSGIIHHVRLQ-GLEP-ATKYYYQCGDPALPG <mark>AMSAVHAFRTMP</mark> AVGPRSYPGRIAVV <mark>GDLG</mark> L	
TaP APhy_b1 C4PKK9 /1-538	83 I T G D F QMG G A V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S L A R E A T G E A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R I L - G L E P - G T K Y Y Y Q C G D P A I P G <mark>A M S A V H A F R T M P</mark> D V G P R S Y P G R I A V V <mark>G D L G L</mark>	
TaP AP hy_b2   C4P KL0   /1-537	82 IT G D F QMG G A V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S L V R E A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P S I P G <mark>A M S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark> :	
HvPAPhy_b2 C4PKL4 /1-537	82 IT GD F QMG G A V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S V V R E A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P A I P G <mark>A M S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark>	
HvPAPhy_b1 C4PKL3 /1-536	82 IT G D F QMG G A V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S V V R E A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P A I P G <mark>A MS A V H A F R T MP</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark> I	
OsP APhy_b   D6QSX9  /1-539	82 V T G D F QM G A A V E P L D P T A V A <mark>S V V R Y G</mark> L A A D S L V R R A T G D A L V Y S Q L Y P F D - G L L N - Y T S A I I H H V R L Q - G L E P - G T E Y F Y Q C G D P A I P A <mark>A M S D I H A F R T M P</mark> A V G P R S Y P G K I A I V <mark>G D L G L</mark> S	
ZmP APhy_b   C4PKL6   /1-544	87 I T G D Y QMG G A V EP L D P G A V G <mark>S V V R Y G</mark> L A A D A L D H E A T G E S L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T R Y V Y R C G D P A I P D <mark>AMS G V H A F R T MP</mark> A V G P G S Y P G R I A V V <mark>G D L G L</mark> S	
MtP APhy Q3ZFI1 /1-543	90 ITGEFQIGENIEPLDPETVG <mark>SIVQYG</mark> RFGRSMNGQAVGYSLVYSQLYPFE-GLQN-YTSGIIHHVRLT-GLKP-NTLYQYQCGDPSLS- <mark>AMSDVHYFRTMP</mark> VSGPKSYPSRIAVV <mark>GDLG</mark> L	
P tP AP 3   V9 LXK5   / 1-564	105 ITGEFQIGNNLKPLDPKSVA <mark>SVVRYG</mark> TRRSQLNRKATGRSLVYSQLYPFL-GLQN-YTSGIIHHVRLT-GLKP-DTLYHYQCGDPSIL- <mark>AMSGTYYFRTMP</mark> DSSSTSYPSRIAIV <mark>GDVG</mark> L	
NtP APhy   A5YBN1   /1-551	89 IT GEYQIGDNIKPLDPSKVG <mark>SVVQYG</mark> KDKSSLRHKAIGESLIYNQLYPFE-GLQN-YTSGIIHHVQLT-GLKP-NTLYYYQCGDPSIP- <mark>AMSTIYHFKTMP</mark> ISSPKSYPKRIAIV <mark>GDLG</mark> L	
LaP APhy   D2 YZL4   / 1-543	87 IT GEFQIGYN I KPLDPKTVS <mark>SVVHYG</mark> TSRTALVREARGQSLIYNQLNPYE - GLQN - YTSGI I HHVQLR - GLEP - STVYYYQCGDPSLQ - <mark>AMSDI YYFRTMP</mark> I SGPKSYPGRVAVV <mark>GDLG</mark> L	
GmPAPhy_b Q93XG4 /1-547	91 V T G E F Q I G L D I K P L D P K T V S <mark>S V V Q Y G</mark> T S R F E L V H E A R G Q S L I Y N Q L Y P F E - G L Q N - Y T S G I I H H V Q L K - G L E P - S T L Y Y Y Q C G D P S L Q - <mark>AMS D I Y Y F R T MP</mark> I S G S K S Y P G K V A V V <mark>G D L G</mark> L	
AtP AP 15   Q95FU3   /1-532	83 <mark>ITGEFQIGKKVKPLDPTSIN<mark>SVVQFG</mark>TLRHSLSHEAKGHSLVYSQLYPFD-GLLN-YTSGIIHHVRIT-GLKP-STIYYYRCGDPSRR-<mark>AMSKIHHFRTMP</mark>VSSPSSYPGRIAVV<mark>GDLG</mark>L</mark>	
AtaPAPhy_a1/F6MIX0//1-549	83 I T G E F QMG G T V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S L V R Q A S G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - A T K Y Y Y Q C G D P A L P G <mark>A M S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark>	
ScPAPhy_a2/F6MIX4//1-543	86 I T G E F QMG G T V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S L V R V A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P A L P G <mark>T MS A V H A F R T MP</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark> I	
TmPAPhy_a1/F6MIW8//1-545	79 IT GEFQMG G T V K PLH P G T V A <mark>S V V R Y G</mark> LA A D S L V R E A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - A T K Y Y Y Q C G D P G I P G <mark>A M S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark>	
TaPAPhy_a3/F6MIW2//1-539	82 IT GEFQMG G T V K P L D P G T V A <mark>S V V R Y G</mark> L A A D S L V R Q A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - A T K Y Y Y Q C G D P A L P G <mark>A M S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark>	
TaP APhy_a2   C4PKK8   /1-549	83 I T G D F QMG G A V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S L V R E A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P A I P G <mark>A M S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark>	
ScP APhy_a 1   F6MIX2   / 1-541	82 IT GEFQMG G T V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S L V R V A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P A L P G <mark>A M S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark> :	
TaP.APhy_b3/F6MIW6//1-536	81 I T G D F QMG G A V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S L V R E A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P A I P G <mark>A T S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark>	
TmP AP hy_b1   F6MIW9   /1-539	84 I T G D F QMG G A V K P L D P G T A G <mark>S V V R Y G</mark> L A A D S L V R E A T G D A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P A I P G <mark>A T S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark> S	
AtaP APhy_b1/F6MIX1//1-538	83 I T G D F QMG G A V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S L A R E A T G E A L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R I L - G L E P - G T K Y Y Y Q C G D P A I P G <mark>A M S A V H A F R T M P</mark> D V G P R S Y P G R I A V V <mark>G D L G L</mark>	
ScP APhy_b1/F6MIX5//1-538	83 I T G D F QMG G A V K P L D P G T V G <mark>S V V R Y G</mark> L A A D S L V R E A T G D V L V Y S Q L Y P F E - G L Q N - Y T S G I I H H V R L Q - G L E P - G T K Y Y Y Q C G D P A I P G <mark>A M S A V H A F R T M P</mark> A V G P R S Y P G R I A V V <mark>G D L G L</mark> I	
' ''	111 I T G D Y Q I G D N I K P L N P S A T A <mark>S V V L Y G</mark> R S I F P L T H Q A T G Y S L V Y N Q L Y P F E - G L K N - Y T S G V I H H V R L T - G L K P - N T T Y F Y Q C G D P S I P - <mark>A M S D I Y H F R T M P</mark> A S G P K S F P G K I A I V <mark>G D L G</mark> L S	
VvP AP   A5 BGI 6   / 1-540	84 ITGEFQIGYNIKPLNPKTVS <mark>SVVRYG</mark> TLRYPLRRKVMGYSLVYNQLYPFE-GLQN-YTSGIIHHVRLA-GLKP-STRYYYRCGDPTI-G <mark>AMSNIYSFRTMP</mark> VSGPRSYPRKIGII <mark>GDLG</mark> L	
PvPAPhy/V7B3Z4//1-546	91 ITGEFQIGFDIKPLDPQTVS <mark>SVVQYG</mark> TSRFDLVHEARGQSLIYSQLYPFD-GLQN-YTSGIIHHVRLI-GLEP-STLYYYQCGDPALQ- <mark>AMSDIYYFRTMP</mark> ISGLHSYPGKVAIV <mark>GDLG</mark> L	
VrP APhy   B5 AR Z7   / 1-547	92 V T G D A Q I G L N V T P V D P A S I G <mark> S E V W Y G</mark> K E S G K Y T S V G K G D S V V S Q L Y P F E - G L WN - Y T S G I I H H V K L E - G L E P - G T R Y Y Y K C G D S S I P - <mark>A M S Q E R F F E T F P</mark> K P S P N N Y P A I A V V <mark>G D L G</mark> L	
AIP AP 15   D7L636   /1-532	83 <mark>ITGEFQIGKKVKPLDPTSIK<mark>SVVQFG</mark>TLRHSLSHEAKGHSLVYSQLYPFD-GLLN-YTSGIIHHVRIT-GLKP-STIYYYRCGDPSRR-<mark>AMSKIHHFRTMP</mark>VSSPSSYPGRIAVV<mark>GDLG</mark>L</mark>	
AtP AP 23   Q6TPH 1   / 1-458	83 V T G D A I V G K D V K P L D P S S I A <mark>S E V WY G</mark> K E K G N YMLK K K G NA T V Y S Q L Y P S D - G L L N - Y T S G I I H H V L I D - G L E P - E T R Y Y Y R C G D S S V P - <mark>A M <u>S</u> E E I S F E T L P</mark> L P S K D A Y P H R I A F V <mark>G D L G L</mark>	
GmP AP 4   V9HXG4   /1-442	70 <mark>  T DDKHSPSYVEYGTLPGRYDS   A EGECTSYNYLL YSSGK   HHAV   G - P LED - NTAY FYRCGGK GA E F<mark>EL</mark> YSSGK   HHAV   G - P LED - NTAY FYRCGGK GA E F<mark>EL</mark></mark>	
IbP AP4   Q9 LL8 1   /1-3 12		53
AtP AP 3   Q8H 129   /1-366		84
AtP AP 8   Q8 VYZ2  /1-335		55
P vP AP 3   D2 D4J4   /1-330		55
StP AP 1   Q6J5M7   /1-328		49
PvPAP4/Q9LL79//1-331		45
AtP AP 7   Q85341   /1-328		51
AtP AP 17   Q95CX8   /1-338		56
BrP AP 17_1/D6MW88//1-337	10	55
OsP AP 1/Q7XH73//1-335		48
GmP AP 2   Q9 LL80   /1-332		53
UACP3 Q707M7 /1-330	6	52
PvPAP5/E2D740//1-326		47 38
MmPAP5/Q05117//1-327		38 38
RnPAP5/P29288//1-327		
HsP AP 5 /P 13686 // 1-325		36 44
SsP AP 5 (P09889 (/1-340		
DrP AP 2   Q75XT1   / 1-339		46
TnP AP 2   Q45755  /1-331	14 KFLAVGDWGG	46
XtP AP 5   Q66  G6   /1-326	15	38
XIP AP 1   Q6GI\G2   /1-325	7PHEE-PSLPHEE-PSL	37
XIP AP 2   Q6IP 56   / 1-326	15	38
DrP AP 1   Q6DHF5   / 1-327	II	33

		KSTPIH <mark>ETYQPRWDYWGRYMEPVTSSTPMMVVE<mark>GNHE</mark>IEEQIGNKTFAAYRSRF 302</mark>
		K S T P I H <mark>E T Y Q P R W D Y W G R Y M E A V T S G T P MMV V E</mark> G N H E I E E Q I G N K T F A A Y R S R F 299
		K S T P I H E T Y Q P R WD Y W G R Y M E P V T S S T P MMV V E <mark>G N H E</mark> I E Q Q I G N K T F A A Y S A R F 298
	198 TYNTTSTVEHMASNQPDLVLLL <mark>GDVSY</mark> ANLYLTN-GTGT <mark>DCYSCSFA</mark>	
		K S T P I H E T Y Q P R WD Y W G R Y M E P V T S S T P MMV V E <mark>G N H E</mark> I E Q Q I G N K T F A A Y S A R F 297
		K S T P I H E T Y Q P R WD Y W G R Y M E P V T S S T P MMV V E <mark>G N H E</mark> I E Q Q I G N K T F A A Y S A R F 297
	198 TYNTTSTVEHMVSNQPDLVLLLGDVSYANLYLTN-GTGTDCYSCSFA	
		K <mark>S T P I H</mark> E T Y Q P R W D Y W G R Y M E P V T S S I P M M V V E <mark>G N H E</mark> I E Q Q I H N R T F A A Y S S R F 302
		N - <mark>T P I H</mark> E T Y Q P R W D Y W G R Y M E P L I S S V P V M V V E <mark>G N H E</mark> I E E Q A V N K T F V A Y S S R F 303
		N - <mark>S P I H</mark> E T Y Q P R W D Y W G R Y M Q P V L S K V P I L V V E <mark>G N H E</mark> Y E E Q A E N R T F L A Y T S R F 318
		D - <mark>T P I H</mark> E T Y Q P R WD Y W G R Y M Q P L V S K I P I M V V E <mark>G N H E</mark> I E E Q A E N Q T F A A Y R S R F 302
LaP APhy   D2 YZL4   / 1-543	202 TYNTTATINHLTSNKPDLLLLI <mark>GDVTY</mark> ANLYLTN-GTGS <mark>DCYSCSFP</mark>	H - <mark>T P I H</mark> E T Y Q P R WD Y W G R F M Q N L V S K V P MMV V E <mark>G N H E</mark> I E K Q A E D K Q F V A Y S S R F 300
		L - <mark>T P I H</mark> E T Y Q P R WD Y W G R F M Q N L V S N V P I M V V E <mark>G N H E</mark> I E K Q A E N R T F V A Y S S R F 304
AtP AP 15   Q95FU3   /1-532	198 TYNTTDTISHLIHNSPDLILLI <mark>GDVSY</mark> ANLYLTN-GTSS <mark>DCYSCSFP</mark>	E - TPIHETYQPRWDYWGRFMENLTSKVPLMVIEGNHEIELQAENKT FEAYSSRF 236
AtaP APhy_a1/F6MIX0//1-549	199 TYNTTSTVDHMASNRPDLVLLV <mark>GDVCY</mark> ANMYLTN-GTGA <mark>DCYSCAFG</mark>	KSTPIHETYQPRWDYWGRYMEAVTSGTPMMVVE <mark>GNHE</mark> IEEQIGNKTFAAYRSRF 298
ScP APhy_a2 / F6MIX4 / /1-543	202 TYNTTSTVDHMMSNRPDLVVLVGDVSYANLYLTN-GTGADCYSCAFG	KSTPIHETYQPRWDYWGRYMEAVTSGTPMMVVE <mark>GNHE</mark> IEEQIGKKTFEAYRSRF 301
TmP APhy a 1/F6MIW8 //1-545	195 TYNTTSTVDHMVSNRPDLVLLVGDVCYANMYLTN-GTGADCYSCAFG	K S T P I H E T Y Q P R W D Y W G R Y M E A V T S G T P MMV V E G N H E I E E Q I R N R T F A A Y R S R F 234
TaP APhy a3 (F6MIW2 )/1-539	198 TYNTTSTVDHMASNRPDLVLLL <mark>GDVSY</mark> ANLYLTN-GTGA <mark>DCYSCAFG</mark>	K S T P I H E T Y Q P R WD Y W G R Y M E A V T S G T P M V V V E G N H E I E E Q I G N K T F A A Y R S R F 297
		K S T P I H E T Y Q P R WD Y W G R Y MEA V T S G T P MMV V E G N H E I E E Q I G N K T F A A Y R S R F 298
		KSTPIHETYOPRWDYWGRYMEAVTSGTPMMVVEGNHEIEEOIGKKTFEAYRSRF 297
TaP APhy b3/F6MIW6//1-536	197 TYNTTSTVEHMASNOPDLVLLLGDVSYANLYLTN-GTGTDCYSCSFA	K S T P I H E T Y Q P R W D Y W G R Y M E S Y T S T T P MMY Y E G N H E I E Q Q I G N K T F A A Y S A R F 296
		K S T P I H E T Y Q P R W D Y W G R Y M E P V T S T T P MMV V E G N H E I E Q Q I G N K T F A A Y S A R F 299
AtaP APhy b1/F6MIX1//1-538	199 TYNTTSTVEHMASNOPDLVLLLGDVSYANLYLTN-GTGTDCVSCSEA	K S T P I H E T Y Q P R WD Y W G R Y M E P V T S S T P M M V V E G N H E I E Q Q I G N K T F A A Y S A R F 238
		N 5 T P I H E T Y Q P R WD Y W G R Y M E P Y T S S T P MMY Y E G N H E I E Q Q I G N K T F A A Y S A R F 298
		0-TPIHETYOPRWDYWGRYMOPLISRIPIMYYEGNHEIEGOAONOTFAAYSSRF 324
		9 - TPIHETY QPRWD YWGRFMQNLVSK V PMMV I EGNHEI EE QAEKKNFVAYSSRF 297
		0-SPIHETYQPRWDYWGRFMQNLVAEVPIMVVEGNHETEEQADNRTFVAYSSRF 304
		- AP I R ET Y - P RWD GWGR FMQNL I S K V P I MV V EGNH ET EE QAD N K T F V A Y S R F 305
		E-TPIHETYOPRWDYWGRFMENLTSKYPLMVIEGNHEIELOAENKTFEAYSSRF 295
		- A P I R E T Y Q P R W D A W G R F M E P L T S K V P T M V I E G N H E I E P Q A S G I T F K S Y S E R F 297
GmP APA IVALY GA 1/1 A42		DCMQHLWDNFGKLVEPFASTRPWMVTEGNHE-EENILLLTDE-FVSYNSRW233
16P AP4 ( 091 18 1 ) /1-912		LTGEHDDAFTESFTDVYTAESLQK - QWYSVLGNHDYRGDAEAQLSSHLRKLDSRWPCLRS 148
		LTSLHDPLFQDSFTNIYTAPSLQK - PWYSVLGNHDYRGDVRAQLSSHLKKLDSKWPCLRS 148
		I I SP Y D S Q F Q D S F T N I Y T A T S L Q K - P WY N V L G N H D Y R G N Y A Q L S P I L R D L D R K W CMR S 175
PUP AP 2 ( D2 D4 14 1 / 1 220		LKGVDDPAFYSSFVDIYTAHSLQK - TWYSVLGNHDYRGDVEAQLSPALKQKDSRWLCLRS 150
FVFAF3 0204J4 /1-330	50 UGT N NUS PVADUMGTV GEKLDTD PVTSTGDN FTEDG	LTGVDDPAFESSFVDTTTAHSLQK - TWYSVLGNHDYRGDVEAQLSPALKQKDSRWLCLKS 150
		LSGVDDPAFEESFINVYTAPSEQK - NWYNVEGNHDYRGDALAQESPIERQRDNRWICMRS 144
PvPAP4/Q9LL79//1-331		LK GVDDPAFELSFSK I Y IAKSLOK - OWYSVLGNHDYR GDVEAOLNI I LOKIDPRWI CORS 140 LK GVNDPSFEASFSH I YTHPSLOK - OWYSVLGNHDYR GNVEAOLSKVLTOKDWRWFCRRS 146
AtP AP / [ 085341 ] / 1-328	52 K G G F N Q S L V A H Q M G V V G E K L D T D F V I S V G D N F V D G G N Q S L V A H Q M G V V G E K L D T D F V I S V G D N F V D G G V V A H Q M G V V G E K L D T D F V I S V G D N F V D G G V V A H Q M G V V G E K L D T D F V I S V G D N F V D G G V V A H Q M G V V G E K L D T D F V I S V G D N F V D G G V V A H Q M G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G D N F V D G G V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S V G E K L D T D F V I S	LK GVNDPSFEASFSHIVIHPSLQK - QWYSVLGNHDYRGNVEAQLSKVLIQKDWKWFCKRS 145 LFSEHDPNFEQSFSNIVTAPSLQK - QWYSVLGNHDYRGDAEAQLSSVLREIDSRWICLRS 151
		LFSEHDPNFEQSFSNIYIAPSLQK - QWYSVLGNHDYRGDAEAQLSSVLREIDSRWICLRS 151 LFSEYDPNFKESFSNIYTAPSLQK - QWYSVLGNHDYRGDSEAQLSSVLREIDSRWICLRS 150
BRY AP 1/_1/D6MW88//1-337		L F S E Y D P N F K E S F S N I Y T A P S L Q K - Q W Y S V L G N H D Y R G D S E A Q L S S V L R E I D S R W I C L R S 150 <mark>L A G V</mark> D D MA F H D S F M D V Y T A Q S L H K - P W Y L V L G N H D Y R G N V L A Q I D P A L R K I D S R F I C M R S 143
USP AP 1/Q7XH73//1-335	49 K G G Y N Q T R V A E Q M G K V A E E T E I D F V V S T G D N F L E N G	-
GmP AP 2   Q9 LL80   / 1-332	54 K G A Y N Q S L V A F Q M G V I G E K L D V D F V I S T G D N F Y D N G	LTGV FDPS FEES FTK I Y TAPS LQK - KWYNV LGNHDYRGNAKAQ I SHV LRYRDNRWV CFRS 148 LTSDQDTA FEES FTNVY TAKS LQK - QWYSV LGNHDYRGDV EAQLSP FLKQ I DNRWLCLRS 147
PvPAP5/E2D740//1-326	48 <u>R G A F N Q S Q V A F Q M G K V G E R L D I D F V V S T G D N F Y D N G</u>	<mark>LISE</mark> HDNA FA ESFTKIYTA ESLQK - QWYSVL <mark>GNHD</mark> YR GDA EA QLSPVLR EMDSRWLCLRS142
MmP AP 5   Q0 5 1 1 7   / 1-3 2 7	DO M D N A D E H T A D E MAA N A K E L A D T M O T MAC A D E L MAC L O D M E W E T C	
D_D AD 5 (D 30 300 / /1 33 7	33 VPNAPPHTAREMANAKETARTVQTMGADPTMSE	<mark>VHDA</mark> SDKRFQETFEDVFSDRALRNIPWYVLA <mark>GNHD</mark> HLGNVSAQIA YSKISKRW 132
KIIF AF 3 [F 2 3 2 6 6 ]/ 1-52 /	39 VPNAP FHTAR EMANAK E I AR TVQ I MGAD FI MSL GDN FY FTG	<mark>V H D A</mark> N D K R F Q E T F E D V F S D R A L R N I P W Y V L A <mark>G N H D</mark> H L G N V S A Q I A Y S K I S K R W 132
HsP AP 5   P 13686   / 1-325	39 V P NA P F H T A R EMA NA K E I A R T V Q I MG A D F I MS L <mark>G D N F Y</mark> F T G	- <mark>V H D A</mark> N D K R F Q E T F E D V F S D R A L R N I P W Y V L A <mark>G N H D</mark> H L G N V S A Q I A Y S K I S K R W 132 - V Q D I N D K R F Q E T F E D V F S D R S L R K V P W Y V L A <mark>G N H D</mark> H L G N V S A Q I A Y S K I S K R W 130
HsP AP 5 (P 23288 () 1-327 HsP AP 5 (P 13686 () 1-325 SsP AP 5 (P 09889 () 1-340	39 V P NA P F H T A R EMA NA K E I A R T V Q I MG A D F I MS L <mark>G D N F Y F T G</mark>	- <mark>VHDA</mark> NDKR FQET FEDV FSDRALRN I PWYVLA <mark>GNHD</mark> HLGNVSAQIA YSK I SKRW 132 - VQDINDKR FQET FEDV FSDRSLRKVPWYVLA <mark>GNHD</mark> HLGNVSAQIA YSK I SKRW 130 - VHDAKDKR FQET FEDV FSDPSLRNVPWHVLA <mark>GNHD</mark> HLGNVSAQIA YSK I SKRW 138
H \$P AP 5   P 1368 6   /1-325 S\$P AP 5   P 09889   /1-340 DrP AP 2   Q75XT1   /1-339	39 V P NA P F H T A R EMA NA K E I A R T V Q I MG A D F I MS L G D N F Y F T G 37 V P NA P F H T A R EMA NA K E I A R T V Q I L G A D F I L S L G D N F Y F T G 45 V P NA P F H T A R EMA NA K A I A T T V K T L G A D F I L S L G D N F Y F T G 47 L P N P P Y V T P I E T A T A R MMA K T A S Q MG A D F I L A Y G D N F Y Y K G	<mark>V H D A</mark> N D K R F Q E T F E D V F S D R A L R N I P WY V L A <mark>G N H D</mark> H L G N V S A Q I A Y S K I S K R W 132 - V Q D I N D K R F Q E T F E D V F S D R S L R K V P WY V L A G N H D H L G N V S A Q I A Y S K I S K R W 133 - V H D A K D K R F Q E T F E D V F S D P S L R N V P WH V L A G N H D H L G N V S A Q I A Y S K I S K R W 138 - V T D V N D P R F Q E T F E D V Y T Q D S L N I - P WY V I A G N H D W V G N V K A Q I E Y S Q K R W 139
H sP AP 5   P 1368 6 /1-325 SsP AP 5   P09889  /1-340 DrP AP 2   Q75XT1  /1-339 TnP AP 2   Q45755  /1-331	39 V P NA P FHTAR EMANAK E I AR TV Q I MGA D F I MS L GD N FY FTG 37 V P NA P FHTAR EMANAK E I AR TV Q I L GA D F I L S L GD N FY FTG 45 V P NA P FHTAR EMANAKA I A TTV K T L GA D F I L S L GD N FY FTG 47 L P N P Y V T P I ETA TAR MMAKTA S QMGA D F I L A V GD N FY Y K G 47 V P Y P P Y I TA V Q K A TA Q EMS K V A EQMGA D F V L A L GD N FY Y K G	VHDA NDKR FQET FEDV FSDRALRN I PWYVLAGNHDHLGNVSAQIA YSK I SKRW 132 - VQDI NDKR FQET FEDV FSDRSLRKVPWVLAGNHDHLGNVSAQIA YSK I SKRW 130 - VHDA KDKR FQET FEDV FSDPSLRNVPWHVLAGNHDHLGNVSAQIA YSK I SKRW 138 - VDVNDPR FQET FEDV YTQDSLN I - PWYVIAGNHDHVGNVKAQIE YSQRSKRW 139 - VDSVDSPR FKQT FEDV YTAKSL - RVPWYVLAGNHAGNVEAQIQ YSQKSDRW 139
H \$P AP 5   P 13686   /1-325 \$\$P AP 5   P09889   /1-340 DrP AP 2   Q7SXT1   /1-339 TnP AP 2   Q4ST55   /1-331 XtP AP 5   Q666 G6   /1-326	39 V P NA P FHTAR EMANAK E I AR TV Q I MGA D F I MS L GD N FY FTG 37 V P NA P FHTAR EMANAK E I AR TV Q I LGA D F I LS L GD N FY FTG 45 V P NA P FHTAR EMANAKA I A TTV K T LGA D F I LS L GD N FY FTG 47 L P N P Y VT P I ETA TAR MMAKTAS QMGA D F I LA V GD N FY YKG 47 V P Y P Y I TA V QKATA Q EMS K VA EQMGA D F V LA L GD N FY YKG 39 L P L P P Y TTR QQ E LVA E EMGKTVAK LGA D F I LS LGD N FY YD G 39 L P L P P Y TTR QQ E LVA E EMGKTVAK LGA D F I LS LGD N FY YD G	- VHDA NDKR FQET FEDV FSDRALRN I PWYVLAGNHDHLGNVSAQIA YSK I SKRW 132 - VQDINDKR FQET FEDV FSDRSLR KVPWYVLAGNHDHLGNVSAQIA YSK I SKRW 130 - VHDAKDKR FQET FEDV FSDPSLR NVPWHVLAGNHDHLGNVSAQIA YSK I SKRW 138 - VHDVNDPR FQET FEDV YTQDSLNI - PWYVIAGNHDHVGNVKAQIE YSQR SKRW 139 - VDVNDPR FQET FEDV YTQDSLNI - PWYVIAGNHDHVGNVKAQIE YSQR SKRW 139 - VDSVDSPR FKQT FEDV YTAKSL - RVPWYVLAGNHDHAGNVEAQIQ YSQK SDRW 139 - VTDV SDPR FKIT FESVYNAESLIN LPWFILAGNHDHKGNVSAQIA YTNVSKRW 132
HsP AP 5   P 13686 (/1-325 SsP AP 5   P09889  /1-340 DrP AP 2   (075XT1/1-339 TnP AP 2   (045755 )/1-331 XtP AP 5   066   G6 //1-326 XIP AP 1   066   G2 / 1-325	39 V P NA P F H T A R EMA NA K E I A R T V Q I MG A D F I MS L G D N F Y F T G 37 V P NA P F H T A R EMA NA K E I A R T V Q I L G A D F I L S L G D N F Y F T G 45 V P NA P F H T A R EMA NA K A I A T T V K T L G A D F I L S L G D N F Y F T G 47 V P Y P P Y V T P I E T A T A R MMA K T A S QMG A D F I L A V G D N F Y Y K G 47 V P Y P Y I T A V Q K A T A Q EMS K V A E QMG A D F V L A L G D N F Y Y K G 39 L P L P P Y T T R Q Q E L V A E EMG K T V A K L G A D F I L S L G D N F Y Y D G 38 L P L P P F T T R Q Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 38 L P L P P F T T R Q Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 39 L P L P P T T R Q Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 30 L P L P P T T R Q Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 30 L P L P P T T R Q Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 30 L P L P P T T R Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 31 L P L P P T T R Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 32 L P L P P T T R Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 34 L P L P P T T R Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 35 L P L P P T T R Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 36 L P L P P T T R Q E L V A E EMS K T V A K L G A D F I L S L G D N F Y Y D G 37 L P L P P T T R Q E L V A E E MS K T V A K L G A D F I L S L G D N F Y Y D G 38 L P L P P T T R Q E L V A E M S M T Y A K L G A D F I L S L G D N F Y Y D G 38 L P L P P T T R Q E L Y A E M S M T Y A K L G A D F I L S L G D N F Y Y D G 37 L P L P P T T R Q E L Y A E M S M T Y A K L G A D F I L S L G D N F Y Y D G 38 L P L P P T T R Q E L Y A E M S M T Y A K L G A D F I L S L G D N F Y Y D G 38 L P L P P T T R Q E L Y A E M S M T Y A K M S M S M S M S M S M S M S M S M S M	- V H D A - V H D A - V Q D I N D K R F Q E T F E D V F S D R A L R N I P W Y V L A G N H D H L G N V S A Q I A Y S K I S K R W 130 - V H D A K D K R F Q E T F E D V F S D P S L R N V P W Y L A G N H D H L G N V S A Q I A Y S K I S K R W 138 - V H D A K D K R F Q E T F E D V T Q D S L R N V P W Y L A G N H D H L G N V S A Q I A Y S K I S K R W 139 - V D V N D P R F Q E T F E D V Y T Q D S L N I - P W Y V I A G N H D H V G N V K A Q I E Y S Q R S K R W 139 - V D V N D P R F Q E T F E D V Y T Q D S L N I - P W Y V I A G N H D H V G N V K A Q I E Y S Q R S K R W 139 - V D V S D P R F K Q T F E D V Y T A K S L - R V P W Y V L A G N H D H A G N V E A Q I Q Y S Q K S D R W 132 - V T D V S D P R F K I T F E S V Y A A E S L I N L P W F I L A G N H D H K G N V S A Q I A Y T N V S T R W 131 - V T D S D P R F K I T F E S V Y S A E S L V K L P W Y I L A G N H D H K G N V S A Q I A Y T N V S T R W 131
HsP AP 5   P 13686   /1-325 SsP AP 5   P09889   /1-340 DrP AP 2   (75XT1   /1-339 TnP AP 2   (45755   /1-331 XtP AP 5   (666   66   /1-326 XIP AP 1   Q66   G6   /1-326 XIP AP 2   CQ6   56   /1-326	39 V P NAP F HTAR EMANAK E I AR TV Q I MGAD F I MS L GD N F Y F T G 37 V P NAP F HTAR EMANAK E I AR TV Q I L GAD F I L S L GD N F Y F T G 45 V P NAP F HTAR EMANAKA I AT TV K T L GAD F I L S L GD N F Y F T G 47 V P NP P Y V T I ETATAR MMAKTAS QMGAD F I L AV GD N F Y Y K G 47 V P Y P Y I T AV QKATAQ EMS K VA EQMGAD F V LA L GD N F Y Y K G 39 L P L P P Y T T R Q E L VA E EMG K TV AK L GAD F I L S L GD N F Y Y D G 38 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 30 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L G D N F Y Y D G 30 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L G D N F Y Y D G 30 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L G D N F Y Y D G 30 L P L P P Y T T R Q E L Y A E EMS K TV AK L GAD F I L S L G D N F Y Y D G 31 L P L P P Y T T R Q E L Y A E EMS K TV AK L GAD F I L S L G D N F Y Y D G 32 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 33 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 34 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E M S K Y A K L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E M S K Y A K L G A F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E M S K Y A K L G A F I L S L G D N F Y Y D G	- VHDA NDKR FQETFEDV FSDRALRN I PWYVLAGNHDHLGNVSAQIA - YSK I SKRW 132 - VQDINDKR FQETFEDV FSDRSLRKVPWVLAGNHDHLGNVSAQIA - YSK I SKRW 133 - VHDA KDKR FQETFEDV FSDRSLRNVPWHVLAGNHDHLGNVSAQIA - YSK I SKRW 138 - VTDV NDPR FQETFEDV YTQDSLNI - PWYVLAGNHDHLGNVSAQIA - YSK I SKRW 139 - VTDV SDPR FKQTFEDV YTQSLI - RVPWYVLAGNHDHAGNVEAQIQ - YSQK SDRW 139 - VTDV SDPR FK TFESV YNAESLI NLPWFILAGNHDHKGNVSAQIA - YTNVSKRW 132 - VTDV SDPR FK I TFESV YNAESLI NLPWFILAGNHDHKGNVSAQIA - YTNVSKRW 131 - VTDV SDPR FK I TFESV YSAESLVKLPWYILAGNHDHKGNVSAQIA - YTNVSTRW 131 - VTDV SDPR FK I TFESVYSSESLI KLPWYILAGNHDHKGNVSAQIA - YTNVSTRW 131
HsP AP 5   P 13686   /1-325 SsP AP 5   P09889   /1-340 DrP AP 2   (75XT1   /1-339 TnP AP 2   (45755   /1-331 XtP AP 5   (666   66   /1-326 XIP AP 1   Q66   G6   /1-326 XIP AP 2   CQ6   56   /1-326	39 V P NAP F HTAR EMANAK E I AR TV Q I MGAD F I MS L GD N F Y F T G 37 V P NAP F HTAR EMANAK E I AR TV Q I L GAD F I L S L GD N F Y F T G 45 V P NAP F HTAR EMANAKA I AT TV K T L GAD F I L S L GD N F Y F T G 47 V P NP P Y V T I ETATAR MMAKTAS QMGAD F I L AV GD N F Y Y K G 47 V P Y P Y I T AV QKATAQ EMS K VA EQMGAD F V LA L GD N F Y Y K G 39 L P L P P Y T T R Q E L VA E EMG K TV AK L GAD F I L S L GD N F Y Y D G 38 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 39 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L GD N F Y Y D G 30 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L G D N F Y Y D G 30 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L G D N F Y Y D G 30 L P L P P Y T T R Q E L VA E EMS K TV AK L GAD F I L S L G D N F Y Y D G 30 L P L P P Y T T R Q E L Y A E EMS K TV AK L GAD F I L S L G D N F Y Y D G 31 L P L P P Y T T R Q E L Y A E EMS K TV AK L GAD F I L S L G D N F Y Y D G 32 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 33 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 34 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E EMS K TV AK L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E M S K Y A K L G AD F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E M S K Y A K L G A F I L S L G D N F Y Y D G 35 L P L P P Y T T R Q E L Y A E M S K Y A K L G A F I L S L G D N F Y Y D G	V H D A N D K R F Q E T F E D V F S D R A L R N I P WY V L A G N H D H L G N V S A Q I A Y S K I S K R W 130 - V H D A K D K R F Q E T F E D V F S D P S L R N V P WY V L A G N H D H L G N V S A Q I A Y S K I S K R W 138 - V H D A K D K R F Q E T F E D V T Q D S L R N V P WY V L A G N H D H L G N V S A Q I A Y S K I S K R W 138 - V T D V N D P R F Q E T F E D V Y T Q D S L N I - P WY V I A G N H D H V G N V K A Q I E Y S Q R S K R W 139 - V D S V D S P R F K Q T F E D V Y T A K S L - R V P WY V L A G N H D H V G N V K A Q I E Y S Q K S D R W 139 - V D V S D P R F K Q T F E D V Y T A K S L - R V P WY V L A G N H D H A G N V E A Q I Q Y S Q K S D R W 132 - V T D V S D P R F K I T F E S V Y A A E S L I N L P WF I L A G N H D H K G N V S A Q I A Y T N V S T R W 131

