Jekyll and Hyde: The switch from environmental resident to antibiotic-resistant superbug in *Pseudomonas aeruginosa*

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But it didn't matter if I drank the stuff

I just kept on changing anyway!

Now I was

Jekyll, Jekyll, Hyde, Jekyll, Hyde, Hyde, Jekyll

Jekyll, Jekyll, Hyde, Jekyll, Hyde!

— Alan "Brain" Power

"Arthur's Almost Live Not Real Music Festival." *Arthur,* created by Marc Brown, Season 3, Episode 11, PBS, 1998

Abstract

Pseudomonas aeruginosa strains embrace numerous strategies to enable their survival across a diverse range of environments. Historically, analysis of the core genome phylogeny has displayed five major clades one of which appeared distant from the other groups. This thesis presents detailed analysis of the divergent clade, characterised by the *P. aeruginosa* PA7 strain, to confirm the 16S rRNA sequence is identical to other *P. aeruginosa* strains and is unlike those belonging to other *Pseudomonas spp.* In contrast, methods utilising the whole genome reveals that this divergent group of PA7-like strains is distinctive enough to form its own separate species. Furthermore, detailed analysis of the *P. aeruginosa* core genome revealed groups of strains linked to either clinical or environmental origins. Niche associated core groups could be characterised by both gene presence and absence, as well as by single nucleotide polymorphisms. In terms of the clustering based on the *P. aeruginosa* accessory genome, few accessory clusters were spread across multiple core groups. This, coupled with a lack of gene flow between the core groups, suggests that the core genome provides a basis for niche adaption that is completed by the characteristics of the accessory genome. Additionally, this thesis sought to investigate how environmental *P. aeruginosa* isolates adapt to clinical niches by using the presence of chloramphenicol and ciprofloxacin antibiotics to simulate a clinical niche. This uncovered the trajectories taken by the organism to resist antibiotic pressure which involved "switching-on" intrinsically encoded efflux pumps. After the removal of antibiotic pressure, the efflux systems were "switched-off" by additional mutations. Whilst these mutations reduce antibiotic tolerance, they also alter fitness to varying degrees relative to the ancestral parent and mutant strains.

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List of abbreviations

AAI – Average amino acid identity

AMR – Antimicrobial resistance

ANI – Average nucleotide identity

ATTC – American Type Culture Collection

AVI – Avibactam

AZT – Aztreonam

BCCM – Belgian Coordinated Collections of Microorganisms

BH – Benjamini-Hochberg

BHI – Brain Heart Infusion

BLAST – Basic Local Alignment Search Tool

BRIG – BLAST Ring Image Generator

CARD – Comprehensive Antibiotic Resistance Database

CAZ – Ceftazidime

CAZ/AVI – Ceftazidime with Avibactam

CHL – Chloramphenicol

CI – Confidence intervals

CIP – Ciprofloxacin

dDDH – digital DNA-DNA hybridisation

DDH – DNA-DNA hybridisation

DNA – Deoxyribonucleic acid

DSZM – Deutsche Sammlung von Mikroorganismen und Zellkulturen

EUCAST – European Committee and Antimicrobial Susceptibility Testing

GBDP – Genome BLAST Distance Phylogeny

GGDC – Genome-to-genome distance calculations

ICNP – International Code of Nomenclature of Prokaryotes

IGB – Integrated Genome Browser

IMP – Imipenem

IQR – Interquartile range

LB – Luria-Bertani Broth

LES – Liverpool Epidemic Strain

LMG – Laboratorium voor Microbiologie, Universiteit Gent

LPSN – List of Prokaryotic names with Standing in Nomenclature

M – Mean

Mdn – Median

MDR – Multidrug resistant

MEM – Meropenem

MFS – Major facilitator superfamily

MGE – Mobile genetic elements

MHA – Mueller-Hinton agar

MHB – Mueller-Hinton broth

MIC – Minimum inhibitory concentration

MLSA – Multilocus sequence alignment

MLST – Multilocus sequence typing

NCTC – National Collection of Type Cultures

NFW – Nuclease free water

OD – Optical Density

PA-CN – Pseudomonas agar supplemented with cetrimide and sodium nalidixate

PCR – Polymerase chain reaction

PIP – Piperacillin

PIP/TAZ – Piperacillin with Tazobactam

QRDR – Quinolone-resistance-determining region

RC – Robust clustering

RES – Reactive electrophilic species

RNA – Ribonucleic acid

RND – Resistance nodulation division

RPM – Revolutions per minute

rRNA – ribosomal RNA

RSCU – Relative synonymous codon usage

SD – Standard Deviation

SNP – Single nucleotide polymorphism

T6SS – Type six secretion system

TAZ – Tazobactam

TOB – Tobramycin

TSA – Tryptic Soy Agar

TYGS – Type Strain Genome Server

vcf – Variant call format

VISA – Vancomycin-intermediate *Staphylococcus aureus*

WGS – Whole Genome Sequencing

XDR – Extensively drug-resistant

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Chapter 1 - Introduction

1.1 Bacterial adaption

The concept of natural selection was first described in 1859 by Charles Darwin (1). It describes the process of evolution whereby organism better adapted to their environment have the highest fitness and will thereby pass on these characteristics through their genes onto their offspring. Over time this process selects the best characteristics to fit the environment leading to changes which refine the organism's ability to survive, resulting in divergence from its original ancestor. In the context of bacteria, species have adapted to specific niches and have been found in numerous environments including soil, water, food, animals, plants, and air. Their ability to grow in these environments can be influenced by factors such as competitors, presence of nutrients, oxygen, temperature, and availability of space. The species which are better adapted to their environmental conditions are the ones which will persist in their environment and pass on their traits.

Bacterial strains can be commensal, being harmless to other organisms, or they can be pathogenic, where they cause disease. Pathogenic strains use a host as their environment and can be either obligate pathogens, where they always cause infection in the hosts, or they can be opportunistic pathogens, only causing disease when the host immune system is compromised. Successful pathogens can be characterised by their production of virulence factors and antimicrobial resistance mechanisms allowing them to invade, evade, persist, and cause disease within the host. The genes encoding these factors can either be intrinsic to the bacteria, acquired through the transfer of genetic material, or develop as the result advantageous mutations (2-4).

1.1.1 Defining a bacterial species

In biology a species is defined as a group of organisms that can reproduce with one another in nature and produce fertile offspring (5). When considering bacteria, reproduction is described as asexual where one "mother" cell undergoes binary fission to produce two "daughter" cells. This allow genetic material to be passed from mother to daughter. Bacteria can also share genetic material between strains considered separate species through mechanisms such as homologous recombination, however this is not generally considered to be a form reproduction (6). Presently, speciation of bacteria is based on a range of specifications including morphological appearance, Gram stain, preferred culture conditions, biochemical tests, serological tests and more recently the genetic characteristics of the bacterium (7).

1.1.2 Bacterial ecotypes in modelling adaption

In nature, bacteria survive within mixed populations that interact with each other and so studying bacteria as single organisms that act alone in their niche is inappropriate. Therefore, bacteria can be modelled as ecotypes which can be defined as a group of bacteria that are ecologically akin in that there is little diversity within the ecotype (8). A single bacterial species can contain multiple ecotypes which contain the characteristics of the species but are distinctive in the way they interact and survive within their environment (9). Hence, two ecotypes can be described as evolutionary lineages which are separate from one another and have their own independent fates. Figure 1-1 depicts the effects of mutation and recombination events on altering the diversity of bacterial ecotypes.