11-D 40		A FP S A E S G S F S P F Y Y S F D A G	ALL X A. COM	
		A FP SK ES ES FS P FY YS FD V G G I H F I MLAA YA N YS K S G D Q Y RWL EK D L - A K V D R S V T P A FP SK ES ES FS P FY YS FD V G		
		A FP S E E S G S S S P F Y Y S FD A G G I H FVMLA S Y A D Y S R S G A Q Y KWL E A D L - E K V D R S V T P 1		
		A F P S T E S G S F S P F Y Y S F D A G		
		A FP S A EN G S F S P F Y Y S F D A G		
		A FP S T E S G S F S P F Y Y S F D A G		
		AFPSTESGSFSPFYYSFDAG		
		A FP S T E S G S F S P F Y Y S F D A G		
		AFPSAESGSFSPFYYSFDAGGIHFIMLAAYDDYSRSGEQYRWLEKDL-SKVDRSVTP		
		AFPSKESDSFSPFYYSFDAGGIHFIMLAAYAAYSKSGEQYRWLEKDL-AKVDRSVTP		
		A FP S K E S D S F S P F Y Y S F D A G		
		AFPSMESESFSPFYYSFDAGGIHFIMLAAYADYSKSGEQYRWLEKDL-AKVDRSVTP		
		A FP S K E S E S F S P F Y Y S F D A G		
		AFPSKESGSPSTFYYSFNAGGIHFVMLGAYISYNKSGDQYKWLERDL-ANVDREVTP		
		AFPSKESGSASTFYYSFNAGGIHFIMLGAYAAYNKSADQYKWLERDL-AKVDRSITP		
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VrP APhy   B5 AR Z7   / 1-547 30	06 -	AFPSEESGSLSTLYYSFNAGGIHFIMLGAYIDYYKNGEQYKWLERDL-ASVDRSITP	N L I <mark>a t</mark> w	H - P P W Y S S Y E V H Y K E A E C M R V E 388
		AFPFKESGSSSTLYYSFNAGGIHFVMLGAYIAYDKSAEQYEWLKKDL-AKVDRSVTP		
		AVPASESGSNSNLYYSFDAG		
GmP AP 4   V9H XG4   / 1-442 23	34 -	KMPFEESGSTSNLYYSFEVAGVHVIMLGSYADYDVYSEQYRWLKEDL-SKVDRKRTP	N L L <mark>V L F</mark>	H - V P W Y N S N K A H Q G A G D D MMA A 316
		VVNTETVDLFFVDTTPFVEEY FNSP EHV YDWRGVFP QQTYTKNVLNGLEYAL-M KSTTK 1		
AtP AP 3   Q8H 129   /1-366 18	80 F	I V N A E I V D L F F V D T T P F V D K Y F - I Q P N	WK I <mark>V IG</mark>	HH-TIKSAGHHGNTIELEKH 264
		V V N A E I V D I F F V D T T P F V D R Y F D - E P K D H V Y D W R G V L P R N K Y L N S L L - T D V D V A L Q E S MA K I		
		I L D G E I V E F F F V D T P F V D E Y F - V D P G E H T Y D WE G V L P RMS Y L S Q L L V D V D S A L - A K S K A K		
		' I V N T D V A E F F F V D T T P F Q D M Y F - T T P K D H T Y D W R N V M P R K D Y L S Q V L K D L D S A L - R E S S A K 1		
PvPAP4/Q9LL79//1-331 14	41 F	I V D T E I A E F F F V D T T P F V D K Y F - L K P K D H T Y D WT G V L P R D K Y L S K L L K D L E I A L - K D S T A K I	WK I <mark>VV</mark> G	HH-PVRSIGHHGDTQELIRH 225
		V L S S GMV D F F F A D T N P F V E K Y F T - E P E D H T Y D WR N V L P R N K Y I S N L L H D L D L E I K K S R A T I		
		V V D A E L V EMF F V D T T P F V K E Y Y T - E A D G H S Y D WR A V P S R N S Y V K A L L R D L E V S L K S S K A R		
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OsPAP1/Q7XH73//1-335 14	44 F	I V S A G I V D F F F V D T T P F Q L Q Y W T - D P G	NK L <mark>AVG</mark>	HH-TMRSVSAHGDTQELLEL 228
GmP AP 2   Q9 LL80   /1-332 14	49 Y	T L N S E N V D F F F V D T T P Y V D K Y F I E D K	NK V V I G	HH-TIKNIGHHGDTQELLIH 233
		I V D S E L V E I F F V D T T P F V E K Y F T E T K H K Y D WQ G I I P Q K S Y I T N L L K D L E L A I K E S T A Q I		
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MmPAP5/Q05117//1-327 13	33 -	NFPSPYYRLRFKIPRTNITVAIFMLDTVMLCGNSDDFASQQPKMPRDLGVARTQLSWLKKQL-AAAKED	Y <b>V L</b> V A G	HY-PIWSIAEHGPTRCLVKN 225
		NFPSPYYRLRFKVPRSNITVAIFMLDTVMLCGNSDDFVSQQPEMPRDLGVARTQLSWLKKQL-AAAKED		
		NFPSPFYRLHFKIPQTNVSVAIFMLDTVTLCGNSDDFLSQQPERPRDVKLARTQLSWLKKQL-AAARED		
		NFPS PYYRLRFKIPRSNVSVAIFMLDTVTLCGNSDDFVSQQPERPRNLALARTQLAWIKKQL-AAAKED		
		NFPYYYYEMNFRIPRTDSTLTIIMLDTVLLCGNSDDFLDQQPRAPRSGVLANRQLLWLQERL-AKSKAD		
TnP AP 2   Q45755   /1-331 14	40 -	K F P A Y Y Y E L N F R I P N T G K T L T I I M L D T V M L C G N S N D F S D E K P Q G P L Y A P D A H R Q L T W L Q E R L - A R S K A D	FLLVAG	HY-PVWSVSEHGPTACLLQR 232
		NYPDYYYDLS FTVPGSNVTVRLLMLDTVELCGNSDDFRDGQPRGPTNLKTAGSQLEWLVEKL-QSAKED		
		NYPDYYYDLAFTIPGSNVTVRILMLDTVQLCGISDDFHDGQPRGPNNLRMAGTQLEWLSEKL-QSSKDD		
		NYPDYYYDLAFTIPGSNVTVRLLMLDTVQLCGISDDFHDGQPRGPNNLKMAGTQLEWLEEKL-QSAKEN		
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HvP APhy_a C4PKL2 /1-544 TaP APhy_a1 C4PKK7 /1-550																												
TaP APhy_a 1 C4PKK7 /1-550 TaP APhy_b1/C4PKK9 /1-538																												
TaP APhy_b2   C4PKL0   /1-537																												
HvPAPhy_b2 C4PKL4 /1-537																												
HvPAPhy_b1/C4PKL3//1-536																												
OsP APhy_b   D6QSX9  /1-539																												
ZmP APhy_b   C4PKL6   /1-544																												
MtP APhy   Q3ZFI 1   / 1-543																												
PtPAP3/V9LXK5//1-564																												
NtP APhy   A5 YBN1   /1-551																												
LaP APhy   D2 YZL4   /1-543																												
GmP APhy_b   Q93XG4   /1-547																												
AtP AP 15   Q9 SF U3   /1-532																												
AtaP APhy_a 1/F6MIX0 //1-549																												
ScP APhy_a2  F6MIX4  /1-543																												
TmP APhy_a 1   F6MIW8   / 1-545																												
TaP AP hy_a3   F6MIW2   /1-539																												
TaP APhy_a2   C4PKK8   /1-549																												
ScP APhy_a1/F6MIX2//1-541																												
TaP APhy_b3   F6MIW 6   /1-536																												
TmP APhy_b1/F6MIW9//1-539																												
AtaP APhy_b1/F6MIX1//1-538	382	MEEL	LYSY	GLDIV	FTGH	I V H <mark>A</mark>	YERS	NRV	F - N Y	TLDP	С G A V H	ISV	GDGGN	R EKMAT	ттнарр	PGRCPI	EPLST	P D D F M -	- G G -	- FCAFN	FTSGPA/	AGSECWD	RQP-	D	YSAYR	ESSFG	HGILE	493
ScP APhy_b1/F6MIX5//1-538																												
RcP AP 1   B9R W G6   / 1-566																												
VvP AP   A5 BGI 6   / 1-540	381	MEEL	LYSY	GVDIV	FNGH	IV H <mark>A</mark>	YERS	NRV	Y - N Y	TLDP	с д р у н	ELMV.	GDGGN	REKMA	I E H A D A	PGKCPI	ЕРЅТТИ	PDTFI-	GG-	- FCATN	FTFGPA	AGKECWD	RQP-	D	FSAFR	ESSFG	HGILE	492
PvPAPhy/V7B3Z4//1-546	388	MEDI		GVDIV	FNGH	і V НА	V E B S	NRV	Y - N Y	S I D P										<b>E O A T N</b>	ETECHES					ETSEC	VGLLE	400
										3 L D F	согун	11 A V	GDGGN	REKMA.	IKFADE	PGHCPI	DPLSTA	ΡΟΡΥΜ-	- G G -	- FCAIN	FIFUFES	S EFCWD	Q P -	D	YSAFR	E 1 3 F 0	TOTLE	450
VrP APhy   B5 AR Z7   / 1-547	389	MENL	LYSY	GVDIV	FNGH	IV H <mark>A</mark>	YERS	NRV	Y - N Y	SLDP	с д р у н	LAV	GDGGN	REKMA	IKFADE	РСНСРІ		S D H F M -	GG-	- FCATN	FTFDQE	SEFCWD	HQP-	D	YSAFR	ETSFG	YGILE	499
VrP APhy  B5 AR Z7  /1-547 AIP AP 15   D7 L636  /1-532	389	MENL	LYSY	GVDIV	FNGH	IV H <mark>A</mark>	YERS	NRV	Y - N Y	SLDP	с д р у н	LAV	GDGGN	REKMA	IKFADE	РСНСРІ		S D H F M -	GG-	- FCATN	FTFDQE	SEFCWD	HQP-	D	YSAFR	ETSFG	YGILE	499
AIP AP 15   D7L636   /1-532 AtP AP 23   Q6TPH 1   /1-458	389 380 381	MENL Meel Meel	L Y S Y ( L Y S Y ( L Y Q Y )	GVDIV <u>GIDIV</u> RVDIV	FNGH FNGH FAGH	IVH <mark>A</mark> IVHA IVHA	YERS	NRV <u>NRV</u> ANRI	Y - N Y <u>Y - N Y</u> Y - N Y	S L D P <u>E L D P</u> T L D P	с	1 A V 1 V V 1 T I	G D G G N <u>G D G G N</u> G D G G N	REKMA <u>REKM</u> A IEKVD'	I K F A D E I E H A D E V D F A D D	Р G H C P I Р G K C P Р G K C <mark>-</mark>	DPLSTS EPLTTF <mark></mark> HSS <sup>V</sup>	S	G G G G	FCATN FCAWN FNSLN	FTFDQE FTPPS LSN	S E F C W D S G K F C W D	H Q P - R Q P -	D D	YSAFR YSAM R	E T S F G E S S F G	YGILE HGILE	499 488 458
AIP AP 15   D7L636   / 1-532 AtP AP 23   Q6TPH 1   / 1-458 GmP AP 4   V9HX G4   / 1-442	389 380 381 317	MENL <u>Meel</u> Meel Mepl	L Y S Y ( L Y S Y ( L Y Q Y ) L Y Q X A :	G V D I V <u>G I D I V</u> R V D I V S V D I V	FNGH FNGH FAGH	1 V H <mark>A 1 V H A</mark> 1 V H A 1 V H A	Y E R S Y E R S Y E R N Y E R S	SNRV S <u>NRV</u> ANRI SKRL	Y - N Y <u>Y - N Y</u> Y - N Y Y - N G	S L D P <u>E L D P</u> T L D P R L D P	C G P V H <u>C G P V Y</u> C G P V Y C G A V H	A V     V V     T	G D G G N <u>G D G G N</u> G D G G N G D G G N	REKMA REKMA IEKVD <sup>V</sup> REGLAI	I K F A D E I E H A D E V D F A D D H K Y I N P	P G H C P I P G K C P P G K C	DPLSTS EPLTTF HSS	S D H F M P D P V M - Y D L F F -	- <mark>G G</mark> - G G -	FCATN FCAWN FNSLN	FTFDQE FTPS LSN	S E F C W D S G K F C W D	H Q P - R Q P -  - Q P -	D D K	Y S A F R <u>Y S A M R</u>  W S E F R	ETSFG ESSFG  EASFG	Y G I L E <u>H G I L E</u>  H G E L K	499 488 458 392
AP AP 15   D7L636 /1-532 AtP AP 23   Q6TPH 1 /1-458 GmP AP 4   V9HXG4  /1-442 IbP AP 4   Q9LL8 1 /1-312	389 380 381 317 233	MENL MEEL MEEL MEPL LLPI	L Y S Y ( L Y S Y ( L Y Q Y ) L Y Q Y I L Y A A S	G V D I V G I D I V R V D I V S V D I V N V D I V	FNGH FNGH FAGH IAGH	IV H <mark>A IV HA</mark> IV HA IV HA IV HA	YERS YERS YERN YERS	S N R V S N R V //N R I S K R L	Y - N Y <u>Y - N Y</u> Y - N Y <u>Y - N G</u> E	S L D P <u>E L D P</u> T L D P R L D P H I S D	C G P V H <u>C G P V Y</u> C G P V Y <u>C G A V H</u> D E S P I	1 A V 1 V V 1 T I 1 T I 0 F M	G D G G N G D G G N G D G G N G D G G N T S G A G	REKMA <u>REKMA</u> IEKVD <sup>I</sup> REGLAI SKAWR	I K F A D E I E H A D E V D F A D D H K Y I N P G D V T MD	P G H C P I P G K C P P G K C R K G V S	D P L S T S E P L T T F <mark>H S S Y</mark>	S D H F M P D P V M Y D L F F	G G - G G -	FCATN FCAWN FNSLN	FTFDQE FT PS	S E F C W D S G K F C W D F F Y D	H Q P - R Q P -  - Q P - G Q	D D K	YSAFR <u>YSAMR</u>  WSEFR FMSV0	ETSFG ESSFG EASFG	Y G I L E H <u>G I L E</u>  H <u>G E L K</u> I G I <b>V</b> F	499 488 458 392 309
AIP AP 15   D7L636 /1-532 AtP AP 23   Q6TPH 1   / 1-458 GmP AP 4   V9HX G4   / 1-442 IbP AP 4   Q9LL8 1   / 1-312 AtP AP 3   Q8H 129   / 1-366	389 380 381 317 233 265	MENL MEEL MEEL LLPI LLPI	L Y S Y I L Y S Y I L Y Q Y I L Y Q A Y L Y A A Y L R T Y I L Q A N	G V D I V G I D I V R V D I V S V D I V N V D I V E V D I V	FNGH FNGH FAGH IAGH MNGH VNGH	IV H <mark>A IV HA</mark> IV HA IV HA IV HA I D HS I D HC	Y E R S Y E R S Y E R N Y E R N L	SNRV SNRV MNRI SKRL	Y - N Y <u>Y - N Y</u> Y - N Y <u>Y - N G</u> E E H	SLDP ELDP TLDP RLDP HISD ISSV	C G P V H C G P V Y C G P V Y C G A V H D E S P I D S N I Q	(   A V ) (   V V ) (   T   ) (   T   ) Q F M (	G D G G N G D G G N G D G G N G D G G N T S G A G S G G G S	REKMA REKMA IEKVD <sup>V</sup> REGLAI SKAWR KAWK	I K FAD E I EHADE V D FAD D H K Y I N P G D V T M D	P G H C P I P G K C P P G K C P G K C R K G V S	D P L S T S E P L T T F <mark>H S S `</mark>	S D H F M P D P V M V D L F F	G G - G G -	FCATN FCAWN FNSLN	FTFDQE FT	SEFCWD SGKFCWD FFYD EMRFYYD	H Q P - R Q P - - Q P - G Q G Q	D D K G G	YSAFR <u>YSAMR</u> WSEFR FMSVC FMSVF	ETSFG ESSFG EASFG LVETD	Y G I L E <u>H G I L E</u> H <u>G E L K</u> I G I V F L R V V F	499 488 458 392 309 343
AIP AP 15 D7L636 /1-532 AtP AP 23 Q6TPH 1 /1-458 GmP AP 4 V9HXG4 /1-42 IbP AP4 Q9LL81 /1-312 AtP AP3 Q8H 129 /1-366 AtP AP8 Q8VV22 /1-335	389 380 381 317 233 265 236	MENL MEEL MEPL LLPI LLPI	L Y S Y I L Y S Y I L Y Q Y I L Y Q Y I L Y A A : L Y S Y I L Y Q Y I L Y A A : L Y A : L	G V D I V G I D I V R V D I V S V D L V B V D L V E V D L V	FNGH FAGH TAGH MNGH VNGH	IV H <mark>A IV HA</mark> IV HA IV HA I D HS I D HC I D HC	Y E R S Y E R N Y E R N Y E R N L L	NRV NRV NRL KRL	Y - N Y <u>Y - N Y</u> <u>Y - N Y</u> E E H E H	SLDP ELDP TLDP RLDP HISD ISSV ISSI	C G P V H C G P V Y C G P V Y C G A V H C G A V H D E S P I D S N I Q N S G I Q	(  A V) (  V V) (  T   ) (  T   ) (  T   ) (  F M T ) (  F M T )	G D G G N G D G G N G D G G N G D G G N T S G A G S G G G S S G G G S	REKMA REKMA IEKVD <sup>I</sup> REGLAI SKAWR KAWK	I K FAD E I EHAD E V D FAD D H K Y I N P G D V T M D D V N D W N	PGHCPI PGKCP PGKC RKGVS	D P L S T S E P L T T F - H S S Y	SDHFM PDPVM- YDLFF	G G G G	FCATN FCAWN FNSLN	FTFDQE FTPS LSN YV-EPE	SEFCWD GKFCWD FFYD MRFYYD RFYYD	H Q P - R Q P - - Q P - G Q G Q G Q	D D K G G	YSAFR YSAMR WSEFR FMSVC FMSVF FMSVF	ETSFG ESSFG EASFG LVETD VSEAE	YGILE HGILE HGELK IGIVF LRVVF LRVVF	499 488 458 392 309 343 313
AIP AP 15   D7L636 /1-532 AtP AP 23   Q6TPH 1   /1-458 GmP AP 4   V9HX G4   /1-442 IbP AP 4   Q9LL8 1   /1-312 AtP AP 3   Q8H 129   /1-366 AtP AP 8   Q8V Y22   /1-335 P V AP 3   D2 D4 /4 / /1-330	389 380 381 317 233 265 236 236	MENL MEEL MEPL LLPI LLPI LLPI	LYSY LYSY LYQYI LYAA LRTYI LQAN LEAN LEAYI	G V D I V G I D I V R V D I V S V D L V N V D L V E V D L V E V D L V	FNGH FAGH TAGH MNGH VNGH		Y E R S Y E R N Y E R N Y E R N L L	NRV NRV NRI KRL	Y - N Y Y - N Y Y - N Y E E H E H	S L D P E L D P T L D P R L D P H I S D I S S V I S S I I S S I I S S I	C G P V H C G P V Y C G P V Y C G A V H D E S P I D S N I Q N S G I Q N S G I H		G D G G N G D G G N G D G G N G D G G N T S G A G S G G G S S G G G S S G G G S	REKMA REKMA IEKVD REGLAI SKAWR KAWK KAWKG KAWSG	I K FADE I EHADE V D FADD H K Y I N P G D V T M D D V N D W N	P G H C P I P G K C P P G K C R K G V S	DPLSTS EPLTTF - HSS KPWSS	S D H F M P D P V M Y D L F F E E L O L	G G G G	FCATN FCAWN FNSLN	FTFDQE FTPS LSN YV-EPE	SEFCWD GKFCWD FFYD MRFYYD RFYYD	H Q P - R Q P - - Q P - G Q G Q G Q G Q	D D K G G G	YSAFR YSAMR WSEFR FMSVC FMSVF FMSVF FMSVF	ETSFG ESSFG EASFG LVETD VSEAE TSEAE	YGILE HGILE HGELK IGIVF LRVVF LRVVF ADIIF	499 488 458 392 309 343 313 313
AP AP 15   D7L636   /1-532 AP AP 23   Q6TPH 1   /1-58 GmP AP 4   V9HX G4   /1-458 IbP AP 4   Q9LL8 1   /1-312 AP AP 3   Q8H 129   /1-366 AP AP 8   Q8V72   /1-335 P vP AP 3   Q6L9X / 1-330 StP AP 1   Q6L9X / 1-330	389 380 381 317 233 265 236 236 230	MENL MEEL MEPL LLPI LLPI LLPI LVPI	L Y S Y I L Y Q Y I L Y Q Y I L Y Q X I L Y Q A N L Q A N I L Q A N I L Q A N I	G V D I V G I D I V R V D I V S V D L V S V D L V E V D L V N V D A V	FNGH FAGH TAGH MNGH VNGH INGH INGH	IVH <mark>A</mark> IVHA IVHA IDHS IDHC IDHC IDHC	Y E R S Y E R N Y E R N Y E R N L L L		Y - N Y Y - N Y Y - N Y E - E H - E H - E H - E H	S L D P E L D P T L D P R L D P H I S D I S S V I S S I I S S I I S S S	C G P V H C G P V Y C G P V Y C G A V H C G A V H D E S P I D S N I Q N S G I H D S P L Q	(   A V (   V V (   T   ) (	G D G G N G D G G N G D G G N G D G G N G D G G N S G G G S S G G G S S G G G S S G G G S S G G G S	REKMA IEKMA IEKVD <sup>1</sup> REGLAI SKAWR KAWK KAWKG KAWSG KAWSG	I K FADE I EHADE V D FADD HK Y I NP G D V TMD D V N D WN D V	P G H C P I P G K C P P G K C R K G V S	D P L S T S E P L T T F H S S <sup>S</sup> K P WS S	S D H F M P D P V M Y D L F F - E E L Q L -	G G - G - G G - G G - G G G - G G G - G G G - G G G - G G - G G - G G - G G - G G G - G G G - G G G - G G G G G - G G G G G - G G G G G - G G G G G G - G	FCATN FCAWN FNSLN	F T F D Q E F T P S L S N Y V - E P E I	SEFCWD SGKFCWD MRFYYD RFYYD RFYYD	H Q P - R Q P - G Q G Q G Q G Q G Q	D D K G G G G G	YSAFR YSAMR FMSVF FMSVF FMSVF FMSVF FMSV7 FMSM0 FMSM0	ETSFG ESSFG EASFG LVETD VSEAE TSEAE (TTESN	YGILE HGILE HGELK IGIVF LRVVF LRVVF ADIIF VWIQF	499 488 458 392 309 343 313 313 307
AIP AP 15   D7L636   /1-532 AtP AP 23   Q6TPH 1   /1-458 GmP, AP 4   V9HXG4   /1-412 IbP AP4   Q9LL8 1   /1-312 AtP AP3   Q8H 129   /1-366 AtP AP8   Q8VYZ2   /1-335 P VP AP3   D2 D414   /1-320 StP AP 1   Q6J5M7   /1-328 P VP AP4 ( 091   79   /1-331	389 380 381 233 265 236 236 230 226	MENL MEEL MEEL LLPI LLPI LLPI LVPI ILPI	LYSY LYQYI LYQYI LYAA LRTYI LQAN LEAYI LQANI LQANI	G V D I V G I D I V R V D I V S V D L V S V D L V E V D L V E V D L V N V D A V	FNGH FAGH TAGH MNGH VNGH TNGH TNGH	IVH <mark>A</mark> IVHA IVHA IDHS IDHC IDHC IDHC	Y E R S Y E R N Y E R N Y E R N L L L L	S N R V S S N R V S M R I S K R L S	Y - N Y Y - N Y Y - N Y Y - N G E H - E H - E H - E H - E H	S L D P E L D P T L D P R L D P H I S D I S S V I S S V I S S S I S S S I S S T	C G P V H C G P V Y C G P V Y C G A V H D E S P I D S N I Q N S G I A N S G I A N S G I H D S P L Q S S O I O	(  A V ( (   V V ( (   T   ) (	G D G G N G D G G N G D G G N T S G A G S G G G S S G G G S	R EKMA I EKVD <sup>1</sup> R EGLAI SKAWR KAWK KAWKGI KAWSGI KSWR KAWKG	IKFADE IEHADE VDFADD HKYINP GDVTMD DVNDWN	P G H C P I P G K C P P G K C R K G V S P Q EM P Q EM	D P L S T S E P L T T F - H S S T K P W S S I	SDHFM PDPVM YDLFF EELQL	G G - G - G G - G G - G G G - G G G - G G - G G - G G - G G - G G - G G - G G - G G - G G - G G - G G G G - G G G G G - G G G G G - G G G G G - G G G G G - G G G G G - G G G G G - G G G G G - G G G G G G - G G G G G G - G G G G G G - G G G G G G G - G G G G G G G - G G G G G G G G - G	FCATN FCAWN FNSLN - FNSLN - DVN	FT FD Q E FT PS LS N P Y V - EP E P K	SEFCWD SGKFCWD MRFYYD RFYYD RFYYD CMKFYYD	H Q P - R Q P - G Q G Q G Q G Q G Q	D D K G G G G G	YSAFR YSAMR FMSVF FMSVF FMSVF FMSV7 FMSM0 FMSM0	ETSFG ESSFG EASFG LVETD VSEAE TSEAE ITSEAE ITSEAE	YGILE HGILE IGIVF LRVVF LRVVF ADIIF VWIQF KSIPK	499 488 458 392 309 343 313 313 307 301
AIP AP 15 [ D7L636]/1-532 AtP AP 23   Q6TPH 1   / 1-458 GmP AP 4   V9HX G4   / 1-422 IbP AP4   Q9LL8 1   / 1-312 AtP AP3   Q8H 129   / 1-366 AtP AP8   Q8VV22   / 1-335 P vP AP3   D2 D4J4   / 1-330 StP AP 1   Q6J5M7   / 1-328 P vP AP4   Q9LL79   / 1-331 AtP AP5 ( Q9SL4 1 / 1-331	389 380 381 317 233 265 236 236 230 226 232	MENL MEEL MEEL LLPI LLPI LLPI LVPI ILPI	LYSY LYSY LYQYI LYQXI LRTYI LQAN LEANI LEANI LEANI LEANI	G V D I V G I D I V S V D L V S V D L V E V D L V E V D L V E V D L V N V D A V N V D A V N V D A V	'FNGH 'FAGH 'IAGH 'MNGH 'NNGH 'INGH 'INGH 'INGH	IV H <mark>A IV H A IV H A ID H S ID H C ID H C ID H C ID H C</mark>	Y E R S Y E R S Y E R N Y E R S L L L L L	SNRV SNRV MNRI SKRL	Y - N Y Y - N Y Y - N Y Y - N G E E H E H E H E H E H E H E H E H E H E H E H E E E E E E E E 	SLDP ELDP TLDP RLDP HISD ISSV ISSV ISSS ISST ISST	CGPVH CGPVY CGPVY CGAVH DESPI DSNIQ NSGIQ NSGIQ NSGIQ SSQIQ SSQIQ	(1 A V ) (1 T 1) (1 T	G D G G N G D G G N G D G G N T S G A G S G G G S S G G G S	R EKMA R EKMA I EKVD R EGLAI S KAWK K AWK K AWK K AWK G K AWK G	IKFADE IEHADE VDFADD HKYINP GDVTMD GDVTMD DV DV - DHLIK	PGHCPI PGKC PGKC RKGVS	DPLSTS EPLTTF HSS KPWSS QRFTMM	SDHFM PDPVM YDLFF EELQL MDKYL	G G - G G -	FCATN FCAWN FNSLN - FNSLN - DVN	FTFDQE FT PS LSN FTF YV FPE	SEFCWD SGKFCWD EMRFYYD RFYYD EMRFYYD EMKFYYD	H Q P - R Q P - G Q G Q G Q G Q G Q G Q G Q	D D G G G G G G	YSAFR YSAMR FMSVC FMSVC FMSVC FMSVC FMSMC FMSMC FMAMC C FMSLE	ETSFG ESSFG LVETD VSEAE TSEAE ITSEAE ITSEA UTTSN	YGILE HGILE IGIVF LRVVF LRVVF ADIIF VWIQF KSIPK AKFIY	499 488 392 309 343 313 313 307 301 308
AP AP 15   D7L636   /1-532 AP AP 23   Q6TPH 1   /1-458 GmP AP 4   V9HX G4   /1-442 IbP AP 4   Q9LL8 1   /1-312 AP AP 3   Q8H 129   /1-366 AP AP 8   Q8V72   /1-355 P vP AP 3   Q6L5M7   /1-328 P vP AP 4   Q9LL79   /1-331 AP AP 7   Q8534 1   /1-328 AP 4 7 12 (052/8 / 1-382	389 380 381 317 233 265 236 236 230 226 232 237	MENL MEEL MEPL LLPI LLPI LLPI LLPI LLPI LLPI	LYSY LYQY LYQY LYQA LRTY LQAN LEAN LEAN LEAN LEAN LEAN	GVDIN GIDIN RVDIN SVDLN EVDLN EVDLN EVDLN NVDAN NVDFN DVDMN KVDLN	FNGH FAGH FAGH MNGH MNGH INGH INGH INGH	IVHA IVHA IVHA IDHS IDHC IDHC IDHC IDHC	Y E R S Y E R N Y E R N Y E R N L L L L L L L L	S N R V S N R V S N R I S K R L S K R L S S K R S S S K S S S S S S S S S S S S S S S S	Y - N Y Y - N Y Y - N Y Y - N G E H E H E H E H E H E H Q H	SLDP ELDP TLDP RLDP HISD ISSV ISST ISST IGS- MSDF	CGPVH CGPVY CGAVH DESPI DSNIQ NSGIQ NSGIQ DSPLQ SSQIQ DSPLQ	(  AV) (  T   ) (  T   ) (  T   ) (  F   T   (  F   T   (  F   T   (  F   T   (  F   T   )   F   T	G D G G N G D G G N G D G G N G D G G N T S G A G S G G G S S G A G S	R EKMA R EKMA I EKVD R EGLAI SKAWR KAWKG KAWKG KAWRG KAWRG	I K FADE I EHADE V D FADD HK Y I NP GD V TMD DV NDWN DV DV	P G H C P I P G K C P P G K C R K G V S P Q E M M G K M G P K E L	D P L S T S E P L T T F - H S S K P W S S I Q R F T MN	S D H F M P D P V M Y D L F F E E L Q L MD K Y L	G G -	FCATN FCAWN FNSLN - FNSLN - DVN	FTFDQE FTPS LSN YV-EPE	SEFCWD SGKFCWD EMRFYYD RFYYD EMKFYYD KLYYD	H Q P - R Q P - G Q G Q G Q G Q G Q G Q G Q G Q		Y S A F R Y S AMR FMS V C FMS V F FMS V V FMS MC FMS MC FMS L F FMS L F FMS L F	ETSFG ESSFG LVETD VSEAE TSEAE ITSEAE ITCTQ VWRFK ITTSK	Y G I L E H G I L E I G I V F L R V V F L R V V F A D I I F V W I Q F K S I P K A K F I Y A F I Y F	499 488 392 309 343 313 313 307 301 308 316
AP AP 15   D7L636   /1-532 AP AP 23   Q6TPH 1   /1-58 GmP AP 4   V9HX G4   /1-458 GmP AP 4   Q9LL8 1   /1-312 AP AP 3   Q8H 129   /1-366 AP AP 8   Q8V721   /1-336 SP AP 1   Q6L5M7   /1-328 P VP AP 4   Q9LL79   /1-331 AP AP 7   Q8528 4   /1-328 BP AP 17 1   D9SCK8   /1-337	389 380 381 317 233 265 236 236 230 226 232 237 236	MENL MEEL MEPL LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPI	LYSY LYQY LYQY LYQA LRTY LQAN LEAN LEAN LEAN LEAN LEAN LEAN LEAN	G V D I V G I D I V R V D I V S V D L V E V D L V E V D L V E V D L V N V D A V N V D A V N V D A V N V D A V D V D M V K V D L V G V D L V	FNGH FAGH FAGH MNGH MNGH INGH INGH INGH INGH	IV H <mark>A IV H A IV H A I V H A I D H C I D H C</mark>	Y E R S Y E R N Y E R N Y E R N L L L L L L L L L L		Y - N Y Y - N Y Y - N Y Y - N G E H E H E H E H E H E H Q H Q H E H	SLDP ELDP TLDP HISD ISSV ISSI IDK ISSS ISST IGS- MSDE ISDE	C G P V H C G P V Y C G P V Y C G A V H D E S P I Q D S N I Q N S G I Q N S G I Q N S G I Q N S G I Q D S P I Q D S P I Q D S P I Q	(  AV) (  T   ) (  T   ) (  T   ) (  F   T   )	G D G G N G D G G N G D G G N T S G A G S G G G S S G A G S S G A G S S G A G S	R EKMA R EKMA I EKVD R EGLA S KAWR KAWKG KAWKG KAWRG KAWRG KAWRG	I K FADE I EHADE V D FADD HKYINP GDV TMD DV NDWN DV DV	P G H C P I P G K C P P G K C R K G V S P Q E M M G K M G C P K E L	D P L S T S E P L T T F - H S S S K P W S S I Q R F T MM	S D H F M P D P V M Y D L F F E E L Q L MD K Y L N P K L L	G G - G G - G G -	FCATN FCAWN FNSLN - FNSLN - DVN	FTFDQE FT	SEFCWD SGKFCWD MRFYYD RFYYD MKFYYD KLYYD KLYYD SVRFYYD	H Q P - R Q P - G Q G Q G Q G Q G Q G Q G Q G Q G Q G Q	D G G G G G G G G G 	Y S A F R Y S AMR FMS V C FMS V F FMS V F FMS MC FMS MC FMS A FMS A FMS A F	ETS FG ESS FG LV ETD VS EA E TS EA E IT ES N UT TS FA VWR FK IT THS K FT HS D	YGILE HGILE HGILF IGIVF LRVVF ADIIF VWIQF KSIPK AKFIY AEIVF AEIVF	499 488 458 392 309 343 313 313 307 301 308 316 315
AP AP 15 [D7L636]/1-532 AtP AP 23   Q6TPH 11/1-458 GmP AP 4  V9HXG4]/1-442 IbP AP4  Q9LL81]/1-312 AtP AP3   Q8H 129]/1-366 AtP AP8   Q8VYZ2]/1-335 P VP AP3   Q6J5M7]/1-328 P VP AP4 [Q8LT9]/1-331 AtP AP7   Q8S341]/1-328 AtP AP7 [Q8S341]/1-328 BrP AP 17 [Q9SCK8]/1-337 OP AP 1007KH73]/1-335	389 380 381 317 233 265 236 236 230 226 232 237 236 229	MENL MEEL MEEL LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPI	LYSY LYQY LYQY LYQA LRTY LCAN LCAN LCAN LCAN LCAN LCAN LCAN LCAN		FNGH FAGH FAGH MNGH VNGH VNGH VNGH VNGH VNGH MNGH		Y E R S Y E R W Y E R W Y E R V L L L L L L L L L		Y - N Y Y - N Y Y - N Y Y - N G E H E H E H E H E H Q H Q H E H E H	SLDP TLDP TLDP TLDP TLDP TLDP TLDP TLSS TSS TSS TSS TSS TSS TSS TSS TSS TS	C G P V H C G P V Y C G P V Y C G A V H D E S P I D S N I Q N S G I Q N S G I Q N S G I Q N S G I Q N S P I Q D S P I Q D S P I Q	(  A V ) (  T   ) Q FM ( P FM ( F F T ) (F F T )	G D G G N G D G G N G D G G N T S G A G S G G G S S G A G S S G A G S S G A G S	R E K MA R E K M D I E K V D R E G L A S K A WR K A WK G K A WK G K A WK G K A WR G K A WR G K A WR G K A WR G	I K F A D E I E H A D E V D F A D D H K Y I N P G D V T M D D V N D W N D V D H L I K H V Q P W D D I T D V D P T I F O O N E	P G H C P I P G K C P R K G V S IP Q EM MG K MG P K E L	DPLSTS EPLTTF - HSSS KPWSSI QRFTMI	S D H F M P D P V M Y D L F F E E L Q L M D K Y L N P K L L	G G - G G - G G -	FCATN FCAWN FNSLN - DVN - MNWWN	FTFDQE FT-PS LSN- YV-EPE - PK	SEFCWD SGKFCWD MRFYYD RFYYD MKFYYD KFYYD KFYYD SVRFYYD	H Q P - R Q P - G Q G Q		Y S A F R Y S AMR FMS V C FMS V C FMS V C FMS V FMS MC FMS A FMS A	ETSFG ESSFG LVETD VSEAE TSEAE UTESN UTESN VWRFK ITTSK FTHSD FTHSD	YGILE HGILE HGILE IGIVF LRVVF ADIIF VWIQF KSIPK AKFIY AEIVF AEIVF AAFAF	499 488 458 392 309 343 313 313 307 301 308 316 315 305
AP AP 15 [D7L636]/1-532 AtP AP 23   Q6TPH 1 /1-458 GmP, AP 4  V9HXG4 /1-422 IbP AP4  Q9LL81 /1-312 AtP AP3   Q8H 129  /1-366 AtP AP3   Q8VYZ2  /1-335 P VP AP3   Q2 D4J4 /1-330 StP AP 1  Q6J5M7]/1-328 P VP AP4   Q9LL79  /1-331 AtP AP 7  Q8S341 /1-328 AtP AP 17   Q9SCX8 /1-338 BrP AP 17_1  D6MW888/1-337 OSP AP 12 (Q7KH73)/1-335 GmP AP2 (Q9LL80)/1-332	389 380 381 233 265 236 236 230 226 232 237 236 237 236 229 234	MENL MEEL MEEL L L P I L L P V F L P V	LYSY( LYQYI LYQA LRTYI LQAN LEAN LEAN LEAN LEAN LEAN KEN LKEN LKEN	G V D I V G I D I V R V D I V S V D L V N V D L V E V D L V E V D L V E V D L V N V D A V N V D A V N V D L V G V D L V G V D L V G V D L V N V D L V	FNGH FAGH TAGH MNGH VNGH VNGH VNGH VNGH NNGH MNGH		Y E R S Y E R W Y E R W Y E R V L L L L L L L L L L L		Y - N Y Y - N Y Y - N Y Y - N G E H E H E H E H E H Q H Q H E H E H E H	SLDP TLDP TLDP HISD ISSV ISSV ISSS ISST IGS- MSDE ISDE ISSR	C G P V H C G P V Y C G P V Y C G A V H D E S P I D S N I Q N S G I H D S P I Q D S P I Q D S P I Q D S P I Q D S S V Q	(  AV) (  T   ) (  T   ) (  T   ) (  T   ) (  F   T ) (  F   T ) (  F   T ) (  F   T ) (  F   T ) (  F   T ) (  F   T )	G D G G N G D G G N G D G G N T S G G G S S G G G S	R E K MA R E K MA I E K V D' R E G L A K A WR K A WR K A WR K A WR K A WR K A WR K A WR G K A WR G K A WR G K A WR G K A WR G K A WR G	I K FADE I EHADE V D FADD HK Y I NP G D V TMD D V NDWN D V	P GH C P I P GK C P R K GV S P Q EM MG K MG ( P K E L	DPLSTS EPLTTF HSS KPWSSI QRFTMI	S D H F M P D P V M Y D L F F E E L Q L M D K Y L N P K L L - D K L Q	G G - G G - G G -	- FCATN - FCAWN - FNSLN DVN MNWWN	F T F D Q E F T P S L S N P K T N N P K S	SEFCWD SGKFCWD MRFYYD RFYYD MKFYYD KLYYD KFYYD SVRFYYD	H Q P - R Q P - G Q G Q		Y S A F R Y S AMR F MS V C F MS V C F MS V C F MS MC F MS MC F MS A F MS A F MS A F MS A F MS A F MS L F MS L F MS L F MS V F MS V M F MS V F MS V M	EASFG EASFG LV ETD VS EAE IT SEAE IT TQTQ VWR FK IT THSK FTHSD FTHSD FTHTD LS ENR	YGILE HGILE HGELK IGIVF LRVVF LRVVF LRVVF KSIPK KSIPK AKFIY AEIVF AEIVF ARFAF LRISF	499 488 458 392 309 343 313 313 307 301 308 316 315 305 311
AP AP 15   D7L636   /1-532 AP AP 23   Q6TPH 1   /1-458 GmP AP 4   V9HX G4   /1-442 IbP AP 4   Q9LL8 1   /1-312 AP AP 3   Q8H 129   /1-366 AP AP 8   Q8V72   /1-355 P vP AP 3   Q L05M7   /1-328 P vP AP 4   Q9LL79   /1-331 AP AP 7   Q8534 1   /1-328 AP AP 7 1 Q C8(8   /1-388 BP AP 17_1   D6MW88   /1-337 OSP AP 1   Q7XH73   /1-325 GmP AP 2   Q9LL80   /1-332 UACP 3   Q707M7   /1-330	389 380 381 233 265 236 236 230 226 232 237 236 229 234 232	MENL MEEL MEEL LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPU LLPL	LYSY( LYSY( LYAA) LYAA LRTYI LQANI LEANI LEANI LEANI LEANI LEANI LEANI LEANI LEANI LEANI LEANI	G V D I V G I D I V R V D I V S V D L V E V D L V E V D L V E V D L V G V D L V	FNGH FNGH FAGH MNGH MNGH INGH INGH MNGH MNGH MNGH MNGH MNGH		Y E R S Y E R W Y E R W Y E R V L		Y - N Y Y - N Y Y - N Y E E H E H E H E H E H E H E H E H E H E H	SLDP ELDP TLDP RLDP HISD ISSV ISSV ISSS ISST ISSE ISSE ISSE ISSE ISSE ISSE ISSE ISSE	C G P V H C G P V Y C G P V Y C G A V H D E S P I D S N I Q N S G I A N S G I A D S P I Q D S P I Q D S P I Q D S P I Q D S S V Q E S S I Q	1	G D G G N G D G G N G D G G N T S G A G S G G G G S S G G G G S S G G G G S S G G G G	R E K MA R E K MA I E K V D' R E G L A K E G L A K A WR K A WR K A WR K A WR G K A WR K K A WR K A WR	I K FADE I EHADE V D FADD H K Y I NP G D V T MD D V N DWN D V D H L I K H V Q P WD D I I FQ NE D T K Q S E D T Q F N	P GH C P C P G K C P P G K C P Q E M P Q E M P K E L P K E L	DPLSTS EPLTTF HSS KPWSSI QRFTMI	S D H F M P D P V M Y D L F F - E E L Q L MD K Y L N P K L L - D K L Q	G G - G G - G G - G G - G D - G D - G D - G G -	- FCATN - FCAWN - FNSLN - DVN	F T F D Q E F T P S L S N Y V - EP E P K	S E F C WD S G K F C WD EMR F Y Y D F F Y Y D F W K F Y Y D K F Y Y D S V R F Y Y D F F Y D EMK F Y Y D C F F Y D EMK F Y Y D C F F Y D C F F Y D	H Q P - R Q P - G Q G Q	D G G G G G G G G G G G G G 	Y S A F R Y S AMR F MS V C F MS V C F MS V C F MS MC F MS MC F MS A F MS A F MS A F MS A F MS V F MS V F MS V K	EASFG EASFG LV ETD TS EAE UT ESN UT CTS VWR FK VWR FK FTHSD FTHSD FTHTD LS ENR UT SQTQ LTQTQ	YGILE HGILE HGELK IGIVF LRVVF LRVVF LRVVF KSIPK KSIPK AKFIY AEIVF AEIVF ARFAF LRISF ATIEF	499 488 458 392 309 343 313 313 307 301 308 316 315 305 311 309
AP AP 15   D7L636   /1-532 AP AP 23   Q6TPH 1   /1-58 GmP AP 4   V9HX G4   /1-458 GmP AP 4   Q9LL8 1   /1-312 AP AP 3   Q8H 129   /1-366 AP AP 8   Q8V721   /1-336 P VP AP 3   Q2 D4J4   /1-330 SFP AP 1 Q 6L5M7   /1-328 AP AP 7   Q8534 1   /1-328 AP AP 7   Q8534 1   /1-328 BP AP 1 7 _ 1   D6MW88   /1-337 OSP AP 1 (Q71H73   /1-335 GmP AP 2   Q2 LL80   /1-332 LIACP 3   Q707M7   /1-330 P VP AP 5   F0740   /1-326	389 380 381 233 265 236 236 236 232 237 236 229 234 232 234 232 238	MENL MEEL MEEL LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPU FLPL LLPI	LYSY( LYQYI LYQA LRTYI LQAN LEAN LEAN LEAN LEAN LEAN LEEN KEN LKEN LKEN LKEN LKAN		FNGH FAGH TAGH MNGH TNGH TNGH TNGH TNGH MNGH MNGH MNGH		Y E R S Y E R W Y E R W Y E R V L		Y - N Y Y - N Y Y - N Y Y - N G E H 	SLDP ELDP TLDP RLDP HISD ISSV ISSV ISST ISST ISDE ISDE ISSE ISSE ISST ISDE ISST	C G P V H C G P V Y C G P V Y C G A V H D E S P I D S N I Q N S G I Q N S G I Q S S Q I Q S S Q I Q H G K T Q D S P I Q D S S Q I Q E S S I Q E S S I Q	(   A V ) (   V V ) (   T   ) (   T   ) (   T   ) (   T   ) (   F   T ) (	G D G G N           G D G G N           G D G G N           G D G G N           T S G A G           S G G G S           S G A G S	R E K MA R E K MA I E K V D' R E G L A S K A WR K A WR K A WR G K A WR K K A WR K A WR	I K FADE I EHADE V D FADD HK Y I NP G D V TMC D V NDWN D V D HL I K HV Q P WC D I D HL I K Q V D P T I F Q Q N E D T K Q S E D I Q C MN	P GH C P I P GK C P P GK C R K GV S P Q EM MG K MG C P K E L 	DPLSTS EPLTTF HSSY KPWSS QRFTMI	S D H FM P D P V M Y D L F F E E L Q L M D K Y L N P K L L - D K L Q	G G - G G - G G - G G - G D - G D - G G - G G -	- FCATN - FCAWN - FNSLN - DVN - MNWWN	FTFDQE FTP LSN- YV-EPEU - PK	S E F CWD S G K F CWD MR F Y Y D - R F Y Y D - R F Y Y D - K F Y Y D - M F F Y D - M F F Y D	H Q P - Q P - Q Q G Q Q	D G 	Y S A F R Y S AMR F MS V C F MS V C F MS V V F MS MC F MS MC F MS A F MS A F MS A F MS A F MS V F MS V	EASFG EASFG LV ETD VS EAE TS EAE UTQTQ VW FAK ITTSK FTHSD FTHSD FTHSD FTHSD IS QTQ LTQTD	YGILE HGILE IGIVF LRVVF LRVVF ADIIF VWIQF KSIPY AEIVF AEIVF AEIVF AEIVF ATIFF ATIFF	499 488 458 392 309 343 313 307 301 307 301 308 316 315 305 311 309 305
AP AP 15 [D7L636]/1-532 AP AP 323 [G6TFH 1]/1-58 GmP AP 4] V9HXG4 //1-458 GmP AP 4] V9HXG4 //1-452 IbP AP 4] Q9LL81 //1-312 AP AP 3] Q8H 129 //1-366 ArtP AP 8] Q8VYZ2 //1-335 P VP AP 3] D2 D4J4 //1-330 StP AP 1] Q6J5M7 //1-328 AP AP 7] Q8S341 //1-328 AP AP 7] Q8S341 //1-328 AP AP 7] Q8S341 //1-328 AP AP 7] Q8S341 //1-328 GmP AP 2] Q9LL80 //1-332 UACP 3] Q707M7 //1-330 P VP AP 5] (005117 //1-326 MmP AP 5] (005117 //1-326	389 380 381 233 265 236 236 230 226 232 237 236 229 234 232 234 232 228 228	MENL MEEL MEEL LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI	LYSY( LYQYI LYQYI LYQAA LRTYI LQAN LEAYI LEAYI LEANI LEANI LEANI LEANI LKEN( LKEN) LKEN( LKEN) LKEN( LKEN)	G V D I V G I D I V R V D I V S V D L V E V D L V E V D L V E V D L V E V D L V D V D M V K V D L V G V D L V D V D V D V G V V D V D V D V D V D V D V D V D V D	FNGH FAGH MNGH INGH INGH INGH INGH INGH MNGH MNGH MNGH MNGH MNGH MNGH		Y E R S Y E R S Y E R N Y E R N L		Y - N Y Y - N Y Y - N Y Y - N G E H E H 	S L D P E L D P T L D P R L D P H I S D V I S S V I S S V I S S S I I S S S T I G S - MS D E I S D E I S S R I S S L I S D T I S D T I S D T I S D T	C G P V H C G P V Y C G P V Y	(   A V (   V V (   T   ) Q FMT Q FMT ( FMT ( FLT ) ( FL	G D G G N           G D G G N           G D G G N           G D G G N           T S G A G           S G G G S           S G A G S           S G A G S           S G A G S           S G A G S           S G A G S           S G A G S           S G A G S           S G A G S           S G A G S           S G A G S           S G A G S	R E K MA R E K MA I E K V D R E G L A S K AWR G K AWK G K AWK G K AWK G K AWR G	I K FADE I EHADE V D FADD H K Y I NPL G D V T NPL G D V T NPL G D V L NPL D U N D V D U N D V I F Q N E U T K Q S E D I Q ET N D L Q MN V R H Q	P GH C P I P GK C P P GK C R K GV S P Q EM MG K MG C P K E L Q Q R	DP L S T S EP L T T F H S S Y K P WS S S QR F T MR N P V T L F	S D H F M P D P V M Y D L F F E E L Q L M D K Y L N P K L L - D K L Q - D K L Q	G G - G G - G G - G D - G D - G G - G -	- FCATN - FCAWN - FNSLN - DVN - MNWWN	FTFDQE FTP LSN- YV-EPEL - PK - TNNPKS	S E F CWD S G K F CWD MR F Y Y D R F Y Y D K F Y Y D L H F F Y D L H F F Y D	$H Q P = \frac{1}{2}$ $G Q = \frac{1}$	D G 	YSAFR YSAMR YSAMR FMSVF FMSVF FMSV7 FMSMC FMSAR FMSAR FMSAR FMSAR FMSVF FMSVF FMSVF FMSVF	ETSFG EASFG UVETO VSEAE TSEAE UTESN UTTSSAE VWRFK UTTSSA FTHSD FTHTD USQTQ LTQTD LTQTD	YGILE HGILE HGELK IGIVF LRVVF ADIIF VWIQF KSIPK AKFIY AEIVF AEIVF AEIVF ARFAF LRISF ATIEF MTILF	499 488 458 392 309 343 313 307 301 307 301 308 316 315 305 311 309 305 308
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AP AP 15   D7L636  /1-532 AP AP 23   Q6TPH 1  /1-458 GmP AP 4   V9HX G4  /1-442 IbP AP 4   Q9LL8 1  /1-312 AtP AP 3   Q8H 129  /1-366 AP AP 8   Q8V72  /1-355 P vP AP 3   Q6L5M7  /1-328 P vP AP 4   Q0LL79  /1-331 AP AP 7   Q8SC48  /1-338 BP AP 17 _ 10 S548  /1-335 GmP AP 2   Q9LC88  /1-335 GmP AP 2   Q9LL80  /1-325 UACP 3   Q70 TM7  /1-305 P vP AP 5   20740  /1-327 RnP AP 5   P1368 6  /1-327 HSP AP 5   P1368 6  /1-327 BP AP 5   P1368 6   P1368 6	389 380 381 317 233 265 236 236 236 232 237 236 232 237 236 232 234 232 234 232 228 228 228 228 228	MENL           MEEL           MEPL           LUPI	LYSY LYQY LYQY LYQA LYQA LQAN LQAN LEAN LEAN LEAN LEAN LEAN LKEN LKEN LKEN LKAN LQAN LQAN	G V D I V G I D I V R V D I V R V D I V R V D I V E V D I V E V D I V E V D I V E V D I V D V D A V N V D I V G V D I V O V D V O V G V D I V O V O V G V D I V O V O V O V O V O V O V O V O V O V	FNGH FAGH MNGH VNGH VNGH INGH INGH MNGH MNGH MNGH MNGH MNGH MNGH MNGH M		Y E R S Y E R M Y E R M Y E R M Y E R M L		Y - NY Y - NY Y - NG Y - E - E - E - E - E - E - E - E - E - E	S L D P E L D P T S D T T S D T T S D T S D T S D T L Q D - L Q D -	C G P V H C G P V Y C G P V Y C G A V H D E S P I Q D S N I Q N S G I H D S P I Q N S G I H D S P I Q H G K T Q D S P I Q C S S I Q E S S S S S S S S S S S S S S S S S S S	I         A           I         T           Q         F           Q         T           Q         T           Q         T           Q         T           Q         T	G D G G N           G D G G N           G D G G N           G D G G N           T S G A G           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G A G S           S G A G S           S G A G S           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N	R E K MA R E K MA I E K V D' R E G L A S K A WR K A WK K A WK G K A WR G K A WR K K A WR K K A WR K K A WR K K A WR K K K A WR K K A WR K K K K K K K K K K K K K K K K K K K	I K FAD E I E HAD E V D FAD D HK Y I ND D V ND WN D V ND WN D V ND WN D V D Y I I FQ N E D T K Q S E D T K Q S E D T Q Q MN V R HQ V R HQ	P GH C P P GK C P P GK C R K GV S P Q EM P Q EM P K E L P Q R	D P L S T S EP L T T F - HS S S R F T M N P V T I I - R K V F - R K V F - R K V F	S D H FM P D P VM YD L F F E E L Q L MD K Y L N P K L L D K L Q P N G Y L P N G Y L	G G - G G - G G - G D - G D - G D - G G - G -	F C A T N F C A WN F N S L N - D V N	FTFDQE FTP LSNP YV-EPE - TNNPK - TNNPK RFF RFF	S E F CWD S G K F CWD MR F Y Y D R F Y Y D K L Y Y D K L Y Y D K K F Y Y D F K L Y Y D K F Y Y D F F Y D K F Y Y D L H F F Y D V Y G S E D S Y G T E D S	$H Q P = \frac{1}{2}$ $G Q = \frac{1}$	D G 	Y S A F R Y S AMR Y S AMR F MS V F F MS V F MS V F F MS V F M	ETS FG ESSFG EASFG VETD VSEAE TSEAE UTQTQ VWRFK FTHSD FTHTD LSENR TSFKE ISSKE ISSKE	YGILE HGILE HGILE IGIVF LRVVF LRVVF ADIIF VWIQF KSIPK AKSIPK AKFIYF AEIVF AEIVF AEIVF ATIEF MTIEF MTITY MSITY	499 488 458 392 309 343 313 307 301 307 301 305 315 305 311 309 305 308 308 306
AP AP 15   D7L636  /1-532 AP AP 23   Q6TPH 1/1-458 GmP AP 4   V9HX G4  /1-442 IbP AP 4   Q9LL8 1/1-312 AP AP 3   Q8H 129  /1-366 AP AP 8   Q8V722  /1-355 P vP AP 3   Q2 D4J4  /1-330 SP AP 1 Q 6L5M7  /1-328 AP AP 7   Q8534 1/1-338 AP AP 7   Q8534 1/1-337 OS <sup>P</sup> AP 1 Q 07XH73  /1-335 GmP AP 2   Q9LL80  /1-332 UACP 3   Q707M7  /1-330 P vP AP 5   Q05117  /1-327 RnP AP 5   P29288  /1-327 HSP AP5   P29288  /1-327 HSP AP5   P13686  /1-325 SS <sup>P</sup> AP 5   P13688  /1-326	389 380 381 317 233 265 236 236 232 232 232 232 232 232 228 2228 2	MENL MEEL MEEL LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPI LLPI	LYSY( LYQY) LYQY LYQA LYQA LQAN LEAY LQAN LEAY LEAY LEAN LEAN LEAN LEAN LEAN LEAN LAAY LAAY LAAY LAAY LAAY	G V D I V G I D I V R V D I V R V D I V S V D I V E V D I V G V T A V G V T A V G V T A V	FNGH FAGH YNGH YNGH YNGH INGH INGH INGH MNGH MNGH MNGH MNGH MNGH MNGH ICGH		Y E R S Y E R M Y E R M Y E R M L		Y - N Y Y - N Y Y - N G Y - E - E H - E H	S L D P E L D P T L D P R L D P H I S D I S S I I S S S I S S T I G S - MS D E I S S T I G S - MS D E I S D E I S S T I S D	C G P V H C G P V Y C G P V Y C G P V H D E S P I Q D S N I Q N S G I H D S P I Q D S P I Q E S P I S	(	G D G G N           G D G G N           G D G G N           T S G A G           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G A G S           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N	R E K MA R E K MA I E K V D' R E G L A S K AWR K AWR K AWR K AWR K AWR G K AWR G K AWR G K AWR G K AWR G K AWR G F MD P S F MD P S	I K FADE I EHADE V DFADD HK Y I ND G D V TMD D V NDWN D V D U NDWN D V D U NDWN D V NDWN D U NDWN I FQQNE D T QQNE D T QQNE D T QQNE D T QQNE D T QQNE D T QQNE D U QQNN V R H Q V R H Q V R H Q	P GH C P I P GK C P P GK C P R K GV S P Q EM P Q EM P K E L P K E L P C E R	D P L S T S EP L T T F - HS S S K P WS S Q R F T MR N P V T I I R K V F - R K V F - R K V F	S D H F M P D P V M Y D L F F E E L Q L M D K Y L N P K L L - D K L Q P N G Y L P N G Y L P N G Y L	G G - G G - G G - G D - G D - G C -	- F C A T N F C A WN - F N S L N D V N	FTFDQE FT P LSN- - TNNPK - RFf RFf RFf	S E F CWD S G K F CWD CMR F Y D R F Y D CMR F Y D MK F Y D MK F Y D CMK F Y D CMF F Y D L H F F Y L H F F Y C M F E S E D S Y G S E D S Y G S E D S	H Q P = - Q P = - Q P = - Q P = - Q P = - Q Q = Q Q = Q Q = Q Q = Q Q = Q Q =	D G 	Y S A F R Y S AMR Y S AMR Y S AMR F MS V C F MS	ETSFG EASFG LVETD VSEAE TSEAE UTTESN UTTESN UTTESN UTTESN ESTR ESTR ESTR ESTR ESTR ESTR ESTR ESTR	YGILE HGILE HGELK IGIVF LRVVF LRVVF ADIIF VWIQF KSIPK AKSIPK AKFIY AEIVF AAEIVF AAEIVF AAEIVF AAEIVF AAEIVF AATIEF ATIEF MTIIY MSITY MSVTY	499 488 458 392 309 343 313 313 307 301 308 316 315 305 311 309 305 308 308 308 308 306 314
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AP AP 15 [D7L636]/1-532 AtP AP 23 [Q6TFH 1]/1-458 GmP AP 4  V9HXG4]/1-422 IbP AP 4] (Q9LL81]/1-312 AtP AP 3] Q8H 129]/1-366 AtP AP 3] Q8H 129]/1-366 AtP AP 3] Q2 D4J4]/1-330 StP AP 1] Q6J5M7]/1-328 P VP AP 4] Q9LL79]/1-331 AtP AP 17 (Q9SCX8]/1-328 AtP AP 71 (Q9SCX8]/1-338 BrP AP 7_1 [D6MWX8]/1-337 OSP AP 1] Q7KH73]/1-335 GmP AP 2] (Q9LL80]/1-322 UACP 3] Q707M7]/1-320 P VP AP 5] [20740]/1-327 RmP AP 5] P13686]/1-325 SSP AP 5] P03889]/1-340 DF4 AP 10 (D711/1-326	383 380 381 317 233 265 236 236 236 232 237 236 232 237 236 232 234 232 232 234 232 232 234 232 232	MENL MEEL MEEL LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI LUPI	LYSY LYSY LYQY LYQY LRTY LQAN LEAY LEAY LEAN LEAN LEAN LEAN LEAN LEAN LEAN LEAN	G V D I V G I D I V R V D I V R V D I V S V D L V E V D L V E V D L V E V D L V G V D L V V G V D L V V G V D L V V D V V V V V V V V V V V V V V	FNGH FNGH FAGH MNGH NNGH INGH INGH INGH INGH MNGH MNGH MNGH MNGH MNGH H I I C G H M C G H H C C G H C C G H C C G H C C C C		Y E R S Y E R S Y E R M Y E R M L		Y - NY Y - NY Y - NY Y - E - E - E - E - E - E - E - E - E - E	S L D P E L D P T L D F T L D F T D F		Q FM U L L L L L L L L L L L L L L L L L L	G D G G N           G D G G N           G D G G N           T S G A G           S G G G S           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N	R EKMA R EKMA I EKVD I EKVD SKAWR SKAWR KAWR KAWR KAWR KAWR G KAWR G KAWR G KAWR G KAWR G KAWR G KAWR G KAWR G F MD P S F MD P S F MD P S	I K F A D E I E H A D E V D F A D D H K Y I ND G D V T MD D V N D WN D V D V T D H L I K H V Q P WD D V D P T I F Q Q N E D I Q E T N D L Q Q MN V R H Q K K H Q K K H Q	P GH C P I P GK C P P GK C P GK GV S R K GV S IP Q EM P K E L P K E L R Q 	DPLSTS EPLTTF HSS KPWSSI QRFTM NPVTIF RKVF RKVF	S D H F M P D P V M Y D L F F E E L Q L M D K Y L D K L Q D K L Q P N G Y L P N G Y L P N G Y L P N G Y L	G G - G G - G G - G D - G D - G G - G C - G G - R G - R G - R G -	FCATN FCAWN FNSLN - DVN - MNWWN	FTFDQE FTBDF PS VV-EPE 	S E F CWD S G K F CWD R F Y D R F Y D R F Y D MR F Y Y D K F Y D K F Y D K F Y D L H F F Y D S V B C D S Y F Y G S E D S Y G T E D S S F G G E D S S	H Q P - G Q G Q C - G Q C - C -		Y S A F R Y S A M R Y S A M R F M S V C F M S V C F M S V C F M S M C F M S M C F M S M C F M S V C	ETS FG EAS FG EAS FG V ETD V SEA E TS EA E TS EA E I T Q T Q V WR FK I T T ST F T H S D F T H T S L S E N R I S Q T Q L T Q T H S K E I S S K E I T S K E	YGILE HGILE HGILE LRUVF LRVVF LRVVF ADIIF VWIQF KSIPK AAFIVF AAFIVF AAFIVF ATIEF ATIEF MTIIF MTIIY MSITY MSVTY MSVTY	499 488 309 343 313 307 301 307 301 308 316 315 305 311 309 305 311 309 308 308 308 308 308
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AP AP 15 [D7L636]/1-532 AP AP 23 [Q6TFH 1]/1-58 GmP AP 4] V9HXG4//1-458 GmP AP 4] V9HXG4//1-442 IbP AP 4] Q9LL81/1-312 AtP AP 3] Q8H129/1-366 AtP AP 3] Q8H129/1-335 P VP AP 3] Q0L79/1-331 AtP AP 1] Q6JX7//1-328 AtP AP 1] Q9LX79/1-332 GmP AP 1] Q9LX79/1-332 GmP AP 2] Q9LL80/1-332 UACP 3] Q707M7//1-330 P VP AP 5] [Q05117]/1-325 SaP AP 5] P2288/1-327 RnP AP 5] P2288/1-327 HSP AP 5] P2288/1-327 HSP AP 5] P2889/1-340 DrP AP 2] Q45755/1-331 XtP AP 5] Q6GI G6/1-325 XIP AP 1] Q6GI IG2/1-325 XIP AP 1] Q6GI IG2/1-325 XIP AP 1] Q6GI IG2/1-325	383 380 381 317 233 235 236 236 232 232 232 232 232 232 232 232	MENLL MEELL MEELL LLPI LLPI LLPI LLPI LLPI LLPI LLPI	LYSY LYGY LYGAN LYGAN LRTY LQAN LEAN LEAN LEAN LEAN LEAN LEAN LEAN LE	GVDIVVE GVDIVE VDIVE VDIVE VDIVE VDIV EVDIV EVDIV EVDIV EVDIV GVDIV GVDIV GVDIV GVDIV GVDIV GVDIV GVDIV GVDIV GVTAN KVTAN KVTAN KVTAN GVTAN	FN GH FN GH FA GH MN GH MN GH LA GH VN GH LA GH VN GH LA GH NN GH MN GH MN GH MN GH CG LC GH LC GH LC GH LC GH LC GH	Image: Constraint of the state of	Y ERS Y ERS Y ERN L		Y - NY Y - NG Y - EH - EH - EH - EH - EH - EH - EH - EH	S L D P T E L D P P T L D P H I S D I S S V I S S V		IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	G D G G N           G D G G N           G D G G N           T S G A G           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N	R EKMA R EKMA I EKVD I EKVD K EGLA SKAWR SKAWR KAWR KAWR KAWR KAWR KAWR G KAWR KA KAWR C KA KAWR C KA KAWR C KA KA KA KA KA KA KA KA KA KA KA KA KA	I K F A D E I E H A D E V D F A D D V D F A D D V N D WN D V N D WN D V N D WN D V D V T D V D P T I F Q Q N E D I Q E T N D V R Q - V R R - Q V R Q - V R R - V R -	P GH C P I P GK C P P GK C R K GV S IP Q EM P K E L P K E L R R Q 	D P L S T S EP L T T F - H S S R P WS S I R F T MR N P V T I F - R K V F - R	S D H F M P D P V M Y D L F F E E L Q L M D K Y L M D K Y L P N G Y L P K G Y L P K G Y L	G G G G G G G G G G G G G G G G G G G	FCATN FCAWN FNSLN - DVN - MNWWN	FTFDQE FTDDF PS SN PK PK PK 	S E F CWD S G K F CWD R F Y D R F Y D R F Y D W K F Y D K F Y D K F Y Y D K F Y Y D K F Y Y D L H F F Y D H Y S S S S Y S S S S S S S S S S S S S	H Q P - Q P - Q P - Q Q - Q D A Q D A Q D A Q D P D Q D P D D D D D D D D D D D D D D D D D		Y S A F R Y S A MR Y S A MR Y S A MR F MS V C F MS	ETS FG EAS FG EAS FG EAS FG EAS FG EAS FG EAS FG TS EAE TS EAE TS EAE TAS	YGILE HGILE HGILE LGIVF LRVVF LRVVF LRVVF ADIIF VWIQF KSIPK ACIVF ACIVF ACIVF ACIVF ACIVF ACIVF MTIF MSITY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY	499 488 458 392 309 343 313 307 301 308 316 315 308 316 315 309 308 308 308 308 308 308 308 308 308 308
AP AP 15, D7L636, /1-532 AP AP 23, Q6TPH 1, /1-458 GmP AP 4 (V9HX G4 /, /1-442 IbP AP 4 (V9HX G4 /, /1-442 IbP AP 4 (Q9LL8 1, /1-312 AP AP 3, Q8H 129 /, /1-356 AP AP 8, Q8V 722 /, /1-335 P vP AP 3 1 Q6L5M7 /, /1-328 P vP AP 4 1 Q9LL79 /, /1-331 AP AP 7, (Q85341 /, /1-328 AP AP 7, (Q85341 /, /1-328 BP AP 17, 1, ID5KW88 /, I-337 OSP AP 1, Q7XH73 /, /1-335 GmP AP 2 (Q9LL80 /, /1-322 UACP3 (Q707M7 /, /1-330 P vP AP 5, [22740 /, /1-326 MmP AP 5, [20751 17 /, /1-327 Rn PAP 5, [P 29288 /, I-327 HSP AP 5, [P 09889 /, I-340 DP AP 2 (Q75XT1 /, /1-339 TnP AP 2 (Q45755 /, -1311 XtP AP 5) [Q6GI G6] /, -1326 XiP AP 10, G6GI G62 /, -1326	383 380 381 317 233 235 236 236 232 232 232 232 232 232 232 232	MENLL MEELL MEELL LLPI LLPI LLPI LLPI LLPI LLPI LLPI	LYSY LYGY LYGAN LYGAN LRTY LQAN LEAN LEAN LEAN LEAN LEAN LEAN LEAN LE	GVDIVVE GVDIVE VDIVE VDIVE VDIVE VDIV EVDIV EVDIV EVDIV EVDIV GVDIV GVDIV GVDIV GVDIV GVDIV GVDIV GVDIV GVDIV GVTAN KVTAN KVTAN KVTAN GVTAN	FN GH FN GH FA GH MN GH MN GH LA GH VN GH LA GH VN GH LA GH NN GH MN GH MN GH MN GH CG LC GH LC GH LC GH LC GH LC GH	Image: Constraint of the state of	Y ERS Y ERS Y ERN L		Y - NY Y - NG Y - EH - EH - EH - EH - EH - EH - EH - EH	S L D P T E L D P P T L D P H I S D I S S V I S S V		IIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIIII	G D G G N           G D G G N           G D G G N           T S G A G           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G G G S           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N           S G A G N	R EKMA R EKMA I EKVD I EKVD K EGLA SKAWR SKAWR KAWR KAWR KAWR KAWR KAWR G KAWR KA KAWR C KA KAWR C KA KAWR C KA KA KA KA KA KA KA KA KA KA KA KA KA	I K F A D E I E H A D E V D F A D D V D F A D D V N D WN D V N D WN D V N D WN D V D V T D V D P T I F Q Q N E D I Q E T N D V R Q - V R R - Q V R Q - V R R - V R -	P GH C P I P GK C P P GK C R K GV S IP Q EM P K E L P K E L R R Q 	D P L S T S EP L T T F - H S S R P WS S I R F T MR N P V T I F - R K V F - R	S D H F M P D P V M Y D L F F E E L Q L M D K Y L M D K Y L P N G Y L P K G Y L P K G Y L	G G G G G G G G G G G G G G G G G G G	FCATN FCAWN FNSLN - DVN - MNWWN	FTFDQE FTDDF PS SN PK PK PK 	S E F CWD S G K F CWD R F Y D R F Y D R F Y D W K F Y D K F Y D K F Y Y D K F Y Y D K F Y Y D L H F F Y D H Y S S S S Y S S S S S S S S S S S S S	H Q P - Q P - Q P - Q Q - Q D A Q D A Q D A Q D P D Q D P D D D D D D D D D D D D D D D D D		Y S A F R Y S A MR Y S A MR Y S A MR F MS V C F MS	ETS FG EAS FG EAS FG EAS FG EAS FG EAS FG EAS FG TS EAE TS EAE TS EAE TAS	YGILE HGILE HGILE LGIVF LRVVF LRVVF LRVVF ADIIF VWIQF KSIPK ACIVF ACIVF ACIVF ACIVF ACIVF ACIVF MTIF MSITY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY MSVTY	499 488 458 392 309 343 313 307 301 308 316 315 308 316 315 309 308 308 308 308 308 308 308 308 308 308

	498 VKNETHALWRWHRNQDLY - GSA - GDEIYIVR - EPERC - L - HKHNSTRPAHGP -
TaP APhy_a 1   C4PKK7   /1-550	499 THALWRWHRNQDHYGSAGDEIYIVREPHRCLHKHNSSRPAHGRSNTTRESGG-
TaP AP hy_b1 C4PKK9 /1-538	494 VKNETYALWKWHRNQDLYQGAV-GDEIYIVR-EPERC-LLKSSIAAYF-
TaP APhy_b2   C4PKL0   /1-537	493 VKNETHALWKWHRNQDLYQGAV-GDEIYIVR-EPERC-LLKSSIAAYF-
HvPAPhy_b2 C4PKL4 /1-537	493 VKNETHALWKWHRNQDLYQGAV-GDEIYIVR-EPGRC-LLSSSIAAYF-
	492 VKNETHALWKWHRNQDLYQGAV-GDEIYIVR-EPERC-LLKSSIAAYF-
OsP APhy_b   D6QSX9  /1-539	494 V K N E T H A L W R W H R N Q D L Y - G S V - G D E I Y I V R - E P D K C - L - I K S S R N R I A Y Y
ZmPAPhy_b C4PKL6 /1-544	499 VRNDTHALWRWHRNQDLHAANVAADEVYIVR - EPDKC - L AKTARLLAY -
	499 V K N E T H A L W S W N R N Q D Y Y - G T A - G D E I Y I V R - Q P D K C P P V M P E E A H N T
PtPAP3/V9LXK5//1-564	516 VKNETHALWTWHRNQDFY-EAA-GDQIYIVR-QPDLCPVQPEAYRLNKPKPQ-
1\tP APhy A5YB\\1 /1-551	500 SETHALWTWHRNQDMYNKAGDIIYIVRQPEKCPVKPKVIKPWPIGEYQFDWI-
LaP APhy   D2 YZL4   /1-543	496 VKNETWALWSWYRNQDSY-NEV-GDQIYIVR-QPHLC-PINQKVCREYFAAI-
GmPAPhy_b Q93XG4 /1-547	500 VKNETWALWSWYRNQDSY-KEV-GDQIYIVR-QPDIC-PIHQRVNIDCIASI-
AtP AP 15   Q95FU3   /1-532	489 MKNETWALWTWYRNQDSS-SEV-GDQIYIVR-QPDRC-PLHHRLVNHC-
/ /	498 THALWRWHRNQDHYGSAGDEIYIVREPHRCLHKHNSSRPAHGRSNTTRESGG-
	497 VKNETHALWRWHRNQDMY - GSA - GDEIYIVR - EPERC - L - HKHNSTRPAHGR -
· _ · · · · ·	494 THALWRWHRNQDHYGSAGDEIYIVREPHRCLHKHNSTRPAHGRQNTTRESGG-
TaP APhy_a3   F6MIW2   /1-539	493 VKNETHALWRWHRNQDMY - GSA - GDEIYIVR - EPHRC - L - HKHNSTRPTHGR -
/_ // //	498 THALWRWHRNQDMYGSAGDEIYIVREPHRCLHKHNSTRPAHGRQNTTRESGG-
·= · · · ·	493 VKNETHALWRWHRNQDMY - GSA - GDEIYIVR - EPERCLHKHKHNSTRPAHGR -
TaP APhy_b3   F6MIW6   /1-536	492 VKNETHALWKWHRNQDLYQGGV-GDEIYIVR-EPERC-LLKSSIAAYF-
TmP APhy_b1 F6MIW9 /1-539	495 VKNETHALWKWHRNQDLYQGVV - ADEIYIVR - EPERC - L LKSSIAAYF -
	494 VKNETHALWKWHRNQDLYQGAV-GDEIYIVR-EPERC-LLKSSIAAYF-
/ /	494 VKNETHALWKWHRNQDLYQGAV - GDEIFIVR - EPERC - L LKSSIAAYF -
	520 VKNETHALWTWHRNQDLY-SSA-GDQIYIVR-QQERC-PVKPK-GAINVLVA-
	493 V K N D T WA L W T W Y R N Q D S R - D N A - G D Q I Y I V R - T P D M C - P T L S A - V T K L W S A A R
· · · · ·	499 VKNETWALWSWYRNQDSY-KEV-GDQIYIVR-QPDIC-PVPQR-VSGDFIASI
VrP APhy   B5 AR Z7   /1-547	500 VKNETWALWSWYRNQDSY-KEV-GDQIYIVR-QPDIC-DVPRKVCRDFTASI-
AP AP 15   D7L636   /1-532	489 MKNETWALWTWYRNQDSS-SQV-GDQIYIVR-QPDRC-PLHHRLVNHC
AtP AP 23   Q6TPH 1   / 1-458	
	393 IVNSTHAFWSWHRNDDD EPVKADDIWITSLVSSRCVDQKTHELRSTLLTP -
	310 Y G C C
	344 Y D V F G H V L H H W K K T Y K E A L Y F A S
	314 Y D G L G H V L H R WS T L K N G V Y S D I
PvPAP3   D2 D4J4   /1-330	314 Y D V Y G K P L H S WS I S K D R
	308 FD I F G N I L H K W S A S K N L V - S I M
	302 L F I M I F L A K F C K L L I C P R G Y V M C M P Y N S L I
	309 Y D V S G N V L H R S S L S K R S A H L
	317 Y D V F G E I L H K W V T S K Q L L H S S V
	316 YNVFGEVLHKWVTSKQLLLSSV
	306 Y D V F G E A L Y H W S F S K A N L Q K V Q S S A S V T E E
	312 FDV FGNA I H K WN T C K FD S S D M
	310 Y D V S G N V L H R L T S S K N L R - S S M
	306 Y D V F G N V L H T L A S S K Q P H S F M
	309 V EASGKSLFKTSLPRRPRP
	309 V EASGKSLFKTSLPRRPRP
	307 I E A S G K S L F K T R L P R R A R P
1 11	315 I EAS GKS L FK TK L P R R A R S E H Q H R R A
	315 I Q A R G T S L Y R A V L K K R D D V L E D D N F
	304 EVAKNQMTLTFFQAR GTSLYRTVLTDRN
	309 V Q S D G K C L Y Q T T L Y P R T F
	308 V Q S N G K C L F Q T T L Y P R T F
	309 V Q S N G K C L F Q T M L Y P R T F
DrP AP 1   Q6DHF5  /1-327	308 LQPDGKCVYQTSV-HKHKVQL

# Figure A4. PAPhy vs Microbial PAPs MSA (See Figure A1 for key)

0 1		
HvP APhy_a   C4PKL2   /1-544	1	
TaP APhy_a 1   C4PKK7   / 1-550	1	
TaP AP hy_b1   C4PKK9   /1-538	1	P LR ED
TaP APhy_b2   C4PKL0   /1-537	1	
HvPAPhy_b2 C4PKL4 /1-537	1	A T A E A S M L E G P S G P V T V
HvPAPhy_b1 C4PKL3 /1-536	1	
OsP APhy_b   D6QSX9   /1-539	1	
ZmP APhy_b   C4PKL6   /1-544	1	
MtP APhy   Q3ZFI 1   / 1-543	1	
PtPAP3/V9LXK5//1-564	1	MASSSLPSISLPVNVFELNNILSLVLKLTITLILLANGAMAMAIPTTLDGPFKPVTIPLDESF
IVtP APhy   A5YBIV1   /1-551	1	
LaP APhy   D2 YZL4   /1-543	1	PSTLEGPFPPLTV
GmP APhy_b   Q93XG4   /1-547	1	
AtP AP 15   Q9 SF U3   /1-532	1	MTFLLLLLFCFLS PAISSAHS PAISSAHSAHS PAISSAHS PAISSA PAISSAHS PAISSAHS PAISSAHS PAISSAHS PAISSAHS PAISSA
AtaPAPhy a1/F6MIX0//1-549	1	
ScP APhy a2 / F6/MIX4 / /1-543	1	
TmP APhy_a1/F6MIW8//1-545	1	
TaP APhy_a3   F6MIW2   /1-539	1	
TaP APhy_a2   C4PKK8  /1-549	1	
ScP APhy a1/F6/MIX2//1-541	1	MWR GS LR LL LL AAA- VTAAA E- GS TLMGP SR PVT - V- ALR ED-
TaP APhy_b3 /F6MIW6 //1-536	1	MG I WR GS LP LL LL A A A A A A E P A S T L E G P S WP V T V P L R E D -
TmP APhy b1/F6MIW9//1-539	1	MW I WR GS LP LL LL AAAAA AAAAA E
AtaP APhy_b1/F6MIX1//1-538	1	MWMWK GS LP LLLL AAAA VAAAA E
ScP APhy_b1/F6MIX5//1-538	1	
RcP AP 1   B9R W G6   /1-566	1	MNP L F L D S C S FMG G L Q Y N R C NMG L L S V P V F A L S F Y V L L S S A T L A A A H G H I P T T L E G P F K P R T -  V P L D O S F
VvP AP   A5 BGI 6   / 1-540	1	MASTLCCVIVVILVNEA ALHARI PTTLDGPFXPVT V
PvP APhy/V7B3Z4//1-546	1	MSTIAFPFLOFHCAFLLLINLLA GFSHCR V PSTLEGPFDPVT V
VrP APhy/ B5 AR Z7 // 1-547	1	MK I CTTLCMLAMY LVMM - STDFITYMAV TESHPTTLDGPFEPVT
AIP AP 15 / D7L636 //1-532	1	MTFLLLLLFCFLSPAI FFADSI
AtP AP 23   Q6TPH 1   / 1-458	1	
GmP AP4   V9HXG4   /1-442	1	MELKOOKLULVIITL LEATAT DS EYV RPLP
MpP AP 1/1-264	-	
OIP AP 2/1-312		
CrP AP 1/1-556	1	
GrP AP 2/1-632	1	MAY SELVIALSA LA LAG - V V NADVOL HADDDDAWLEK DERENMI
CrP AP 3/1-629	1	MAQSE LA LA LA SA LV LA AAVV NA EVOLHTAD DD
GP AP 4/1-691	1	
CrP AP 5/1-637	1	MAPRALLVILLIGUG
MpP AP4/1-377	1	
MpP AP 2/1-832	- 1	
OIP AP 1/1-539		
MpP AP 3/1-454		
CrP AP 5/1-435		
СГР АР 6/1-435 АГР АР / Q12546 //1-614	1	
	1	
AnidP AP   Q92200   /1-618	1	
LeP AP   Q05205  /1-539	1	
MbP AP   A0 A1R3Y2F9   /1-434	1	
MtubPAP (P9WL81)/1-529	1	
BcP AP   B4 BKR2   / 1-561	1	mond.
BmaPAP   A0A0H2WHP3   /1-560	1	MJ NK
BpsP AP   Q63X35  /1-560	1	

					4.00
HvP APhy_a   C4PKL2   /1-544		R G H A V D L P D - T D - P R V Q	R I		102
TaP APhy_a1 C4PKK7 /1-550		R G H A V D L P D - T D - P R V Q	R I	- A T GWA P EQ I A V - A L S A A P - T S A W V S W - I T G E F Q M G G T V - K P L - D P V S W - I T G E F Q M G G T V - K P L - D P	99
TaP APhy_b1 C4PKK9 /1-538		R G H A V D L P D - T D - P R V Q	8 I	- V T GWA P EQ I A V - A L S A A P T S A W V S W - I T G D F Q M G G A V - K P L - D P V S W - I T G D F Q M G G A V - K P L - D P	98
TaPAPhy_b2 C4PKL0 /1-537			R I	- V T GWA P E Q I A V - A L S A A P T S A W V S W - I T G D F Q MG G A V - K P L - D P	97
HvP APhy_b2   C4PKL4   /1-537		R G H A V D L P D - T D - P R V Q	R F		97
HvPAPhy_b1/C4PKL3//1-536		R G H A V D L P D - T D - P R V Q	R F	- V T GWA P E Q I A V - A L S A A P T S A W V S W - I T G D F Q MG G A V K P L - D P	97
OsP AP hy_b   D6QSX9  /1-539		R G H A V D L P D - T D - P R V Q	R F		97
ZmPAPhy_b C4PKL6 /1-544		R G H A V D L P D - T D - P R V Q	R F		102
MtP APhy   Q3ZFI 1   / 1-543		R G N A V D I P D - T D - P L V Q	R I		105
P tP AP 3   V9 LXK5   / 1-564		R G N T I D L P D - T D - P R V Q	R 1		120
NtP APhy   A5YBN1 /1-551	48	R G H A V D <mark>L P D -</mark> T D <mark>- P R V Q</mark>	R 1		104
LaP APhy   D2 YZL4   / 1-543	46	P T V S I D L P D - T D - P R V R	R I	- V H G F Q P E Q I S L - S L S T S H H S L W V S W - I T G E F Q I G Y N I K P L - D P	102
GmP APhy_b   Q93XG4   /1-547	50	R	R F	- V R G F E P E Q I S V - S L S T S H D S V W I S W - V T G E F Q I G L D I K P L - D P	106
AtP AP 15   Q95FU3   /1-532	42	R G Q A I D L P D - T D - P R V R	R F	- V I G F E P E Q I S L - S L S S D H D S I W V S W - I T G E F Q I G K K V K P L - D P	98
AtaP APhy_a 1/F6MIX0 //1-549	42	R G H A V D L P D - T D - P R V Q	R F	- A T G WA P E Q I A V - A L S A A P T S A W V S W - I T G E F Q MG G T V K P L - D P	98
ScP APhy_a2  F6MIX4  /1-543	45	R G H A V D L P D - T D - P R V Q	R F	- A N GWA P E Q I A V - A L S A A P T S A W V S W - I T G E F Q MG G T V K P L - D P	101
TmP APhy_a1/F6MIW8//1-545	38	R G H A V D L P D - T D - P R V Q	R F	- A T GWAP E Q I T V - A L S A A P T S A W V S W - I T G E F Q MG G T V K P L - H P	94
TaP APhy a3 (F6MIW2 )/1-539	41	R G H A V D L P D - T D - P R V Q	R F	- A T GWA P E Q I A V - A L S A A P T S A W V S W - I T G E F Q MG G T V K P L - D P	97
TaP APhy a2   C4PKK8   /1-549	42	R G H A V D L P D - T D - P R V Q	R F	- V T GWAP E Q I A V - A L S A A P T S A W V S W - I T G D F Q MG G A V K P L - D P	98
ScP APhy_a 1/F6MIX2//1-541	41	R G H A V D L P D - T D - P R V Q	R F	- A N GWA P E Q I A V - A L S A A P T S A W V S W - I T G E F Q MG G T V K P L - D P	97
TaP APhy b3/F6MIW6//1-536	40	R G H A V D L P D - T D - P R V Q	R F	- V T GWAP EQ I AV - A L S A A P T S A W V S W - I T G D F Q MG G A V K P L - D P	96
TmP APhy b1/F6MIW9//1-539	43	R G H A V D L P D - T D - P R V Q	R F	- V T GWAP E Q I A V - A L S A A P T S A W V S W - I T G D F G MG G A V K P L - D P	99
AtaP APhy b1/F6MIX1//1-538		R G H A V D L P D - T D - P R V Q	R F	- V T GWAP E Q I A V - A L S A A P T S A W V S W - I T G D F QMG G A V K P L - D P	98
ScP APhy b1/F6MIX5//1-538		R G H A V D L P D - T D - P R V Q	R		98
RcP AP 1/B9RW G6//1-566		R G H A I D L P D - S D - P R V Q	8		126
VvP AP   A5 BGI 6 /1-540		R G K A V D L P D - T D - P R V R			99
PvPAPhv/V7B3Z4//1-546		R G N A V D L P P - S D - P R V R			106
VrP APhy/85ARZ7//1-547		R R G S D D L P M - T H - P R L R			107
AIP AP 15   D7L636   /1-532		R G K A I D L P D - T D - P R V R		VTGFFEQIAL AISS-F-ISSWW	
AtP AP 15   07 L636   / 1-532 AtP AP 23   Q6TPH 1   / 1-458				VIGPEPEQIAL-SLSSDH-OSIW	98
1 - 11		RKTLTTIPWDSIS	_	NY 35 DFF EQIAL-ALSI-FF - ISNW	
GmP AP 4   V9H X G4   / 1-442	33	RKILIIPWDSIS	K	- AHSSYP QQVHI-SLAGDKHMKVIW-IIDDKHSPSP	"
MpP AP 1/1-264					
OIP AP 2/1-312					
CrP AP 1/1-556					104
CrP AP 2/1-632		V G S V A G <mark> C F D -</mark> Q N I P A V G <mark></mark>	W		131
CrP AP 3/1-629		V G S V A G <mark></mark> C Y D <mark>- Q G I</mark> P A V G <mark></mark>	_		136
CrP AP 4/1-69 1		V A A V T E <mark> Q P D</mark> P K I Q I H V D			
CrP AP 5/1-637		<u>R R S L V E</u> <mark>Q D S V A D</mark> - <mark>A R L Q</mark>	R	- A S D C E P L E V H L - A L G E R D G D L R V QW - R T K G F G C P S T V T WG R S D L T Q Q	84
MpPAP4/1-377	-	<u></u> <mark></mark>			25
MpP AP 2/1-832		P LAA I E <mark>PSS</mark> LRE <mark>-</mark> TP <mark>-</mark> PRLR <mark></mark>	R F		132
OIP AP 1/1-539	48				111
MpPAP3/1-454	40	<mark>sglr</mark> ge <mark>Rr-Plar</mark>	S S	S S S S S D P Q R S A S P N A W - V E D D A R R A P E A R S A S P N A	81
CrP AP 6/1-435	17	<mark>YD</mark> <mark>LED</mark> -ED <mark></mark>	R F	F I S G V - EKAGAK R N T Y ELQLK R K K	48
A/P AP   Q12546 /1-614	46	NGNGKG <mark></mark> FPRLVEPPAVK <mark></mark>	P	- A T A N P R N N V N V I S L S Y I P K G M H I H Y - Q T P F - G L P F - G L	94
AnidP AP   Q92200   /1-618	51	N G N G K G F P R L V E A P A V K	P F	- S A H P K N N V N V I - S L S Y L P D G M H H Y - Q T P F - G L	99
LeP AP   Q05205   /1-539	40	ТТН 5 К Р <mark>V S A</mark> <mark>A S A L</mark>	R	- G T P L A K A G A A D - R V C E A G A K W - L R V G F K Q L	81
				- T S G F	9
MbP AP   A0 A1R 3 Y2F 9   / 1-434		<u> </u>		1301	
MbP AP   A0 A1R3Y2F9   /1-434 MtubP AP   P9 WL81   /1-529	6	R R R F L T	v	GTGVGAGGTAL - LSSHPRGPAVW- YQRGRS GAPPVGGLH L QFGRN	75
	6 20	R R F L T <mark> T G</mark> - <mark>A A A V</mark>	_	- <mark>G T G V G A G G T A L</mark> - L S S H P R G P A V W Y Q R G R S G A P P V G G L H L Q F G R N	-
MtubP AP (P9WL81)/1-529	6 20 25	R R F L T <mark> </mark>	A 8	- <mark>G T G V G A G G T A L</mark> - L S S H P R G P A V W Y Q R G R S G A P P V G G L H L Q F G R N	75
MtubP AP   P9WL81   / 1-529 BcP AP   B4 BKR2   / 1-561	6 20 25 25	R R F L T <mark> </mark>	A S R <u>A A</u> A	- <mark>G T G V G A G G T A L</mark> <mark>L S S H P R G P A</mark> V W Y Q R G R S -  G A P P V G G L H L Q F G R N Y Q R G R S G A P P V G G L H L Q F G R N	75 82 82

Indexp_10(m12)(1/24)       10       Indexp_10(m12)(1/24)       10       Indexp_10(m12)(1/24)       Indexp_10(m12)(1/24) <td< th=""><th></th><th></th><th></th><th></th><th></th></td<>					
The Phy.21 (CHURS) (1-333       33	HvPAPhy_a C4PKL2 /1-544 103				
The PPU_21_CONTUNITION       Image: Control of the PU_21_CONTUNITION       <					000 MET 100 E
H####p_10(EVLA[/358]       Image: Constraint of the constraint					
HP ###p_1 (UPLI) (1.34       B       A A D S V W E       A TO D A V V S L       P 12         Di ###p_1 (DENLS) (1.34       D       A A D S V W E       A TO D A V V S L       P 12         Di ##p_1 (DENLS) (1.34       D       A A D S V W E       A TO D A V V S L       P 12         Di ##p_1 (DENLS) (1.34       D       A A D S V W E       A TO D A V V S L       P 12         Di ##p_1 (DENLS) (1.34       D       A A D S V W E       A TO D A V V S L       P 12         Di ##p_1 (DENLS) (1.34       D       A A D S V W E       A TO D A V V S L       P 12         Im##p_1 (DENLS) (1.34       D       A Y S L       P 12       P 12 <td></td> <td></td> <td></td> <td></td> <td></td>					
0 0 PPH_2   0 CAD3   1/33       9					
Bin MMPRUID       Control (1) - 20       A + 0 + 0 + 0 = - + 0 + 0 + 0 + 0 + 0 + 0 + 0 + 0 + 0 +	HvP APhy_b1 C4PKL3 /1-536 98	 G T V G <mark>S V</mark>	V R Y G L A /	A D S V V R E A	TGD - A L V Y S Q L Y P 129
Mm <sup>2</sup> my (132311)/143       105       FT V 0       Q       P F 65 NM 0 Q       A V 0 * 1 UY 5 Q       FT 55         ImP Phy (132312)/143       105       S V 0       Q       C N 1 S Q       N 1 O 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q       S V 0 C       C N 1 S Q					
hp###jU003/jU03       11	ZmP APhy_b   C4PKL6   /1-544 10	 G A V G <mark>S V</mark>	V R Y G L A /	A D A L D H E A	TGE-SLVYSQLYP 134
InterAmp/201211/1231       105       S.K.Y.G.S.L.Y.K.L.       A.I.G.S.L.I.Y.K.L.       A.I.G.S.L.I.Y.K.L.       P.I.G.S.S.L.H.K.       A.I.G.S.L.I.Y.K.L.       P.I.G.S.S.L.H.K.       A.I.G.S.L.I.Y.K.L.       P.I.G.S.S.L.Y.K.L.       P.I.G.S.S.LYK.L.       P.I.G.S.S.LYK.L.S.S.S.LYK.L.       P.I.G.S.	MtP APhy/Q3ZFI1//1-543 10	 E T V G <mark>S I</mark>	V Q Y G R F (	G R S M N G Q A	VGY-SLVYSQLYP 137
Lup APW, 1002LAJ (1243 102       I.Y. N. E.       A.R. G., S.L. I.Y. N.L.       T.S. R.T. L.Y. R.E.       A.R. G., S.L. I.Y. N.L.       Y.Y. S. Y.         ADD APPL 3103Y01 (1357 1)       T.S. R.T. L.Y. R.E.       A.R. G., S.L. I.Y. N.L.       Y.Y. S. Y.       Y.Y. Y.Y. Y.       Y.Y. Y.Y	PtPAP3/V9LXK5//1-564 12:	 K S V A <mark>S V</mark>	V R Y G T R F	R S Q L N R K A	TGR - SLVYSQL YP 152
Gm PHP1p1033KG1/1547       107       K T Y 5 0       Y 0 1       T S F F E V H E       A R 0 0 S L V N 0 L       Y F 130         Acc P PHp121F0AND(1/548       9       C T Y 6 S L       Y N 0       A S 0 D A LV Y S 0 L       Y F 130         Acc P PHp21F0AND(1/548       9       C T Y 6 S L       Y N 0       C A AD S LV N 0       A S 0 D A LV Y S 0 L       Y F 133         Tm PHp21F0AND(1/548       9       C T Y 6 S L       Y N 0       C AAD S LV N 0       A S 0 D A LV Y S 0 L       Y F 133         Tm PHp21F0AND(1/548       9       C T Y A S L       N N 0       C AAD S LV N 0       A AT 0 D A LV Y S 0 L       Y F 133         Tm PHp21F0AND(1/548       9       C T Y A S L       N N 0       C AAD S LV N 0       A T 0 D A LV Y S 0 L       Y F 133         Tm PHp21F0AND(1/548       9       C T Y G S L       Y N 0       C AAD S LV N 0       Y N 0       Y D A LV Y S 0 L       Y F 133         Tm PHp21F0AND(1/548       9       C T Y G S L       Y N 0       C AAD S LV N E       A T 0 D A LV Y S 0 L       Y F 133         SchPhp21F0AND(1/548       9       C T Y G S L       Y N 0       C AAD S LV N E       A T 0 D A LV Y S 0 L       Y F 133         SchPhp21F0AND(1/548       9       C T Y G S LV N E       A T 0 D A LV Y S 0 L       Y F 133					
nbr#pis(100FUS(1):A32       9	LaP APhy   D2 YZL4   / 1-543 10	 K T V S <mark>S V</mark>	<mark>V Н Y</mark> <mark>G</mark> T S F	R T A L V R E A	R G Q - S L I Y N Q L N P 134
Aub Phy.g.1 (FONM) (1/349       30       0.00000       0.00000	GmP APhy b/Q93XG4//1-547 10	 	<u> v q y</u> <mark>с</mark> т s ғ	R F E L V H E A	R G Q - S L I Y N Q L Y P 138
SrPP1_021FEMX8/1/1-34       102       0.17 (0.17)       132         TimP2Phy_121FEMX8/1/1-34       5       0.17 (A. V. S. Q	AtP AP 15   Q95FU3   /1-532 9	 T S I N <mark>S V</mark>	V Q F G T L F	R H S L S H E A	KGH - S L V Y S Q L Y P 130
TmP #P_121[F6WW2[1/34]       5	AtaP APhy a 1/F6MIX0 //1-549 9	 G T V G <mark>S V</mark>	V R Y G L A /	A D S L V R Q A	SGD - ALVYSQL YP 130
To PPW_23/F6WW2/1/343       9	ScP APhy a2 (F6MIX4)/1-543 10:	 G T V G <mark>S V</mark>	V R Y G L A /	A D S L V R V A	TGD - A L V Y S Q L Y P 133
Tor Phylog J (OPK/3(1)-54)       9	TmP APhy a 1/F6MIW8 //1-545 9	 G T V A S V	V R Y G L A /	A D S L V R E A	TGD - A LV Y S Q L Y P 126
TorP#J_g2 (OPK/SI)(1-54)       9	TaP APhy a3 (F6M) W2 (/1-539 98	 G T V A S V	V R Y G L A /	A D S L V R Q A	TGD - ALVYSQL YP 129
ScPP#pr_01[F6MUS[/154]       95	TaP APhy a2   C4PKK8   /1-549 9	 	V R Y G L A /	A D S L V R E A	TGD - ALVYSOL YP 130
Tor#Phy_j_3[r6MW*j/.536       97       0       0       0       VI       LAD 5 LV E       A T C D A LV Y S Q L       VF       131         Torm Phy_j_3[r6MW*j/.538       93       0       0       VI       LAAD 5 LV E       A T C D A LV Y S Q L       VF       133         Acr Phy_j_3[r6MW*j/.538       93       0       0       VI       LAAD 5 LV E       A T C D A LV Y S Q L       VF       133         Acr Phy_j_5[r6MW*j/.538       93       0       0       VV       LAAD 5 LV E       A T C D A LV Y S Q L       VF       133         Acr Phy_j_5[r6MW*j/.538       13       0       0       VV       LAAD 5 LV E       A T C D A LV Y S Q L       VF       133         Acr Phy_j_5[r6MW*j/.536       137       A T C D A LV Y S Q L       VF       133       A T C D A LV Y S Q L       VF       133         VP APH_j/10232/J.546       107       LAAD 5 LV E       A T C D A LV Y S Q L       VF       133         Ar P 23 [07L6W*j/.527       138       A T C D A LV Y S Q L       VF       138       A T C D A LV Y S Q L       VF       138         Ar P 23 [07L6W*j/.527       138       A T C D A LV Y S Q L       VF       138       A T C D A LV Y S Q L       VF       139         Ar P 23 [07L6W*j/.5		 G T V G S V	V R Y G L A /	ADSLVRVA	TGD - ALVYSQL YP 129
TmP#Pu_D_LIFEMAWI/1-333       100       OT AG DV       VT V       CLAADS LVR E       AT GD ~ ALVY SQ.L       VP       131         AmaPPu_D_LIFEMAXI/1-338       9       OT VG V       VT V       CLAADS LVR E       AT GD ~ ALVY SQ.L       VP       130         SeP Pu_D_LIFEMAXI/1-338       9       OT VG V       VT V       CLAADS LVR E       AT GD ~ LVY SQ.L       VP       130         ReP #1 JEFEMAXI/1-338       100       AT GD ~ LVY SQ.L       VP       130       AT GD ~ LVY SQ.L       VP       131         ReP #1 JEFEMAXI/1-348       100       AT GD ~ LVY SQ.L       VP       131       Pr PAPHy/D/17532/1/1-547       108       AT GO ~ LVY SQ.L       VP       133         Pr PAPHy/D/S32/1/1-547       108       AS 1G O E       VW V       G 12 K P L VH AL       VP       133         AP PAP JD/OTGS//1-532       9       AS 1G O E       VW V       G 12 K P L VH AL       VP       133         AP PAP JD/OTGS//1-532       9       S 1 A D E       VW V       G 12 K P L VH AL       VP       133         AP PAP JD/OTGS//1-542       9       S 1 A D E       VW V       G 12 K P L VH AL       VP       133         GM PAP JJ-120       G 12 K P L VH AL	/= / //	 	V R Y G L A /	A D S L V R E A	TGD - ALVYSOL YP 128
AmpPerp_1p_1[F6WX1/1/338       9		 G T A G S V	V R Y G L A /	A D S L V B E A	TGD - ALVYSOL YP 131
SPPPhp_allFoNUS(J-333         9	·= · · · · ·				
RcP # 1198W 06/1/566       12 ************************************					
V##       V	RcP AP 1/B9RW G6//1-566 12	 	VIVGRS	I F P I T H O A	TGY-SLVYNOLYP 158
P##APhy/PS324/1.46       107       0.01%       5 %       0.01%       G T & F D & V H E       A & R & Q - S & L Y & S & L       Y F       138         WP#APhy/BS4R27/1.47       108       0.01%       A & S & I & S & V & V & G & L & V & Y & S & V & Y & Y & F       139         AP# P23/GETFH1/1.438       19       0.01%       S & I & S & V & V & V & V & F       0 & F & K & G & N & V & Y & S & V & Y & F       130         Gm/P AP / J12.44       78       0.01%       S & V & V & V & V & V & V & V & V & V &					
WP#Phy[53427/L147       138					
APP P15/D7.636 // 532       9					
ARP #23[06TFH1]/1458       99       SSIASE       VWY       GK EK GN YMLK					
GmP #4 i (V9HX64i / 1-42       78       78       VEV       GTLP GR YDSI       AEGE-CTS YNYL       104         MPP #2 1/-264       0P #2 2/-321       0P #2 1/-355       015       AG & SDV       VEV       GTSR SS LKAR       AY GA & GY YT QD       Y1 35         OP #2 1/-323       131       AG & SDV       VEV       GTSR SS LKAR       AY GA & GY YT QD       Y1 35         OP #2 1/-323       137       KTYA AV       KTYA AV       RKA G       WTKH       SG SV VIN VRA       Y1 55         OP #2 1/-323       137       KTYA AV       RKA AV       RKA       OK AK - GWYKH       SG S. VIN VLRA       Y1 55         OP #2 1/-513       RS       SS       QP AS YP YS PR RAA QG CY GK KD KK KK KD DD DD DD AP AP PH T       AP 280         OP #2 1/-513       RS       QP AS YP YS PR RAA QG CY GK KD KK KK KD DD DD DD AP AP PH T       AP 280         OP #2 1/-513       RS       QP AS YP YS PR RAA QG CY GK KD KK KK KD DD DD CP AY PH T       AP 280         OP #2 1/-513       RS       QS       QP 4 AS YP YS PR RAA QG CY GK KD KK KK KD DD DD CP AY PH T       AP 280         OP #2 1/-513       RS       QA AP D       SR R       AF 26 S S YY YP SP RAA QG CY GK KD KK KK KD DD DD CP AP PH T       AP 280         OP #2 1/-513       RS       QP AP F       GT SA SAPP AR RE RER					
MpP.PP_1/1-264       OPAP2/1-312       OPAP2/1-312       OPAP2/1-312       OPAP2/1-312       OPAP2/1-629       137       OPAP2/1-631       137       S G S V INVLRA - VT       155         OPAP2/1-631       137       S VR OP VALIS FMRHG FD RAV EAARS AP I QV LRP NEP LQV HLALT GT AG EMR V QWNT R DV GV AP V KW       GP AS V/ S F R R AA Q G C V G K K D K K K K K D D D D D D D G P AY PHT AP 280         OPAP2/1-631       75       S G S V I NVLRA - VY I S F R R AA Q G C V G K K D K K K K K D D D D D D D G P AY PHT AP 280       GP AS V/ S F R R AA Q G C V G K K D K K K K K D D D D D D D G P AY PHT AP 280         OPAP2/1-832       133       OPAP2/1-832       133       AC V A R C ED V EV R       R L Q Q A Q Q       S R R					
OP AP2/1-312					
OP AP 1/1-556       105       AG & S DV       VR Y       G T S R S S LK A R       A Y G A & G G Y Y T Q D       Y Y       135         OP AP 2/1-629       132       DV C G L       K T Y AAVRKA G AK G       WT K H       T G S & VUN V LR A       YT 165         OP AP 3/1-629       137       S K T Y AAV       S G S & VIN V LR A       YS       155         OP AP 3/1-631       T Y S Y R QP V A I S FMR H G F D R AV EAAR S AP I QV LR P NE P LQV H LA LT GT A G EMR V QWN TR DV GV AP QV RW       G A K G WY K H       G A K G QP LL S       A G G A S V P Y S P R RAA Q G C V G KK DK KK KK DD DD D D G P A Y P H T       AP 20         OP AP 3/1-637       FS       G G M E 2 V Z Y RW       G G M E 2 V Z Y RW       G G G M E 2 V L S       A G G S V V Y S P R RAA Q G C V G KK DK KK KK KK DD D D D G P A Y P H T       AP 20         OP AP 3/1-737       FS       G G M E 2 V Z Y RW       G G G M E 2 V L S       A G G S V V Y S P R RAA Q G C V G KK D KK KK KK V L S E V D F E V L 201         OP AP 1/1-539       112       A C V AR C E D V E V R       V L T E D G AS N A S S A A P A R E R E R A R HW G A Y A P R A D V K Y A V S E V D F E V L 201         OP AP 1/1-539       112       A C V AR C E D V E V R       V L T E D G AS N A P A R E R E R A R HW G A Y A P Y R A D V K Y A V K K Y A V L S E V D F E V L 211         OP AP 1/1-539       112       G R N A S H G A R       L T Y       R V G M G A Y A H V       P A T T T Y D A	. ,	 			
CP AP 2/1-632       132       DV C G L       K T V A A V R K A G A K G - WT K H       T G S - VV N Y L R A Y T 165         CP AP 3/1-629       137       K T Y A A V       R K A        G A K & G WY K H       S G S - VI N Y L R A Y T 165         CP AP 3/1-629       137       K T Y A A V       R K A        G A K & G WY K H       S G S - VI N Y L R A Y T 165         CP AP 4/1-691       174       S Y R Q P V A I S FMR H G F D R A V E A R S A P I Q V L R P N E P L Q V H L A L T G T A G EMR Y QWN T R D V G V A P Q K R W       G A K S G WY K P R R A A Q G C V G K K D K K K K K D D D D D G P A P Y H T A P 260         CP AP 4/1-377       26       G G N E L V L R P N E P L Q V H L A L T G T A G EMR Y Q Q A P Q D       S R R L Q A G Q P L L S       A E G S S Y V I S E G L M 116         Mp P AP 2/1-832       133       A C V A R C E D V V E V R       V L T E D G AS I A S S A A P A E R E R A R HWV G A Y A P V K Y A V L S E V D P E Y L 201         Q A P A D / A P Y 3/1-354       112       G R N A S H G A R       L T D D D R . D A P V K A V K J E E V D P Y L 201         Q A P AP (212346/1-614       9       V L T E D G AS I A S S A A P A R E R E R A R HWV G A Y A P V K Y A V L S E V D P Y L 201         Q A P AP (212346/1-614       9       V L T E D G AS I A S A P A R E R E A R H WV G A Y A P Y R A P P 113         Q A P AP (212346/1-614       9       V G L P A V K W G T S P A N L N S T A Q G Y S H Y D R T P S 102		 A G - S D V	V R V	R S S I K A R	YGA - GGYYTOD YY 135
CP AP3/1-629       137       KTYA AV       RKA       GAK       GWVKH       SGS-VINYLRA       YS       165         CP AP4/1-691       174       SYR QP VAIS FMR HGFDRAV EAAR SAPIQVLRP NEPLQV HLALTG AG EME V GWN TR DV GVAP QVRW       GP AS VP YS PR RAAQGCVGKK DKKKKK KDDDDDDGPAYPHT       AP 280         CP AP5/1-637       85       QQA P QD       SR R       GG SON ELLVLS       AEGS-SYVISEG       LM 116         MpP AP2/1-837       CS       GG SON ELLVLS       AEGS-SYVISEG       LM 116         MpP AP2/1-832       133       ACVA R CEDVVEVR       VILTEDGAS NASSAAP AR ER ERAR HWV GAYAP PR ADV TAVAP VK YAV LS EVD PEYL 201         OIP AP1/1-339       I12       GR NAS HGAR       LTY       RV GNGAYAHV       PATTT TYDARD LC       GAP 149         MpP AP3/1-454       82       PILE DD       VN F       GAS AH PLILT       DD DR - DAP VK YAV LS EVD PEYL 201         OF AP46/1-435       49       LI       VK       G SS AP AR ER ERAR HWV GAYAP PR ADV TAVAP VK YAV LS EVD PEYL 201         OR AP4 [012546]/1-614       95       PILE DD       VN F       GAS AH PL LILT       DD DR - DAP 1454         Apf AP [02200]/1-618       100       VR W       G SS PR NLNS T       AQGY - SHTYDR T       PS 125         Anid PA [02220]/1-618       100       VR W       G SP AN LV LT       SS G GD KL					
CP AP4/1-691       174       S Y R Q P V A I S FMR H G F D R A V E A A R S A P I Q V LR P N E P L Q V H L A LT G T A G EMR V QWN T R D Y G V A P Q V R W       G P A S V P Y S P R R A A Q G C V G K K D K K K K K K D D D D D G P A Y P H T A P       280         CP AP5/1-637       85       Q Q A P Q D       S R R       R L Q A G Q P L L S       A E G S - S Y V I S E G       L M 116         Mp AP4/1-377       26       G S V       Y Q Y A P F       G G G N A S S A A P A R E R E R A R HWY G A Y A P P R A D Y T A Y A P V K Y A V L S E V D P E Y L 201         OP A P1/1-333       133       A C V A R C E D V E V R       Y L T E D G AS N A S A A P A R E R E R A R HWY G A Y A P P R A D Y T A Y A P V K Y A V L S E V D P E Y L 201         OP AP2/1-433       12       G R N A S H G A R       P I L E D D       V N F       G A S A H P L I L T       D D D R - D A P P P R A       P P 113         CP AP 6/1-435       49       V I L       G Q L P A       V R W       G K S P A N L N K Y       A Q Q Y S H Y Y D R T L P S 125         Anid P A (92200/1-614       95       G Q Q P S       V R W       G K S P A N L N K Y       A Q Q Y S H Y Y D R T L P S 125         Anid P A (92200/1-614       95       G Q Q P S       V R W       G K S P A N L N K Y       A Q Q Y S H Y D R T P S 125         Anid P A (92200/1-614       95       G G Q L P A       V R W       G K S P A N L N K Y       A Q Q Y S H Y D R T					
CPAP5/1-637       85       QQAP					
MpP AP4/1-377       26       C       V Q Y AP F       G G G N E E LV LS       A T G E - ER A F       52         MpP AP2/1-832       133       A C V A R C E DV V E V R       V T T T E D G AS N A S S A A P A R E R E R A R HWV G A Y A P V R Y AV LS E V D P E V L       201         OIP AP 1/1-339       112       G R NA S H G AR       LT Y       R V G NG A Y A H V       P A T T T Y D A R L C G A P 1 H3         OP AP 4/1-359       112       G R NA S H G AR       LT Y       R V G NG A Y A H V       P A T T T Y D A R L C G A P 1 H3         OP AP 6/1-435       49       V F L       G A S A H P L I L T       D D D T D A P P P A A P P R A U Y G L       G I S I G       V V G L V L I LG LA       Y G T 2         AP AP (122546)/-1541       9       V G L       G I S I G       V V G L V L I LG LA       Y G T 2         AP AP (022200)/1-618       100       G Q A P S       V R W       G K D P R N L N K V       A H G W S H Y D R T - P S 125         AnidP AP (02220)/1-618       100       G Q A P S       V R W       G T S P A N L N K V       A H G W S H Y D R T - P S 130         MbP AP (AA IR3Y2F9)/1434       10       S G G A P S       V R W       G T S P A N L N K V       S G G G K L V       100         MbP AP (P W W B 1/1-522)       76       S V V A E T - R S 19       S G G S V V A E T - R S 19       130					
MpP AP2/1-832       133       A C V A R C E D V V E V R       V T L T E D G AS N A S S A A P A R E R E R A R HWV G A Y A P P R A D V T A V A P V K Y A V L S E V D P E Y L       201         OIP AP 1/1-539       112       G R N A S H G A R       L T Y       R V G N G A Y A H V       P A T T T T Y D A R D L C       G A P       149         MpP AP3/1-454       82       P I L E D D       V N F       G A S A H P L I L T       D D D R       D D D R       D D D R       D D D R       D D D R       P P       113         OP AP 6/1-435       49       V I L T C D D R       D R       D R <td></td> <td></td> <td></td> <td></td> <td></td>					
OP AP 1/1-539       112					
MpP AP3/1454       82       PILEDD       VIF       GASAHPLILT       DDDR-DAPPPRA       PP       113         CPAP6/1435       49       VIF       GISIG       VIF       GISIG       VVGLVALILGLA       YG       72         APAP (12546/1-614       95       VIF       GISIG       VIF       GISIG       VVGLVALILGLA       YG       72         APAP (12546/1-614       95       GQLPA       VRW       GISIG       VVGLVALILGLA       YG       72         AnidP AP (092200)/1-618       100       GQAPS       VRW       GTSPANLNKV       AHGW-SHTVDRT       PS       130         LeP AP (092205/1/-539       82       KL       AGY       DSLVLT       SSGGDK LV       100         MbPAP (A0AIR3Y2F9/1/434       10       SVVA ET       RS       19         MtubPAP (P9WU81/1/529       76       SVVA ET       RS       19         MtubPAP (A0AHR3Y2F9/1/434       0       SVVA ET       RS       114         BCPAP (P8WU81/1529       ASTEMP       VVGLVALTD       SGGSVVAET       RS       114         BCPAP (44EK2/1/1561       83       VVAET       VVGLVAET       SGGSVVAET       SI       114         BcPAP (A0AD82WHP3/1/560       83       VKF					
CP AP 6/1-33       49       V G L       G I S I G       VV G LV A L I LG LA       Y G       72         AP AP [0.12546]/1-514       95       G Q L P A       V R W       G K D P R N L N S T       A Q G Y S H T Y D R T       P S       125         AnidP AP [0.92200]/1-618       100       G Q A P S       V R W       G T S P A N L N K V       A H GW S H T Y D R T       P S       130         LP AP [0.0250]/1-539       82       K L       A G Y       D S LV L T       S S G G D K L V       100         Mb2 AP [99W181]/1-529       76       S VV A E T       R S       19         MtubPAP [940A1R3Y2F9]/1-151       83       A S T E MY       V K W T T D T V G N P R VML G T P       T S G F G S V R LY D C       105         Bm0 PAP [A0ADR3 WH79]/1-560       83       V R F       A G P E A WR T       V H G V Q R T Y T D G       105					
A/P AP   (J12546)/1-614       95       0 Q Q Q Q Q   /1-618       100       0 Q Q Q Q Q   /1-618       100       0 Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q					
AnidP AP   092200 /1-618       100					
LeP AP   Q05205   /1-539         82         KL         A G Y         D S L V L T         S S G G D K L V         100           MbP AP   A0 AIR3Y2F9   /1-434         10         -					
MbPAP         AQAIR3Y2F9//1-434         10           MtubPAP         F9WL81//1-529         76         SVVVAET         R S         19           MtubPAP         P9WL81//1-529         76         VSWH TT DT V GNP R VML GT P         TS G F G S V V A ET         R S         114           BcPAP         J44EKR2//1-561         83         A R I         V A D G EP A R T         V H G V Q R L Y D G         105           BmaP AP         J40A0H2WHP3//1-560         83         V R F         A G P N EAWR T         V H G V Q R T Y D G         105	· · · · · · · · · · · · · · · · · · ·				
MtubP AP (P9WL81)/1-329         76         V SWH TTDTV GNPRVMLGTP         TSGFGSVVVAET         RS         114           BcP AP (B4EKR2)/1-361         83         A R I         V A D G EP AR T         V H GV QR L Y D G         105           BmaP AP (A0A0H2WHP3)/1-360         83         V R F         A G P N EAWR T         V H GV QR T Y TD G         105					
BcP AP   64 BtR2 / 1/-5.61         83         A R I         V A D G E P A R T         V H G V - Q R L Y T D G         105           BmaP AP   A0 A0H2 WHP3 / 1/-5.60         83         V R F         A G P N E AWR T         V H G V - Q R T Y T D G         105					
8maP AP /A0 ADH2WHP3 //1-560 83					
	6psr Ar   Q65755  /1-560 8:	 	AG	r N EAWN I V	<u></u> 105