In Figure 1-1a, an adaptive mutation occurs within one strain in Ecotype 1. This mutation improves the fitness of the strain providing it with the ability to outcompete the other strains within its ecotype without affecting Ecotype 2 due to the ecological differences between them. This is termed periodic selection and results in the selection of distinct strains within the

ecotype (8). An example of this includes the acquisition of antibiotic resistance genes such as $bla_{CTX\text{-}M}$ which provide a fitness advantage to strains when antibiotics such as cefoxitin are prevalent in the environment (10). Therefore, strains containing the advantageous genotype will proliferate and overtake the existing strains within the ecotype.

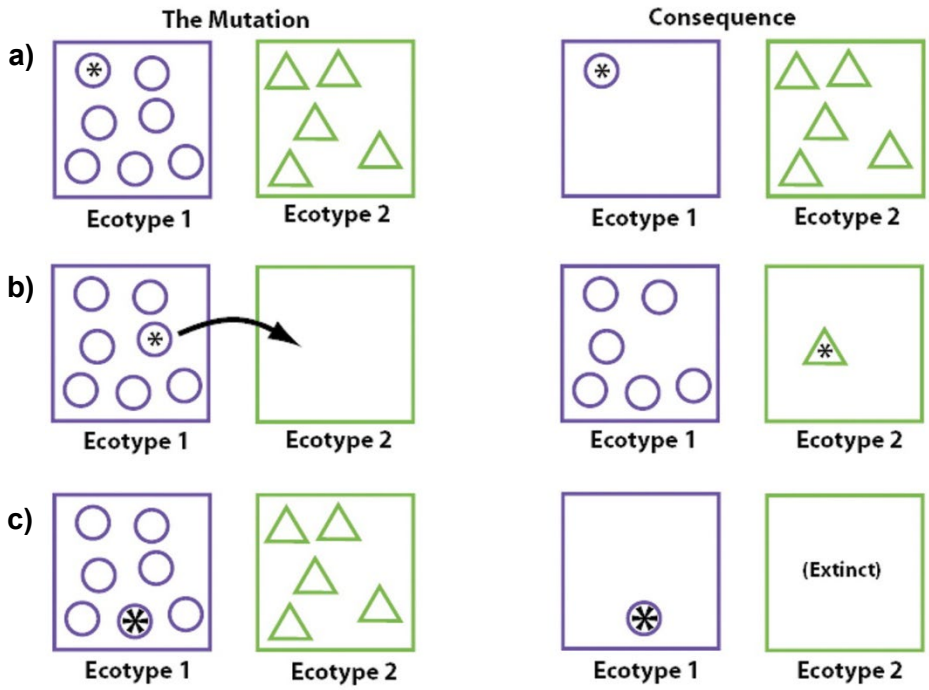

Figure 1-1: Effects of mutation and recombination events in shaping ecotype diversity. Events depicted include a) Periodic selection mutations, b) Ecotype-forming mutations, and c) Speciation-quashing mutations. Shapes depict like strains belonging to an ecotype with those marked with an asterisk (*) indicating mutants containing adaptive mutations. Image based on Figure 1 from Cohan et al (8)

In ecotype-forming mutations (Figure 1-1b) a mutation or recombination event within a strain creates a mutant in Ecotype 1 that can utilise new resources resulting in its colonisation of a new ecological niche. This mutant is distinctive from the strains within its original ecotype, Ecotype 1, and forms the separate Ecotype 2. As a result, the mutant strain is no longer subject to conditions imposed on strains within Ecotype 1 (8). This has been observed in experiments with *Escherichia coli* grown in a minimal amount of glucose and abundance of citrate (11). Citrate was not the favoured substrate by the *E. coli* strain forming the initial ecotype. However, mutations in strains resulting in the ability to effectively metabolise citrate provide them with

the ability to utilise a new resource that is inaccessible to the strains present in its original ecotype. Thus, a new ecotype was formed by the citrate metabolising mutants and though it was competitive with the strains in the original ecotype, an extinction event did not occur (11).