			G L E P G T K Y Y		
			G L E P A T K Y Y		
			G L E P G T K Y Y		
			G L E P G T K Y Y		
HvP APhy_b2   C4PKL4   / 1-537	130 F	E G L Q N Y T S G I I H H V R L Q	G L E P G T K Y Y	Y Q - C G D P	A I P G
HvPAPhy b1/C4PKL3//1-536	130 F	EGLQNYTSGIIHHVRLQ	GLEPGTKYY	Y Q - C G D P	A I P G
OsP APhy b/D6QSX9//1-539	130 F	D G L L N Y T S A I I H H V R L Q	GLEPGTEYF	Y Q - C G D P	A I P A
ZmP APhy_b   C4PKL6   /1-544	135 F	EGLQN Y T S G I I H H V R L Q	GLEPGTRYV	Y R - C G D P	A I P D
MtP APhy   Q3ZFI 1   / 1-543	138 F	EGLQN YTSGII HHVRLT	GLKPNTLYQ	Y Q - C G D P	S L S -
			GLKPDTLYH		
			GLKPNTLYY		
			GLEPSTVYY		
			GLKPSTIYY		
			GLEPATKYY		
			GLEPGTKYY		
			GLEPATKYY		
			GLEPGTKYY		
			GLKPSTIYY		
			G L E P E T R Y Y		
1 11	_		PLEDNTAYF		
MpP AP 1/1-264					
OIP AP 2/1-312			G L MA G E R Y S		
			GLKSATRYY		
			H L D P N T F Y Y		
			D L L P D T A Y W		
	53 V		E L R P G E K I A		
MnP AP 2/1-832			V A E A V A V A R R R V T WS S G R S A A A N P R L S WWR G P S E A N A S T V V A		
					H
OIP AP 1/1-539	150 A	N S F G Y R H P G Y V H T A A I V			
OIP AP 1/1-539 MpP AP 3/1-454	150 A 114 L	D P E A R D R	A L D A R R A P W	L N - C D D L	
OIP AP 1/1-539 MpP AP 3/1-454 CrP AP 6/1-435	150 A 114 L 73 L	D P E A R D R D D G V E P E A R D R		LN - C D D L	
OIP AP 1/1-539 MpP AP 3/1-454 CrP AP 6/1-435 A/P AP   Q12546 /1-614	150 A 114 L 73 L 126 C	D P EAR DR			A A N G
01P AP 1/1-539 MpP AP 3/1-454 CrP AP 6/1-435 A/P AP   Q12546 /1-614 AnidP AP   Q92200  /1-618	150 A 114 L 73 L 126 C 131 C	D P EAR DR			A A N G
OIP AP 1/1-539 MpP AP3/1-454 CPP AP6/1-435 AfP AP (012546/1/1-614 AnidP AP (092200/1/1-618 LeP AP (005205/1/1-539	150 A 114 L 73 L 126 C 131 C 101 F	D P EAR DR			
OIP AP 1/1-539 MpP AP3/1-454 CPP AP6/1-435 AfP AP (012546/1/1-614 AnidP AP (092200/1/1-618 LeP AP (005205/1/1-539	150 A 114 L 73 L 126 C 131 C 101 F	D P EAR DR			
0/P AP 1/1-539 MpP AP3/1-454 OP AP 6/1-435 A/P AP (012546/1-614 AnidP AP (092200/1-618 LeP AP (005205/1-539 MbP AP (A0 A1R3Y2F9/1-434	150 A 114 L 73 L 126 C 131 C 101 F 20 Y	D P EAR DR		L N - C D D L	
OIP AP 1/1-539 MpP AP 3/1-454 CrP AP 6/1-435 A/P AP (012546)/1-614 AnidP AP (005205)/1-618 LeP AP (005205)/1-539 MbP AP (ADAIR3Y2F9)/1-434 MtubP AP (P9WL81)/1-529	150 A 114 L 73 L 126 C 131 C 101 F 20 Y 115 Y	D P EAR DR	G L E P D T T Y Y G L E P D T T Y Y H L K P E T T Y Y G E C V D I Q P Y N L T P D T D V V	L N - C D D L	A A N G G T D - S A G T G T G T G
OIP AP 1/1-339 MpP AP3/1-454 OP AP6/1-435 AfP AP   012546/1-1514 AnidP AP   092200  /1-618 LeP AP   005205  /1-539 MbP AP   A0 A183Y2F9  /1-434 MtubP AP   P3WL81  /1-529 BcP AP   64 Br.82  /1-561	150 A 114 L 73 L 126 C 131 C 101 F 20 Y 115 Y 106 L	D P EAR DR	A L DA R R A P W           G L E P D T T Y Y           H LK P E T T Y Y           G E C V D I Q P Y           N L T P D T D Y V           N L T P D T D Y V	L N - C D D L	A A N G G T D - S A 

HvP APhy_a   C4PKL2  /1-544	174	- SAVHAFRTM	P A A G P R S - 1	PG	R I A V V G	D L (	g L T Y N	T T S T V D	HM	T 214
TaP APhy_a 1   C4PKK7   / 1-550	171	- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L (	g L T Y N	T T S T V D	HM/	A 211
TaP APhy_b1 C4PKK9 /1-538	170	- SAVHAFRTM	P D V G P R S - 1	PG	R I A V V G	D L (	g L T Y N	T T S T V E	HM/	A 210
TaP APhy_b2   C4PKL0   /1-537	169	- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L (	g L T Y N	T T S T V E	HM/	A 209
HvP APhy_b2/C4PKL4//1-537	169	- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L (	g L T Y N	T T S T V E	HM/	A 209
HvP APhy b1/C4PKL3//1-536	169	- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L (	g L T Y N	T T S T V E	HM/	A 209
OsP APhy_b   D6Q5X9   /1-539	169	- S D I H A F R T M P	P A V G P R S - Y	PG	K I A I V G	D L C	g L T Y N	T T S T V E	HMN	v 209
ZmP APhy_b   C4PKL6   /1-544	174	- S G V H A F R T M P	P A V G P G S - Y	PG	R I A V V G	D L (	g L T Y N	T T S T V D	H L M	v 214
MtP APhy/Q3ZFI1//1-543	176	- S D V H Y F R T MP	P V S G P K S - Y	PS	R I A V V G	D L (	g L T Y N	T T S T V N	HM	1 216
PtPAP3/V9LXK5//1-564	191	- SGTYYFRTMP	P D S S S T S - Y	PS	R I A I V G	D V (	g L T Y N	T T S T V S	HM	1 231
NtP APhy   A5YBN1   /1-551		- STIYHFKTM	P   S S P K S - Y	РК	R I A I V G	D L (	G L T Y N	T T S T V S	HLN	M 215
LaP APhy/D2YZL4//1-543	173	- S D I Y Y F R T M P	P   S G P K S - Y	PG	R VAVV G	D L (	g L T Y N	T T A T I N	HL1	T 213
GmP APhy b/Q93XG4//1-547	177	- SDIYYFRTM	P   S G	PG	K V A V V G	D L C	g L T Y N	T T T I G	H L '	T 217
AtP AP 15   Q95FU3   /1-532	169	- SKIHHFRTM	P V S S P S S - Y	PG	R I A V V G	D L C	g L T Y N	TTDTIS	H L	1 209
AtaP APhy_a 1/F6MIX0 //1-549	170	- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L C	G L T Y N	T T S T V D	HM/	A 210
		- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L C	g L T Y N	T T S T V D	HMI	M 213
TmP APhy a 1/F6MIW8//1-545	166	- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L C	g L T Y N	T T S T V D	H MI	V 206
TaP APhy a3 (F6MIW2 )/1-539	169	- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L C	g L T Y N	TTS TVD	HM/	A 209
TaP APhy a2   C4PKK8   /1-549	170	- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L C	g L T Y N	T T S T V D	HM/	A 210
ScP APhy a 1/F6MIX2 //1-541	169	- SAVHAFRTM	P A V G P R S - Y	PG	R I A V V G	D L C	g L T Y N	T T S T V D	HMN	V 209
TaP APhy b3 (F6MIW6)/1-536		- SAVHAFRTM	P A V G P R S - Y	P G	R I A V V G	D L C	g L T Y N	T T S T V E	HM/	A 208
TmP APhy b1/F6MIW9//1-539		- SAVHAFRTM					g L T Y N			
		- SAVHAFRTM	P D V G P R S - Y	P G	R I A V V G	D L (	g L T Y N	T T S T V E	HM/	A 210
ScP APhy b1/F6MIX5//1-538			PAVGPRS-)	PG	R I A V V G	D L (	g L T Y N	TTSTVE		
RcP AP 1   B9RW G6   /1-566							g L T Y N		H L	
VvP AP   A5 BGI 6   /1-540		- SNIYSERTME	PVSGPRS-)	PR	K   G     G	D L (	g L T Y N	STATID		
PvP APhy/V7B3Z4//1-546							g L T Y N			
VrP APhy   B5 AR Z7   / 1-547		- SOERFFETFF	PKPSPNN-)	PA	R I A V V G	D L (	g L T R N	STSTID		
							g L T Y N			
							g L T S N			
GmP AP 4   V9HXG4   /1-442	133	A E F E L K T P F	P A Q	PI	T FAVAG	D L (	g Q T G W	TKSTLA	HI/	D 168
MpP AP 1/1-264							g			
OIP AP 2/1-312	28	- ETTRSFRAPH	<mark>К</mark> ТРКК	H G	KETTK - LAVVG	рто	g Q T D V	T R E V L T	HV	R 69
GrP AP 1/1-556							s		KM0	
GrP AP 2/1-632		- MGEYRFKTLF	P G P G	PL	R VGLIA	D V (	g	S S D T R D		
CrP AP 3/1-629	205	- V G E Y R F K T L F	P G P G	PL	R VGL   A	D I (	g 0 T V N	SSDTRD	HLN	M 246
CrP AP 4/1-69 1	336	- SKEYSFVSAF	P P A G P A G	T V	R A L F V A	D M0	G Q A E V D G S L E G S Q M L P S L N T T M L M Y R	D T L A S Y	RE4	A 396
			D F T S P K S	R G	SDSRFSFIAFG	D M0	g E S HV	KSKKAPMASRTVD		G 198
MpP AP 4/1-377	92	- ER FWF FHKRS	SPEQIRAGE	PL	R MIAVC	D V (	g H S D	S T G V L D	LVRAEVHGVDGADADV	A 146
MpP AP 2/1-832	321	- GGTLSYRLSD	DAGGSFPPPDAPPLTIAVPPCA	RDQGRNETAPF	RPETLAMEA	D M0	GRGTDDDARTWQEYGS PAFN	VSKRLA	S D /	A 404
				K T			GRGSNDDAETWRAYGQ PSLN		RD/	A 239
			Р Р Т Р Р К Т	L	S F F T L G	D wo	g V R G L R G T	D S R A V A	RAN	M 180
							g R A G N	D NQRRTA		
							g Y T N A			
							g			
							C D T S G			
							GR L A D G R Y V S D N I G S P F A G D			
							GR L A D G R Y V S D N I G S P F A G D			
BcP AP   B4 B(R2   /1-561							A T P N			
							T P N T G WV			
							A T P N T G W V			
, , <i>n</i>										-

		285 <mark>S C S F G K S T P I H</mark> E T
		282 <mark>S C A F G K S T P I H</mark> E T Y Q P R WD Y WG R Y M E A V T S G T P MMV V E <mark>G N H E</mark> 282
		281
		С Y <mark>S C S F A K S T P I H</mark> E T
		С Y <mark>S C S F A K S T P I H E T</mark>
HvP APhy_b1/C4PKL3//1-536 210 SN Q P - DLVLLVGDV	SYANLYLTN-GTGTD	280 <mark>S C S F A K S T P I H E T</mark>
OsP APhy b / D6Q5X9 / /1-539 210 SN Q P - D L V L L L G D V	SYANLYLTN-GTGTD	280 Y Q P RWD Y WG R Y ME P V T S R I P MMV V E G N H E 280
ZmP APhy b/C4PKL6//1-544 215 RN R P - DLVLLLGDV	CYANLYLTN-GTGAD	285
MtP AP hy / Q3ZFI 1 / / 1-543 217 SN H P - D L I L L V G D A	SYANMYLTN-GTGSD	286
PtPAP3/V9LXK5//1-564 232 SN R P - D L I L L V G G V	TYANLYLTN-GTGSD	2 Y <mark>S C S F A N - S P I H</mark> E T Y Q P R WD Y WG R Y M Q P V L S K V P I L V V E <mark>G N H E</mark>
NtP APhy   A5YBN1   /1-551 216 GN D P - N L V L L V G D V	TYANLYLSN-GTGSD	285
LaP APhy/D2YZL4//1-543 214 SN K P - D L L L L I G D V	TYANLYLTN-GTGSD	283
GmP APhy b/ Q93X G4 / /1-547 218 SN E P - D L L L L I G D V	TYANLYLTN-GTGSD	287
AtP AP 15 / Q9SFU3 / /1-532 210 HN S P - D L I L L I G D V	SYANLYLTN-GTSSD	279
AtaPAPhy a1/F6MIX0//1-549 211 SN R P - DLVLLVGDV	CYANMYLTN - GTGAD 0	21 <u>S C A F G K S T P I H</u> E T Y Q P R WD Y WG R Y MEAV T S G T P MMV Y E <mark>G N H E</mark>
ScP APhy a2 / F6MIX4 / /1-543 214 SN R P - DLVVLV GDV	SYANLYLTN-GTGAD	284
TmP APhy a 1/F6/VIW8 / 1-545 207 SN R P - DLVLLVGDV	CYANMYLTN-GTGAD	277 <mark>S C A F G K S T P I H</mark> E T
TaP APhy a3 / F6/VIW2 / /1-539 210 SN R P - DLV LLLGDV	SYANLYLTN-GTGAD	280 S C A F G K S T P I H E T
		281
ScP APhy a1/F6MIX2//1-541 210 SN R P - DLVVLVGDV	SYANLYLTN-GTGAD	280 Y S C A F G K S T P I H E T Y O P R WD Y WG R Y MEA Y T S G T P MMY Y E G N H E
TaP APhy b3 (F6M) W6 (/1-536 209 SN 0 P - D L V L L L G D V	SYANLYLTN - GTGTD G	279
TmP APby b1/E6MIW9//1-539 212 SK 0 P - D L V L L L G D V	SYANLYLTN - GTGTD	282 Y
AtaP APhy b1/F6/MIX1//1-538 211 SN 0 P - D L V L L L G D V	SYANLYLTN - GTGTD G	281
ScP APby b1/F6MIX5//1-538 211 SN L P - D L V L L L G D V	SYANLYLTN - GTGTD	281
RCP AP 1/B9RWG6//1-566 238 SN N P - D       V GD A	TYANIYITN - GTGAD	Y
		280 Y S C S F P Q - T P I H E T
PvP APbv / V7 B374 / /1-546 218 NN E P - D           G D V	TYANIYITN - GTGSD	287 - K C S F P Q - S P I H E T Y Q P R WD Y WGR FMQ N L V A E V P I MV V E G N H E
		288
		279 S C S F P E - T P I H E T
AtP AP 23 ( 06 TP H 1 / 1-458 210 EN - D P - S L V     V G D	TYANOYRTIGGKGVP	280 C F S C S F P D - A P I R E T
GmPAP41V9HXG41/1-442 169 Q.CKY.D.V.Y.L.P.G.D.L	S Y A D	MQH LWD N F G K LV E P F A S T R P WMY T E G N H E
		FP P R WD T F G R LA E P LMS K V P M L V V A G N H D
0/PAP2/1-312 70 DALGDS-ELLIHTGDV	S Y A D	FAP R WD S F G T L S E F L L D G MP M L T V P G N H D 118
CP 4P 1/1-556 219 L S N P - D L L L V G D E	A V A N L E D E R - G	A F NY G P V V S N G L T V S
		YY
CP 4P3/1-529 247 AN K P - O V V I MV G D N	Τ Υ Α	Y GALDTEVRNSK GT
CP4P4/1-691 397 FA S G G A V P P V T L I V H N G D I	S V S R	FS TQWDN FMQQ I EP VAAAMP YMV TP GN H E
CP4P5/1-637 199 0 ELEB	A V A D	K WWD S FMAAL EP LAAS RP YMV GLIGNH FAGP C RD TN 257
		YMDD LOP LAAY VP YMV SP GN H E 195
		Y G S V WD E WG E Q I T P WA S R V P F L T C V G N H E
		YAS VWD EWAA Q I TP WAS R V P F I S N LGN H E 287
CP245/1-435 117 AD VAGCMPP - A EVVS T GDN	EVPS	D - DV 0 FD - ES FR I Y TAK ELQ V PWY V MG NHD 173
		YNGTSSTLPGGGPLPEEYKKPLPAGEIPDQGGPQGGDMSVLYESNWDLWQWLNNVTLKIPYMVLPGNHE
		V - NSR - YAPTWGR F - KALTSPSP - GNHD - 221
Mic AP (40/20/20/20/20/20/20/20/20/20/20/20/20/20	CYANI AOD	
MtubP AP (POW/1811/1-529 209	CYANLESSAGE	R I R T WS DWFD N N T R S A R Y R P WMP A A G N H E R I R T WS DWFD N N T R S A R Y R P WMP A A G N H E 255
PRAPIRA (F31/102) 200	CYANI	NPAHOP EVWDRANDTAAN NATAAN NATAAN 238
		NFAHQP 238
		AVWRDFGNNNQTSAANRFWWRFCFGNHE 238
apa A (dosto)/1900 105 Yu - Aven Fur - LFHELNOOL		236

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		I E - E Q I						
		I E - E Q I				- G S F S		
		I E - Q Q I						
		I E - Q Q I						308
		I E - Q Q I				- E S F S	\$	308
		I E - Q Q I G N				- E S F S	\$	308
		I E - E Q I D N						
		I E - Q Q I H N				- G S S S	\$	313
		I E - E Q A V N				- G S S S		
PtPAP3/V9LXK5//1-564 302	2 - 1	Y E - E Q A E N	LA Y	TSRF	A F P S K E S	- G S L S	\$	329
NtP APhy   A5 YBN 1   / 1-551 286	6 - 1	I E - E Q A E N	ΑΑΥ	RSRF	A F P S K E S	- G S S S	\$	313
LaP APhy   D2 YZL4   / 1-543 284	4 - 1	I E - K Q A E D	/ A Y	SSRF	A F P S E E S	- G S S S	s	311
GmPAPhy_b/Q93XG4//1-547 288	3 - 1	I E - K Q A E N	/ A Y	SSRF	A F P S Q E S	- G S S S	\$	315
AtP AP 15   Q95FU3   /1-532 280	- C	I E - L Q A E N	EA Y	SSRF	A F P F N E S	- G S S S	s	307
AtaP APhy_a1/F6MIX0//1-549 282	2 -	I E - E Q. I G N	4 A Y	RSRF	A F P S T E S	- G S F S	s	309
ScP APhy a2   F6MIX4   /1-543 285	5 - 1	I E - E Q I	E A Y	RSRF	A F P S A E N	- G S F S	s	312
TmPAPhy a1/F6MIW8//1-545 278	3 - 1	I E - E Q I R N	Α.Α Y	RSRF	A F P S T E S	- G S F S	s	305
TaP APhy a3/F6MIW2//1-539 281	1 - 1	I E - E Q I	ад Y	RSRF	A F P S T E S	- G S F S	s	308
		I E - E Q I						
ScP APhy a 1/F6MIX2 //1-541 281	1 -	I E - E Q I	EA Y	RSR F	A F P S A E S	- G S F S	5	308
		I E - Q Q I						
		I E - Q Q I				- D S F S	5	310
		I E - Q Q I				- FS FS	5	309
		IE-QQIKTFA						
		I E - QQA QN						
		I E - EQA						
		T E - EQART FV						
		T E - E Q A D N						
		I E - L Q.A E N						
		I E - P Q A						
		EENILLDEFV						
		V A - Q N G						
		ME-LQLSMFK						
		ME-LQL						
		LETEGIPAVINNITISFSFPTN				GD   T (		
		R D WP G T						
		V D - P S						
		VD-PS						
		Y D A T P D T WQ H V N H T S S G K I S P R						
		Y D A T P D T WQ H V N H T S S G K T S P R						
		A D S S N WP E S R V A D E Y G V D D S G G						
		H R G S V A D V S L L N T G						
		A E F D G P H N I L T A Y L N D D I A N G T A P T D N L T Y Y S C P P S Q R N F T A E F D G P G N P I T A Y L N E G I P N G T WAA E N L T Y Y S C P P S Q R N F T						
		Y S T T G A						248
		N E - V G N						189
		N E - V G N G P						
		I E - FHN						
BpsPAP   Q63X35   / 1-560 239	- e	IE-FHNQGLD	υδλ	LARY	ILPENGT	KFA	<u> </u>	265

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GmP APhy_b   Q93XG4   /1-547	316		FYYSFNAG	G	
AtP AP 15   Q95FU3   /1-532	308	<u></u> 1	LYYS F N A G	G	;
AtaP APhy_a 1/F6MIX0 //1-549	310		FYYS FD A G	G	,
ScP APhy_a2  F6MIX4  /1-543	313		FYYS FD A G	G	1
TmP APhy_a1/F6MIW8//1-545	306		FYYS FD A G	G	,
				G	
TaP AP hy_a2   C4PKK8  /1-549	310	F	FYYS FD A G	G	,
ScP APhy_a1/F6MIX2//1-541	309		FYYS FD A G	G	į
TaP APhy b3 (F6MIW6)/1-536	308		FYYS FD A G	G	
				G	
AtaP APhy b1/F6MIX1//1-538	310		FYYS FD A G	GAAYADYS-KS-334	,
ScP APhy_b1/F6/MIX5//1-538	310	F	FYYS FD A G	G	,
RcP AP 1 / B9RW G6 / /1-566	336		FYYSFNAG	G	J
VvP AP   A5 BGI 6   /1-540	309		FYYSFNAG	G	j.
PvPAPhy/V7B3Z4//1-546	316		LYYS F N A G	GG-IHFIMLYD-KK - 340	J
VrP APhy   B5 AR Z7   /1-547	317		LYYS F N A G	GGAYIDYY-KN 341	
AIP AP 15   D7L636   /1-532	308		LYYS F N A G	G	
AtP AP 23   Q6TPH 1   /1-458	309		I L Y Y S F D A G	GG-VHFVML	j.
GmP AP4   V9HXG4   /1-442	245		I L Y Y S F E V A	A	J
MpP AP 1/1-264	97		(DWFSHDVG	G	/
OIP AP 2/1-312	145		LFWSHEVG	G	,
GrP AP 1/1-556	315	F	FYYSANVG	G	J
CrP AP 2/1-632	354		I L Y Y S T I I A	A	J
GrP AP 3/1-629	354		I L Y Y S T V I G	GNN Y V P FH - K G - 379	J
CrP AP 4/1-69 1	486		MWYAFEYG	G	J
GrP AP 5/1-637	316	ALRRELQQDDAVGAGTGVSRRRRVEHNPF	FWYS FD YA	A	1
MpP AP4/1-377	220		I HYYSLDIG	G	
				G	
OIP AP 1/1-539	329		DWFAVTFG	GNTEVN	
MpP AP 3/1-454	273	F	AGVDANGADLGAG	G	1
GrP AP 6/1-435	219		RWNASMGG	GVV T R I A L P P D A A T G A P R S - L D L V M L D T T P I I Y Q Y A G A S W V D F L - N G F 273	1
				G	
				G	
				G N T MS G G T - V A 273	
MbP AP   A0 A1R3Y2F9   /1-434	190		LWYS FTAG	G	,
				G	
BcP AP   B4 BKR 2  /1-561	266		RWYS FRVS	S	;
				G	
				G	

HvP APhy_a   C4PKL2   /1-544	339 G E Q Y R W L E K D L A K V D R S V T P - W - L V	A G W H <mark>A F</mark>	P W Y T	ТҮКК	A H Y R E V	ECMRVAM EEL	L Y S H G L D I A F T <mark>G H</mark>	VHAYERSNRV - 412
	336 G E Q Y R W L E K D L A K V D R S V T P - W - L V							
TaP AP hy_b1 C4PKK9 /1-538	335 G E Q Y R W L E K D L A K V D R S V T P - W - L V	A G W Y <mark>A F</mark>	P W Y S	ТҮКК	A H Y R E A	ECMRVAM EEL	L Y S Y G L D I V F T <mark>G H</mark>	VHAYERSNRV - 408
	334 G E Q Y R W L E K D L A K V D R S V T P - W - L V							
	334 G D Q Y R W L E K D L A K V D R S V T P - W - L V							
	334 - D Q Y R W L E K D L A K V D R S V T P - W - L V							
	334 G K Q Y K W L E K D L A K V D R S V T P - W - V I							
	339 G A Q Y K W L E A D L E K V D R S V T P - W - L I							
	340 G D Q Y K W L E K D L A S L D R E V T P - W - L V							
	355 G D Q Y K W L E E D L A N V D R E V T P - W - L V							
NtP APhy   A5YBN1   /1-551	339 D D Q Y K W L E R D L A N V D R T V T P - W - L V	A T W H <mark>P P</mark>	P W Y S	ΤΥΤ	A H Y R E A	ECMKVAM EEL	L Y E C G V D L V F N <mark>G H</mark>	VHAYERSNRV - 412
	337 G K Q Y K W L E R D L A S V D R S E T P - W - L V							
	341 A E Q Y K W L E R D L E N V D R S I T P - W - L V							
	333 <u>A E Q Y E W L K K D L A K V D R S V T P - W - L V A</u>							
	335 G E Q Y R W L E K D L A K V D R S V T P - W - L V							
	338 G E Q Y R W L E K D L A K V D R S V T P - W - L V							
	331 G E Q Y R W L K K D L A K V D R A V T P - W - L V							
	334 G E Q Y R W L E K D L A K V D R S V T P - W - L V							
	335 G E Q Y R W L E K D L A K V D R S V T P - W - L V							
	334 G E Q Y R W L E K D L S K V D R S V T P - W - L V							
	333 G E Q Y R W L E K D L A K V D R S V T P - W - L V							
	336 G E Q Y R W L E K D L A K V D R S V T P - W - L V							
	335 G E Q Y R W L E K D L A K V D R S V T P - W - L V A							
	335 G E Q Y R W L E K D L A K V D R S V T P - W - L V							
	361 G D Q Y K W L E R D L A N V D R E V T P - W - L V A							
	334 A D Q Y K W L E R D L A K V D R S I T P - W - L I							
	341 A D Q Y K W L E R D L A S V D R S I T P - W - L V A							
	342 G E Q Y K W L E R D L A S V D R S I T P - W - L I							
	333 <u>A E Q Y E W L K K D L A K V D R S V T P - W - L V A</u>							
	334 G L Q Y A W L K E D L S K V D R A V T P - W - L V A							
	270 <u>SEQ YRWLKEDLSK VD RKRTP - W - LL</u>							
	128 A P M F E W L K G D L A S I D R A L T P - W - V I V							
	176 T P Q MAWL R K D L A T I N R Q Y T P - W - V V							
	340 TPQ YDWLVRDLSS VD RSVTP - W - VV							
	380 T P Q Y Q WAMK E F A S V D R K M T P - W - L F V							
	380 T P Q Y EWAMK E F A S V D R K M T P - W - L F V							
	510 S E Q Y Q F M V K T L A S V D R R R T P - W - L V							
	369 S S Q A A W L E A D L A A A D R C A T P - W - V V							
	252 NKMYDWLEADLAAANANRAKTP-W-IV							
	538 S P Q H A F L E A A L A T A N R N R A E T P - W - V F I							
	353 S A Q G E W L K R E L S S I D R A K T P - W - V V							
	329 NAQ WAWLERVLSDATADIGGGKAEKPTWR - V							
	274 NAQDADAIKSSLQQQLNASYANGSAAAGGSS-WR-L							
	438 Y E Q WHWL Q Q D L A K V D R S K T P - W - V I V							
	444							
	274 Q A Q I D W L K A D L A A N T K P C T A /							
	226 G E Q R R W L Q A E L A N A R R D S E I D W - V V							
	321 G E Q R R W L Q A E L A N A R R D S E I D W - V V							
	326 G E Q T R W L E R T L R H A A H D D D I D W - I V V							
	326 G E Q T R W L E Q T L R R A S R D R D I D W - I V							
BpsP AP   Q63X35  /1-560	326 <u>G E Q T R W L E Q T L R R A S R D R D I D W - I V</u>		UALS	55K	TG NGSD	KGIREAWLPL	FDRYGVDLVLCG	UHDYERSFPVR 401

								440
TaP APhy_a1 C4PKK7 /1-550								
TaP AP hy_b1 C4PKK9 /1-538								436
								435
HvPAPhy_b2 C4PKL4 /1-537								435
								434
								435
ZmP APhy_b   C4PKL6   /1-544	413	F -	 чγтι	. D A	C G P V H I S V G D G G N		ЕКМАТАН	440
MtP APhy   Q32FI 1   / 1-543	414	Y -						441
PtPAP3/V9LXK5//1-564	429	Y .	 чγтι	. D P	C G P V H I T V G D G G N		ЕКМАУРН	456
IVtP APhy   A5YBIV1   /1-551								440
LaP APhy/D2YZL4//1-543	411	Y -	 NYNI	. D P	CGPVHITIGDGGN		ЕКМАТКЕ	438
GmP APhy b/Q93XG4//1-547	415	Y .	 NYNI	. D P	CGPVYITVGDGGN		ЕКМАТКЕ	442
AtaP APhy a 1/F6MIX0 //1-549	409	F -	 N Y Т I	. D P	CGAVHISVGDGGN		ЕКМАТТН	436
ScP APhy a2 (F6MIX4)/1-543	412	F -	 V Y Т I	D P	CGAVHISVGDGGN		ЕКМАТТН	439
TmP APhy a 1/F6MIW8//1-545								432
TaP APhy_a3 / F6/MIW2 / /1-539			NY T I	. D P	CGAVHISVGDGGN		ЕКМАТТН	435
			NY T I	D P	CGAVHISVGDGGN		ЕКМАТТН	436
ScP APhy a 1/F6/MIX2 //1-541								
			 NY T I	D P	CGAVHISVGDGGN		ЕКМАТТН	434
RcP AP 1   B9RW G6   /1-566								
GmP AP 4 / V9HX G4 / /1-442	344	Y .	 NG R I	. D P	CGAVHITIGDGGN		E G L A	368
MpP AP 1/1-264	202	R	 оwке	D A	C G A V H L T V G D G G N		E	223
OIP AP 2/1-312	250	н.	 ) F H V	ие	CGPVHVVVGDGGN		E	271
		Y.	 νQΤΕ	D A	CGTVY-TAGNAG		VGLNTEF	438
CrP AP 2/1-632	454	γ.	 с Y К F	D S	CGP   Y   T   GD G G N		EGPYRNF	481
			( Y K F	D T	CGP   Y   T   GD G G N		EGPYRNE	481
CrP AP 4/1-691	590	Y .	 3 G A (	: Q Р	PRPDGSQ TAPVHLVTGHAG		A G L S L N <mark>-</mark>	621
CrP AP 5/1-637	446	G	 vксv	E E	EDQLGGVAGRSSASEGIRHIVLGTAG		HVLSSVE	485
MpP AP 2/1-832	634	F -	 рат.	R	AGK TRK SYGTRGCVA		SEPTIDA	661
OIP AP 1/1-539	443	G S T S F -	 ۷Vs4	D E	GCAAFSRLVDG		V A T Y	468
MpP AP 3/1-454			 					
GrP AP 6/1-435	358		 < s A [	) D P	V H Y I T S G A G S D		RKGEFDD	383
A/P AP   Q12546 /1-614	506		 LΥ	P	L G A N G T		DTAAIVN	522
AnidP AP   Q92200   /1-618	512	F -	 РМТА	N			DESSIAD	527
						A F Y G I S G S H A L L E A S N D S T F G V L K L T L S A T G Y T G D F V I		
MbP AP   A0 A1R3 Y2F9   /1-434	302	GALGTDTRTPIPV	 DT R S	DLIDST	R G T V H L V I G G G G T		K	339
								434
BcP AP   B4 BKR 2   / 1-561	402	G C	 NHRAGVDAKTGEVVETI	Q P	R P V G S N D P N R T T F D T S H G T I H L I L G G G G T	A P L D V Y G	ENPSTGE	466
						A P L D V Y G	ENPATGL	466
						S A P L D V Y G		