Speciation-squashing mutations, Figure 1-1c, are the result of mutant strain that develops a fitness advantage so great that allows it to not only out-compete the strain within its own ecotype, Ecotype 1, but also strains within the other ecotypes present in the environment, Ecotype 2. The result of a mutation with such capabilities results in the extinction of Ecotype 2, leaving the mutant strain the sole survivor of the environment (8). This is evident in *Pseudomonas aeruginosa* where the acquisition of type six secretion systems (T6SS) provides strains with the ability to secrete effector proteins into nearby bacterial species including *P. aeruginosa* (12). To survive these attacks, strains require immunity proteins that are restricted to the *P. aeruginosa* species. Therefore, the strains containing the T6SS can successfully target strains present in another ecotype in addition to strains within its own ecotype that do not possess the immunity proteins (13).

In nature it is not required for an advantageous mutation to be exclusive to a singular ecotype as recombination events can occur within and between species. Additionally, it is not required for all strains within an ecotype to be identical copies of one another. Therefore, a small degree of diversity represented through allelic variation can be expected within the ecotype. These different alleles will coexist in the ecotype until the developments of a strain with a sufficiently increased fitness. Cohan *et al.* took this into account when proposing the "Adapt Globally Act Locally" model which is depicted in Figure 1-2 (8).

Within the Adapt Globally Act Locally model, strains within Ecotype 1 and Ecotype 2 express slight variation across their genome which is not sufficient to provide increased fitness over

other members in the population. Then, specific mutations arise which provide an adaptive advantage within the ecotype, and through periodic selection (Figure 1-2a) the mutant becomes the sole inhabitant of the ecotype without effecting other ecotypes within the environment (Figure 1-2b). The adaptive mutation can also be advantageous in other ecotypes which is possible if recombination occurs between the mutant of Ecotype 1 and Ecotype 2 allowing for the transfer of only advantageous mutations (Figure 1-2b). This leads to the generation of a new mutant which retains the genetic material of its parent but with the addition of the advantageous mutation that proliferated in Ecotype 1. Following this, the new mutant is able to proliferate in Ecotype 2 without effecting Ecotype 1 as it does not contain all the characteristics required to be present in the ecotype nor is it competing for the same resources (Figure 1-2c). Hence, it is possible for recombination events to take place between ecotypes that can provide strains with fitness advantages. Such events can be observed in the human gut where multiple species and strains co-exist. Within this environment genes like *ermB,* which provides resistance to macrolides, can be transferred between different species providing multiple ecotypes the ability to survive in conditions where the antibiotic is present (14).