HMP#Mp_0[0H2]/JAM       G				
bp APPU_D_10PUSU_1A33       0	HvPAPhy a/C4PKL2//1-544 4	441 🗛	A D E	Y 486
The PMPs_12 (ORUS)(1331       0 <td>TaP APhy a 1 (C4PKK7 //1-550 4</td> <td>438 🔺</td> <td>A D E</td> <td>Y 483</td>	TaP APhy a 1 (C4PKK7 //1-550 4	438 🔺	A D E	Y 483
The PPUP_L2 (0PL/L2)/337       40       00	TaP APhy b1/C4PKK9//1-538 4	437 4	A D D	Y 482
Hire Area, Jack (2014).1333 - 13       G				V 481
InterAmp_al (2013)(31)336       35       55       0	<i>i i i</i>			V 491
0 0 #P#ip_0 (DGCD2) (DFL6)(J-344       0	·= · · · ·			
DimPRING       CIP DI ALL	<i>i i i</i>			
MM <sup>2</sup> /PPi/123711/1243       44       0 <td>/ / /</td> <td></td> <td></td> <td></td>	/ / /			
PP#481/02US(1)/548       427       00				
Ind PMP (JAST) (JAST)       441       0 <td>MitP APhy/Q32-11//1-543 4</td> <td>442</td> <td>ADE CPEPTTPD CPEPTTPD</td> <td></td>	MitP APhy/Q32-11//1-543 4	442	ADE CPEPTTPD	
List Perploy 1202(4):434       43       5			A D E	F 504
0m APHy_1023K041(J-347       443       00	11tP APhy   A5YB111/1-551 4	441 🗚	A D E	Y 486
AP# P13 (DSF13(1)-532       435       0.0       0.				
And PAPs_1 [FORM 0]./1-33       437       A0       C       C P D P K K P II       C A G F F S G A A A G F C       D D P Y S A V 82         Ser PAPs_1 [FORM 0]./1-33       433       A0       C       C A G F F S G A A A G F C       D D P Y S A V 82         Tim PAPs_2 [FORM 0]./1-34       433       A0       C A G F F S G A A A G F C       D D P Y S A V 82         Tim PAPs_2 [FORM 0]./1-34       433       A0       C A G F F S G A A A G F C       D D P Y S A V 82         Tim PAPs_2 [FORM 0]./1-34       437       A0       C A G F F S G A A A G F C       D D P Y S A V 82         Tim PAPs_2 [FORM 0]./1-34       437       A0       C A G F F S G A A A G F C       D D P Y S A V 82         Tim PAPs_2 [FORM 0]./1-34       437       A0       C C G F F T S G A A A G F C       D D P Y S A V 82         Tim PAPs_2 [FORM 0]./1-34       437       A0       C C G F F T S G A A A G F C       D D P Y S A V 82         Tim PAPs_2 [FORM 0]./1-34       433       A0       C C G F F T S G A A A G F C       D D P Y S A V 82         SerPAPs_2 [FORM 0]./1-34       43       A0       C C G F F T S G A A A G F C       D O P Y S A V 82         SerPAPs_2 [FORM 0]./1-34       43       A0       C C F F T S G A A A G F C       D O P Y S A V 82         SerPAPs_2 [FORM 0]./1-34       43       A0 <td< td=""><td></td><td></td><td></td><td></td></td<>				
SPAPUP_27[FMWW]/J=34       440       A       C       PD P R K K H       F       C       C       F N TO P AA D R TC       D       D D P V S A V SS         To P P R K K H       F A       C       C       C A F N T S G A A A D R C       D       D D P V S A V SS         To P P R K K H       F A       C       C A F N T S G A A A D R C       D D P V S A V SS         To P P R K K H       F A       C A F N T S G A A A D R C       D D P V S A V SS         To P P R K K H       F A       C A F N T S G A A A D R C       D D P V S A V SS         To P P R K K H       F A       C A F N T S G A A A D R C       D D P V S A V SS         SP P N F, S P A A D R C       F A A D R C       C A F F N T S G A A A D R C       D D P V S A V SS         SP P N F, S P A A D R C       F A A D R C       C A F F N T S G A A A D R C       D D P V S A V SS         SP P N F, S P A A D R C       F A A D R C       F A A D R C       D D P V S A V SS       D D P V S A V SS         To P P R K F N D C A A D R C       F A A D R C       F A A D R C       F A A D R C       D D P V S A V SS         To P A P N J S N SS S S A D D       F A A D R C       F A A D R C       F A A D R C       D D P V S A V SS         S A A D D P V S A V SS S S A D D       F A A D R C       F A A D R C       F A A D R C	AtP AP 15   Q9 SF U3   / 1-532 4	435 🧕	A D D P V M - G F C A W N F T P S D K F C W D R Q P D Y S A	L 477
Tim PPup_12 i FOMW (1/54)       43       0       -	AtaPAPhy_a1/F6MIX0//1-549 4	437 🤺	A D E A F I - G F C A S N F T S G P A A G R F C W D R Q P D Y S A	Y 482
TorAPby_03/F0M W(1/33)       43       0       - <td>ScP APhy_a2   F6MIX4   /1-543 4</td> <td>440 A</td> <td>A D E A F I - G F C G F N F T S G P A A G R Y C W D R Q P D Y S A</td> <td>Y 485</td>	ScP APhy_a2   F6MIX4   /1-543 4	440 A	A D E A F I - G F C G F N F T S G P A A G R Y C W D R Q P D Y S A	Y 485
TOP #Phy_021 (EMSX) 1/-54       435       DC       Im #Phy_021 (EMSX) 1/-54       435       A00       Im #Phy_021 (EMSX) 1/-54       A35       C       Im #Phy_01 (EMSX) 1/-54       A35       C       Im #Phy_01 (EMSX) 1/-54       A35       C       Im #Phy_01 (EMSX) 1/-54	TmPAPhy_a1/F6MIW8//1-545 4	433 🗛	A D E A F I - G F C A S N F T S G P A A G R F C W D R Q P D Y S A	Y 478
scPePhy_01[F6XXV]/J-341       456       A D E       O E       C P D P E V E T       D E       C C P N E T S O P A A G V C       N       O E D V S A V 40         TorPAPhy_01[F6XXV]/J-334       438       A D D       O E       C P E L S T P D       D E H       C C A N E T S O P A A G S F C       O E D V S A V 40         TorPAPhy_01[F6XXV]/J-334       437       A D D       O E       C P E L S T P D       D E H       C C A N E T S O P A A G S F C       O E D V S A V 40         ScPAPhy_01[F6XXV]/J-334       437       A D D       O E       C P E L S T P D       O E H       C C A N E T S O P A A G S F C       O E D V S A V 40         ScPAPhy_01[F6XXV]/J-334       437       A D D       O E       O E P E L S T P D       O E H       C C A N E T S O P A A G S F C       O E Q P D V S A V 40         ScPAPhy_01[F6XXV]/J-334       437       A D D       O E D C D P D S T T P D       C E H       C C A N E T S O P A G S F C       O E Q P D V S A V 40         VPAPhy[V323Z/J-547       44       A D E       O E D C D P D IS T P D D       C F H       C C A N E T S O P A G S F C       O E Q P D V S A F 60         VPAPhy[V323Z/J-547       44       A D E       O C P P D IS T P D D       C F H       C C A N E T S O P A G S F C       O E Q P D V S A F 60         GW PAP/1/323Z T S A M S D D       O E D D D <td< td=""><td>TaP APhy a3 (F6MIW2 (/1-539 4</td><td>436 🗚</td><td>A D E</td><td>Y 481</td></td<>	TaP APhy a3 (F6MIW2 (/1-539 4	436 🗚	A D E	Y 481
scPePhy_01[F6XXV]/J-341       456       A D E       O E       C P D P E V E T       D E       C C P N E T S O P A A G V C       N       O E D V S A V 40         TorPAPhy_01[F6XXV]/J-334       438       A D D       O E       C P E L S T P D       D E H       C C A N E T S O P A A G S F C       O E D V S A V 40         TorPAPhy_01[F6XXV]/J-334       437       A D D       O E       C P E L S T P D       D E H       C C A N E T S O P A A G S F C       O E D V S A V 40         ScPAPhy_01[F6XXV]/J-334       437       A D D       O E       C P E L S T P D       O E H       C C A N E T S O P A A G S F C       O E D V S A V 40         ScPAPhy_01[F6XXV]/J-334       437       A D D       O E       O E P E L S T P D       O E H       C C A N E T S O P A A G S F C       O E Q P D V S A V 40         ScPAPhy_01[F6XXV]/J-334       437       A D D       O E D C D P D S T T P D       C E H       C C A N E T S O P A G S F C       O E Q P D V S A V 40         VPAPhy[V323Z/J-547       44       A D E       O E D C D P D IS T P D D       C F H       C C A N E T S O P A G S F C       O E Q P D V S A F 60         VPAPhy[V323Z/J-547       44       A D E       O C P P D IS T P D D       C F H       C C A N E T S O P A G S F C       O E Q P D V S A F 60         GW PAP/1/323Z T S A M S D D       O E D D D <td< td=""><td>TaP APhy a21C4PKK81/1-549 4</td><td>437 🔺</td><td>A D E</td><td>Y 482</td></td<>	TaP APhy a21C4PKK81/1-549 4	437 🔺	A D E	Y 482
TOPAPH_12/FGMV6/[1.38       433       0 <td>ScP APhy a 1/E6/MIX21/1-541 4</td> <td>436 🔺</td> <td>A D F</td> <td>Y 481</td>	ScP APhy a 1/E6/MIX21/1-541 4	436 🔺	A D F	Y 481
The Perpu DJ [F6 MW3 [/1-33       43       00	TaP APhy b3/F6MIW6//1-536 4	435 4	A D D	
Avp Phi_DLIGENXL/[1-33       437       00       0<			ADD	
ScP APU, b1F6MX3/L-338       32       00       0 </td <td>Atop APby, b1/E6MIX1//1-538 4</td> <td>437</td> <td>ADD DEM G. G. ECAENETS GPAAGS EC</td> <td></td>	Atop APby, b1/E6MIX1//1-538 4	437	ADD DEM G. G. ECAENETS GPAAGS EC	
Rchw JJSSW WG(J).356       43       0.0       P 0.0       P D S TTP 0       E FL       0.0       C P D Y S AY 508         Whe Al X5866/J.304       43       0.0       P 0.0       P 0.0       P 0.0       C P E S TTP 0       T FL       0.0       0.0       P 0.0       D P V S AY 508         Whe Al X5866/J.304       43       0.0       P 0.0				
VP.PP (NSSGE)[/1:40       435       0.0       P CATNETTED       FCATNETTEDPAGE				
P# P#NPi/03232/1/1546       443       A D E       OH Q D V S A F 487         WP PMV/03232/1/1547       443       A D E       OH Q D V S A F 487         WP PMV/03232/1/1547       443       A D E       OH Q D V S A F 487         WP PMV/03232/1/1547       443       A D E       OH Q D V S A F 487         WP PAV0/0427/1147       36       A D E       OH Q D V S A F 487         MP PA 23/060PH 1/1447       36       A D D       P V M Q D V S A F 487         MP PA 243/060PH 1/1447       36       A D D       P Q F XWA F 780         MP PA 21/2564       32       A D S D S I T F SR P T S V D T       A S N         OP P4 21/2564       39       A D S D S I T F SR P T S V D T       A S N         OP P4 21/2564       39       A D S D S I T F SR P T S V D T       A S N         OP P4 21/2564       39       A D S D S I T F SR P T S V D T       A S N         OP P4 21/2564       39       A D S D S I T F SR P T S V D T       A S N         OP P4 21/2564       39       A D S D S I T F SR P T S V D T       A S N         OP P4 21/2564       39       A D S D S I T F SR P T S V D T       A S N         OP P4 21/2564       39       A D S D S I T F SR P T S V D T       A S N P O P A A S A R P S O P V T N A A Q P P A M S R P O P A S A R P S O P V T N A A Q P A M		405		
WP APP/19374227/1/1547       444       0.E	VVP AP   A3 BGI 6  / 1-340 4	436	ADA	F 481
AP AP 15 107 L656 (1/1-52)       435       AD E       P G K       C P E L TT P D       P V M G C G .       F C A WH FT P .       5 C K F C .       W.       P D R D P X S AM 477         AP AP 23 (0 GPH 1/1/1-43       36       AD E       P G K .       C P H S Y D .       L F F       F N S L N L S N       458         GMP AP 1/1/2-41       214       .       .       N R Q F KW S E F       811       N R Q F KW S E F       811         MP AP 1/1/2-41       214       .	PVPAPhy/V/B324//1-546 4	443	ADE CONFICATION OF CONFICATIONO OF CONFICATION OF CONFICATIONO OF CONFICATIONO OF CONFICATIONO OF CONFICATIONO OF CONFICATIONO OF CONFICATION	F 487
APP #23 (GGTPH1/J-148       455       DD       P & K       C       H S S Y D       LF F       FN S L N L S N       MP       P K W S S V       FQ P XWS S F       FG P XWS S F	VrP APhy  B3 AR 27   / 1-347 4	444	ADE PGH. CPUPISTSD. HEN.G. G. FCATNFIPDUESTEPC. W. DRUPDYSA	F 488
GmPA4/V9HX64//142       369       ImpAP1/1242       369       ImpAP1/1244       244         MpPAP1/1244       224       GP Y G Q SWS       EP Q P XWS EF 381         GP Y G Q SWS       GP Y G Q SWS       EP Q P XWS F 288         GP Y G Q SWS       GP Y G Q SWS       EP Q P XWS F 288         GP Y G Q SWS       GP Y G Q SWS       EP Q P XWS F 288         GP Y G Q SWS       GP Y G Q SWS       EP Q P XWS F 288         GP Y G Q SWS       VD EI NP NN KY Y CEA LOT G GK SP VA LAAS NP S GWGP Q Y Q A HAP G C P TV T FQ P A       TSV DN - G LLV S NMT AA GQ P AMG FC         GP P A93/1-629       482       VD EI NP NN KY Y CEA LNY G G LG P V AMAAS KP S GWGP G Y Q T Q A HAP G C P TV T FQ P A       TSV DN - G LLV LS NMT AA GQ P AMG FC       0       NS Q P TWS AY 570         GP P A93/1-629       482       VD EI NP N T NK T Y CEA LNY G G LG P V AMAAS KP S GWGP G Y Q T Q A HAP G C P TV T FQ P A       TSV D N - G LLV LS NMT AA GQ P AMG FC       0       NS Q P TWS AY 570         GP A93/1-629       482       VD EI NP N T NK T Y CEA LNY G G LG P V AMAAS KP S GWGP G Y Q T Q A HAP G C P TV T FQ P A       TSV D N - G LLV LS NMT AA GQ P AMG FC       0       NS Q P TWS AY 570         GP A93/1-629       480       D Q	AIP AP 15   D7L636   / 1-532 4	435	ADEPVM_IGGFCAWNFTPSGKFCWDRIQPDYSA	M 477
MpPAP_J1-264       224       GP Y GQ SWS       FP Q P SWS A F       240         OP X P2/1-312       272       GP Y GQ SWS       FP Q P SWS A F       240         OP X P2/1-312       272       GP Y GQ SWS       FP Q P SWS A F       240         OP X P2/1-321       272       GP Y GQ SWS       FP Q P SWS A F       240         OP X P2/1-321       272       GP Y GQ SWS       FP Q P SWS A F       240         OP X P2/1-321       282       V D E I NP N N K TY C EA LOT GG K SP V A LA AS NP S GWOP GY Q R Q A HAP G CP TV T FQ P A       TS V DN       G I LV P S NMT AA G Q P AMG F C       Q       NS Q P TWS A H       570         OP X P3/1-629       482       V D E I NP N T N K TY C EA LOT GG K SP V A LA AS KP S GWOP GY Q R A HAP G CP TV T FQ P A       TS V DN       G I LV P S NMT AA G Q P AMG F C       Q       NS Q P TWS A H       570         OP X P3/1-637       486       D D       K DW       C EE V LN E F O FG R E DV D G D TMS F S F I R T ED G SV G D R LT LR SK I AP GD A C SS R AAWT LAS GRK QE D EE E Q D E E K E 544       MpPAP2/1-337       S FV V G S A G A G F TK T A T Y NA P F S D V TM       Y E Y GY LR I T V V NR T H LY G E F       722         MP AP X/1-339       465       SH       S V L M L A Y AAT G G A V       S FV V G S A G A G F TK T A T Y NA P F S D V TM       Y E Y GY LR I T V V NR T H LY G E F       722         MP AP X/1-339				
OP AP2/1-312       272       GP Y G N SWM       EP OP S Y S A F       288         OP AP2/1-356       433       AD S D S L T R FS R P T S Y D T       A S M       C T R P V Y T N A       T L V Y I A G       G L Y C F       T N A A S Q P M KG C       P       D T Q P AWS A R       489         OP AP2/1-621       482       V D E I N P N N N K T Y C E A L D T G G K S P V A LA A S N P S GWG P G Y Q T Q A H A P G C P T V T F Q P A       T S V D N       G L L V S N MT A A S Q P A MG F C       Q       N S Q P T WS A H       570         OP AP2/1-621       482       V D E I N P N T N K T Y C E A L N Y G G L G P V A MA A S K P S GWG P G Y Q T Q A H A P G C P T V T F Q P A       T S V D N       G L L V S N MT A A G Q P A MG F C       Q       N S Q P T WS A Y       570         OP AP2/1-631       622       V D E I N P N T N K T Y C E A L N Y G G L G P V A MA A S K P S GWG P G Y Q T Q A H A P G C P T V T F Q P A       T S V D N       G L L V S N MT A A G Q P A MG F C       Q       N S Q P T WS A Y       570         M P AP2/1-317       W G D Q       K D Q       K D Q       K D Q       K D Q A C S S R A A WT L A S G R X Q Q E E E Q D E E K E       564         M P AP2/1-332       45 S H       M D Q       V V H       A Y A A G A A Y       S F V Y G S A G A G F T T K A Y N A P F S D Y T M       Y E Y G Y H K I Y Y N R T H L Y G E 722         M P AP2/1-333       41 D M       M D Q       <		369 -		F 381
CPAP1/1-536       439       ADS DS LT R FS R P T S Y D T       AS N       CT R P V V TNA       T L V Y I AG       G       K I C P       T R D P V S GK Y C       P       D T Q P AWS AR       499         CPAP2/1-632       422       V D E I N P N TN K T Y C E AL LA T G GK S P V A LAA S N P S GW C G Y Q T Q A HA P G C P T V T F Q P A       T S V D N       G I L V P S NIT A A G Q P AMG F C       0       N S Q P T WS A H       570         CPAP2/1-631       422       V D E I N P N TN K T Y C E AL LA Y G G L G P V A MA A S K P S GW G Q Y Q T Q A HA P G C P T Y T F Q P A       T S V D N       G I L V P S NIT A A G Q P AMG F C       0       N S Q P T WS A H       570         CPAP2/1-631       480       D D Q       K D W       C E E V L N E F G F G R F D V D G D T MS F S F I R T E D G S V G O R L T R S K I A P G D A C S S R A AWT L A S G K A Q E Q E E K E 564         MpPAP2/1-832       662       N G D       V W H       A Y A A T G A A V       S F V V G S A G A G F T K T A T Y N A P F S D V T M       E       429         MpPAP2/1-832       643       N G D       Y W H       A Y A A T G A A V       S F V V G S A G A G F T K T A T Y N A P F S D V T M       F L V S G Y G A S G A G F T K T A T Y N A P F S D V T M       F L V G Y L R T T V N A P F S D V T M       F L V G Y L R T V V K G U V S R F       -       429         O P A P / 1/1-533       845       Y U H A Y A A T G A A V       S F V V G S A G A G F T K T A				F 240
CP AP 2/1-632       482       V D E I N P N N N K T Y C EA LQ T G G K S P V A LAA S N P S G WG P G Y Q R Q A HA P G C P T V T F Q P A       T S V D N       G I L V P S N M T AA G Q P A MG F C       Q       N S Q P T WS A H 570         CP AP 3/1-639       482       V D E I N P N N N K T Y C EA LUT G G L G P V A MAA S K P S G WG P G Y Q T Q A HA P G C P T V T F Q P A       T S V D N       G L V P S N M T AA G Q P A MG F C       Q       N S Q P T WS A H 570         CP AP 3/1-639       482       V D E I N P N N N K T Y C EA LUT G G L G P V A MAA S K P S G WG P G Y Q T Q A HA P G C P T V T F Q P A       T S V D N       G L V S N M T AA G Q P A MG F C       Q       N S Q P T WS A H 570         CP AP 3/1-639       482       D D Q       K D W       C E E V L N E F G F G R F D V D G D T MS F F I A T E D G S V A D R L T L R S K I A P G D A CS S R A W T L A S G R K Q E Q E E E Q D E E K S 64         M P P A2/1-832       662       N G D       V V H       A Y A A T G A V       S F V V G S A G A G F T K T A T Y N A P F S D V T M       Y E Y G Y L R I T V V N R T H L Y G E F 722         M P P A2/1-832       662       N G D       V V H       A Y A A T G A V       S F V V G S A G A G F T K T A T Y N A P F S D V T M       Y E Y G Y L R I T V V N R T H L Y G E F 722         M P P A2/1-533       K L D M       P G G       A Y A A T G A V       S F V V G S A G A G F T K T A T Y N A P F S D V T M       Y Y Y G Y L R I T V V N R T H L Y G E F 722         M P P A2/1-533       <				
CP AP3/1-629       482       V D E I N P N T N K T Y C EA LN Y G G L G P V AMAA SK P S G W G P G Y Q T Q A HA P G C P T Y T F Q P A       T S V D N       G L V L S NMT AA G Q P AMG F C       Q       O       N S Q P T WS A Y 570         CP AP4/1-691       622       VA N P L P       P W L       EHL G       L       W       636         CP AP5/1-637       KD Q       KD Q       CE EV LN E F G F G R F D V D G D T MS F S F I R T E D G S V G D R L T L R S K I A P G D A C S S R A AWT L AS G R K Q E Q E E E Q D E E K 564         Mp AP4/1-377       VV H       A Y A A T G A A V       S F V V G S A G A G F T K T A T Y N A P F S D V T M       Y E Y G Y L R I T V V N R T H L Y G E F 722         OP A P1/1-337       458       S H       P G G       A P V       S V L V       G       T G G A P H T K N A I G A S F M       E       98         Mp A P3/1454       415       P G G       A P V       S V L V       G       T G G A P H T K N A I G A S F M       E       98         Mp A P3/1454       415       P C A P A S (1 4 3 34       D M       P A R       V A K R T R A R       G C A Q A V V K G Q L V S R F       R R A P       442         C P A P (J 12546//1-614       523       N T       P A R       Y A H N G K S I T       H I N G M G N I E S H S E F S D G       E G L T N I T A L S 63         A M P P (J 25205//1-61457       S N Q Q	CrP AP 1/1-556 4	439 A	A D S D S L T R F S R P T S Y D T <mark> </mark>	R 499
CP AP 4/1-691       622       FRUE       FUE	CrP AP 2/1-632 4	482 🗸	V D E I N P N N N K T Y C E A L Q T G G K S P V A L A A S N P S G WG P G Y Q R Q A H A P G C P T V T F Q P A <mark> </mark>	H 570
CPAP5/1-637       486       DDQ       KDW       CEEV LNEEGEGR FDV DGD TMS FS FIRTEDGSV GDR LTLRSK IAP GDACSSRAAWTLASGRK QEQEE EQD EEK E 564         MpPAP2/1-337       MpPAP2/1-337       SFVVG SAGAG GFTK TATY NAP FS DV TM       YEYGYLR I TVVNR TH LY GE F 722         OIPAP1/1-539       465       SH       PGG       APV       SVL -V       G       TGGAP HTK NA I GAS FM       E       498         MpPAP2/1-832       65 SH       PGG       APV       SVL -V       G       TGGAP HTK NA I GAS FM       E       498         MpPAP3/1-54       415       PAR       VAK RTRAR       G       RV VR GQ LV SR F       E       498         MpPAP3/1-54       415       PAR       VAK RTRAR       G       RV VVR GQ LV SR F       E       442         GP AP6/1-435       384       LDM       DT RTRDA       LFLSDTQG       FV AVVLS GS QMR V HFY       TT EQS GP TY 426         A/P AP [Q12546]/1-614       523       NNT       TY       YAHNGKS IT       HI I N GMA GN I ES HS EF SD G       EG LT N I T AL 563         A/P AP [Q02200]/1-615       528       NQO       PNT       TNS GK SMT       HI I N GMA GN I ES HS & WED GO       EG L T N I T AL 563         LeP AP [Q02200]/1-615       529       0T D HF       TO SK K GS SMT       HI I N SM GG V I S SHS & WED GO & GG & GG & G	CrP AP 3/1-629 4	482 🚺	<u>V D E I N P N T N K T Y C E A L N Y G G L G P V AMAA S K P S GWGP G Y Q T Q A HA P G</u> C P T V T F <u>Q P A P T WS A</u>	Y 570
MpP AP4/1-377       Mp AP2/1-832       662       NGD       VVH       A YAATGAAV       S FVV GSA GAG FTK TATY NAP FS DVTM       Y EY GY LR I TVV NR TH LY GE F       722         OIP AP 1/1-539       469       SH       PGG       APV       SVL V       G       TGGA PH TK NA I GAS FM       E       498         MpP AP3/1-434       415       PAR       VA K R TR AR       G       RV V K G QL VS R F       R R A P       442         CP AP 6/1-435       384       LDM       D TR TR DA       LF LS DT Q G       FV AVV LS GS QMR V H FY       TT E QS GP TY       426         A/P AP (Q12546()/1-614       523       NN T       Y       Y A HN GK S I T       HI I N GMA GN I ES HS EFS D G       E G L T N TA L       563         A/P AP (Q32200)/1-618       528       NQ O       PNT       TNS GK SMT       HI I N GMA GN I ES HS EFS D G       E G L T I TA L       563         LeP AP (Q32201/1-518       540       DT FT       TNS GK SMT       HI I N GMA GN I ES HS       WFD GG       E G L T I TA L       563         MbP AP (D32205/1/1-539       407       TD H F       TG F       C NK GS GN P T QT LT LNS VR DV TVK S G G       S R D N GA T LY AD GS D G Q V E DA M       NV S S AA GK T 474         MbP AP (DA1RSY2F9/1/1-539       430       PT N       A LL FP Q P R       C	CrP AP 4/1-691 6	622 -		- 636
Minp AP (153)       Minp AP (153)<	CrP AP 5/1-637 4	486 🛛	D D Q	E 564
OPAP 1/1-539       469       SH       PGG       APV       SVL       V       G       TGGAP HTK NA IGAS FM       E       498         MpP AP3/1-454       415       PAR       VAKRTRAR       G       RV VVR GQLVSR F       RR AP       442         CPAP6/1-435       384       LDM       DTRTRDA       LFLSDTQG       FVAVVLSGSQMRVHFY       TTEQSGPT 426         A/P / Q12546/1-614       523       NNT       Y       VAKRTRAR       HI INGMA GNIESHSESD G       EG       LTNTK 426         A/P / Q12505//1-614       523       NNT       Y       VAHNGKSIT       HI INGMA GNIESHSESD G       EG       LTNTK 4563         AnidP AP (Q3200)/1-614       523       NO       TGT       CNK GS GNP P TOTLTLINSVR DV TV KS GG       S RD NGAT LYAD GS D GG QV LR GLMAW       NV S S A GKK 474         MbPAP (Q32005//1-539       407       TDHF       TGT       CNK GS GNP P TOTLTLINSVR DV TV KS GG       S RD NGAT LYAD GS D GG QV LR GLMAW       NV S S A GKK 474         MbPAP (Q3205//1-539       407       TDHF       G       VG GAV LR GLMAW       NV S S A GKK 474         MbPAP (P9WL81//1-529       435       PTN       ALL FP QP R       CQV IT - G       VG DF DP A I R R KP S I FV       L       ED A P - WS A F 381         MtubPAP (P9WL81//1-529       435 <td>MpPAP4/1-377</td> <td></td> <td></td> <td>-</td>	MpPAP4/1-377			-
MpPAP3/1454       415       PAR       VAKRTRAR       G       RV VVR GQLVSRF       RR AP       442         CPAP6/1435       384       LDM       DTRTRDA       LFLSDTQG       FVAVVLSGSQMRVHFY       TTEQSGFTY       426         A/P AP (212546/1-614       523       NNT       Y       YAHNGKSIT       HI INGMAGNIESHSEFSDG       EG       EG       LTITAL       563         AnidPAP (292200/1-614       528       NQQ       PNT       TNS GKSMT       HI I NGMAGNIESHSEFSDG       EG       EG       LTITAL       563         LeP AP (092200/1-614       528       NQQ       PNT       TNS GKSMT       HI I NGMAGNIESHSEFSDG       EG       LTITAL       569         LeP AP (092200/1-614       528       NQQ       PNT       TNS GKSMT       HI I NGMAGNIESHSEFSDG       EG       LTITAL       569         LeP AP (005205/1-539       407       TOHF       TGT       CNK GS SNPP TQTLTLINSVRDVTVKSGG       SR DN GATLVAD GSD GG QV LR GLMAW       NV S S A A GK K       474         MbPAP (A0AIR3Y2F9/1/1434       340       PTN       ALLFP QP R       CQV I T       G       VGD FDP A I RR KP S I FV       L       ED A P - WS A F 381         MtubPAP (P9WL81/1/529       435       PTN       ALLFP QP R       CQV I T       G	MpPAP2/1-832 6	662 🚺	N G D	F 722
MpPAP3/1454       415       PAR       VAKRTRAR       G       RV VVR GQLVSRF       RR AP       442         CPAP6/1435       384       LDM       DTRTRDA       LFLSDTQG       FVAVVLSGSQMRVHFY       TTEQSGFTY       426         A/P AP (212546/1-614       523       NNT       Y       YAHNGKSIT       HI INGMAGNIESHSEFSDG       EG       EG       LTITAL       563         AnidPAP (292200/1-614       528       NQQ       PNT       TNS GKSMT       HI I NGMAGNIESHSEFSDG       EG       EG       LTITAL       563         LeP AP (092200/1-614       528       NQQ       PNT       TNS GKSMT       HI I NGMAGNIESHSEFSDG       EG       LTITAL       569         LeP AP (092200/1-614       528       NQQ       PNT       TNS GKSMT       HI I NGMAGNIESHSEFSDG       EG       LTITAL       569         LeP AP (005205/1-539       407       TOHF       TGT       CNK GS GNP PTQTLTLINSVRDVTVKSGG       SR DN GATLVAD GSD GG QV LR GLMAW       NV S S A A GK K       474         MbPAP (A0AIR3Y2F9/1/1434       340       PTN       ALLFP QPR       CQV I T       G       VGD FDP A I RR KP S I FV       L       ED A P - WS A F 381         MtubPAP (P9WL81/1/529       435       PTN       ALLFP QPR       CQV I T       G	OIP AP 1/1-539 4	469 8	SH	- 498
A/P AP   Q12546i / 1-614       523       NNT       EG       LTN ITAL       563         AnicP AP   Q92200 / 1-618       528       NQQ       PNT       TNSGKSMT       HIINGMAGNIESHSEFSDG       EG       LTN ITAL       563         LeP AP   Q05205 / 1-539       407       TDHF       TDHF       CNK GS GNP FOLLTLINSVR DVTVK SGG       SR DNGAT LYAD GS DGGV LR GLAW       NV S SAA GKT       474         MbP AP   Q05205 / 1-539       407       TDHF       CNK GS GNP FOLLTLINSVR DVTVK SGG       SR DNGAT LYAD GS DGGV LR GLAW       NV S SAA GKT       474         MbP AP   Q05205 / 1-539       407       TDHF       CNK GS GNP FOLLTLINSVR DVTVK SGG       SC DNGAT LYAD GS DGGV LR GLAW       NV S SAA GKT       474         MbP AP   Q05205 / 1-539       407       TDHF       COV IT       G       VGD FOP A I R R KP SI FV       L       ED AP - WS AF       881         MtubPAP   P9WL81 / 1-529       435       PTN       ALL FP QP R       CQV I T       G       VGD FOP A I R R KP SI FV       L       ED AP - WS AF       476         BCPAP   B4B/R2 / 1/-561       457       AQ AK V FTK       PNR       PV P GT AP N       TV V       R       QP AD A L ED A I       W       SAP 503         BCPAP RP AP	MpP AP 3/1-454 4	415 -	P A R V A K R T R A R V A K R T R A R V Y A K R T R A P V Y R G U V S R F	- 442
A/P AP   Q12546i / 1-614       523       NNT       EG       LTN ITAL       563         AnicP AP   Q92200 / 1-618       528       NQQ       PNT       TNSGKSMT       HIINGMAGNIESHSEFSDG       EG       LTN ITAL       563         LeP AP   Q05205 / 1-539       407       TDHF       TDHF       CNK GS GNP FOLLTLINSVR DVTVK SGG       SR DNGAT LYAD GS DGGV LR GLAW       NV S SAA GKT       474         MbP AP   Q05205 / 1-539       407       TDHF       CNK GS GNP FOLLTLINSVR DVTVK SGG       SR DNGAT LYAD GS DGGV LR GLAW       NV S SAA GKT       474         MbP AP   Q05205 / 1-539       407       TDHF       CNK GS GNP FOLLTLINSVR DVTVK SGG       SC DNGAT LYAD GS DGGV LR GLAW       NV S SAA GKT       474         MbP AP   Q05205 / 1-539       407       TDHF       COV IT       G       VGD FOP A I R R KP SI FV       L       ED AP - WS AF       881         MtubPAP   P9WL81 / 1-529       435       PTN       ALL FP QP R       CQV I T       G       VGD FOP A I R R KP SI FV       L       ED AP - WS AF       476         BCPAP   B4B/R2 / 1/-561       457       AQ AK V FTK       PNR       PV P GT AP N       TV V       R       QP AD A L ED A I       W       SAP 503         BCPAP RP AP				
AnidPAP   Q92200 /1-618       528       N.Q.       P.N.T.       T.N.S.G.K.S.M.T.       H.I.I.N.G.       MG.G.N.I.E.S.H.S.       WFDEG.       E.G.LTEITAK       569         LeP AP   Q05205   /1-539       407       TDH F       TGT       C.N.K.G.S.G.N.P.T.Q.T.LT.L.N.S.V.R.DV.T.V.K.S.G.G.       S.R.D.N.G.A.T.LY.A.D.G.S.D.G.G.Q.V.L.G.LMAW       NV S.S.A.G.K.T. 474         MbP AP   A0A1R3Y2F9   /1-434       340       P.T.N.       A.L.L.F.P.Q.P.R.       C.Q.V.I.T.G.       V.G.D.F.P.A.L.F.P.S.F.V.       L       ED.A.P. WS.A.F. 381         MtubP AP   P9WL81   /1-529       435       P.T.N.       A.L.L.F.P.Q.P.R.       C.Q.V.I.T.G.       V.G.D.F.P.A.L.F.P.Q.P.R.       ED.A.P. WS.A.F. 476         BC PAP   B4B/K2 / /1-561       467       A.Q.A.K.V.F.T.K.       P.N.R.       P.N.R.       P.V.P.G.A.P.N.       T.V.P.R.       Q.P.A.D.A.L.E.P.Q.P.N.       S.A.F. 503         BC PAP   B4B/K2 / /1-561       467       A.Q.A.K.V.F.T.K.       P.N.R.       P.N.R.       P.V.P.G.A.P.N.       T.V.P.R.       Q.P.A.D.A.L.E.P.Q.P.N.       S.A.F. 503         BC PAP   B4B/K2 / /1-561       467       A.Q.A.K.V.F.T.K.       P.N.R.       P.V.P.G.A.P.N.       T.V.P.R.       Q.P.A.D.A.L.E.P.Q.P.N.       S.A.F. 503         BC PAP   B4B/K6 / / A.Q.A.K.V.F.T.K.       P.N.R.       P.V.P.G.A.P.N.       T.V.P.R.       Q.P.A.D.A.L.E.P.Q.P.N.       S.A.F.	A/P AP (012546)/1-614	523 👖	NNT	563
LeP AP   Q05205   /1-539       407       TDH F       TDH F       NV S S A G K T       474         MbP AP   A0 AIR3Y2F9   /1-434       340       PTN       A LL FP Q P R       CQV I T       G       V GD FD P A I R R K P S I FV       L       ED A P       WS S A A G K T       474         MbP AP   A0 AIR3Y2F9   /1-434       340       PTN       A LL FP Q P R       CQV I T       G       V GD FD P A I R R K P S I FV       L       ED A P       WS A F       381         MtubP AP   P9WL81   /1-529       435       PTN       A LL FP Q P R       CQV I T       G       V GD FD P A I R R K P S I FV       L       ED A P       WS A F       476         Browner AP   A0 ALV FTK       PTN       A LL FP Q P R       CQV I T       G       V GD FD P A I R R K P S I FV       L       ED A P       WS A F       476         Browner AP   A0 ALV FTK       PTN       A LL FP Q P R       CQV I T       G       V GD A P A DA LED A I       W       S A R       503         Browner AP   A0 ALV FTK       PNR       PV P GA P N       TEV P N       G       O DA V ED A I       S A P       503         Browner AP   A0 ALV FTK       PNR       PV P GA P N       TEV P N       G       O DA V ED A I       S A P       503	AnidP AP ( 092200 1 / 1-619	528		K 569
MbPAP   A0 AIR3Y2F9  /1434       340       PTN       ALLFP QPR       CQV I T       G       VGD FDP A I R R K P S I FV       L       ED AP       WSA F 381         MtubPAP   P9WL81   /1-529       435       PTN       ALLFP QPR       CQV I T       G       VGD FDP A I R R K P S I FV       L       ED AP       WSA F 476         BCPAP   84BK2 / /1-561       467       AQAKV FTK       PNR       PVP GTAP N       TVV       R       QP AD ALED AI       W       SA R 503         BmcPAP   40 ANUMP24 (/550       457       AQAKV FTK       PNR       PVP GTAP N       TVV       AD AV ED AI       SA P 503	LeP AP (005205)/1-520 A	407		
MtubPAP [P9WL81]/1-529       435       PTN       ALLFPQPR       CQVIT       G       VGDFDPAIRRKPSIFV       L       EDAP       BDAP       W       SAF 503         Bmm2P8 (AMANUMPSI():50, 457 NOAVYETK       PNR       PVPGTAPN       TFV       R       SAF 503         Bmm2N       PVPGTAPN       FVPGTAPN       FVPGTAPN       SAF 503	MAD AD LAD A 10 2 V 2 G 1 / 4 4 4 4	240		E 201
BCPAP/B4BK72//1-561 467 A QA K V F T K	NOT AF   AD ALKST2F5   / 1-434 3	425		F 470
	NITUDE AF (FSWL81)/1-529 4	+35 -	EDAP WSA	F 4/6
BMBY AP   AUAUM 2WHY 3   / 1-360 467   QARVETK Bp\$P AP   Q63X35   / 1-560 467   QARVETK W SAR 503	BCP AP   B4 BKK2  /1-561 4	46/	TEV-R UPADALEDAT	K 503
Bpsr Pr (L65X35)/1-560 467 EDA L SAR 503	Brand AP (AD ADH2 WHP3)/1-560 4	467	PURKVETK OT ADAVEDAT	K 503
	BpsPAP   Q63X35  /1-560 4	467	RUARVIELN. PVP GAAPN. SA	<u>R</u> 503

LUD ADD - LOADKID / A CAA															
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OsP APhy_b   D6QSX9   /1-539	483 R E	- S S F G H G I	LEVKN	IE	- THALWR -	WHR N Q I	) L Y - G S V - G D	E	I Y	IVREPDKC	- L I K -	S S R N R I	AYY		
ZmP APhy_b   C4PKL6   /1-544	488 R E	- S S F G H G V	L E V R N	ID	- THALWR -	WHR N Q (	DLHAANVAAD	E	V Y	IVREPDKC	- L	AKTARL	LAY		
MtP APhy   Q32FI 1   / 1-543	488 R E	- S S F G H G I	L E V K N	IE	- THALWS -	WNR NQ (	OYY-GTA-GD	E	I Y	IVRQPDKC	- P	P V MP E E	AHNT-		
PtPAP3/V9LXK5//1-564	505 R E	- S S F G H G I	LEVKN	IE	- THALWT -	WHR N Q (	DFY-EAA-GD	Q	I Y	IVRQPDLC	- P V Q P E -	- A Y R L N K P	К P Q		
NtP APhy   A5YBV11   /1-551	487 R E	- S S F G H G I	LEVKS	8 E	- THALWT -	WHR N Q (	DMY - NKA - GD	1	I Y	IVRQPEKC	- P V K P K -	V I K P W P	IGEYQ	FDWI	
LaP APhy   D2 YZL4   / 1-543	485 R E	- S S F G Y G I	LEVKN	IE	- TWALWS -	WYRNQ	DSY-NEV-GD	Q	I Y	IVRQPHLC	- PINQK -	V C R E Y F	AAI		
GmP APhy b/Q93XG4//1-547	489 R E	- S S F G Y G I	LEVKN	IE	- TWALWS -	WYRNQ	OSY-KEV-GD	Q	I Y	IVROPDIC	- PIHQR -	VNIDCI	A S I		
AtP AP 15   Q95FU3   /1-532	478 R E	- S S F G H G I	LEMKN	IE	- TWALWT -	WYR N 0.	DSS-SEV-GD	9	I Y	IVROPDRC	- P	LHHRLV	NHC		
AtaP APhy a 1/F6MIX0 //1-549	483 R E	- S S F G H G I	LEVKN	VE	- THALWR -	WHR NO.	DHY-GSA-GD	E	IY	IVREPHRC	- L HK -	HNSSRP	AHGRS	NTTRESG	G
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					T MALE L MALT	MV P N O I		0	L V	IVETEDMO	DTICA	VTVIWS	A A B		
								Q							
PvPAPhy/V7B3Z4//1-546	488 R E	- T S F G Y G I	LEVKN	IE	- TWALWS -	WYRNQ	ОSY-КЕV-GD	Q	I Y	IVRQPDIC	- P V P Q R -	V S G D F I	A S I		
P vP AP hy   V7 B3Z4   / 1-546 VrP AP hy   B5 AR Z7   / 1-547	488 R E 489 R E	- T S F G Y G I - T S F G Y G I	LEVKN LEVKN	V E	- TWALWS - - TWALWS -	WYRNQI WYRNQI	О S Y - К EV - G D О S Y - К EV - G D	Q	Y   Y	IVRQPDIC IVRQPDIC	- P V P Q R - - D V P R K -	V S G D F I V C R D F T	ASI ASI		
P vP AP hy   V7B3Z4   /1-546 VrP AP hy   B5ARZ7   /1-547 AIP AP 15   D7L636   /1-532	488 RE 489 RE 478 <u>RE</u>	- T S F G Y G I - T S F G Y G I - S S F G H G I	LEVKN LEVKN LEMKN	V E	- TWALWS - - TWALWS - - TWALWT -	WYRNQI WYRNQI WYRNQI	D S Y - K EV - G D D S Y - K EV - G D D S S - S Q V - G D	Q	Y   Y   Y	V R Q P D   C   V R Q P D   C   V R Q P D   C	- P V P Q R - - D V P R K - - P	V S G D F I V C R D F T L H H R L V	ASI ASI NHC		
P vP APhy   V7B324   /1-546 VrP APhy   B5ARZ7   /1-547 AIP AP 15   D7L636   /1-532 AtP AP 23   Q6TPH 1   /1-458	488 RE 489 RE 478 <u>RE</u> 	- T S F G Y G I - T S F G Y G I - S S F G H G I	LEVKN LEVKN LEMKN	VE	- TWA LWS - - TWA LWS - - TWA LWT -	WYRNQI WYRNQI WYRNQI	D S Y - K E V - G D D S Y - K E V - G D D S S - S Q V - G D	Q	Y   Y   Y	I V R Q P D I C I V R Q P D I C I V R Q P D R C	- P V P Q R - - D V P R K - - P	V S G D F I V C R D F T L H H R L V	ASI ASI NHC	<u> </u>	· · · · · · · · · · · ·
P vP APhy V783Z4 /1-546 VrP APhy B5ARZ7 /1-547 AIP AP 15 D7L636 /1-532 AtP AP 23 Q6TPH1 /1-458 GmP AP4 V9HXG4 /1-442	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u>	- T S F G Y G I - T S F G Y G I - S S F G H G I - A S F G H G E	LEVKN LEVKN <u>LEMKN</u>  LKIVN	N E	- TWA LWS - - TWA LWS - - TWA LWT - - THA FWS -	WYRNQI WYRNQI WYRNQI	D S Y - K EV - GD D S Y - K EV - GD D S S - S QV - GD D S - S PV K AD	Q	Y   Y   Y 	I V R Q P D I C I V R Q P D I C I V R Q P D R C I V R Q P D R C I V S S R C	- P V P Q R - - D V P R K - - P  - V - D Q K T I	V S G D F I V C R D F T L H H R L V  H E L R S T L L	ASI ASI <u>NHC</u> TP		
P vP AP hy   V783Z4   /1-546 VrP AP hy   85 AR Z7   /1-547 AP AP 15   D71.636   /1-532 AtP AP 23   Q6TPH 1   /1-458 GmP AP 4   V9HXG4   /1-442 MpP AP 1 /1-264	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u> 241 R E	- T S F G Y G I - T S F G Y G I - S S F G H G I - A S F G H G E - G S F G A G R	L E V K N L E V K N L E MK N  L K I V N L E I L N	N E	- TWA LWS - - TWA LWS - - TWA LWT - - THA FWS - - THA SWE -	WYRNQI WYRNQI WYRNQI WHRNDI WHRNDI	D S Y - K EV - G D D S Y - K EV - G D D S S - S Q V - G D D EP V K A D	Q	Y   Y   Y   W   T S	I V R Q P D I C I V R Q P D I C I V R Q P D R C I V R Q P D R C I V S S R C	- P V P Q R - - D V P R K - - P - V - D Q K T I	V S G D F I V C R D F T L H H R L V H E L R S T L L	ASI ASI NHC TP		
P vP APhy/V783Z4//1-546 VrP APhy/B5ARZ7//1-547 AIP AP 15/D7L636//1-532 AtP AP 23/Q6TPH1//1-458 GmP AP4/V9HXG4//1-442 MpP AP 1/1-264 OIP AP2/1-312	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u> 241 R E 289 R E	- T S F G Y G I - T S F G Y G I - S S F G H G I - A S F G H G E - G S F G A G R - G S F G A G S	LEVKN LEVKN LEMKN LEIVN LEINN LEINN	N E	- TWA LWS - - TWA LWS - - TWA LWT - - THA FWS - - THA SWE - - THA TWE -	WYRNQI WYRNQI WYRNQI WHRNDI WRR	DSY-KEV-GD DSY-KEV-GD DSS-SQV-GD DDEPVKAD	Q	- I Y - I Y - I WI T S	I V R Q P D I C I V R Q P D I C I V R Q P D R C I V R Q P D R C	- P V P QR - - D V P R K - - P - V - D QK T I	V S G D F I V C R D F T L H H R L V H E L R S T L L	ASI ASI NHC TP		
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P vP APhy/V783Z4//1-546 VrP APhy/85AR27//1-547 AP AP 15/D7L636//1-532 ArP AP 23/Q6TPH 1//1-458 GmP AP 4/V9HXG4//1-442 MpP AP 1/1-264 OIP AP 2/1-312 CrP AP 1/1-556 CrP AP 2/1-632	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u> 241 R E 289 R E 500 R E 571 R D	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGE - GS FGAGR - GS FGAGS - AAHGFVT - PS FGHAI	LE VKN LE VKN LE MKN LE ILN LE ILN LT IHN LD FLT LE LQS	N E	- TWA LWS - - TWA LWS - - TWA LWT - - THA FWS - - THA FWS - - THA TWE - - TRA VIK - - SVARFS -		D S Y - K EV - GD D S Y - K EV - GD D S S - S QV - GD D EP V K A D D G EA - T E E G N A V S MD	Q	- I Y	I V R Q P D I C I V R Q P D I C I V R Q P D R C I V R Q P D I C V R Q P D I C I V R Q P D I C V R Q P D I C I V R Q P D I C V R Q P D I C V R Q P D I C I V R Q P D I C V R Q P	- P V P QR - - D V P RK - - P - V - D QK T I  - P - A S R -	V S G D F I V C R D F T L H H R L V H E L R S T L L N Q A R K P MP S S EM	ASI ASI <u>NHC</u> <u>TP</u> RSVQR IMMGRR	Q	
P vP AP hy   V783Z4  /1-546 VrP AP hy   85 AR 27 //1-547 AP AP 15   071636  /1-532 AtP AP 23   06TPH 1  /1-458 GmP AP 4   V9HXG4  /1-442 MpP AP 1/1-264 OIP AP 2/1-632 CrP AP 2/1-652 CrP AP 2/1-629	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u> 241 R E 289 R E 500 R E 571 R D 571 R D	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGE - GS FGAGR - GS FGAGS - AAHGFVT - PS FGHAI - PS FGHAI	LE VKN LE VKN LE ILN LE ILN LT ILN LD FLT LE LQS LD LMS	N E	- TWA LWS - - TWA LWS - - TWA LWT - - THA FWS - - THA SWE - - THA TWE - - TRAV IK - - SVAR FS - - TSAH FR -		0 S Y - K EV - GD 0 S Y - K EV - GD 0 S S - S QV - GD 0 D EP V K AD 0 D EP V K AD 0 D G EA - T E 6 G - NAV S MD E G N - AV A - MD	Q Q D S D D	- I Y		- P V P QR - - D V P RK - - P - V - D QK T I  	V S G D F I V C R D F T L H H R L V HELRSTLL N Q A R K P M P S S EM A S R MA G	A S I A S I N H C T P R S V Q R IMMG R R	Q	
P vP APhy/V783Z4//1-546 VrP APhy/B5ARZ7//1-547 AIP AP 15/D7L636//1-532 AtP AP 23/Q6TPH1/1/1458 GmP AP4/V9HXC4//1442 MpP AP 1/1-264 OIP AP2/1-312 CrP AP 1/1-556 CrP AP2/1-632 CrP AP3/1-629 CrP AP4/1-691	488 R E 489 R E 478 <u>R E</u> 241 R E 289 R E 500 R E 571 R D 571 R D 637 -	- TS FGYGI - TS FGYGI - SS FGHGI - AS FGHGE - GS FGAGR - GS FGAGS - AAHGFVT - PS FGHAI - PS FGHAI - PS FGHAI	LE VKN LE VKN LE ILN LE ILN LT ILN LD LQS LE LMS ME AN	N E	- TWA LWS - - TWA LWS - - THA LWS - - THA FWS - - THA FWS - - THA FWE - - TRAV IK - - SVAR FS - - TSAH FR - - TSAH FR -		D S Y - K EV - G D D S Y - K EV - G D D S S - S QV - G D D D E P V K A D A P D - G E A - T E E G N A V S MD D G Q L - MD	Q Q D S D D D S	- I Y I Y I Y	IVRQPDIC IVRQPDIC IVRQPDIC LV-SSRC LTRDLS-C VLERLGAC VLERLGAC	- P V P Q R - - D V P R K - - P	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - NQARKP - ASRMAG AAAEAEAG	A S I A S I N H C T P R S V Q R IMMG R R MMG R R A R G	Q	
P vP AP hy   V7 8324  /1-546 VrP AP hy   85 AR27  /1-547 AIP AP 15   D7 L636  /1-532 AF AP 23   Q6TPH 1  /1-458 GmP AP 4   V9HXG4  /1-442 MpP AP 1/1-264 OIP AP 2/1-312 CrP AP 1/1-556 CrP AP 2/1-632 CrP AP 3/1-659 CrP AP 5/1-631 CrP AP 5/1-631	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u> 241 R E 289 R E 500 R E 571 R D 571 R D 637 - 565 E Q	- TS FGYGI - TS FGYGI - SS FGHGI - AS FGHGE - GS FGAGR - GS FGAGR - GS FGAGR - AHG FV T - PS FGHAI - PS FGHAI WG YMR - DQ EEQDQ	LE VKN LE VKN LE IVN LE I LN LE I LN LT I LN LD FLT LD LNS LD AN ED EEE	V E	- TWA LWS - - TWA LWS - - TWA LWS - - THA FWS - - THA SWE - - TRAV IK - - SVAR FS - - TSAH FR - - TSAH FR - - TSAH FR -		D S Y - K EV - G D D S Y - K EV - G D D S S - S QV - G D D E P V K A D A P D - G E A - T E E G - N A V S MD E G N - A V A - MD E G N - A Q L - MD E A E Q D Q E - D D	Q Q Q D D S D C C C C C C C C C C C C C C C C	- I Y I Y I Y	IVRQPDIC IVRQPDIC IVRQPDC LV-SSRC LTRDLS-C VLERLGAC VLERLGAC VLERLDSC LSKPADF	- P V P Q R - - D V P R K - - P - V - D Q K T I     	- VSGDFI - VCRDFT - LHHRLV - LHHRLV - NQARKP - NQARKP - MSSEM - ASRMAG AAAEAAEAG - SKLQLQ	A S I A S I N H C T P R S V Q R IMMG R R MMG R R A R G S A G A A	Q MMS A MMS A	
P vP APhy/V783Z4//1-546 VrP APhy/B5AR27//1-547 AIP AP 15/D7L636//1-532 AIP AP 23/Q6TPH 1/1-458 GmP AP 4/V9HXG4//1-442 MIP AP 1/1-264 OIP AP 2/1-312 CrP AP 1/1-556 CrP AP 2/1-632 CrP AP 3/1-629 CrP AP 3/1-631 OF AP 5/1-637 MIPP AP 4/1-377	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u> 241 R E 289 R E 500 R E 571 R D 637 - 565 E Q 374 -	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGI - GS FGAGR - GS FGAGR - AAHGFVT - PS FGHAI WGYMR - DQE EQDQ	LE VKN LE	V E	- TWA LWS - - TWA LWS - - TWA LWS - - THA FWS - - THA SWE - - THA TWE - - TRA V IK - - TRA V IK - - TS AH FR - - TS MR V E - DE QD E QD E E		D S Y - K EV - GD D S Y - K EV - GD D S S - S QV - GD D EPVKAD A P D - GEA - T E E G - NAV S MD E G N - AVA - MD D G Q L - MD C A E Q D Q E - D D	Q Q	- I Y I Y I Y I Y	LV S S R C LV S S R C LV S S R C L T R D L S - C V L E R L G A C V L E R L G A C V L E R L D S C A L S K P A D F E V R E Q G V D	- P V P QR - - D V P R K - - P - V - D QK T I - P - A - S R - - G E R FMA A /	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AAAEAEAG - SKLQLQ	A S I A S I N H C T P R S V Q.R IMMG R R MMG R R A R G S A G A A	Q	
P vP APhy/V783Z4//1-546 VrP APhy/B5AR27//1-547 AP AP IS B5AR27//1-547 AP AP 23/Q6TPH 1//1-458 GmP AP 4/V9HXG4//1-442 MpP AP 1/1-264 OIP AP 2/1-812 CrP AP 1/1-556 CrP AP 2/1-632 CrP AP 3/1-691 CrP AP 5/1-637 MpP AP 4/1-377 MpP AP 2/1-832	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u> 241 R E 289 R E 500 R E 571 R D 637 - 565 E Q 374 - 723 Q E	- TS FGYGI - TS FGYGI - SS FGHGE - GS FGAGR - GS FGAGR - GS FGAGR - AAHGFVT - PS FGHAI - PS FGHAI WGYMR - DQ E E QDQ - TQ FGK GV	LE VKN LE	N E	- TWA LWS - - TWA LWS - - TWA LWS - - THA FWS - - THA SWE - - THA SWE - - TRA VIK - - SVA FFS - - SVA FFS - - TS AH FR - - TS MR VE - DE QD E QD E E DADADAPT -		0 S Y - K EV - GD 0 S Y - K EV - GD 0 S S - S QV - GD 0 D EPVKAD 0 D G EA - T E E G NAV S MD E G N - AV A - MD 0 G Q L - MD 0 G Q L - MD 0 ND 8 F G S G Y T S E E	Q	- I Y I Y I Y	IVRQPDIC IVRQPDIC IVRQPDIC IVRQPDRC IVRQPDRC VLRLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC	- P V P QR - - D V P RK - - P - V - D QK T I - P - A S R -  G ER FMA A/  C LR G R R G	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - NQARKP - ASRMAG AAAEAEAG - SKLQLQ	A S I A S I N H C T P R S V Q.R IMMG R R MMG R R A R G S A G A A A D D D L	Q	EALIVSR
P vP AP hy V783Z4 //1-546 VrP AP hy   B5ARZ7 //1-547 AIP AP 15   D71636 //1-532 AtP AP 23   Q6TPH 1//1-458 GmP AP 4 / V9HXG4 //1-442 MPP AP 1/1-264 OIP AP 2/1-312 CrP AP 1/1-556 CrP AP 2/1-632 CrP AP 3/1-629 CrP AP 4/1-691 CrP AP 5/1-637 MPP AP 4/1-377 MPP AP 2/1-832 OIP AP 1/1-532	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u> 241 R E 289 R E 500 R E 571 R D 571 R D 571 R D 637 - 565 E Q 374 - 733 Q E 499 K E	- TS FGYGI - TS FGYGI - S FGHGE - GS FGAGR - GS FGAGS - AAHGFVT - PS FGHAI - PS FGHAI - PS FGHAI - TQ FGKGV LY EYGYVR	LE VKN LE	N E	- TWA LWS - - TWA LWS - - TWA LWS - - THA SWE - - THA SWE - - THA SWE - - TRA VIK - - SVAR FS - - SVAR FS - - TSAH FR - DEQD EQD E E DADADAP T - - TH - LYG -	WY R N QI WY R N QI WY R N QI WR R - WR R - Y F R N L J Y F R N L J WY K N L WY K N L V F K N L V F K N L V F K N L T K R K R T K R K R	D S Y - K EV - GD           D S Y - K EV - GD           D S Y - K EV - GD           D S S - S QV - GD           D D EP V KAD           D D GEA - TE           E G - NAVS MD           E G - A V A - MD           D G QL - MD           E A E QD QE - DD           S FGS GYTS EE           S AD - G QV - LD	Q Q D S D D S D S D E E E V E E T E A GAA LAA LAWLT A	- I Y	IVR QPDIC IVR QPDIC IVR QPDIC LVR SSRC VLR LGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC	- P V P QR - - D V P RK - - P  	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AAAEAEAG - SKLQLQ - FRDERV	ASI ASI NHC RSVQR IMMGRR MMGRR ARG - SAGAA ADDDL	Q	EALIVSR
P vP APhy/V783Z4//1-546 VrP APhy/B5AR27//1-547 AIP AP 15/D7L636//1-532 AIP AP 23/Q6TPH1//1-458 GmP AP 4/V9HXG4//1-442 MpP AP 1/1-264 OIP AP 2/1-312 CrP AP 1/1-556 CrP AP 2/1-632 CrP AP 3/1-631 CrP AP 5/1-637 MpP AP 4/1-832 OIP AP 1/1-539 MpP AP 3/1-454	488 R E 489 R E 478 <u>R E</u> 382 <u>R E</u> 241 R E 289 R E 500 R E 571 R D 637 - 565 E Q 374 - 723 Q E 499 K E 443 R Q	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGI - GS FGAGR - GS FGAGR - AAHGFVT - PS FGHAI - PS FGHAI WGYMRI - DQ EEQDQ TQ FGKGV - TQ FGKGV - RDVIHHV	LE VKN LE	I E	- TWA LWS - - TWA LWS - - TWA LWS - - THA SWE - - THA SWE - - THA SWE - - TRA VIK - - SVAR FS - - TSAH FR - - TSAH SWE - - TSAH SWE - - TH - LYG -		D S Y - K EV - G D D S Y - K EV - G D D S S - S QV - G D D E P V K A D A P D - G E A - T E E G - N A V S MD E G N - A V A - MD E G N - A V A - MD E A D Q E - D D S F G S G Y T S E E S A D - G G V - L	Q Q D S D D S D S D E E EV E ET EA GAA LAA LAWLT A	- I Y I Y	IVRQPDIC IVRQPDIC IVRQPDC IVRQPDC IVRQPDC VRRLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC VLERLGAC	- P V P QR - - D V P R K - - P	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AAAEAEAG - SKLQLQ - SKLQLQ	A S I A S I N H C R S V Q R IMMG R R MMG R R A R G - S A G A A - S A G A A -	Q	EALIVSR
P vP APhy/V783Z4//1-546 VrP APhy/B5AR27//1-547 AIP AP 15/D7L636//1-532 AIP AP 23/Q6TPH 1/1-458 GmP AP 4/V9HXG4//1-442 MIP AP 1/1-264 OIP AP 2/1-312 CP AP 1/1-556 CP AP 3/1-631 CP AP 3/1-631 CP AP 3/1-631 OIP AP 4/1-377 MIPP AP 4/1-372 MIP AP 4/1-332 OIP AP 1/1-539 MIP AP 3/1-454 CP AP 6/1-435	488 R E 489 R E 478 R E 2478 R E 241 R E 289 R E 500 R E 571 R D 571 R D 571 R C 374 - 723 Q E 499 K E 443 R Q 427 T R	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGI - GS FGAGR - GS FGAGR - GS FGAGR - A HGFVT - PS FGHAI - PS FGHAI - DQ E EQDQ - TQ FGKGV LY EVGYVR - RDV I HHV	LE VK N LE	V E	- TWA LWS - - TWA LWS - - TWA LWS - - THA FWS - - THA SWE - - THA SWE - - TRA VIK - - TRA VIK - - SVAR FS - - TSAH FR - - TSAH FR - DEQDEQDEE DADADAPT - - TH - LYG -		D S Y - K EV - G D D S Y - K EV - G D D S S - S QV - G D D E P V K A D A P D - G E A - T E E G - N A V S MD E G N - A V A - MD D G Q L - MD D G Q L - MD S F G S G Y T S E S A D - G G V - L D 	Q Q D S D D S D S D E E EV E E T E A GAA LAA LAWLT A	- I Y	V R Q P D I C I V R Q P D I C I V R Q P D R C I V R Q P D R C I V R Q P D R C V L R L G A C V L E R L G A C V A V A G A R A C I V R Q P D R C V A V A G A R A C V A V A G A R A C V A V A G A R A C V A V A V A V A V A V A V A V A V A V A	- P V P QR - - D V P R K - - P	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AAAEAEAG - SKLQLQ - FRDERV	ASI ASI NHC RSVQR IMMGRR MMGRR ARG - SAGAA ADDDL	0	EALIVSR
P vP APhy/V783Z4//1-546 VrP APhy/V783Z4//1-546 AP AP J5 [D7L636//1-532 AtP AP 23 [Q6TPH 1]/1-458 GmP AP 4   V9HXG4//1-442 MpP AP 1/1-264 OIP AP 2/1-832 OP AP 3/1-629 OP AP 3/1-637 MpP AP 4/1-837 MpP AP 4/1-837 MpP AP 2/1-832 OIP AP 1/1-539 MpP AP 3/1-454 OP AP 6/1-435 AP AP (212546)/1-614	488         R         E           499         R         E           478         R         E           382         R         E           241         R         E           289         R         E           500         R         E           571         R         D           637         -         -           765         E         Q           374         -         -           723         Q         E           443         R         Q           427         T         R           564         L         D	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGI - GS FGAGR - GS FGAGR - GS FGAGR - AAHGFVT - PS FGHAI - PS FGHAI WGYMR - DQ E EQDQ - TQ FGKGV LY EYGYVR - RDV I HHV	LE VKN LE VKN LE IKN LE ILN LT FLT LE LQS LD LQS LD LQS LD EEE LDR FA ITR LT AFN LR IFN	V E	- TWA LWS - - TWA LWS - - TWA LWS - - THA FWS - - THA SWE - - THA SWE - - TRA VIK - - SVA FFS - - SVA FFS - - TS AH FR - - TS MR VE - DE QD E QD E E DA DA DA PT - - TH - LY G -	WYRNQI WYRNQI WYRNQI WRR WRR WRR WRR YFRNLJ WYKNL WKR WRR WRR 	D         S         Y         K         E         G           D         S         Y         K         E         G           D         S         Y         K         E         G           D         S         Y         K         E         G           D         S         S         Q         Y         G           D         S         S         Q         Y         G           D         -         E         Q         -         -           A         P         D         G         E         -         -           A         P         D         G         E         -         -         -           C         -         -         N         N         S         M         -         -         N         N           S         F         G         Y         -         -         N         N         -         N	Q Q	- I Y	I V R Q P D I C I V R Q P D I C I V R Q P D R C I V R Q P D R C I V R Q P D R C V L R L D S C V L E R L D S C C S C S C S C S C S C S C S C S C	- P V P QR - - D V P RK - - P - P - P - A S R -  G ER F MA A A  C L R G R R G	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AAAEAEAG - SKLQLQ - FRDERV	A S I A S	Q	EALIVSR
P vP APhy/V783Z4//1-546 VrP APhy/B5AR27//1-547 AIP AP 15/D7L636//1-532 AIP AP 23/Q6TPH 1//1-458 GmP AP 4/V9HXG4//1-442 MIP AP 2/1-312 CrP AP 2/1-312 CrP AP 2/1-632 CrP AP 2/1-637 MIP AP 4/1-691 CrP AP 5/1-637 MIP AP 4/1-832 OIP AP 1/1-539 MIP AP 2/1-832 OIP AP 1/1-539 MIP AP 2/1-454 CrP AP 6/1435 AJP AP (212246//1-614 Anicl AP (202200//1-618	488         R         E           499         R         E           478         R         E           382         R         E           241         R         E           250         R         E           571         R         D           637         -         -           723         Q         E           499         K         E           427         T         R           564         R         Q           570         L         D	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGI - GS FGAGS - AAHGFVT - PS FGHAI - PS FGHAI - UQ EQDQ - TQ FGKGV LY EYGYUR - RDVIHHV KVHYGFSK KTHFGFSK	LE VKN LE VKN LE ILN LE ILN LT ILN LD FLT LE LQS LD FLT LE ASN ED EEE LDR FA ITR LT AFN LT IFN LT IFN	V E	- TWA LWS - - TWA LWS - - TWA LWS - - THA SWE - - THA SWE - - THA SWE - - THA SWE - - TSAH FR - - TALKWE - - TH - LYG - - TALKWE - - TALKWE -		D S Y - K EV - G D D S Y - K EV - G D D S S - S QV - G D D E P V K A D D G E A - T E E G - N A V S M D E G N - A V A - M D D G Q L - M D E A E Q D Q E - D D S F G S G Y T S E S A D - G G V - L D D G G V - L D D G G V - L D D G T V - G D	Q Q D S D D S D S D E E E V E E T E A GAA LAA LAWLT A S S E S E S	- I Y I Y	IVR QP DIC IVR QP DIC IVR QP DR C IVR QP DR C VL RL GA C VL ER LGA	- P V P QR - - D V P R K - - P	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AA EA EA G - SKLQLQ - FRDERV - FRDERV	A S I A A S I A N H C T P R S V Q R IMMG R R MMG R R A R G S A G A A  S A G A A  	Q	EALIVSR
P vP APhy/V783Z4//1-546 VrP APhy/B5AR27//1-547 AIP AP 15/D7L636//1-532 AIP AP 23/Q6TPH1//1-458 GmP AP 4/V9HXG4//1-442 MpP AP 1/1-264 OIP AP 2/1-312 CrP AP 2/1-632 CrP AP 2/1-651 CrP AP 2/1-651 CrP AP 2/1-651 CrP AP 4/1-651 CrP AP 4/1-651 OIP AP 4/1-377 MpP AP 4/1-377 MpP AP 4/1-359 OIP AP 1/1-539 MpP AP 3/1-454 CrP AP 6/1-435 AFP AP (Q12546)/1-614 AnidP AP (Q2200)/1-618	488         R         E           498         R         E           478         R         E           382         R         E           241         R         E           241         R         E           283         R         E           500         R         E           571         R         D           573         R         -           723         Q         E           493         R         Q           443         R         Q           427         T         R           570         K         E           443         R         Q           427         T         R           570         L         T	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGI - GS FGAGR - GS FGAGR - GS FGAGR - AHGFVT - PS FGHAI WGYMRI - DQ EEQDQ - DQ EEQDQ - TQ FGKGV - RDV IHVV - RDV IHVV - RDV IHVV	LE VKN LE	I E	- TWA LWS - - TWA LWS - - TWA LWS - - THA SWE - - THA SWE - - THA SWE - - TRA VIK - - SVAR FS - - TS AH FR - - TY U VU VU VU VU VI		D S Y - K EV - G D D S Y - K EV - G D D S S - S QV - G D D - E P V K A D D - E P V K A D C - G C A - T E E G - NAV S MD E G N - A V A - MD D - G Q L - MD S F G S G Y T S E E S A D - G G V - G D G T V - G D G T V - G D G T V - G D G S T - G D A S Y S G V S LG S	Q Q D S D D S D E E E V E E T E A GAALAALAWLT A S S E E K K	- I Y	I V R Q P D I C I V R Q P D I C I V R Q P D R C I V R Q P D R C I V R Q P D R C V L R L G S C V L E R L G S C S C V L E R L G S C S C S C S C S C S C S C S C S C S	- P V P QR - - D V P RK - - P	- VSGDFI - VCRDFT - UCRDFT - UCRDFT - NQARKP - NQARKP - MPSSEM - ASRMAG AAAEAEAG - SKLQLQ - SKLQLQ - SKLQLQ - SKLQLQ - VAGGKK - NQGKK	A S I A S I NHC T P T	Q	EALIVSR
P vP APhy/V783Z4//1-546 VrP APhy/V783Z4//1-547 AP AP 15/D7L636//1-532 AP AP 23/Q6TPH1//1-458 GmP AP 4/V9HXG4//1-442 MpP AP 1/1-264 OIP AP 2/1-312 OP AP 2/1-312 OP AP 2/1-632 OP AP 2/1-632 OP AP 2/1-631 OP AP 2/1-631 OP AP 4/1-691 OP AP 5/1-637 MpP AP 4/1-377 MpP AP 2/1-339 OIP AP 1/1-539 MpP AP 3/1-454 OP AP 6/1435 AJP AP (Q12546//1-614 AnidP AP (Q05205//1-539 MbP AP (ADA1R3Y2F3//1-434	488         R         E           498         R         E           478         R         E           382         R         E           244         R         E           244         R         E           283         R         E           500         R         E           571         R         D           637         -         -           723         Q         E           493         R         Q           427         T         R           570         K         E           443         R         Q           427         T         C           570         L         D           475         L         D	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGI - GS FGAGR - GS FGAGR - GS FGAGR - A HGFVT - PS FGHAI - PS FGHAI - DQ E EQDQ - DQ E EQDQ - TQ FGK GV L Y EYGYVR - RDVI HW - RDVI HW - RDVI HW - RDVI HWYGFSK RTHFGFSK - RDNP YGF	LE VKN LE VKN LE IHN LT IHN LT LT LE LQS LD FLT LE LQS LD EE LD EE LT AFN LT FN LT VKN SD RST	V E	- TWA LWS - - TWA LWS - - TWA LWS - - THA SWE - - THA SWE - - THA SWE - - TRA VIK - - SVAR FS - - TSAH FR - - TSAH FR - - TSAH FR - - DE QD E QD E E DA DA DA PT - - TH - LYG - - TH - LYG - - TYV NWE - - TYV LYRA - TYV LYRA		D S Y - K EV - GD           D S Y - K EV - GD           D S S - S QV - GD           D D - EPVKAD           D D - GEA - TE           E G - NAVS MD           E G - NAVS MD           E G - AVA - MD           D - G QL - MD           S FGS GYTS EE           S A D - G QV - GD           G QT S - GO           G S T - GO	Q Q D S D D D E E E V E E T E A GAA LAA LAWL T A S S K	- I Y	V R Q P D I C I V R Q P D I C I V R Q P D R C I V R Q P D R C I V R Q P D R C V L R L G A C V L E R L G A C A C V L E R L G A C A C V L E R L G A C A C A C A C A C A C A C A C A C A	- P V P QR - - D V P R K - - P	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AAAEAEAG - SKLQLQ - FRDERV - FRDERV - VAGGKK - QSIALN - QSIALN	A S I A S I NHC T P T P T P S A G A A A D D D L  S A G A A A D D D L  L H S V S G A A G F S R G G -	Q	EALIVSR
P vP. APhy/V78324//1-546 VrP APhy/V78324//1-546 VrP APhy/85 AR271/1-547 AP AP 15 [D7L636//1-532 AtP AP 23 [Q6TPH 1/1/1458 GmP AP 4  V9HXG4//1-442 MpP AP 1/1-264 O(P AP 2/1-632 OP AP 3/1-629 OP AP 3/1-629 OP AP 3/1-637 MpP AP 2/1-832 O(P AP 1/1-539 MpP AP 2/1-832 O(P AP 1/1-539 MpP AP 3/1-454 OP AP 6/1-435 AP AP (Q12546//1-614 AnidP AP (Q92200 //1-618 LeP AP (Q05205)/1-539 MbP AP (A0AIR3Y2F9//1-434 MtuD AP (P9WL81/1-529	488         R         E           493         R         E           478         R         E           382         R         E           241         R         E           283         R         E           241         R         E           283         R         E           501         R         D           571         R         D           637         -         -           723         Q         E           443         R         Q           443         R         Q           447         R         D           570         LD         S70           475         R         D           477         R         D	- TS FGYGI - TS FGYGI - SS FGYGI - SS FGYGI - GS FGAGR - GS FGAGR - GS FGAGR - AHGFVT - PS FGHAI - WGYMR - DQ E QDQ - TQ FGKGV LY EYGYVR - RDNPYGF - RDNPYGF - RDNPYGF	LE VKN LE VKN LE IKN LE ILN LT FLT LE LQS LD LQS LD LQS LD EE LDR FA ITR LT AFN LT FN LT FN VA FDV	V E	- TWA LWS - - TWA LWS - - TWA LWS - - THA FWS - - THA SWE - - THA SWE - - TRA VIK - - SVA FFS - - SVA FFS - - TS AH FR - - TS MR VE - DE QD E QD E E DA DA DA PT - - TH - LY G - - - TH - LY G - - - TY LYRA - TY D LYRA - STTS I KA T -		D S Y - K EV - GD           D S Y - K EV - GD           D S Y - K EV - GD           D S S QV - GD           D D EPVKAD           D D G QL - MD           S F G S GYT S EE           S AD - G GV - LD           G TV - GD           G TV - GD           G TV - GD           G T - GD           S F G S GYT S EE           S AD - G GV - LD           G T - GD           G T GP	Q Q	- I Y	IVR QP DIC           VIRLGAC           VIERLGAC           VIERLGAC           VIERLGAC           VIERLGAC           VIERLGAC           VIERLGAC           VIERLGAC           VIRD           IVRD           IVRD           IVRD           IVRD           IVRD           IVRD           VIPQ           IVRD           IVRD           IVRD	- P V P QR - - D V P R K - - P - P - P - A S R -  G ER F MA A A  C L R G R R G	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AAAEAEAG - SKLQLQ - FRDERV - FRDERV - VAGGKK - TIN - QSIALN - FTLTKP	A S I A A S I A T P	Q	EALIVSR
P vP APhy/V78324//1-546 VrP APhy/V78324//1-546 VrP APhy/85AR27//1-547 AIP AP 15/D7L636//1-532 AIP AP 25/D7L636//1-532 GmP AP 4/V9HXG4//1-442 MpP AP 1/1-264 OIP AP 2/1-312 GP AP 2/1-632 GP AP 2/1-632 GP AP 2/1-637 MpP AP 4/1-691 GP AP 2/1-637 MpP AP 2/1-832 OIP AP 2/1-832 OIP AP 2/1-832 OIP AP 2/1-353 MpP AP 3/1-454 GP AP 6/12256//1-614 AnidP AP (005205//1-539 MbP AP (A0ALR3Y2F5)/1-434 MtubP AP (A0ALR3Y2F5)/1-434 MtubP AP (A0ALR3Y2F5)/1-529 BcP AP (BALR3/2/1-561	488         R         E           489         R         E           478         R         E           382         R         E           241         R         E           289         R         E           500         R         E           571         R         D           637         -         7           723         Q         E           443         R         Q           447         T         R           564         L         D           5704         R         D           5704         R         D	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGI - GS FGAGR - GS FGAGS - AAHGFVT - PS FGHAI - PS FGHAI - DQ EEQDQ - TQ FGKGV - TQ FGKGV - TQ FGKGV - RDVIHHV - WHYGFSK RTHFGFSK GAQVKLQV - RDNPYGF - TG TGYGI	LE VKN LE VKN LE ILN LE ILN LT ILN LD FLT LE LQS LD FLT LE AS LT AFN LT AFN LT FDN SD RST VA FDV AV FDV	I       E	- TWA LWS - - TWA LWS - - TWA LWS - - THA SWE - - THA SWE - - THA SWE - - T HA SWE - - T SAH FR - - T SAH		D S Y - K EV - G D           D S Y - K EV - G D           D S S - S QV - G D           D D - E P V K A D           D D - G EA - T E           E G - NAV SMD           E G - NAV SMD           D - G EA - T E           E G - NAV SMD           B F G S G Y T S E E           S A D - G G V - L D           S A D - G G V - L D           S - G S T - G G           D - G G S T - G D           A S Y S G V S L G S           S P F G G L T - V I           S A D H P T A Q Y	Q Q D S D D S D E EV E E T E A GAA LAA LAWL T A S S E E V E T E A GAA LAA LAWL T A S B E E E E V E T E A GAA LAA LAWL T A S S E E E V E T E A GAA LAA LAWL T A S S E E V E T E A GAA LAA LAWL T A S S E E E V E E T E A GAA LAA LAWL T A S S E E E E V E E T E A GAA LAA LAWL T A S S E	- I Y I Y	I V R Q P D I C I V R Q P D I C I V R Q P D R C I V R Q P D R C I V R Q P D R C V L R L G A C V C A C A C A C V C A C A C A C V C A C A C A C A C V C A C A C A C A C A C A C A C A C A C	- P V P QR - - D V P R K - - P	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AAAEAEAEA - SKLQLQ - SKLQLQ - SKLQLQ - FRDERV - VAGGKK - TIN - QSIALN - FTLTKP	A S I A A S I A A S I A T P	Q	EALIVSR
P vP AP hy/V78324//1-546 VrP AP hy/V78324//1-546 VrP AP hy/E5 AR27//1-547 AP AP 15/D7L636//1-532 GmP AP 23 (06TPH 1//1-458 GmP AP 4/V9HXG4//1-442 MpP AP 1/1-256 OP AP 2/1-632 OP AP 2/1-632 OP AP 2/1-631 OP AP 2/1-631 OP AP 4/1-691 OP AP 4/1-691 OP AP 4/1-691 OP AP 4/1-877 MpP AP 4/1-837 MpP AP 4/1-377 MpP AP 4/1-614 OP AP 6/1-435 A/P AP (012546//1-614 AnidP AP (02200)/1-618 LeP AP (005205/1-539 MbP AP (A0AIR3Y2F9/1/1-434 MtubP AP (A0AIR3Y2F9/1/1-434	488         R         E           498         R         E           478         R         E           382         R         E           2441         R         E           284         R         E           2441         R         E           289         R         E           500         R         E           571         R         D           557         R         Q           374         -         -           723         Q         E           443         R         Q           427         T         R           570         L         T           382         R         L           570         L         T           382         R         L           477         R         D           504         R         D           504         R         R	- TS FGYGI - TS FGYGI - SS FGHGI - SS FGHGI - GS FGAGR - GS FGAGR - GS FGAGR - AHGFVT - PS FGHAI WGYMRI - DQ EEQDQ - TQ FGKGV - RDVIHV KVHYGFSK RTHFGFSK RTHFGFSK RTHFGFSK RDNPYGF - RDNPYGF - RDNPYGF - RDYGYGI - TGTGYGI	LE VKN LE	I       E	- TWA LWS - - TWA LWS - - TWA LWS - - THA SWE - - THA SWE - - THA SWE - - TRA VIK - - SVAR FS - - TS AH FR - - TS AH FR - - TS M FR - - TS CONTROL - - TY DLY - - TY DLY - - TY DLY - - TY DLY RA - TY SIKAT - - ST SIKAT - - SH TT I TMR - - SH TT VN -		D S Y - K EV - G D         D S Y - K EV - G D         D S S - S QV - G D         D D - E P V K A D         D D - G C A - T E         G C - NAV S MD         E G - NAV S MD         E G - AVA - MD         D - G QL - MD         S A D A G GV - G D         S F G S G Y T S E E         S A D A G GV - G D         G T V - G D         G T V - G D         G T V - G D         G T V - G D         G T V - G D         A S Y S GV S LG S         G P F G G L T - V I         G A D Q H P T A Q Y         G A D Q H P T A E Y	Q Q	- I Y I Y	IVRQPDIC           VIRL           IVRQC	- P V P QR - - D V P R K - - P	- VSGDFI - VCRDFT - LHHRLV HELRSTLL - NQARKP - MPSSEM - ASRMAG AAAEAEAG - SKLQLQ - S	A S I A S I NH C T P T P T P S A G A A A G G A A A D D D L  S A G A A A D D D L  S A G A A S A A G A S A S A A A G A S A S A A G A S A S A A A A A A A A A A A A A A A A	Q MMS A MMS A S A S L A A D E T D K E	EALIVSR

#### Table A2. PAP I motif conservation

Metal ligands are coloured in dark red. Conservation is shown in a blue to white gradient, with no substitutions with respect to the literature motif being the darker blue and over three substitutions being white. The PAPhy group includes characterised and predicted PAPhy sequences. The HMW Plant PAPs group includes HMW plant PAP and PAPhy outlier sequences. \*The two bacterial PAPs that contain GDLG PAP I motif have a four residues insertion in the middle (**GD**QSTPA**LG**).

		M	otif						Gro	up					
		PA	NP I			PAPhy	HMW Plant PAPs	HMW Animal PAPs	LMW Plant PAPs	LMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
Residue	1	2	3	4	Sequences	29	42	10	13	10	12	2	6	124	100
Literature	G	D	х	G	Substitutions	29	41	8	13	10	5	0	2	108	87.1
	G	D	L	G	0	28	36	1	0	0	0	0	2*	67	54.0
	G	D	W	G	0	0	0	0	13	10	2	0	0	25	20.2
	G	D	Μ	G	0	0	4	6	0	0	1	0	0	11	8.9
	G	D	т	G	0	0	0	1	0	0	2	0	0	3	2.4
	G	D	V	G	0	1	0	0	0	0	0	0	0	1	0.8
	G	D	Т	G	0	0	1	0	0	0	0	0	0	1	0.8
	А	D	Μ	G	1	0	0	0	0	0	3	0	0	3	2.4
	Ν	D	Μ	G	1	0	0	0	0	0	0	2	0	2	1.6
Observed	S	D	L	G	1	0	1	0	0	0	0	0	0	1	0.8
	А	D	V	G	1	0	0	0	0	0	1	0	0	1	0.8
	С	D	V	G	1	0	0	0	0	0	1	0	0	1	0.8
	А	D	Т	G	1	0	0	0	0	0	1	0	0	1	0.8
	G	D	L	А	1	0	0	0	0	0	0	0	3	3	2.4
	G	D	L	S	1	0	0	1	0	0	0	0	0	1	0.8
	G	D	Т	С	1	0	0	0	0	0	0	0	1	1	0.8
	А	D	V	S	2	0	0	0	0	0	1	0	0	1	0.8
	-	-	-	-	4	0	0	1	0	0	0	0	0	1	0.8

			Moti	f						Grou	ıp					
		I	ΡΑΡ Ι	I			PAPhy	HMW Plant PAPs	HMW Animal PAPs	LMW Plant PAPs	LMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
Residue	1	2	3	4	5	Sequences	29	42	10	13	10	12	2	6	124	100
Literature	G	D	x	x	Y	Substitutions	28	42	9	13	10	12	2	6	122	98.4
	G	D	L	S	Y	0	0	31	0	0	0	3	2	0	36	29.0
	G	D	Ν	F	Y	0	0	0	0	13	10	2	0	0	25	20.2
	G	D	V	S	Y	0	15	0	0	0	0	1	0	0	16	12.9
	G	D	F	А	Y	0	0	0	7	0	0	2	0	0	9	7.3
	G	D	L	С	Y	0	0	2	0	0	0	0	0	5	7	5.6
	G	D	V	С	Y	0	5	0	0	0	0	0	0	0	5	4.0
	G	D	V	Т	Y	0	5	0	0	0	0	0	0	0	5	4.0
	G	D	Μ	Т	Y	0	0	5	0	0	0	0	0	0	5	4.0
	G	D	Т	S	Y	0	0	2	0	0	0	1	0	0	3	2.4
Observed	G	D	L	Т	Y	0	1	1	0	0	0	0	0	0	2	1.6
Observed	G	D	L	А	Y	0	0	0	1	0	0	1	0	0	2	1.6
	G	D	А	S	Y	0	1	0	0	0	0	0	0	0	1	0.8
	G	D	А	Т	Y	0	1	0	0	0	0	0	0	0	1	0.8
	G	D	L	Ρ	Y	0	0	1	0	0	0	0	0	0	1	0.8
	G	D	Ν	T	Y	0	0	0	1	0	0	0	0	0	1	0.8
	G	D	Ν	S	Y	0	0	0	0	0	0	1	0	0	1	0.8
	G	D	Ν	Т	Y	0	0	0	0	0	0	1	0	0	1	0.8
	G	D	Ν	А	Y	0	0	0	0	0	0	0	0	1	1	0.8
	R	D	F	А	Y	1	0	0	1	0	0	0	0	0	1	0.8
	G	G	V	т	Y	1	1	0	0	0	0	0	0	0	1	0.8

 Table A3. PAP II motif conservation (See Table A2 caption)

		N	lotif						Grou	h					
		PA	AP III			PAPhy	HMW Plant PAPs	HMW Animal PAPs	LMW Plant PAPs	LMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
Residue	1	2	3	4	Sequences	29	42	10	13	10	12	2	6	124	100
Literature	G	Ν	н	E/D	Substitutions	29	40	10	13	10	9	2	6	119	96.0
	G	Ν	н	E	0	29	38	9	0	0	6	2	5	89	71.8
	G	N	н	D	0	0	2	1	13	10	3	0	1	30	24.2
0	А	N	н	Е	1	0	0	0	0	0	2	0	0	2	1.6
Observed	G	N	Y	Е	1	0	1	0	0	0	0	0	0	1	0.8
	G	D	н	D	1	0	0	0	0	0	1	0	0	1	0.8
	G	S	н	Е	1	0	1	0	0	0	0	0	0	1	0.8

Table A4. PAP III motif conservation (See Table A2 caption)

		М	otif						Grou	р					
		PA	P IV			PAPhy	HMW Plant PAPs	HMW Animal PAPs	LMW Plant PAPs	LMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
Residue	1	2	3	4	Sequences	29	42	10	13	10	12	2	6	124	100
Literature	v	х	х	Н	Substitutions	1	31	1	12	10	9	2	5	71	57.3
	V	L	М	Н	0	0	20	0	0	0	0	0	0	20	16.1
	v	V	G	н	0	0	0	0	9	1	1	0	0	11	8.9
	v	А	G	н	0	0	0	0	0	9	0	0	0	9	7.3
	v	L	V	н	0	0	5	0	0	0	0	0	0	5	4.0
	v	Т	G	н	0	0	0	0	3	0	1	0	0	4	3.2
	v	Q	М	н	0	0	0	0	0	0	0	0	3	3	2.4
	v	Q	F	н	0	0	0	0	0	0	2	0	0	2	1.6
	v	С	М	н	0	0	0	0	0	0	0	0	2	2	1.6
	v	М	S	н	0	0	0	0	0	0	0	2	0	2	1.6
	v	М	F	н	0	0	0	1	0	0	1	0	0	2	1.6
Observed	v	т	W	н	0	1	0	0	0	0	0	0	0	1	0.8
Observed	v	L	F	н	0	0	1	0	0	0	0	0	0	1	0.8
	v	L	L	н	0	0	1	0	0	0	0	0	0	1	0.8
	v	V	М	н	0	0	1	0	0	0	0	0	0	1	0.8
	v	V	т	н	0	0	1	0	0	0	0	0	0	1	0.8
	v	М	V	н	0	0	1	0	0	0	0	0	0	1	0.8
	v	Т	V	н	0	0	1	0	0	0	0	0	0	1	0.8
	v	G	G	н	0	0	0	0	0	0	1	0	0	1	0.8
	v	G	T	н	0	0	0	0	0	0	1	0	0	1	0.8
	v	н	G	н	0	0	0	0	0	0	1	0	0	1	0.8
	v	V	F	н	0	0	0	0	0	0	1	0	0	1	0.8
	А	G	W	н	1	17	0	0	0	0	0	0	0	17	13.7

Table A5. PAP IV motif conservation (See Table A2 caption)

	М	otif						Grou	ıp					
	PAI	P IV			PAPhy	HMW Plant PAPs	HMW Animal PAPs	LMW Plant PAPs	LMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
А	Т	W	Н	1	7	0	0	0	0	0	0	0	7	5.6
А	А	W	н	1	0	4	0	0	0	0	0	0	4	3.2
А	S	W	н	1	2	1	0	0	0	0	0	0	3	2.4
А	Y	F	н	1	0	0	0	0	0	0	0	1	1	0.8
А	А	W	н	1	1	0	0	0	0	0	0	0	1	0.8
А	V	G	н	1	0	0	0	1	0	0	0	0	1	0.8
А	М	W	н	1	0	0	0	0	0	1	0	0	1	0.8
А	т	Μ	н	1	0	1	0	0	0	0	0	0	1	0.8
А	L	W	н	1	0	1	0	0	0	0	0	0	1	0.8
А	V	V	н	1	0	1	0	0	0	0	0	0	1	0.8
Т	М	G	н	1	0	0	3	0	0	0	0	0	3	2.4
т	Y	G	н	1	0	0	3	0	0	0	0	0	3	2.4
т	F	G	н	1	0	0	1	0	0	0	0	0	1	0.8
F	L	А	н	1	0	2	0	0	0	0	0	0	2	1.6
F	S	А	н	1	0	1	0	0	0	0	0	0	1	0.8
F	А	G	н	1	0	0	0	0	0	1	0	0	1	0.8
L	Y	G	н	1	0	0	1	0	0	0	0	0	1	0.8
L	G	G	н	1	0	0	0	0	0	1	0	0	1	0.8
T	S	G	н	1	0	0	1	0	0	0	0	0	1	0.8
А	G	w	Y	2	1	0	0	0	0	0	0	0	1	0.8

		Mo	otif						Gro	up					
		РА	ΡV			PAPhy	HMW Plant PAPs	HMW Animal PAPs	LMW Plant PAPs	LMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
Residue	1	2	3	4	Sequences	29	42	10	13	10	12	2	6	124	100
Literature	G	н	х	н	Substitutions	29	42	2	13	10	12	2	6	116	93.5
	G	н	V	Н	0	28	42	0	0	0	6	0	0	76	61.3
	G	н	D	н	0	0	0	1	13	7	1	0	4	26	21.0
	G	н	Е	н	0	0	0	0	0	3	2	0	2	7	5.6
	G	н	Т	н	0	1	0	0	0	0	0	2	0	3	2.4
Observed	G	н	N	н	0	0	0	0	0	0	2	0	0	2	1.6
	G	н	К	н	0	0	0	1	0	0	0	0	0	1	0.8
	G	н	н	н	0	0	0	0	0	0	1	0	0	1	0.8
	А	Н	Е	н	1	0	0	8	0	0	0	0	0	8	6.5

Table A6. PAP V motif conservation (See Table A2 caption)

#### Table A7. PAPhy 1 motif conservation

Conservation is shown in a blue to white gradient, with no substitutions with respect to the literature motif being the darker blue and over three substitutions being white. Substitutions are shown in bold. LMW PAPs were not included in the PAPhy motif analysis.