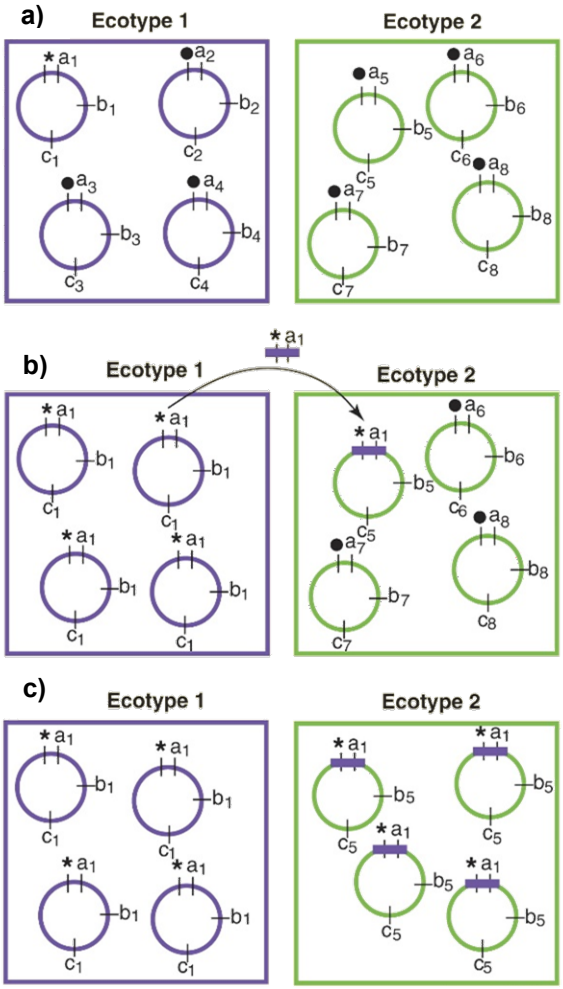

Figure 1-2: Illustration of the "adapt globally, act locally" concept described by Cohan et al. *a) an adaptive mutation marked by an asterisk (*) increases fitness of a singular strain in Ecotype 1. b) the adaptive mutant along with its specific configuration of alleles takes over Ecotype 1 and transfers the adaptive mutation through recombination to a strain belonging to Ecotype 2. c) the adaptive mutant in Ecotype 2 now has the fittest phenotype resulting in the mutant and its alleles becoming dominant in Ecotype 2. Each circle represents an individual strain with gene represented by letters with allele variants numbered. Image is based on Figure 3 from Cohan et al (8)*

1.1.3 The role of mutations

Species of bacteria adapt to fit their ecological niches, however stress caused by limitations in resources essential for their survival or the presence of a competitor can act as a driving force to select mutations. Mutations are heritable changes to the bacterial genome caused by insertion, deletion, duplication, substitutions, and inversions of a single or series of bases. They can be synonymous, where the resulting mutation is silent with the amino acid coded for

remaining the same, therefore the protein translated retains its original structure and function (15). However, some mutations are nonsynonymous where changes lead to: missense mutations, where the amino acid coded for changes and can result in a structural change to the translated protein; nonsense mutations, where a premature stop codon results in early termination of the protein that is no longer functional; and frameshift mutations, where the reading frame changes resulting in the translation of non-functional proteins (16).

Changes to the non-coding regions, known as the intergenic regions, can affect the regulation and expression of the genes surrounding it. This is due to intergenic regions containing elements such as: promoters, which provide a binding site for RNA polymerase; operators, which act as binding sites for regulatory proteins; terminators, which mark the site for RNA polymerase to stop synthesising RNA; and small RNAs, which influence metabolism and cellular responses. Therefore, it is possible for intergenic regions to be under selection in environments where mutations in these regions play roles in adaption to the environment (17). Within *P. aeruginosa,* adaptive intergenic regions have been identified which can aid in the organism's adaption to a cystic fibrosis host (17-19). Whilst the specific function of the intergenic region involved was not identified in these studies, the changes seen in the intergenic regions aided in the tolerance towards antibiotics and improved nutrient acquisition thus creating a strain that is better adapted to its environment.

In terms of bacterial fitness, mutations can have beneficial, neutral, and deleterious effects which may alter the competitiveness of the strain (20). Whilst the majority of mutations are deleterious, a minority may increase fitness and are therefore beneficial (21). Bacteria carrying these mutations are more likely to survive in the environment due to natural selection.

The rate at which mutations occur in bacteria can also affect their ability to produce antibiotic resistant strains. In *E. coli*, overexpression of the AcrAB-TolC efflux pump, which can be caused by the presence of an antibiotic, is associated with decreased expression of *mutS* which is involved in repairing DNA mismatches (22). Therefore, these strains have higher mutation rates which can increases the chances of acquiring permanent antibiotic resistance (22). Additionally, deficiencies in MutS production by *P. aeruginosa* have shown that the resulting hypermutating phenotype facilitates the rapid acquisition of resistance in comparison to wild type strains (23). Though hypermutation can lead to the acquisition of antibiotic resistance, this strategy is only viable as a selection strategy under extreme conditions. This is due to the inability of *mutS* mutants to repair DNA mismatches which results in a strain more likely to develop mutations in useful genes that decrease fitness when compromised. This is evident in *mutS* mutants which are outcompeted by wildtype strains in competition assays (24).