									Mo	tif												G	iroup					
									PAP	hy 1									PAPhy	Predicted PAPhy	PAPhy outliers	HMW Plant PAPs	HMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
Residue	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Sequences	14	15	2	40	10	12	2	6	101	100
Literature	R	G	H/V/Q/N	А	V/I	D	L/	I P	D/E	ΞТ	D	Р	R/L	V	Q	R	R/N/T	Substitutions	10	10	0	0	0	0	0	0	20	19.8
	R	G	Н	А	V	D	L	Ρ	D	Т	D	Ρ	R	V	Q	R	R	0	8	10	0	0	0	0	0	0	18	17.8
	R	G	Ν	А	V	D	I	Р	D	т	D	Ρ	L	V	Q	R	Ν	0	1	0	0	0	0	0	0	0	1	1.0
	R	G	Н	А	V	D	L	Р	D	Т	D	Р	R	V	Q	R	т	0	1	0	0	0	0	0	0	0	1	1.0
	R	G	Q	А	Т	D	L	Ρ	D	т	D	Ρ	R	V	R	R	R	1	1	0	0	0	0	0	0	0	1	1.0
	R	G	V	А	V	D	L	Ρ	E	Т	D	Ρ	R	V	R	R	R	1	1	0	0	0	0	0	0	0	1	1.0
	R	G	Ν	т	Т	D	L	Ρ	D	Т	D	Ρ	R	V	Q	R	т	1	1	0	0	0	0	0	0	0	1	1.0
	R	G	Н	А	Т	D	L	Р	D	S	D	Р	R	V	Q	R	Т	1	0	1	0	0	0	0	0	0	1	1.0
	R	G	к	А	I	D	L	Р	D	Т	D	Ρ	R	V	R	R	R	2	0	1	0	0	0	0	0	0	1	1.0
	R	G	К	А	V	D	L	Р	D	Т	D	Р	R	V	R	R	R	2	0	1	0	0	0	0	0	0	1	1.0
Observed	R	G	Ν	А	V	D	L	Р	Р	S	D	Р	R	V	R	R	R	3	0	1	0	0	0	0	0	0	1	1.0
Observed	Р	т	V	S	Ι	D	L	Р	D	Т	D	Р	R	V	R	R	Ν	4	1	0	0	0	0	0	0	0	1	1.0
	R	R	G	S	V	D	L	L	Р	Т	D	Р	R	V	Α	К	т	7	0	0	0	1	0	0	0	0	1	1.0
	R	R	G	S	D	D	L	Р	м	т	н	Ρ	R	L	R	К	Ν	9	0	1	0	0	0	0	0	0	1	1.0
	R	Q	G	S	Ν	D	v	Р	L	Т	D	Ρ	R	L	Α	Ρ	R	9	0	0	0	1	0	0	0	0	1	1.0
	R	Q	G	S	D	D	v	Ρ	L	Т	D	Ρ	R	L	Α	Р	R	9	0	0	0	1	0	0	0	0	1	1.0
	R	Q	G	s	D	D	v	Р	L	т	D	Р	R	L	v	Р	R	9	0	0	0	1	0	0	0	0	1	1.0
	R	R	G	S	D	D	L	Р	м	D	н	Р	R	L	R	к	R	10	0	0	1	0	0	0	0	0	1	1.0
	R	R	G	s	Е	D	v	Р	L	S	D	Р	R	L	Α	Р	R	10	0	0	0	1	0	0	0	0	1	1.0
	R	Q	G	S	D	Е	v	Ρ	I	Т	Ε	Ρ	R	L	Α	Ρ	С	12	0	0	0	1	0	0	0	0	1	1.0
	R	R	s	L	V	Ε	Q	D	s	v	Α	D	Α	R	L	Q	R	14	0	0	0	0	0	1	0	0	1	1.0

			Ν	/lotif								Group					
			PA	Phy 2				PAPhy	Predicted PAPhy	PAPhy outliers	HMW Plant PAPs	HMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
Residue	1	2	3	4	5	6	Sequences	14	15	2	40	10	12	2	6	101	100
Literature	S	V/I	V	R/Q	Y/F	G	Substitutions	13	13	0	0	0	0	0	0	26	25.7
	S	V	V	R	Y	G	0	9	11	0	0	0	0	0	0	20	19.8
	S	- I	V	Q	Y	G	0	1	0	0	0	0	0	0	0	1	1.0
	S	V	V	Q	F	G	0	1	1	0	0	0	0	0	0	2	2.0
	S	V	V	Q	Y	G	0	2	1	0	0	0	0	0	0	3	3.0
	S	V	V	н	Y	G	1	1	0	0	0	0	0	0	0	1	1.0
	S	V	V	L	Y	G	1	0	1	0	0	0	0	0	0	1	1.0
	S	V	V	E	Y	G	1	0	0	0	1	0	0	0	0	1	1.0
	S	V	V	Е	Y	G	1	0	0	0	0	1	0	0	0	1	1.0
	S	I	V	Е	Y	G	1	0	0	0	0	2	0	0	0	2	2.0
	S	т	V	R	Y	G	1	0	0	0	1	0	0	0	0	1	1.0
	S	E	V	R	Y	G	1	0	0	0	1	0	0	0	0	1	1.0
	S	E	V	Q	F	G	1	0	0	0	0	2	0	0	0	2	2.0
Observed	S	к	V	Q	Y	G	1	0	0	0	1	0	0	0	0	1	1.0
	S	к	V	Q	F	G	1	0	0	0	1	0	0	0	0	1	1.0
	S	V	V	Q	Y	Α	1	0	0	0	0	0	1	0	0	1	1.0
	D	V	V	R	Y	G	1	0	0	0	0	0	1	0	0	1	1.0
	S	E	V	w	Y	G	2	0	1	1	3	0	0	0	0	5	5.0
	S	Y	V	E	Y	G	2	0	0	1	0	0	0	0	0	1	1.0
	S	Μ	V	E	Y	G	2	0	0	0	1	0	0	0	0	1	1.0
	S	т	V	F	Y	G	2	0	0	0	1	0	0	0	0	1	1.0
	S	E	V	L	Y	G	2	0	0	0	1	0	0	0	0	1	1.0
	S	E	V	v	Y	G	2	0	0	0	1	0	0	0	0	1	1.0
	S	Q	V	н	Y	G	2	0	0	0	1	0	0	0	0	1	1.0
	S	R	V	E	Y	G	2	0	0	0	0	1	0	0	0	1	1.0
	Р	Α	V	R	w	G	3	0	0	0	0	0	0	1	0	1	1.0
	Р	S	V	R	W	G	3	0	0	0	0	0	0	1	0	1	1.0

Table A8. PAPhy 2 motif conservation (See Table A7 caption)

							Motif										G	iroup					
							PAPhy 3							PAPhy	Predicted PAPhy	PAPhy outliers	HMW Plant PAPs	HMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
Residue	1	2	3	4	5	6	7	8	9	10	11	12	Sequences	14	15	2	40	10	12	2	6	101	100
Literature	А	Μ	S	х	х	H/Y	A/Y/H	F	R/K	Т	Μ	Р	Substitutions	14	10	0	0	0	0	0	0	24	23.8
	А	Μ	S	А	V	Н	А	F	R	Т	Μ	Ρ	0	6	7	0	0	0	0	0	0	13	12.9
	А	Μ	S	D	Т	Н	А	F	R	Т	Μ	Ρ	0	1	0	0	0	0	0	0	0	1	1.0
	А	Μ	S	G	V	Н	А	F	R	Т	Μ	Ρ	0	1	0	0	0	0	0	0	0	1	1.0
	А	Μ	S	D	V	Н	Y	F	R	Т	Μ	Р	0	1	0	0	0	0	0	0	0	1	1.0
	А	Μ	S	G	Т	Y	Y	F	R	Т	Μ	Р	0	1	0	0	0	0	0	0	0	1	1.0
	А	Μ	S	Т	Т	Y	Н	F	К	Т	Μ	Ρ	0	1	0	0	0	0	0	0	0	1	1.0
	А	Μ	S	D	Т	Y	Y	F	R	Т	Μ	Р	0	2	1	0	0	0	0	0	0	3	3.0
	А	Μ	S	К	Т	Н	Н	F	R	Т	Μ	Р	0	1	1	0	0	0	0	0	0	2	2.0
	Α	Μ	S	D	I	Y	Н	F	R	Т	Μ	Р	0	0	1	0	0	0	0	0	0	1	1.0
	A	Μ	S	N	I	Y	S	F	R	Т	Μ	Р	1	0	1	0	0	0	0	0	0	1	1.0
	т	Μ	S	A	V	Н	A	F	R	Т	Μ	Р	1	0	1	0	0	0	0	0	0	1	1.0
Observed	A	Т	S	A	V	Н	A	F	R	Т	Μ	Р	1	0	2	0	0	0	0	0	0	2	2.0
	A		S	Q	E	R	F	F	E	Т	F	Р	4	0	1	0	0	0	0	0	0	1	1.0
	A	Μ	S	E	E	I	S	F	E	Т	L	Р	4	0	0	1	0	0	0	0	0	1	1.0
	G	L	S	D	E	R	S	F	R	Т	L	Р	5	0	0	0	1	0	0	0	0	1	1.0
	G	L	S	D	E	Н	S	F	Т	Т	L	Р	5	0	0	0	1	0	0	0	0	1	1.0
	Т	F	S	A	E	H -	S	F	Т	Т	L	Р	5	0	0	0	1	0	0	0	0	1	1.0
	G	w	S	A	1	F	Q	F	R	T	V	Р	5	0	0	0	0	1	0	0	0	1	1.0
	G	w	S	A	V	F	N	F	к	T	Р 	P	5	0	0	0	0	1	0	0	0	1	1.0
	G	w	S	A	E	F	Y	F	H	і т	T T	P	5	0	0	0	0	1	0	0	0	1	1.0
	ĸ	D	S	A	V	R	S	F	к т	I T	т	P	5	0	0	0	0	0	1	0	0	1	1.0
	G	L	S	D	E	R	S	F	T	і т	L	P	6	0	0	0	1	0	0	0	0	1	1.0
	G	L	S	G	E	L	S	F	E	I C	L	P	6	0	0	0	2	0	0	0	0	2	2.0
	G	w	S	К	E	Y	S	F	v	S	Α	Р	6	0	0	0	0	0	1	0	0	1	1.0

Table A9. PAPhy 3 motif conservation (See Table A7 caption)

	Motif													e	iroup										
							P	APhy	4							PAPhy	Predicted PAPhy	PAPhy outliers	HMW Plant PAPs	HMW Animal PAPs	Microalgal PAPs	Fungal PAPs	Bacterial PAPs	Total	%
Residue	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Sequences	14	15	2	40	10	12	2	6	101	100
Literature	D	С	Y	S	С	S/A	F	х	х	х	Т	Р	Ι	н	Substitutions	13	12	0	0	0	0	0	0	25	24.8
	D	С	Y	S	С	S	F	G	К	S	Т	Ρ	Т	н	0	1	0	0	0	0	0	0	0	1	1.0
	D	С	Y	S	С	А	F	G	К	S	Т	Ρ	Т	н	0	1	6	0	0	0	0	0	0	7	6.9
	D	С	Y	S	С	S	F	Α	К	S	Т	Ρ	1	н	0	4	3	0	0	0	0	0	0	7	6.9
	D	С	Y	S	С	S	F	А	Ν	S	Т	Ρ	I.	н	0	1	1	0	0	0	0	0	0	2	2.0
	D	С	Y	S	С	А	F	Α	К	S	Т	Ρ	1	н	0	1	0	0	0	0	0	0	0	1	1.0
	D	С	Y	S	С	S	F	S	Ν	-	Т	Ρ	I.	н	0	1	0	0	0	0	0	0	0	1	1.0
	D	С	Y	S	С	S	F	Ν	D	-	т	Ρ	I	н	0	1	0	0	0	0	0	0	0	1	1.0
	D	С	Y	S	С	S	F	Ρ	Н	-	Т	Ρ	1	н	0	1	0	0	0	0	0	0	0	1	1.0
	D	С	Y	S	С	S	F	Ρ	L	-	Т	Ρ	I.	н	0	1	0	0	0	0	0	0	0	1	1.0
	D	С	Y	S	С	S	F	Ρ	Е	-	Т	Ρ	I	н	0	1	1	0	0	0	0	0	0	2	2.0
Observed	D	С	Y	S	С	S	F	Р	Q	-	Т	Ρ	I.	Н	0	0	1	0	0	0	0	0	0	1	1.0
	D	С	Y	S	С	S	F	А	Ν	-	S	Ρ	I	н	1	1	0	0	0	0	0	0	0	1	1.0
	D	С	Y	К	С	А	F	Р	Q	-	Т	Р	I	Н	1	0	1	0	0	0	0	0	0	1	1.0
	D	С	Y	К	С	S	F	Р	Q	-	S	Ρ	I	н	2	0	1	0	0	0	0	0	0	1	1.0
	S	С	Y	S	С	А	F	Ρ	D	-	Α	Р	I	R	3	0	1	0	0	0	0	0	0	1	1.0
	Ρ	С	F	S	С	S	F	Р	D	-	Α	Ρ	Ι	R	4	0	0	1	1	0	0	0	0	2	2.0
	Ρ	С	F	S	С	S	F	Ρ	К	-	Α	Ρ	Ι	R	4	0	0	0	1	0	0	0	0	1	1.0
	Ρ	С	F	S	С	S	F	Ρ	Ν	-	Α	Ρ	Ι	R	4	0	0	0	1	0	0	0	0	1	1.0
	Ρ	С	Y	S	С	А	F	Ρ	D	-	S	Ρ	т	R	4	0	0	0	1	0	0	0	0	1	1.0
	Ρ	С	F	S	С	S	F	Ρ	D	-	Α	Ρ	L	R	5	0	0	0	2	0	0	0	0	2	2.0
	D	Ν	Y	G	Α	L	S	Ρ	D	D	L	G	D	S	9	0	0	0	0	0	1	0	0	1	1.0
	D	Ν	Y	G	Α	L	D	Т	Е	V	R	Ν	S	К	9	0	0	0	0	0	1	0	0	1	1.0

## Table A10. PAPhy 4 motif conservation (See Table A7 caption)

#### Table A11. BLASTP search of PAPhy consensus against the non-redundant protein sequences database

Results table for the BLAST search performed against the whole non-redundant protein sequences database using the PAPhy consensus sequence as query. Results shaded pink correspond to already characterised or predicted PAPhy.

Accession #	Description	Score (Bits)	E Value
AEO00268.1	recTaPAPhy_b2_delta_C-t_cMyc_6xHIS [synthetic construct]	1015	0
AEE99723.1	PAPhy_b2 [Triticum aestivum]	1013	0
ACR23329.1	purple acid phosphatase isoform b2 [Triticum aestivum]	1012	0
AEO00269.1	recTaPAPhy_b2_delta_C-t_6xHIS [synthetic construct]	1010	0
AEE99733.1	PAPhy_b1 [Secale cereale]	1010	0
AEE99727.1	PAPhy_b1 [Triticum monococcum]	1005	0
AEO00267.1	recTa_PAPhy_b1_delta_C-t_6xHIS [synthetic construct]	1003	0
AEO00271.1	recHvPAPhy_b2_delta_C-t_6xHIS [synthetic construct]	997	0
AEE99729.1	PAPhy_b1 [Aegilops tauschii]	996	0
ACR23328.1	purple acid phosphatase isoform b1 [Triticum aestivum]	994	0
AEE99722.1	PAPhy_b1 [Triticum aestivum]	994	0
AEE99724.1	PAPhy_b3 [Triticum aestivum]	993	0
ACR23333.1	purple acid phosphatase isoform b2 [Hordeum vulgare]	991	0
AEE99725.1	PAPhy_b3 [Triticum aestivum]	989	0
XP_003567420.1	PREDICTED: purple acid phosphatase 15 [Brachypodium distachyon]	988	0
ACR23332.1	purple acid phosphatase isoform b1 [Hordeum vulgare]	987	0
AEE99735.1	PAPhy variant b1 [Hordeum vulgare]	985	0
ACR23327.1	purple acid phosphatase isoform a2 [Triticum aestivum]	984	0
AEO00270.1	recHvPAPhy_a_delta_C-t_6xHIS [synthetic construct]	977	0
AEE99720.1	PAPhy_a3 [Triticum aestivum]	977	0
XP 020191825.1	purple acid phosphatase 15-like [Aegilops tauschii subsp. tauschii]	975	0
AEO00266.1	recTaPAPhy_a1_delta_C-t_6xHIS [synthetic construct]	975	0
ACR23331.1	purple acid phosphatase isoform a [Hordeum vulgare]	974	0
		974	
AEE99728.1	PAPhy_a1 [Aegilops tauschii]	972	0
AEE99717.1	PAPhy_a1 [Triticum aestivum]		0
XP_020155451.1	purple acid phosphatase 15-like [Aegilops tauschii subsp. tauschii]	972	0
ACR23326.1	purple acid phosphatase isoform a1 [Triticum aestivum]	971	0
AEE99730.1	PAPhy_a1 [Secale cereale]	967	0
AEE99732.1	PAPhy_a2 [Secale cereale]	966	0
AEE99719.1	PAPhy_a2 [Triticum aestivum]	961	0
AEE99726.1	PAPhy_a1 [Triticum monococcum]	954	0
AEG77017.1	purple acid phosphatase isoform b [Hordeum vulgare subsp. vulgare]	953	0
ABF99890.1	Ser/Thr protein phosphatase family protein, expressed [Oryza sativa Japonica Group]	951	0
XP_015631975.1	PREDICTED: purple acid phosphatase 15 [Oryza sativa Japonica Group]	944	0
ADG07931.1	purple acid phosphatase isoform b [Oryza sativa Japonica Group]	944	0
AEO00272.1	recOsPAPhy_b_delta_C-t_6xHIS [synthetic construct]	944	0
XP_015690330.1	PREDICTED: purple acid phosphatase 15 [Oryza brachyantha]	943	0
BAF13805.1	Os03g0848200 [Oryza sativa Japonica Group]	942	0
EEC76531.1	hypothetical protein OsI_14321 [Oryza sativa Indica Group]	941	0
KQK86187.1	hypothetical protein SETIT_034687mg [Setaria italica]	938	0
XP_012698453.1	purple acid phosphatase 15 [Setaria italica]	938	0
PAN44018.1	hypothetical protein PAHAL_I01134 [Panicum hallii]	932	0
AFV28975.1	purple acid phosphatase [Triticum aestivum]	924	0
XP_021308311.1	purple acid phosphatase 15 [Sorghum bicolor]	915	0
AEO00273.1	recZmPAPhy_b_delta_C-t_6xHIS [synthetic construct]	900	0
ACR23335.1	purple acid phosphatase isoform b [Zea mays]	900	0
XP_010233761.1	PREDICTED: purple acid phosphatase 15-like [Brachypodium distachyon]	896	0
XP_008667173.1	uncharacterized LOC100272946 isoform X1 [Zea mays]	890	0
ONM11578.1	Purple acid phosphatase 15 [Zea mays]	884	0
ONM11581.1	Purple acid phosphatase 15 [Zea mays]	878	0
EEE60297.1	hypothetical protein OsJ_13361 [Oryza sativa Japonica Group]	838	0
NP_001140870.1	uncharacterized LOC100272946 precursor [Zea mays]	837	0
OVA06852.1	Phosphoesterase domain [Macleaya cordata]	835	0
XP_011041900.1	PREDICTED: purple acid phosphatase 15-like isoform X1 [Populus euphratica]	832	0

Accession #	Description	Score (Bits)	E Value
BAS87356.1	Os03g0848200 [Oryza sativa Japonica Group]	831	0
XP_011041903.1	PREDICTED: purple acid phosphatase 15-like isoform X4 [Populus euphratica]	831	0
XP_011041902.1	PREDICTED: purple acid phosphatase 15-like isoform X3 [Populus euphratica]	831	0
XP_011041901.1	PREDICTED: purple acid phosphatase 15-like isoform X2 [Populus euphratica]	831	0
XP_012071127.2	purple acid phosphatase 15 isoform X2 [Jatropha curcas]	831	0
KDP39361.1	hypothetical protein JCGZ_01118 [Jatropha curcas]	830	0
XP_006420927.1	hypothetical protein CICLE_v10004642mg [Citrus clementina]	828	0
XP_006420928.1	hypothetical protein CICLE_v10004642mg [Citrus clementina]	828	0
XP_006493060.1	PREDICTED: purple acid phosphatase 15 isoform X2 [Citrus sinensis]	827	0
KDO42829.1	hypothetical protein CISIN_1g008312mg [Citrus sinensis]	827	0
XP_021595347.1	purple acid phosphatase 15-like isoform X4 [Manihot esculenta]	825	0
XP_015574076.1	PREDICTED: purple acid phosphatase 15 isoform X1 [Ricinus communis]	825	0
XP_002323987.2	serine/threonine protein phosphatase [Populus trichocarpa]	825	0
XP_021595346.1	purple acid phosphatase 15-like isoform X3 [Manihot esculenta]	824	0
 OM071036.1	hypothetical protein CCACVL1_18488 [Corchorus capsularis]	824	0
XP 015574077.1	PREDICTED: purple acid phosphatase 15 isoform X2 [Ricinus communis]	824	0
 XP_009385494.1	PREDICTED: purple acid phosphatase 15 [Musa acuminata subsp. malaccensis]	824	0
	acid phosphatase, putative [Ricinus communis]	824	0
AGL44402.1	calcineurin-like phosphoesterase [Manihot esculenta]	824	0
OM088642.1	hypothetical protein COLO4_20148 [Corchorus olitorius]	824	0
XP 015574078.1	PREDICTED: purple acid phosphatase 15 isoform X3 [Ricinus communis]	824	0
CDP11126.1	unnamed protein product [Coffea canephora]	823	0
XP 006493059.1	PREDICTED: purple acid phosphatase 15 isoform X1 [Citrus sinensis]	823	0
XP 008792903.1	PREDICTED: purple acid phosphatase 15-like [Phoenix dactylifera]	822	0
XP 010926759.1	PREDICTED: purple acid phosphatase 15-like [Elaeis guineensis]	820	0
AFY06666.1	purple acid phosphatase [Citrus trifoliata]	820	0
GAU48994.1	hypothetical protein TSUD_88670 [Trifolium subterraneum]	820	0
XP 021641480.1	purple acid phosphatase 15-like isoform X2 [Hevea brasiliensis]	819	0
XP 021641479.1	purple acid phosphatase 15-like isoform X1 [Hevea brasiliensis]	819	0
XP 016566379.1	PREDICTED: purple acid phosphatase 15 isoform X2 [Capsicum annuum]	818	0
XP_009611646.1	PREDICTED: purple acid phosphatase 15 isoform X2 [Nicotiana tomentosiformis]	818	0
XP 016566378.1	PREDICTED: purple acid phosphatase 15 isoform X1 [Capsicum annuum]	817	0
 XP_004247857.1	PREDICTED: purple acid phosphatase 15 isoform X1 [Solanum lycopersicum]	817	0
 XP_003601637.1	purple acid phosphatase superfamily protein [Medicago truncatula]	817	0
 AAX71115.1	phytase [Medicago truncatula]	816	0
XP 015086742.1	PREDICTED: purple acid phosphatase 15 isoform X1 [Solanum pennellii]	816	0
_ XP_012481726.1	PREDICTED: purple acid phosphatase 15-like isoform X1 [Gossypium raimondii]	816	0
XP_010326830.1	PREDICTED: purple acid phosphatase 15 isoform X2 [Solanum lycopersicum]	816	0
XP_009611645.1	PREDICTED: purple acid phosphatase 15 isoform X1 [Nicotiana tomentosiformis]	816	0
XP_016724292.1	PREDICTED: purple acid phosphatase 15-like [Gossypium hirsutum]	816	0
XP_006601875.1	PREDICTED: purple acid phosphatase 15-like isoform X1 [Glycine max]	816	0
XP_004502218.1	PREDICTED: purple acid phosphatase 15-like isoform X1 [Cicer arietinum]	816	0
PHU21359.1	Purple acid phosphatase 13 [Capsicum chinense]	815	0
GAV67690.1	Metallophos domain-containing protein/Metallophos_C domain-containing protein [Cephalotus follicularis]	815	0
XP_015086743.1	PREDICTED: purple acid phosphatase 15 isoform X2 [Solanum pennellii]	815	0
XP 019180960.1	PREDICTED: purple acid phosphatase 15-like [Ipomoea nil]	815	0

## Table A12. BLASTP search of PAPhy consensus against the non-redundant protein sequences database excluding plant sequences

Results table for the BLAST search performed against the non-redundant protein sequences database using the PAPhy consensus sequence as query and restricting the output to non-plant sequences. Results shaded pink correspond to already characterised or predicted PAPhy.

Accession #	Description	Score (Bits)	E Value
AEO00268.1	recTaPAPhy_b2_delta_C-t_cMyc_6xHIS [synthetic construct]	1015	0
AEO00269.1	recTaPAPhy_b2_delta_C-t_6xHIS [synthetic construct]	1010	0
AEO00267.1	recTa_PAPhy_b1_delta_C-t_6xHIS [synthetic construct]	1003	0
AEO00271.1	recHvPAPhy_b2_delta_C-t_6xHIS [synthetic construct]	997	0
AEO00270.1	recHvPAPhy_a_delta_C-t_6xHIS [synthetic construct]	977	0
AEO00266.1	recTaPAPhy_a1_delta_C-t_6xHIS [synthetic construct]	975	0
AEO00272.1	recOsPAPhy_b_delta_C-t_6xHIS [synthetic construct]	944	0
AEO00273.1	recZmPAPhy_b_delta_C-t_6xHIS [synthetic construct]	900	0
XP_005642760.1	Metallo-dependent phosphatase [Coccomyxa subellipsoidea C-169]	442	2.00E-147
GAQ89001.1	hypothetical protein KFL_004780010 [Klebsormidium nitens]	377	7.00E-122
XP_011400105.1	Purple acid phosphatase 15 [Auxenochlorella protothecoides]	374	8.00E-121
XP_005651640.1	Metallo-dependent phosphatase [Coccomyxa subellipsoidea C-169]	328	4.00E-104
GAQ79694.1	purple acid phosphatase [Klebsormidium nitens]	335	5.00E-104
GAQ84117.1	Purple acid phosphatases superfamily protein [Klebsormidium nitens]	318	4.00E-100
XP_011400106.1	Purple acid phosphatase 15 [Auxenochlorella protothecoides]	315	3.00E-98
GAQ81065.1	hypothetical protein KFL_000700010 [Klebsormidium nitens]	312	6.00E-95
GAX79017.1	hypothetical protein CEUSTIGMA_g6457.t1 [Chlamydomonas eustigma]	302	3.00E-92
GAX79015.1	hypothetical protein CEUSTIGMA_g6455.t1 [Chlamydomonas eustigma]	300	7.00E-91
XP_011398238.1	Purple acid phosphatase 18 [Auxenochlorella protothecoides]	295	8.00E-91
XP_005645010.1	Metallo-dependent phosphatase [Coccomyxa subellipsoidea C-169]	298	2.00E-89
XP_004994476.1	hypothetical protein PTSG_04388 [Salpingoeca rosetta]	291	2.00E-89
XP_005644436.1	Metallo-dependent phosphatase [Coccomyxa subellipsoidea C-169]	289	4.00E-87
XP_001743494.1	hypothetical protein [Monosiga brevicollis MX1]	283	2.00E-86
XP_005650419.1	Metallo-dependent phosphatase [Coccomyxa subellipsoidea C-169]	268	3.00E-79
XP_013898053.1	hypothetical protein MNEG_8929 [Monoraphidium neglectum]	259	8.00E-79
KDD75912.1	hypothetical protein H632_c440p0 [Helicosporidium sp. ATCC 50920]	261	2.00E-78
XP_001695912.1	predicted protein [Chlamydomonas reinhardtii]	261	3.00E-77
XP_001693551.1	predicted protein [Chlamydomonas reinhardtii]	248	3.00E-71
GAX82085.1	hypothetical protein CEUSTIGMA_g9513.t1 [Chlamydomonas eustigma]	248	3.00E-71
XP_005845616.1	hypothetical protein CHLNCDRAFT_58566 [Chlorella variabilis]	247	7.00E-71
XP_008867791.1	hypothetical protein H310_04978 [Aphanomyces invadans]	241	1.00E-70
XP_002956809.1	hypothetical protein VOLCADRAFT_77270 [Volvox carteri f. nagariensis]	243	2.00E-69
XP_008604917.1	hypothetical protein SDRG_01179 [Saprolegnia diclina VS20]	234	2.00E-68
GAX77692.1	hypothetical protein CEUSTIGMA_g5135.t1 [Chlamydomonas eustigma]	240	2.00E-68
XP_012194718.1	hypothetical protein SPRG_01129 [Saprolegnia parasitica CBS 223.65]	233	9.00E-68
XP_009838177.1	hypothetical protein H257_12603 [Aphanomyces astaci]	232	2.00E-67
KDD71970.1	hypothetical protein H632_c4075p0 [Helicosporidium sp. ATCC 50920]	226	1.00E-66
XP_019576941.1	PREDICTED: bifunctional purple acid phosphatase 26 [Rhinolophus sinicus]	230	3.00E-66
XP_009529776.1	hypothetical protein PHYSODRAFT_560568 [Phytophthora sojae]	227	5.00E-65
OWZ23938.1	Iron(III)-zinc(II) purple acid phosphatase [Phytophthora megakarya]	227	6.00E-65
ETP45786.1	hypothetical protein F442_07863 [Phytophthora parasitica P10297]	228	1.00E-64
OQR85020.1	purple acid phosphatase 20-like [Achlya hypogyna]	224	1.00E-64
ETM47648.1	hypothetical protein L914_07645 [Phytophthora parasitica]	227	2.00E-64
KUG00586.1	Purple acid phosphatase 18 [Phytophthora nicotianae]	226	6.00E-64
XP_008904647.1	hypothetical protein PPTG_10898 [Phytophthora parasitica INRA-310] hypothetical protein F444 07968 [Phytophthora parasitica P1976]	226	8.00E-64
ETO76675.1		225	8.00E-64
KXZ54062.1	hypothetical protein GPECTOR_5g17 [Gonium pectorale] probable purple acid phosphatase [Cyanidioschyzon merolae strain 10D]	227	1.00E-63
XP_005535638.1 CEG46048.1	probable purple acid phosphatase [Cyanidioschyzon meroiae strain 100] probable purple acid phosphatase 20-like [Plasmopara halstedii]	226 218	2.00E-63 2.00E-62
KUF96465.1	hypothetical protein AM588_10006046 [Phytophthora nicotianae]	218	2.00E-62 2.00E-61
OQS06871.1	purple acid phosphatase 20-like [Thraustotheca clavata]	217 214	7.00E-61
CCI46862.1	unnamed protein product [Albugo candida]	214 215	1.00E-61
	Iron(III)zinc(II) purple acid phosphatase putative [Albugo laibachii Nc14]	215	1.00E-60 1.00E-60
CCA24554.1 XP 005786596.1	hypothetical protein EMIHUDRAFT 462501 [Emiliania huxleyi CCMP1516]	215	
VL_0021002001	hypothetical protein Elvinourar i 402501 [Ennildhid huxleyi CCMP1516]	221	3.00E-60

Accession #	Description	Score (Bits)	E Value
KOO29270.1	purple acid phosphatase 22-like protein [Chrysochromulina sp. CCMP291]	218	5.00E-60
<pre><p_005535955.1< pre=""></p_005535955.1<></pre>	probable purple acid phosphatase protein [Cyanidioschyzon merolae strain 10D]	216	1.00E-59
<pre>(P_008867792.1</pre>	hypothetical protein, variant 1 [Aphanomyces invadans]	208	1.00E-59
(P_009040156.1	hypothetical protein AURANDRAFT_2456 [Aureococcus anophagefferens]	206	8.00E-59
<pre>KP_002500568.1</pre>	predicted protein, partial [Micromonas commoda]	206	4.00E-58
EWM24423.1	putative purple acid phosphatase 20 [Nannochloropsis gaditana]	209	6.00E-58
<pre>(P_001418076.1</pre>	predicted protein [Ostreococcus lucimarinus CCE9901]	202	3.00E-57
OLQ13473.1	Purple acid phosphatase 18 [Symbiodinium microadriaticum]	205	9.00E-56
(P_011400104.1	Purple acid phosphatase 15 [Auxenochlorella protothecoides]	202	9.00E-56
<pre>(P_003057348.1</pre>	predicted protein [Micromonas pusilla CCMP1545]	195	2.00E-55
<pre>(P_004344296.1</pre>	calcineurin-like phosphoesterase [Capsaspora owczarzaki ATCC 30864]	200	2.00E-55
<pre>(P_002908896.1</pre>	Iron(III)-zinc(II) purple acid phosphatase, putative [Phytophthora infestans T30-4]	200	7.00E-55
EWM24421.1	ser thr protein phosphatase family expressed [Nannochloropsis gaditana]	201	8.00E-55
GAY02812.1	Hypothetical protein PINS_010626 [Pythium insidiosum]	206	3.00E-54
(P_008867793.1	hypothetical protein, variant 2 [Aphanomyces invadans]	191	3.00E-53
OUS47827.1	purple acid phosphatase-like protein [Ostreococcus tauri]	199	9.00E-53
KP_003079493.1	Iron/zinc purple acid phosphatase-like C-terminal domain [Ostreococcus tauri]	198	9.00E-53
KOO30306.1	purple acid phosphatase 18-like protein [Chrysochromulina sp. CCMP291]	196	1.00E-52
CCI46863.1	unnamed protein product [Albugo candida]	182	6.00E-50
<pre>KP_005792093.1</pre>	hypothetical protein EMIHUDRAFT_62631 [Emiliania huxleyi CCMP1516]	181	4.00E-49
OLP85966.1	Purple acid phosphatase 18 [Symbiodinium microadriaticum]	189	4.00E-48
<pre>(P_007513930.1</pre>	predicted protein [Bathycoccus prasinos]	187	5.00E-48
<pre>(P_005790588.1</pre>	hypothetical protein EMIHUDRAFT_62875 [Emiliania huxleyi CCMP1516]	177	9.00E-48
OLQ04592.1	Purple acid phosphatase 18 [Symbiodinium microadriaticum]	187	2.00E-47
EWM20876.1	purple acid phosphatase isoform b2 [Nannochloropsis gaditana]	184	2.00E-47
(P_005822961.1	hypothetical protein GUITHDRAFT_165854 [Guillardia theta CCMP2712]	182	6.00E-47
(P_004334080.1	Serine/threonine phosphatase [Acanthamoeba castellanii str. Neff]	173	3.00E-45
OIR12952.1	hypothetical protein BEU05_00010 [Marine Group III euryarchaeote CG- Bathy2]	168	5.00E-43
AIF02460.1	purple acid phosphatase [uncultured marine group II/III euryarchaeote KM3_157_C11]	163	2.00E-41
<pre>KP_005851825.1</pre>	hypothetical protein CHLNCDRAFT_133298 [Chlorella variabilis]	160	3.00E-41
<pre>(P_004336336.1</pre>	Ser/Thr phosphatase family protein [Acanthamoeba castellanii str. Neff]	155	7.00E-39
(P_009497258.1	hypothetical protein H696_05131 [Fonticula alba]	160	1.00E-38
(P_020892703.1	probable inactive purple acid phosphatase 2 isoform X2 [Exaiptasia pallida]	158	2.00E-38
<pre>(P_022792006.1</pre>	probable inactive purple acid phosphatase 9 [Stylophora pistillata]	156	1.00E-37
<pre>KP_020892702.1</pre>	nucleotide pyrophosphatase/phosphodiesterase-like isoform X1 [Exaiptasia pallida]	155	2.00E-37
<pre><p_004352814.1< pre=""></p_004352814.1<></pre>	Ser/Thr phosphatase family superfamily protein [Acanthamoeba castellanii str. Neff]	154	3.00E-37
(P_020428169.1	hypothetical protein PPL_10614 [Polysphondylium pallidum PN500]	152	4.00E-37
OIR14055.1	hypothetical protein BEU04_03530 [Marine Group III euryarchaeote CG- Bathy1]	152	4.00E-37
<pre>(P_015779285.1</pre>	PREDICTED: probable inactive purple acid phosphatase 2 [Acropora digitifera]	154	6.00E-37
(P_015775723.1	PREDICTED: probable inactive purple acid phosphatase 2 [Acropora digitifera]	153	1.00E-36
<pre>(P_020907484.1</pre>	probable inactive purple acid phosphatase 9 [Exaiptasia pallida]	152	2.00E-36
OIR23119.1	hypothetical protein BET99_00210 [Marine Group III euryarchaeote CG- Epi2]	150	2.00E-36
PBO81240.1	hypothetical protein COC13_03450 [Euryarchaeota archaeon]	149	6.00E-36
OZJ01427.1	hypothetical protein BZG36_05750 [Bifiguratus adelaidae]	149	1.00E-35
XP_004992544.1	iron/zinc purple acid phosphatase-like protein [Salpingoeca rosetta]	148	2.00E-35
XP_004354481.1	Ser/Thr phosphatase, putative [Acanthamoeba castellanii str. Neff]	145	3.00E-35

## Table A13. BLASTP search of PAPhy consensus against the non-redundant protein sequences database including only prokaryotic sequences

Results table for the BLAST search performed against the whole non-redundant protein sequences database using the PAPhy consensus sequence as query and restricting the output to prokaryotic sequences. Results shaded pink correspond to already characterised or predicted PAPhy.

Accession #	Description	Score (Bits)	E Value
WP_091112253.1	hypothetical protein [Nocardioides psychrotolerans]	120	6.00E-26
	hypothetical protein [Armatimonadetes bacterium GXS]	116	6.00E-25
WP_091025310.1	hypothetical protein [Nocardioides szechwanensis]	117	8.00E-25
CUU36519.1	Calcineurin-like phosphoesterase [Armatimonadetes bacterium GXS]	115	1.00E-24
WP_076414819.1	hypothetical protein [Shewanella sp. UCD-KL12]	118	2.00E-24
WP_072261434.1	MULTISPECIES: hypothetical protein [unclassified Armatimonadetes]	111	2.00E-23
CUU34844.1	Calcineurin-like phosphoesterase [Armatimonadetes bacterium DC]	111	3.00E-23
WP_077753580.1	hypothetical protein [Shewanella psychrophila]	112	2.00E-22
WP_033526872.1	phosphoesterase [Streptomyces galbus]	110	3.00E-22
PIV54789.1	hypothetical protein COS16_09190 [Candidatus Desantisbacteria bacterium CG02_land_8_20_14_3_00_49_13]	111	4.00E-22
WP_016432483.1	hypothetical protein [Streptomyces sp. HGB0020]	109	5.00E-22
WP_094056248.1	phosphoesterase [Streptomyces sp. XY006]	109	5.00E-22
WP_067027069.1	phosphoesterase [Streptomyces sp. RV15]	109	6.00E-22
PCK09148.1	metallophosphoesterase [Alteromonadaceae bacterium]	108	7.00E-22
WP_030942929.1	phosphoesterase [Streptomyces sp. NRRL S-646]	108	1.00E-21
WP_095985775.1	metallophosphoesterase [Cystobacter fuscus]	107	1.00E-21
WP_083940956.1	hypothetical protein [Pseudoduganella violaceinigra]	108	1.00E-21
WP_053760021.1	phosphoesterase [Streptomyces sp. AS58]	108	1.00E-21
WP_079064155.1	phosphoesterase [Streptomyces sp. NRRL F-4489]	107	2.00E-21
WP_020942412.1	phosphoesterase [Streptomyces collinus]	107	2.00E-21
WP_019990122.1	T9SS C-terminal target domain-containing protein [Rudanella lutea]	107	2.00E-21
KUL39863.1	phosphoesterase [Streptomyces sp. NRRL F-4489]	107	2.00E-21
OGS18554.1	hypothetical protein A3J83_07560 [Elusimicrobia bacterium RIFOXYA2_FULL_40_6]	107	2.00E-21
WP_046913510.1	phosphoesterase [Streptomyces stelliscabiei]	107	3.00E-21
WP_003993161.1	phosphoesterase [Streptomyces viridochromogenes]	107	3.00E-21
WP_067440252.1	phosphoesterase [Streptomyces lincolnensis]	107	3.00E-21
WP_097249307.1	phosphoesterase [Streptomyces sp. 1222.2]	107	3.00E-21
WP_025356225.1	phosphoesterase [Kutzneria albida]	107	3.00E-21
WP_099881855.1	hypothetical protein [Massilia sp. B2]	107	3.00E-21
WP_095753102.1	phosphoesterase [Streptomyces sp. SA15]	107	3.00E-21
WP_099151811.1	hypothetical protein [Lewinella nigricans]	108	3.00E-21
SHM97906.1	Phosphodiesterase/alkaline phosphatase D [Streptomyces yunnanensis]	107	3.00E-21
WP_013050969.1	hypothetical protein [Shewanella violacea]	108	3.00E-21
WP_099943464.1	phosphoesterase [Streptomyces sp. 93]	107	3.00E-21
AHH96072.1	phosphoesterase [Kutzneria albida DSM 43870]	107	3.00E-21
WP_079182190.1	phosphoesterase [Streptomyces yunnanensis]	107	3.00E-21
WP_097224693.1	phosphoesterase [Streptomyces sp. OV198]	107	4.00E-21
WP_054234561.1	phosphoesterase [Actinobacteria bacterium OK006]	107	4.00E-21
SFG82570.1	Fibronectin type III domain-containing protein [Duganella sp. CF458]	107	4.00E-21
WP_083550613.1	hypothetical protein [Chitinophaga jiangningensis]	107	4.00E-21
SHM57947.1	Por secretion system C-terminal sorting domain-containing protein [Chitinophaga jiangningensis]	107	4.00E-21
WP_089901422.1	metallophosphoesterase [Chitinophaga arvensicola]	106	5.00E-21
SEW53952.1	Purple acid Phosphatase, N-terminal domain [Chitinophaga arvensicola]	106	5.00E-21
WP_079470159.1	metallophosphoesterase [Chitinophaga ginsengisegetis]	106	6.00E-21
EKX65667.1	Tat pathway signal sequence domain protein [Streptomyces ipomoeae 91-03]	106	6.00E-21
EGD44950.1	putative phosphoesterase [Nocardioidaceae bacterium Broad-1]	105	6.00E-21
WP_078875737.1	phosphoesterase [Streptomyces sp. 769]	106	6.00E-21
WP_071899680.1	metallophosphoesterase [Cystobacter ferrugineus]	105	6.00E-21
WP_079142593.1	phosphoesterase [Streptomyces noursei]	106	6.00E-21
ANZ16104.1	phosphoesterase [Streptomyces noursei ATCC 11455]	106	7.00E-21
WP_030256863.1	hypothetical protein [Streptacidiphilus jeojiense]	105	8.00E-21
WP_089098575.1	phosphoesterase [Streptomyces hyaluromycini]	105	8.00E-21

Accession #	Description	Score (Bits)	E Value
WP_099920509.1	phosphoesterase [Streptomyces sp. 94]	105	9.00E-22
WP_099931504.1	phosphoesterase [Streptomyces sp. 70]	105	9.00E-22
WP_095852448.1	phosphoesterase [Streptomyces sp. Ag82_01-15]	105	9.00E-22
WP_067370936.1	phosphoesterase [Streptomyces olivochromogenes]	105	9.00E-22
WP_069571735.1	phosphoesterase [Streptomyces lydicus]	105	9.00E-2
WP_093485332.1	MULTISPECIES: phosphoesterase [Streptomyces]	105	1.00E-2
WP_052067226.1	phosphoesterase [Streptomyces mirabilis]	105	1.00E-2
WP_048580595.1	phosphoesterase [Streptomyces viridochromogenes]	105	1.00E-20
WP_081967121.1	hypothetical protein [Kitasatospora sp. NRRL B-11411]	105	1.00E-20
SEE57537.1	Phosphodiesterase/alkaline phosphatase D [Streptomyces sp. 2314.4]	105	1.00E-2
WP_013927818.1	metallophosphoesterase [Runella slithyformis]	106	1.00E-2
PIG76172.1	calcineurin-like phosphoesterase family protein [Streptomyces sp. 70]	105	1.00E-2
WP_079023518.1	phosphoesterase [Streptomyces sp. NRRL B-24891]	104	1.00E-2
WP_093474453.1	phosphoesterase [Streptomyces sp. 1222.5]	105	1.00E-2
WP_015809161.1	metallophosphoesterase [Pedobacter heparinus]	103	2.00E-2
SHH67224.1	Fibronectin type III domain-containing protein [Massilia sp. CF038]	105	2.00E-2
WP_002624649.1	hypothetical protein [Cystobacter fuscus]	104	2.00E-2
WP_078914265.1	hypothetical protein [Streptomyces sp. NRRL S-384]	105	2.00E-2
WP_060896173.1	phosphoesterase [Streptomyces diastatochromogenes]	104	2.00E-2
WP_084185652.1	metallophosphoesterase [Chitinophaga niabensis]	104	2.00E-2
WP_072363078.1	metallophosphoesterase [Chitinophaga sancti]	104	2.00E-2
WP_006602914.1	phosphoesterase [Streptomyces auratus]	104	2.00E-2
WP 062723243.1	phosphoesterase [Streptomyces caeruleatus]	104	2.00E-2
WP 086934137.1	hypothetical protein [Agarilytica rhodophyticola]	105	2.00E-2
WP 046729223.1	phosphoesterase [Streptomyces humi]	104	2.00E-2
WP 075031618.1	phosphoesterase [Streptomyces mirabilis]	104	3.00E-2
WP 005479953.1	calcineurin-like phosphoesterase [Streptomyces bottropensis]	104	3.00E-2
WP 073561531.1	metallophosphoesterase [Archangium sp. Cb G35]	103	3.00E-2
	phosphoesterase [Streptomyces torulosus]	104	3.00E-2
WP_033212942.1	phosphoesterase [Kitasatospora phosalacinea]	104	3.00E-2
WP 055541125.1	phosphoesterase [Streptomyces neyagawaensis]	103	3.00E-2
WP 077348043.1	metallophosphoesterase [Algoriphagus sp. A40]	103	3.00E-2
WP 052856304.1	MULTISPECIES: phosphoesterase [Streptomyces]	103	3.00E-2
WP 051399878.1	hypothetical protein [Amycolatopsis halophila]	103	3.00E-2
WP_062708967.1	phosphoesterase [Streptomyces regalis]	103	4.00E-2
WP 012142094.1	hypothetical protein [Shewanella sediminis]	105	4.00E-2
WP 068141167.1	hypothetical protein [Roseimaritima ulvae]	104	4.00E-2
WP 051661797.1	phosphoesterase [Streptomyces albulus]	103	4.00E-2
OOG76730.1	metallophosphoesterase [Algoriphagus sp. A40]	103	4.00E-2
AIA06105.1	phosphoesterase [Streptomyces albulus]	103	4.00E-2
WP_016575024.1	MULTISPECIES: phosphoesterase [Streptomyces]	103	4.00E-2
WP_086603297.1	phosphoesterase [Streptomyces swartbergensis]	103	4.00E-2
WP_053164936.1	phosphoesterase [Streptomyces swartbergenss]	103	4.00E-2
WP_083727071.1	metallophosphoesterase [[Flexibacter] sp. ATCC 35208]	103	4.00E-2
WP_067301171.1	phosphoesterase [Streptomyces griseochromogenes]	103	4.00E-2
WP_087301171.1 WP_099970780.1	phosphoesterase [Streptomyces griseocinomogenes]	103	5.00E-2
WP_099970780.1 WP 093697627.1	phosphoesterase [Streptomyces sp. 2231.1]	103	5.00E-2
09309/02/.1	phosphoesterase [Streptomyces sp. 2231.1] phosphoesterase [Streptomyces sp. 0K228]	103	J.00E-2

## Appendix 2. Supplemental information

#### Table A14. List of primers used for cloning and mutagenesis

The sequences of the primers used for cloning PAPhy genes in pOPIN vectors have the 5' pOPIN extensions coloured in grey. In the sequence of the primers used for QuickChange<sup>M</sup> mutagenesis, codons introducing the desired mutation are coloured red. The first T<sub>m</sub> corresponds to the overlapping sequence and the second T<sub>m</sub> to the non-overlapping sequence of the primers. In the sequence of the primers used for the cloning of GmPAPhy\_b into the Gateway<sup>M</sup>-compatible pPICZ $\alpha$ -DEST, the generic parts of the primers are coloured grey. The first T<sub>m</sub> corresponds to the overlapping sequence and the second T<sub>m</sub> to full length of the primers.

Name	Sequence	T <sub>m</sub> (°C)	Product size (bp)	Application
TaPAPhyA1-F1	AAGTTCTGTTTCAGGGCCCGGAGCCGGCGTCGACGCTCA	65.3	1559	Cloning of TaPAPhy_a1 from pPICZα into pOPINB
TaPAPhyA1-R1	ATGGTCTAGAAAGCTTTACAAGCACCTGTGCGGCTCC	63.1	1559	Cloning of TaPAPhy_a1 from pPICZα into pOPINB
TaPAPhyB-F1	AAGTTCTGTTTCAGGGCCCGACTCTGGAGGGCCCGTCT	60.5	1556	Cloning of TaPAPhy_b1/2 from pPICZα into pOPINB/K
TaPAPhyB-R1	ATGGTCTAGAAAGCTTTA <b>TTTGAGCAGGCATCTTTCCGG</b>	59.8	1556	Cloning of TaPAPhy_b1/2 from pPICZα into pOPINB/K
HvPAPhyA-F1	AAGTTCTGTTTCAGGGCCCGTCGACGCTCGCTGGCCCGT	65.3	1556	Cloning of HvPAPhy_a from pPICZa into pOPINB
HvPAPhyA-R1	ATGGTCTAGAAAGCTTTACTTGTGCAAGCACCTCTCCGG	63.7	1556	Cloning of HvPAPhy_a from pPICZa into pOPINB
OsPAPhyB-F1	AAGTTCTGTTTCAGGGCCCGGCTCCTTCGTCGACGTTGG	61.0	1565	Cloning of OsPAPhy_b from pPICZa into pOPINB
OsPAPhyB-R1	ATGGTCTAGAAAGCTTTATTTGATCAGGCACTTGTCAGGC	60.3	1565	Cloning of OsPAPhy_b from pPICZa into pOPINB
ZmPAPhyB-F1	AAGTTCTGTTTCAGGGCCCGGAGCCGGCGTCGACGCTGT	65.3	1565	Cloning of ZmPAPhy_b from pPICZa into pOPINB
ZmPAPhyB-R1	ATGGTCTAGAAAGCTTTAGAGGCACTTGTCGGGCTCCCT	65.7	1565	Cloning of ZmPAPhy_b from pPICZa into pOPINB
GmPAPhyT-F1	AAGTTCTGTTTCAGGGCCCGGACCCGGTGACCGTCCCGTT	65.5	1541	Cloning of GmPAPhy_b from pET15b into pOPINB
GmPAPhyT-R1	ATGGTCTAGAAAGCTTTACACACGCTGATGAATCGGGCAAATG	64.6	1541	Cloning of GmPAPhy_b from pET15b into pOPINB
TaB2_H229A-F1	CCCATCGCTGAGACGTACCAGCCGCGCTG	46.0, 56.0	4623	Introducing mutation H229A into TaPAPhy_b2-pGAPZαA
TaB2_H229A-R1	GTCTCAGCGATGGGCGTGGACTTGGCGAAC	46.0, 54.3	4623	Introducing mutation H229A into TaPAPhy_b2-pGAPZαA
TaB2_K348A-F1	ACCTACGCTGCTCACTACAGGGAGGCAGAG	42.0, 54.3	4623	Introducing mutation K348A into TaPAPhy_b2-pGAPZαA
TaB2_K348A-R1	TGAGCAGCGTAGGTGCTGTACCATGGCGC	42.0, 53.3	4623	Introducing mutation K348A into TaPAPhy_b2-pGAPZαA
TaB2_K410A-F1	GCGAGGCTATGGCCACCACCCACGCCG	42.0, 50.0	4623	Introducing mutation K410A into TaPAPhy_b2-pGAPZαA
TaB2_K410A-R1	GCCATAGCCTCGCGGTTCCCGCCGTCG	42.0, 50.0	4623	Introducing mutation K410A into TaPAPhy_b2-pGAPZαA
attB1_GmPAPhy-F1	CAAAAAAGCAGGCTTCGACCCGGTGACCGTCCCG	65.1, 75.5	1541	Cloning GmPAPhy_b from pOPINB into Gateway compatible pPICZ $\alpha$ -DEST
CHis_GmPAPhy-R1	TTTAATGATGATGATGATGATGCACCCCCCCCCCCCCCC	61.4, 71.4	1541	Cloning GmPAPhy_b from pOPINB into Gateway compatible pPICZ $\alpha$ -DEST
attB1	GGGGACAAGTTTGTACAAAAAAGCAGGCTTC	46.6, 66.8	1548	Generic cloning into Gateway compatible pPICZ $\alpha$ -DEST with C-6xHis tag
CHis-attB2-pPICZ	GGGGACCACTTTGTACAAGAAAGCTGGGTTTTTAATGATGATGATGATGA	47.0, 72.7	1548	Generic cloning into Gateway compatible pPICZ $\alpha$ -DEST with C-6xHis tag

#### Table A15. Original PAPhy constructs

The parameters for each protein sequence were computed with the ExPASy ProtParam tool (Gasteiger *et al.*, 2005). ' $\epsilon$ ', extinction coefficient at 280 nm measured in water assuming all cysteine residues are reduced; 'A 0.1% (= 1 g L<sup>-1</sup>)' absorbance at 280 nm of a 0.1% protein solution (equivalent to 1 g L<sup>-1</sup>) assuming all cysteine residues are reduced.

Construct	MW (kDa)	ε (M⁻¹ cm⁻¹)	A 0.1% (= 1 g L <sup>-1</sup> )
GmPAPhy_b-pET15b	59.58	121130	2.033

MGSSHHHHHHSSGLVPRGSHMDPVTVPFDPALRGVAVDLPETDPRVRRRVRGFEPEQISVSLSTSHDSVWISWVTGEFQIGLDIKPLDPKTVSSV VQYGTSRFELVHEARGQSLIYNQLYPFEGLQNYTSGIIHHVQLKGLEPSTLYYYQCGDPSLQAMSDIYYFRTMPISGSKSYPGKVAVVGDLGLTYNTT TTIGHLTSNEPDLLLLIGDVTYANLYLTNGTGSDCYSCSFPLTPIHETYQPRWDYWGRFMQNLVSNVPIMVVEGNHEIEKQAENRTFVAYSSRFAFP SQESGSSSTFYYSFNAGGIHFIMLGAYINYDKTAEQYKWLERDLENVDRSITPWLVVTWHPPWYSSYEAHYREAECMRVEMEDLLYAYGVDIIFNG HVHAYERSNRVYNYNLDPCGPVYITVGDGGNREKMAIKFADEPGHCPDPLSTPDPYMGGFCATNFTFGTKVSKFCWDRQPDYSAFRESSFGYGIL EVKNETWALWSWYRNQDSYKEVGDQIYIVRQPDICPIHQRV

			1 000	
TaPAPhy_a1-pPICZαA	57.26	110700	1.933	

EPASTLTGPSRPVTVALREDRGHAVDLPDTDPRVQRRATGWAPEQIAVALSAAPTSAWVSWITGEFQMGGTVKPLDPGTVGSVVRYGLAADSLV RQASGDALVYSQLYPFEGLQNYTSGIIHHVRLQGLEPATKYYYQCGDPALPGAMSAVHAFRTMPAVGPRSYPGRIAVVGDLGLTYNTTSTVDHMA SNRPDLVLLVGDVCYANMYLTNGTGADCYSCAFGKSTPIHETYQPRWDYWGRYMEAVTSGTPMMVVEGNHEIEEQIGNKTFAAYRSRFAFPSTE SGSFSPFYYSFDAGGIHFLMLGAYADYGRSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYTTYKAHYREVECMRVAMEELLHSHGLDIAFTG HVHAYERSNRVFNYTLDPCGAVHISVGDGGNREKMATTHADEPGHCPDPRPKPNAFIGGFCASNFTSGPAAGRFCWDRQPDYSAYRESSFGHGI LEVKNETHALWRWHRNQDHYGSAGDEIYIVREPHRCLHKHHHHHH

TaPAPhy_b1-pPICZαA         57.10         113680         1.991
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TLEGPSRPVTVPLREDRGHAVDLPDTDPRVQRRVTGWAPEQIAVALSAAPTSAWVSWITGDFQMGGAVKPLDPGTVGSVVRYGLAADSLAREA TGEALVYSQLYPFEGLQNYTSGIIHHVRILGLEPGTKYYYQCGDPAIPGAMSAVHAFRTMPDVGPRSYPGRIAVVGDLGLTYNTTSTVEHMASNQP DLVLLLGDVSYANLYLTNGTGTDCYSCSFAKSTPIHETYQPRWDYWGRYMEPVTSSTPMMVVEGNHEIEQQIGNKTFAAYSARFAFPSMESESFSP FYYSFDAGGIHFIMLAAYADYSKSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYSTYKAHYREAECMRVAMEELLYSYGLDIVFTGHVHAYER SNRVFNYTLDPCGAVHISVGDGGNREKMATTHADDPGRCPEPMSTPDAFMGGFCAFNFTSGPAAGSFCWDRQPDYSAYRESSFGHGILEVKNE THALWKWHRNQDLYQGAVGDEIYIVREPERCLLKHHHHHH

	TaPAPhy_b2-pPICZαA	57.1	113680	1.991	
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TLEGPSRPVTVPLREDRGHAVDLPDTDPRVQRRVTGWAPEQIAVALSAAPTSAWVSWITGDFQMGGAVKPLDPGTVGSVVRYGLAADSLVREA TGDALVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTKYYYQCGDPSIPGAMSAVHAFRTMPAVGPRSYPGRIAVVGDLGLTYNTTSTVEHMASNQ PDLVLLLGDVSYANLYLTNGTGTDCYSCSFAKSTPIHETYQPRWDYWGRYMEPVTSSTPMMVVEGNHEIEQQIGNKTFAAYSARFAFPSMESESFS PFYYSFDAGGIHFIMLAAYADYSKSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYSTYKAHYREAECMRVAMEELLYSYGLDIVFTGHVHAYE RSNRVFNYTLDPCGAVHISVGDGGNREKMATTHADDPGRCPEPMSTPDAFMGGFCAFNFTSGPAAGSFCWDRQPDYSAYRESSFGHGILEVKN ETHALWKWHRNQDLYQGAVGDEIYIVREPERCLLKHHHHHH

	TaPAPhy_b2-pGAPZαA	57.49	113680	1.978	
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EPASTLEGPSRPVTVPLREDRGHAVDLPDTDPRVQRRVTGWAPEQIAVALSAAPTSAWVSWITGDFQMGGAVKPLDPGTVGSVVRYGLAADSLV REATGDALVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTKYYYQCGDPSIPGAMSAVHAFRTMPAVGPRSYPGRIAVVGDLGLTYNTTSTVEHMAS NQPDLVLLLGDVSYANLYLTNGTGTDCYSCSFAKSTPIHETYQPRWDYWGRYMEPVTSSTPMMVVEGNHEIEQQIGNKTFAAYSARFAFPSMESE SFSPFYYSFDAGGIHFIMLAAYADYSKSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYSTYKAHYREAECMRVAMEELLYSYGLDIVFTGHVH AYERSNRVFNYTLDPCGAVHISVGDGGNREKMATTHADDPGRCPEPMSTPDAFMGGFCAFNFTSGPAAGSFCWDRQPDYSAYRESSFGHGILE VKNETHALWKWHRNQDLYQGAVGDEIYIVREPERCLLKHHHHHH

EPPSTLAGPSRPVTVTPRENRGHAVDLPDTDPRVQRRATGWAPEQVAVALSAAPTSAWVSWITGEFQMGGTVKPLDPRTVGSVVRYGLAADSL VREATGDALVYSQLYPFEGLHNYTSGIIHHVRLQGLEPGTKYYYQCGDPAIPGAMSAVHAFRTMPAAGPRSYPGRIAVVGDLGLTYNTTSTVDHM TSNRPDLVVLVGDVSYANMYLTNGTGTDCYSCSFGKSTPIHETYQPRWDYWGRYMEPVTSSTPMMVVEGNHEIEEQIGNKTFAAYRSRFAFPSA ESGSFSPFYYSFDAGGIHFIMLGAYADYGRSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYTTYKAHYREVECMRVAMEELLYSHGLDIAFTG HVHAYERSNRVFNYTLDPCGAVYISVGDGGNREKMATTHADEPGHCPDPRPKPNAFIAGFCAFNFTSGPAAGRFCWDRQPDYSAYRESSFGHGI LEVKNETHALWRWHRNQDLYGSARDEIYIVREPERCLHKHHHHH

OsPAPhy_b-pPICZaA 57.33	112190	1.957	
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APSSTLAGPTRPVTVPPRDRGHAVDLPDTDPRVQRRVKGWAPEQIAVALSAAPSSAWVSWVTGDFQMGAAVEPLDPTAVASVVRYGLAADSLV RRATGDALVYSQLYPFDGLLNYTSAIIHHVRLQGLEPGTEYFYQCGDPAIPAAMSDIHAFRTMPAVGPRSYPGKIAIVGDLGLTYNTTSTVEHMVSN QPDLVLLLGDVSYANLYLTNGTGTDCYSCSFANSTPIHETYQPRWDYWGRYMEPVTSRIPMMVVEGNHEIEEQIDNKTFASYSSRFSFPSTESGSFS PFYYSFDAGGIHFVMLAAYADYSKSGKQYKWLEKDLAKVDRSVTPWVIAGWHAPWYSTFKAHYREAECMRVAMEELLYSYAVDVVFTGHVHAY ERSNRVFNYTLDPCGPVHISVGDGGNREKMATSYADEPGRCPDPLSTPDPFMGGGFCGFNFTSGPAAGSFCWDRQPDYSAYRESSFGHGILEVK NETHALWRWHRNQDLYGSVGDEIYIVREPDKCLIKHHHHHH

Construct	MW (kDa)	ε (M <sup>-1</sup> cm <sup>-1</sup> )	A 0.1% (= 1 g L <sup>-1</sup> )
ZmPAPhy_b-pPICZαA	56.97	112190	1.969

EPASTLSGPSRPVTVAIGDRGHAVDLPDTDPRVQRRVTGWAPEQVAVALSASPTSAWVSWITGDYQMGGAVEPLDPGAVGSVVRYGLAADALD HEATGESLVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTRYVYRCGDPAIPDAMSGVHAFRTMPAVGPGSYPGRIAVVGDLGLTYNTTSTVDHLVR NRPDLVLLLGDVCYANLYLTNGTGADCYSCAFAKSTPIHETYQPRWDYWGRYMEPVTSSIPMMVVEGNHEIEQQIHNRTFAAYSSRFAFPSEESGS SSPFYYSFDAGGIHFVMLASYADYSRSGAQYKWLEADLEKVDRSVTPWLIAGWHAPWYTTYKAHYREAECMRVEMEELLYAYGVDVVFTGHVH AYERSNRVFNYTLDACGPVHISVGDGGNREKMATAHADEAGHCPDPASTPDPFMGGRLCAANFTSGPAAGRFCWDRQPEYSAYRESSFGHGVL EVRNDTHALWRWHRNQDLHAANVAADEVYIVREPDKCLHHHHHH

#### Table A16. Cloned PAPhy constructs

The parameters for each protein sequence were computed with the ExPASy ProtParam tool (Gasteiger et al., 2005). ' $\epsilon$ ', extinction coefficient at 280 nm measured in water assuming all cysteine residues are reduced; 'A 0.1% (= 1 g L<sup>-1</sup>)' absorbance at 280 nm of a 0.1% protein solution (equivalent to 1 g L<sup>-1</sup>) assuming all cysteine residues are reduced. In the TaPAPhy\_b2 mutant sequences, the mutated residues are coloured in red.

Construct	MW (kDa)	ε (M⁻¹ cm⁻¹)	A 0.1% (= 1 g L <sup>-1</sup> )
GmPAPhy_b-pOPINB	59.58	121130	2.033

MGSSHHHHHHSSGLEVLFQGPDPVTVPFDPALRGVAVDLPETDPRVRRRVRGFEPEQISVSLSTSHDSVWISWVTGEFQIGLDIKPLDPKTVSSVV QYGTSRFELVHEARGQSLIYNQLYPFEGLQNYTSGIIHHVQLKGLEPSTLYYYQCGDPSLQAMSDIYYFRTMPISGSKSYPGKVAVVGDLGLTYNTTT TIGHLTSNEPDLLLLIGDVTYANLYLTNGTGSDCYSCSFPLTPIHETYQPRWDYWGRFMQNLVSNVPIMVVEGNHEIEKQAENRTFVAYSSRFAFPS QESGSSSTFYYSFNAGGIHFIMLGAYINYDKTAEQYKWLERDLENVDRSITPWLVVTWHPPWYSSYEAHYREAECMRVEMEDLLYAYGVDIIFNGH VHAYERSNRVYNYNLDPCGPVYITVGDGGNREKMAIKFADEPGHCPDPLSTPDPYMGGFCATNFTFGTKVSKFCWDRQPDYSAFRESSFGYGILE VKNETWALWSWYRNQDSYKEVGDQIYIVRQPDICPIHQRV

	GmPAPhy_b-pPICZa-DEST	58.10	121130	2.085	
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DPVTVPFDPALRGVAVDLPETDPRVRRRVRGFEPEQISVSLSTSHDSVWISWVTGEFQIGLDIKPLDPKTVSSVVQYGTSRFELVHEARGQSLIYNQL YPFEGLQNYTSGIIHHVQLKGLEPSTLYYYQCGDPSLQAMSDIYYFRTMPISGSKSYPGKVAVVGDLGLTYNTTTIGHLTSNEPDLLLLIGDVTYANL YLTNGTGSDCYSCSFPLTPIHETYQPRWDYWGRFMQNLVSNVPIMVVEGNHEIEKQAENRTFVAYSSRFAFPSQESGSSSTFYYSFNAGGIHFIML GAYINYDKTAEQYKWLERDLENVDRSITPWLVVTWHPPWYSSYEAHYREAECMRVEMEDLLYAYGVDIIFNGHVHAYERSNRVYNYNLDPCGPV YITVGDGGNREKMAIKFADEPGHCPDPLSTPDPYMGGFCATNFTFGTKVSKFCWDRQPDYSAFRESSFGYGILEVKNETWALWSWYRNQDSYKE VGDQIYIVRQPDICPIHQRVHHHHHH

	TaPAPhy_b2-pOPINB	58.58	113680	1.941	
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MGSSHHHHHHSSGLEVLFQGPTLEGPSRPVTVPLREDRGHAVDLPDTDPRVQRRVTGWAPEQIAVALSAAPTSAWVSWITGDFQMGGAVKPL DPGTVGSVVRYGLAADSLVREATGDALVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTKYYYQCGDPSIPGAMSAVHAFRTMPAVGPRSYPGRIAV VGDLGLTYNTTSTVEHMASNQPDLVLLLGDVSYANLYLTNGTGTDCYSCSFAKSTPIHETYQPRWDYWGRYMEPVTSSTPMMVVEGNHEIEQQI GNKTFAAYSARFAFPSMESESFSPFYYSFDAGGIHFIMLAAYADYSKSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYSTYKAHYREAECMRV AMEELLYSYGLDIVFTGHVHAYERSNRVFNYTLDPCGAVHISVGDGGNREKMATTHADDPGRCPEPMSTPDAFMGGFCAFNFTSGPAAGSFCW DRQPDYSAYRESSFGHGILEVKNETHALWKWHRNQDLYQGAVGDEIYIVREPERCLLK

TaPAPhy_b2-pOPINK	84.22	156540	1.859	

MAHHHHHHMSPILGYWKIKGLVQPTRLLLEYLEEKYEEHLYERDEGDKWRNKKFELGLEFPNLPYYIDGDVKLTQSMAIIRYIADKHNMLGGCPKE RAEISMLEGAVLDIRYGVSRIAYSKDFETLKVDFLSKLPEMLKMFEDRLCHKTYLNGDHVTHPDFMLYDALDVVLYMDPMCLDAFPKLVCFKKRIEA IPQIDKYLKSSKYIAWPLQGWQATFGGGDHPPKSDLSSGLEVLFQGPTLEGPSRPVTVPLREDRGHAVDLPDTDPRVQRRVTGWAPEQIAVALSA APTSAWVSWITGDFQMGGAVKPLDPGTVGSVVRYGLAADSLVREATGDALVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTKYYYQCGDPSIPGA MSAVHAFRTMPAVGPRSYPGRIAVVGDLGLTYNTTSTVEHMASNQPDLVLLLGDVSYANLYLTNGTGTDCYSCSFAKSTPIHETYQPRWDYWGR YMEPVTSSTPMMVVEGNHEIEQQIGNKTFAAYSARFAFPSMESESFSPFYYSFDAGGIHFIMLAAYADYSKSGEQYRWLEKDLAKVDRSVTPWLV AGWHAPWYSTYKAHYREAECMRVAMEELLYSYGLDIVFTGHVHAYERSNRVFNYTLDPCGAVHISVGDGGNREKMATTHADDPGRCPEPMSTP DAFMGGFCAFNFTSGPAAGSFCWDRQPDYSAYRESSFGHGILEVKNETHALWKWHRNQDLYQGAVGDEIYIVREPERCLLK

TaPAPhy_b2_H229A-pGAPZαA	57.42	113680	1.980	

EPASTLEGPSRPVTVPLREDRGHAVDLPDTDPRVQRRVTGWAPEQIAVALSAAPTSAWVSWITGDFQMGGAVKPLDPGTVGSVVRYGLAADSLV REATGDALVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTKYYYQCGDPSIPGAMSAVHAFRTMPAVGPRSYPGRIAVVGDLGLTYNTTSTVEHMAS NQPDLVLLLGDVSYANLYLTNGTGTDCYSCSFAKSTPIAETYQPRWDYWGRYMEPVTSSTPMMVVEGNHEIEQQIGNKTFAAYSARFAFPSMESE SFSPFYYSFDAGGIHFIMLAAYADYSKSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYSTYKAHYREAECMRVAMEELLYSYGLDIVFTGHVH AYERSNRVFNYTLDPCGAVHISVGDGGNREKMATTHADDPGRCPEPMSTPDAFMGGFCAFNFTSGPAAGSFCWDRQPDYSAYRESSFGHGILE VKNETHALWKWHRNQDLYQGAVGDEIYIVREPERCLLKHHHHHH

TaPAPhy_b2_K348A-pGAPZαA	57.43	113680	1.979	

EPASTLEGPSRPVTVPLREDRGHAVDLPDTDPRVQRRVTGWAPEQIAVALSAAPTSAWVSWITGDFQMGGAVKPLDPGTVGSVVRYGLAADSLV REATGDALVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTKYYYQCGDPSIPGAMSAVHAFRTMPAVGPRSYPGRIAVVGDLGLTYNTTSTVEHMAS NQPDLVLLLGDVSYANLYLTNGTGTDCYSCSFAKSTPIHETYQPRWDYWGRYMEPVTSSTPMMVVEGNHEIEQQIGNKTFAAYSARFAFPSMESE SFSPFYYSFDAGGIHFIMLAAYADYSKSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYSTYAAHYREAECMRVAMEELLYSYGLDIVFTGHVH AYERSNRVFNYTLDPCGAVHISVGDGGNREKMATTHADDPGRCPEPMSTPDAFMGGFCAFNFTSGPAAGSFCWDRQPDYSAYRESSFGHGILE VKNETHALWKWHRNQDLYQGAVGDEIYIVREPERCLLKHHHHHH

Construct	MW (kDa)	ε (M <sup>-1</sup> cm <sup>-1</sup> )	A 0.1% (= 1 g L <sup>-1</sup> )
TaPAPhy_b2_K410A-pGAPZαA	57.43	113680	1.979

EPASTLEGPSRPVTVPLREDRGHAVDLPDTDPRVQRRVTGWAPEQIAVALSAAPTSAWVSWITGDFQMGGAVKPLDPGTVGSVVRYGLAADSLV REATGDALVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTKYYYQCGDPSIPGAMSAVHAFRTMPAVGPRSYPGRIAVVGDLGLTYNTTSTVEHMAS NQPDLVLLLGDVSYANLYLTNGTGTDCYSCSFAKSTPIHETYQPRWDYWGRYMEPVTSSTPMMVVEGNHEIEQQIGNKTFAAYSARFAFPSMESE SFSPFYYSFDAGGIHFIMLAAYADYSKSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYSTYKAHYREAECMRVAMEELLYSYGLDIVFTGHVH AYERSNRVFNYTLDPCGAVHISVGDGGNREAMATTHADDPGRCPEPMSTPDAFMGGFCAFNFTSGPAAGSFCWDRQPDYSAYRESSFGHGILE VKNETHALWKWHRNQDLYQGAVGDEIYIVREPERCLLKHHHHHH

HvPAPhy a-pOPINB	58.75	113680	1 935	
	50.75	113000	1.555	

MGSSHHHHHHSSGLEVLFQGPSTLAGPSRPVTVTPRENRGHAVDLPDTDPRVQRRATGWAPEQVAVALSAAPTSAWVSWITGEFQMGGTVKP LDPRTVGSVVRYGLAADSLVREATGDALVYSQLYPFEGLHNYTSGIIHHVRLQGLEPGTKYYYQCGDPAIPGAMSAVHAFRTMPAAGPRSYPGRIA VVGDLGLTYNTTSTVDHMTSNRPDLVVLVGDVSYANMYLTNGTGTDCYSCSFGKSTPIHETYQPRWDYWGRYMEPVTSSTPMMVVEGNHEIEE QIGNKTFAAYRSRFAFPSAESGSFSPFYYSFDAGGIHFIMLGAYADYGRSGEQYRWLEKDLAKVDRSVTPWLVAGWHAPWYTTYKAHYREVECM RVAMEELLYSHGLDIAFTGHVHAYERSNRVFNYTLDPCGAVYISVGDGGNREKMATTHADEPGHCPDPRPKPNAFIAGFCAFNFTSGPAAGRFC WDRQPDYSAYRESSFGHGILEVKNETHALWRWHRNQDLYGSARDEIYIVREPERCLHK

OsPAPhy b-pOPINB	58.80	112190	1.908	
OSFAFIIY_D-POFIND	J0.60	112190	1.908	

MGSSHHHHHHSSGLEVLFQGPAPSSTLAGPTRPVTVPPRDRGHAVDLPDTDPRVQRRVKGWAPEQIAVALSAAPSSAWVSWVTGDFQMGAA VEPLDPTAVASVVRYGLAADSLVRRATGDALVYSQLYPFDGLLNYTSAIIHHVRLQGLEPGTEYFYQCGDPAIPAAMSDIHAFRTMPAVGPRSYPGK IAIVGDLGLTYNTTSTVEHMVSNQPDLVLLLGDVSYANLYLTNGTGTDCYSCSFANSTPIHETYQPRWDYWGRYMEPVTSRIPMMVVEGNHEIEE QIDNKTFASYSSRFSFPSTESGSFSPFYYSFDAGGIHFVMLAAYADYSKSGKQYKWLEKDLAKVDRSVTPWVIAGWHAPWYSTFKAHYREAECMR VAMEELLYSYAVDVVFTGHVHAYERSNRVFNYTLDPCGPVHISVGDGGNREKMATSYADEPGRCPDPLSTPDPFMGGGFCGFNFTSGPAAGSFC WDRQPDYSAYRESSFGHGILEVKNETHALWRWHRNQDLYGSVGDEIYIVREPDKCLIK

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MGSSHHHHHHSSGLEVLFQGPEPASTLSGPSRPVTVAIGDRGHAVDLPDTDPRVQRRVTGWAPEQVAVALSASPTSAWVSWITGDYQMGGAV EPLDPGAVGSVVRYGLAADALDHEATGESLVYSQLYPFEGLQNYTSGIIHHVRLQGLEPGTRYVYRCGDPAIPDAMSGVHAFRTMPAVGPGSYPG RIAVVGDLGLTYNTTSTVDHLVRNRPDLVLLLGDVCYANLYLTNGTGADCYSCAFAKSTPIHETYQPRWDYWGRYMEPVTSSIPMMVVEGNHEIE QQIHNRTFAAYSSRFAFPSEESGSSSPFYYSFDAGGIHFVMLASYADYSRSGAQYKWLEADLEKVDRSVTPWLIAGWHAPWYTTYKAHYREAECM RVEMEELLYAYGVDVVFTGHVHAYERSNRVFNYTLDACGPVHISVGDGGNREKMATAHADEAGHCPDPASTPDPFMGGRLCAANFTSGPAAGR FCWDRQPEYSAYRESSFGHGVLEVRNDTHALWRWHRNQDLHAANVAADEVYIVREPDKCL

#### Table A17. Summary of the PAPhy expression trials in *E. coli* hosts

The levels of protein expression are represented as '-', no expression; '+?'no clear expression; '+', low expression; '++', expression; '+++' or '++++' high expression. The solubility test results are represented as '-', insoluble; 'n/a', not applicable. The phytase activity test results are represented as '+?', no clear activity; '-', no activity; 'n/a', not applicable.

Construct	Induction method	Strain	Induction length	[IPTG] (mM)	т (°С)	Expression	Solubility	Activity
GmPAPhy_b-pET15b	b IPTG BL21 (DE3) pLysS		5 h	0 - 1	37	-	n/a	n/a
		Rosetta 2 (DE3) pLysS	4 h - O/N	0 - 0.5	25 - 30	-	n/a	n/a
	Ro		O/N	0 - 0.5	25 - 30	+	-	n/a
		SHuffle T7	O/N	0 - 0.5	16 - 37	-	n/a	n/a
	Autoinduction	SHuffle T7	O/N	n/a	25 - 37	-	n/a	n/a
GmPAPhy_b-pOPINB Autoinduction		SHuffle T7	O/N	n/a	25 - 37	+?	-	+?
		SHuffle T7 Express	O/N	n/a	25 - 37	+?	-	-
HvPAPhy_a-pOPINB	IPTG	SHuffle T7	O/N	0 - 0.5	16 - 37	++++	-	n/a
		SHuffle T7 Express		0 - 0.5	16 - 37	++	-	n/a
		ArcticExpress (DE3) RP	3 days	0 - 0.5	12	+++	-	n/a
Autoinduction		Autoinduction SHuffle T7		n/a	25 - 37	++++	-	n/a
		SHuffle T7 Express	O/N	n/a	25 - 37	+++	-	n/a
		ArcticExpress (DE3) RP	6 days	n/a	12	+++	-	n/a
OsPAPhy_b-pOPINB	IPTG	SHuffle T7	O/N	0 - 0.5	16 - 37	+++	-	n/a
		SHuffle T7 Express	O/N	0 - 0.5	16 - 37	+++	-	-
		ArcticExpress (DE3) RP	3 days	0 - 0.5	12	+++	-	n/a
	Autoinduction	SHuffle T7	O/N	n/a	25 - 37	+++	-	n/a
		SHuffle T7 Express	O/N	n/a	25 - 37	+++	-	n/a
		ArcticExpress (DE3) RP	6 days	n/a	12	+++	-	n/a
ZmPAPhy_b-pOPINB	Autoinduction	SHuffle T7	O/N	n/a	25 - 37	+?	-	-
		SHuffle T7 Express	O/N	n/a	25 - 37	+?	-	-
TaPAPhy_b2-pOPINB	Autoinduction	SHuffle T7	O/N	n/a	25 - 37	++++	-	+?
		SHuffle T7 Express	O/N	n/a	25 - 37	++++	-	-
TaPAPhy_b2-pOPINK	Autoinduction	SHuffle T7	O/N	n/a	25 - 37	+	-	n/a
		SHuffle T7 Express	O/N	n/a	25 - 37	+	-	n/a
		BL21 (DE3)	O/N	n/a	25 - 37	++++	-	n/a

#### Table A18. Protonation state of TaPAPhy\_b2 structure for MD simulations at pH 5.5.

The protonation state of histidine (HIS) and aspartate (ASP) residues was manually selected upon careful inspection of their environment. The protonation state of glutamate (GLU) residues was assigned automatically by the GROMACS 4.6.5 package (Hess *et al.*, 2008).

Residue #	Residue type	Location	Protonation state
7	GLU	Surface	Deprotonated
19	GLU	Surface	Deprotonated
20	ASP	Surface	Deprotonated
23	HIS	Surface	Proton in N $\delta1$ and N $\epsilon2$
26	ASP	Buried	Proton in Oδ2
29	ASP	Surface	Deprotonated
31	ASP	Buried	Deprotonated
44	GLU	Buried	Deprotonated
65	ASP	Surface	Deprotonated
76	ASP	Surface	Deprotonated
91	ASP	Surface	Deprotonated
96	GLU	Surface	Deprotonated
100	ASP	Surface	Deprotonated
111	GLU	Surface	Deprotonated
122	HIS	Buried	Proton in Nδ1
123	HIS	Buried	Proton in Nɛ2
130	GLU	Surface	Deprotonated
141	ASP	Surface	Deprotonated
152	HIS	Surface	Proton in N $\delta1$ and N $\epsilon2$
174	ASP	Fe ligand	Deprotonated
186	GLU	Surface	Deprotonated
187	HIS	Buried	Proton in Nδ1
194	ASP	Surface	Deprotonated
201	ASP	Fe ligand	Deprotonated
216	ASP	Surface	Deprotonated
229	HIS	InsS <sub>6</sub> ligand	Proton in N $\delta1$ and N $\epsilon2$
230	GLU	Buried	Deprotonated
237	ASP	Buried	Deprotonated
244	GLU	Surface	Deprotonated
256	GLU	Buried	Deprotonated
259	HIS	PO <sub>4</sub> ligand	Proton in N $\delta$ 1 and N $\epsilon$ 2
260	GLU	Buried	Deprotonated
262	GLU	Buried	Deprotonated
283	GLU	Buried	Deprotonated
285	GLU	Surface	Deprotonated
295	ASP	Surface	Deprotonated
300	HIS	Buried	Proton in N $\delta1$ and N $\epsilon2$
309	ASP	Surface	Deprotonated
315	GLU	Surface	Deprotonated
321	GLU	Surface	Deprotonated
323	ASP	Buried	Deprotonated
328	ASP	Surface	Deprotonated
340	HIS	Fe ligand	Proton in Nδ1

Residue #	Residue type	Location	Protonation state
350	HIS	PO <sub>4</sub> ligand	Proton in N $\delta$ 1 and N $\epsilon$ 2
353	GLU	InsS <sub>6</sub> ligand	Deprotonated
355	GLU	Buried	Deprotonated
362	GLU	Buried	Deprotonated
363	GLU	Surface	Deprotonated
371	ASP	Buried	Deprotonated
377	HIS	Fe ligand	Proton in N <sub>2</sub>
379	HIS	Fe ligand	Proton in Nδ1
382	GLU	Buried	Deprotonated
393	ASP	Buried	Deprotonated
399	HIS	Buried	Proton in Nɛ2
404	ASP	Buried	Proton in Oδ2
409	GLU	PO₄ ligand	Deprotonated
415	HIS	Buried	Proton in Nδ1
417	ASP	Buried	Deprotonated
418	ASP	Surface	Deprotonated
424	GLU	Surface	Deprotonated
430	ASP	Buried	Proton in Oδ2
453	ASP	Surface	Deprotonated
457	ASP	Surface	Deprotonated
463	GLU	Buried	Deprotonated
468	HIS	Buried	Proton in Nɛ2
472	GLU	Surface	Deprotonated
476	GLU	Surface	Deprotonated
478	HIS	Surface	Proton in Nδ1 and Nε2
484	HIS	Surface	Proton in Nδ1
488	ASP	Surface	Deprotonated
496	ASP	Buried	Deprotonated
497	GLU	Surface	Deprotonated
503	GLU	Surface	Deprotonated
505	GLU	Surface	Deprotonated

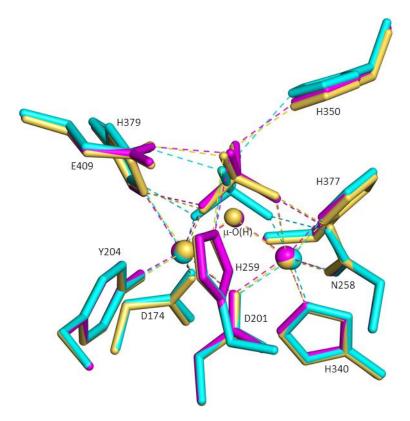


Figure A5. Superimposed active sites of the TaPAPhy\_b2:PO<sub>4</sub> structures

Comparison of the three states of the active site obtained in the different TaPAPhy\_b2:PO<sub>4</sub> crystal structures. Cyan, product-bound state. Magenta, substrate-bound state. Yellow, regeneration state.

#### Table A19. Comparison of the active sites of plant PAPhy with TaPAPhy\_b2 as reference

Amino acid positions compared corresponded to (1) non-conserved residues within 10 Å of the phosphate ion in the TaPAPhy\_b2 structure, (2) non-conserved residues forming part of PAPhy motifs or in their vicinity, or (3) non-conserved residues forming part of PAP motifs or in their vicinity. Residues in each of the positions analysed that did not show conservation when compared to TaPAPhy\_b2 were shaded in lilac (TaPAPhy\_a1), green (HvPAPhy\_a), orange (OsPAPhy\_b), yellow (ZmPAPhy\_b) or pink (GmPAPhy\_b).

TaPAPhy_b2	TaPAPhy_b1	TaPAPhy_a1	HvPAPhy_a	OsPAPhy_b	ZmPAPhy_b	GmPAPhy_b	Motif	b → a	Cereal $\rightarrow$ Soybean
His23	His23	His23	His23	His22	His22	Val14	PAPhy 1	n/a	$His \rightarrow Val$
Leu199	Leu199	Val199	Val199	Leu198	Leu198	lle189	n/a	n/a	n/a
Ser203	Ser203	Cys203	Ser203	Ser202	Cys202	Thr193	PAP 2	n/a	n/a
Leu207	Leu207	Met207	Met207	Leu206	Leu206	Leu197	n/a	$Leu \to Met$	n/a
Thr215	Thr215	Ala215	Thr215	Thr214	Ala214	Ser205	n/a	n/a	n/a
Ser221	Ser221	Ala221	Ser221	Ser220	Ala220	Ser211	PAPhy 4	n/a	n/a
Ala223	Ala223	Gly223	Gly223	Ala222	Ala222	Pro213	PAPhy 4	n/a	Ala/Gly $\rightarrow$ Pro
Lys224	Lys224	Lys224	Lys224	Asn223	Lys223	Leu214	PAPhy 4	n/a	Lys/Asn → Leu
Ser225	Ser225	Ser225	Ser225	Ser224	Ser224	Deletion	PAPhy 4	n/a	Ser $\rightarrow$ Deletion
Gln263	Gln263	Glu263	Glu263	Glu262	Gln262	Lys252	n/a	n/a	Gln/Glu → Lys
Ala306	Ala306	Ala306	Ala306	Ala305	Ser305	Ala295	n/a	n/a	n/a
Ala308	Ala308	Ala308	Ala308	Ala307	Ala307	lle297	n/a	n/a	n/a
Ala341	Ala341	Ala341	Ala341	Ala340	Ala340	Pro330	n/a	n/a	n/a
Ser345	Ser345	Thr345	Thr345	Ser344	Thr344	Ser334	n/a	n/a	n/a
Thr346	Thr346	Thr346	Thr346	Thr345	Thr345	Ser335	n/a	n/a	n/a
Tyr347	Tyr347	Tyr347	Tyr347	Phe346	Tyr346	Tyr336	n/a	n/a	n/a
Lys348	Lys348	Lys348	Lys348	Lys347	Lys347	Glu337	n/a	n/a	$Lys \to Glu$
Ala354	Ala354	Val354	Val354	Ala353	Ala353	Ala343	n/a	Ala $\rightarrow$ Val	n/a
Ser401	Ser401	Ser401	Ser401	Ser400	Ser400	Thr390	n/a	n/a	n/a
Thr413	Thr413	Thr413	Thr413	Thr412	Thr412	lle402	PAPhy 5	n/a	$Thr \to Ile$
Thr414	Thr414	Thr414	Thr414	Ser413	Ala413	Lys403	PAPhy 5	n/a	Thr/Ser/Ala $\rightarrow$ Lys
His415	His415	His415	His415	Tyr414	His414	Phe404	PAPhy 5	n/a	n/a
Asp418	Asp418	Glu418	Glu418	Glu417	Glu417	Glu407	PAPhy 5	n/a	n/a

TaPAPhy_b2	TaPAPhy_b1	TaPAPhy_a1	HvPAPhy_a	OsPAPhy_b	ZmPAPhy_b	GmPAPhy_b	Motif	b → a	Cereal $\rightarrow$ Soybean
Pro419	Pro419	Pro419	Pro419	Pro418	Ala418	Pro408	PAPhy 5	n/a	n/a
Arg421	Arg421	His421	His421	Arg420	His420	His410	PAPhy 5	n/a	n/a
Glu424	Glu424	Asp424	Asp424	Asp423	Asp423	Asp413	PAPhy 5	n/a	n/a
Met426	Met426	Arg426	Arg426	Leu425	Ala425	Leu415	PAPhy 5	n/a	n/a
Ser427	Ser427	Pro427	Pro427	Ser426	Ser426	Ser416	PAPhy 5	Ser $\rightarrow$ Pro	n/a
Thr428	Thr428	Lys428	Lys428	Thr427	Thr427	Thr417	PAPhy 5	Thr $ ightarrow$ Lys	n/a
Asp430	Asp430	Asn430	Asn430	Asp429	Asp429	Asp419	PAPhy 5	$Asp \to Asn$	n/a
Ala431	Ala431	Ala431	Ala431	Pro430	Pro430	Pro420	PAPhy 5	n/a	n/a
Phe432	Phe432	Phe432	Phe432	Phe431	Phe431	Tyr421	PAPhy 5	n/a	n/a
Met433	Met433	lle433	lle433	Met432	Met432	Met422	PAPhy 5	$Met \to lle$	n/a

# Appendix 3. Recombinant expression of GST-PNGase F and GST-Endo F1 in *Escherichia coli*

This appendix reports the expression and purification of the recombinant fusion protein glycosidases GST-PNGase F and GST-Endo F1, used in **Chapter 3** for the enzymatic deglycosylation of TaPAPhy\_b2 to generate samples for X-ray crystallography. Constructs for the expression of the two glycosidases with GST fusion tags in *Escherichia coli* were obtained from Dr Yoav Peleg (The Israel Structural Proteomics Center, The Weizmann Institute of Science, Rehovot, Israel) and expressed and purified following the procedure described by the original source of the plasmids (Grueninger-Leitch *et al.*, 1996).

## A3.1. Materials and methods

### A3.1.1. Transformation

Upon arrival, pGEX3 constructs containing the glycosidase coding sequences were transformed into *E. coli* Stellar competent cells (Clontech-Takara) for plasmid sequencing, storage and propagation following protocol in **Chapter 3, section 3.1.1.4.** Colonies were selected in LB agar plates with ampicillin (100 µg mL<sup>-1</sup>) and grown in 10 mL LB liquid culture containing the same antibiotic for plasmid extraction. Purified plasmids were used for the transformation of BL21 *E. coli* expression strain.

#### A3.1.2. Expression

A small-scale expression trial to check for recombinant protein expression and solubility was performed as described for the PAPhy enzymes in **Chapter 3, section 3.1.1.5.** 200  $\mu$ L of BL21 overnight cultures resulting from the transformation of each of the two glycosidase constructs were inoculated into 10 mL of LB media with ampicillin (100  $\mu$ g mL<sup>-1</sup>), grown at 37°C and 180 rpm to an OD<sub>600</sub> of 0.8 and cooled down to room temperature before induction with 0.2 mM IPTG. Expression was left to carry on for 4 h at 22°C and 180 rpm before samples were taken to check for total cell and soluble fraction recombinant protein expression on SDS-PAGE.

Once the production of soluble protein was confirmed, the expression of recombinant glycosidases was scaled-up to a total of 1 L of culture media per enzyme, distributed between two 2 L conical flasks with 500 mL each. The same protocol as for the expression trial was followed. Expression cultures were centrifuged for 20 min at 7500 x g and 4°C in a standing high-speed centrifuge in order to separate the cells from the culture media. Cell pellets for each glycosidase were resuspended in 30 mL of cold lysis buffer (50 mM Tris/HCl pH 8.0, 0.5% (v/v) triton X-100), snap-frozen in liquid nitrogen and stored at -80°C ready for purification.

#### A3.1.3. Purification

Frozen pellets were left to defrost at room temperature before subjecting them to three cycles of cell lysis per glycosidase using a French press. The soluble fractions were separated from cell debris by centrifugation for 20 min at 48000 x g and 4°C in a standing high-speed centrifuge. Recombinant glycosidases were purified from the soluble fractions following a two-step purification protocol.

The first purification step consisted of GST affinity chromatography in an ÅKTA Pure chromatography system (GE Healthcare), using a 1 mL GSTrap 4B cartridge (GE Healthcare) for each glycosidase, at 4°C and a flow rate of 0.3 mL min<sup>-1</sup>. The soluble fractions were loaded onto the corresponding GSTrap 4B cartridges after preequilibration with 10 CV of binding buffer (50 mM Tris/HCl pH 8.0). The cartridges were then washed with binding buffer until a stable UV signal was registered by the ÄKTA system. The recombinant proteins were eluted with a gradient of 0–10 mM of reduced glutathione, resulting from the gradual mixing of binding buffer and elution buffer (50 mM Tris/HCl pH 8.0, 10 mM reduced glutathione), and a 20 mL step with elution buffer. 2 mL fractions were collected during the elution and results were assessed by running denatured samples of the peak fractions on SDS-PAGE. Fractions containing the recombinant glycosidases were concentrated bellow 1 mL using 10 kDa MWCO centrifugal filters (Merck) before further purification.

The second step of glycosidase purification was performed at 4°C by gel filtration on a HiLoad 16/600 Superdex 75 pg column (GE Healthcare) pre-equilibrated and eluted at a flow rate of 0.4 mL min<sup>-1</sup> with 50 mM Tris/HCl pH 8.0 and 200 mM NaCl. The elution was carried out collecting 2 mL fractions and results were assessed by running denatured samples of the peak fractions on SDS-PAGE. Fractions containing pure glycosidases were pooled and concentrated for dialysis before storage in the recommended buffer (Grueninger-Leitch *et al.*, 1996). GST-PNGase F was dialysed against 50 mM Tris/HCl pH 8.0 and 2.5 mM EDTA, while GST-Endo F1 was dialysed against 10 mM sodium acetate pH 5.5. After dialysis, the glycosidases were diluted in the appropriate dialysis buffer containing 50% (v/v) glycerol and stored at -20°C in 1 mg mL<sup>-1</sup> aliquots.

## A3.2. Results and discussion

## A3.2.1. Transformation

The pGEX3 constructs encoding the fusion glycosidases GST-PNGase F and GST-Endo F1 were successfully transformed into *E. coli* for plasmid propagation and expression. Sequences of the glycosidases without the GST fusion tag are collected in Table A20. The parameters for each glycosidase were computed with the addition of the GST tag.

The parameters for each protein sequence were computed with the ExPASy ProtParam tool (Gasteiger *et al.*, 2005). ' $\epsilon$ ', extinction coefficient at 280 nm measured in water assuming all cysteine residues are reduced; 'A 0.1% (= 1 g L<sup>-1</sup>)' absorbance at 280 nm of a 0.1% protein solution (equivalent to 1 g L<sup>-1</sup>) assuming all cysteine residues are reduced.

Construct	MW (kDa)	MW + GST tag (kDa)	ε (M <sup>-1</sup> cm <sup>-1</sup> )	A 0.1% (= 1 g/L)
PNGaseF-pGEX3	31.69	61.76	116200	1.928
APADNTVNIKTFDKVKNAFG EIDVTDFKSLLSGNTELKIYTET PYDAGSRGCAEWCFRTHTIA NGDAFYAISSFVIAKSNTPISA	WLAKGREYSVDFDIVYG	TPDYKYSAVVPVIQYNKSSIE	OGVPYGKAHTLGLKKNIQI	
EndoF1-pGEX3	34.78	58.66	75180	1.315
	CDLYNLDGVFFDDEYSA	QTPPPSGFVTPSNNAAARL	AYETKQAMPNKLVTVYV	YLKPLQDKGIKVILSILGNHDR /SRTSSFPTAVDGVNAGSYVD KLIAKELYGDELVYSNTPYSKD

## A3.2.2. Expression

Good levels of recombinant protein expression were observed in BL21 cultures after 4 h at 22°C for both glycosidases. While most of the expressed GST-Endo F1 was detected in the soluble fraction, little soluble protein was detected for GST-PNGase F

Table A20. Constructs for the expression of recombinant glycosidases with GST fusion tags in E. coli

compared to the total cell protein samples, indicating that a considerable portion of this protein ended up in inclusion bodies (data not shown).

### A3.2.3. Purification

The results of the GST affinity purification of GST-PNGase F and GST-Endo F1 recombinant glycosidases are displayed in Figure A6A and Figure A6B, respectively. A yield of 8.4 mg L<sup>-1</sup> was obtained for GST-PNGase F after the first purification step, while 17.2 mg L<sup>-1</sup> were obtained for GST-Endo F1.

The results of the gel filtration step of GST-PNGase F and GST-Endo F1 recombinant glycosidases are displayed in Figure A7A and Figure A7B, respectively. A total of 4.5 mg L<sup>-1</sup> of GST-PNGase F were obtained at the end of the purification, in contrast to 11.3 mg L<sup>-1</sup> of GST-Endo F1.

## A3.3. Conclusions

The successful expression and purification of two recombinant glycosidases with GST fusion tags in *E. coli* achieved in this appendix allows for the reduction of costs in the generation of deglycosylated recombinant protein samples for X-ray crystallography obtained from *Pichia pastoris* expression. The activity of the recombinant glycosidases *versus* equivalent commercial enzymes is compared in **Chapter 3, section 3.2.2.3.3**.

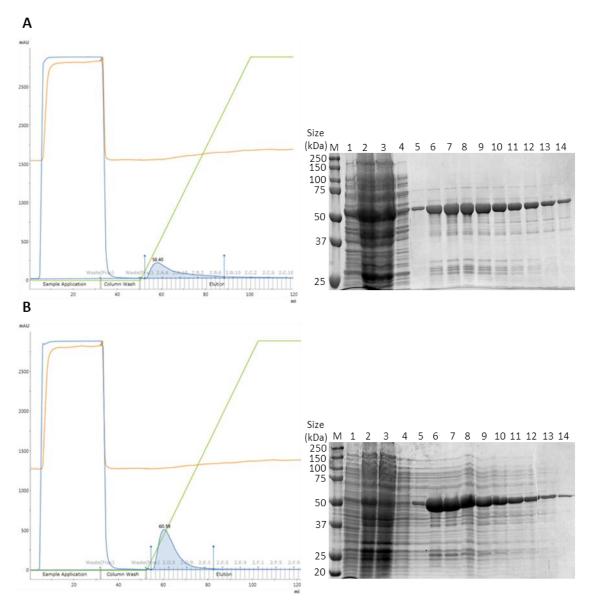


Figure A6. GST affinity purification of recombinant glycosidases

Chromatograms and 10% (v/v) acrylamide SDS-PAGE gels with results of the GST affinity purification of recombinant GST-PNGase F (**A**) and GST-Endo F1 (**B**). In chromatograms: blue line, UV trace; orange line, conductivity trace; green line, concentration of elution buffer. In gels: lane M, dual colour protein standards (BIO-RAD); lane 1, total cell protein; lane 2, soluble fraction; lane 3, column flow-through; lane 4, column was; lanes 5 to 14, peak elution fractions containing recombinant glycosidase.

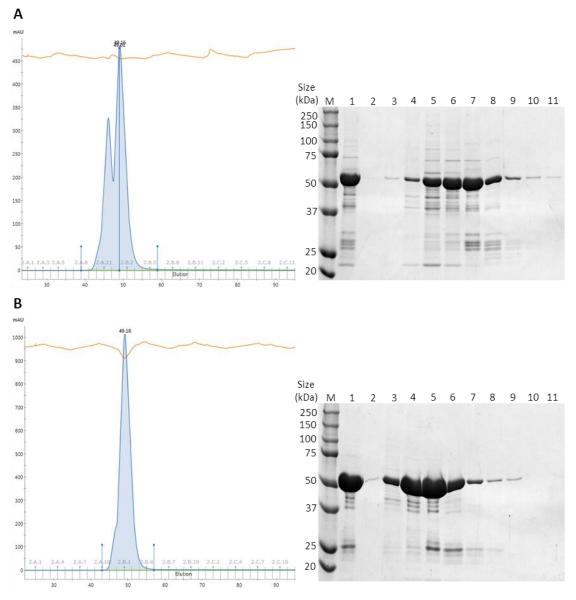


Figure A7. Gel filtration purification of recombinant glycosidases

Chromatograms and 10% (v/v) acrylamide SDS-PAGE gels with results of the GST affinity gel filtration purification of recombinant GST-PNGase F (**A**) and GST-Endo F1 (**B**). In chromatograms: blue line, UV trace; orange line, conductivity trace; green line, concentration of elution buffer. In gels: lane M, dual colour protein standards (BIO-RAD); lane 1, GST affinity purified protein; lanes 2 to 11, peak elution fractions containing pure recombinant glycosidase.

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