1.1.4 Transfer of genetic material

Vertical gene transfer involves the transfer of genetic material from a parent cell to its offspring. As bacteria replicate the bacterial genome is copied with offspring inheriting the parental genome, including the traits which it codes for. Traits are not just derived from the parent cell and instead may be acquired from other strains and species through the horizontal transfer of genetic material such as mobile genetic elements (MGE) which are transferred between bacterial cells. MGEs can encode enzymes and proteins that give bacteria a competitive advantage with the mechanisms responsible for their transfer including conjugation, transduction, and transformation (Figure 1-3) (4).

Bacterial conjugation involves the transfer of a MGE from cell to cell (Figure 1-3a). In the process two bacterial cells are physically connected to one another through a pilus which creates a channel for the donor cell to transfer the MGE across to a recipient cell (25). The use

of bacterial conjugation has been implicated in the antibiotic resistance of many species due to its ability to transfer plasmids containing antibiotic resistant genes to strains that were originally susceptible (4). The ability of a plasmid to conjugate into another organism relies on transfer genes which initiate the formation of the pilus that facilitates the transfer of the plasmid to a recipient (26). Without these genes the plasmid would not be able to be transferred via conjugation to a recipient cell and will therefore need to exploit other mechanisms, which can include exploiting a conjugative plasmid, to facilitate transfer (27-29).

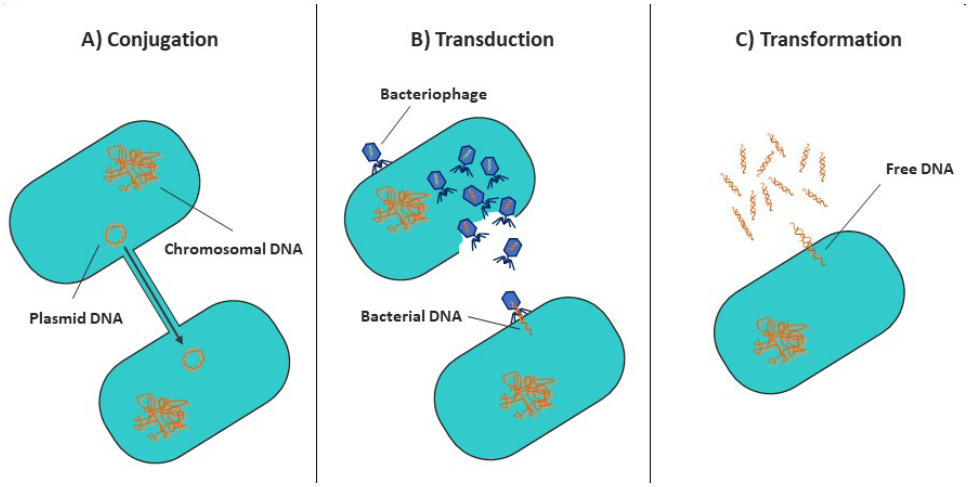

Figure 1-3: Mechanisms of horizontal gene transfer. A) Conjugation, where genetic material is transferred from a donor cell to a recipient. B) Transduction, where a bacteriophage incorporates and transports bacterial DNA to a recipient cell. C) Transformation, where free DNA released from either living or decaying cells is integrated into the recipient cell.

Transduction occurs when a bacteriophage inserts itself and the genetic material it is transporting into a recipient cell (Figure 1-3b). The genetic material transported by the bacteriophages can then be incorporated into the bacterial chromosome by recombination or from a plasmid where it will be expressed and replicated by the host cell's machinery (30). Strains of *Staphylococcus aureus* have evolved to use transduction for its own advantage by manipulating bacteriophages to spread pathogenicity islands containing virulence factors such as the toxic shock toxin (31, 32). These pathogenicity islands incorporate both the genes of the

bacteriophage itself as well as accessory genes like *tsst* (Figure 1-4) (32). Thus, enabling both the bacteriophage and the virulence gene to be transferred together.

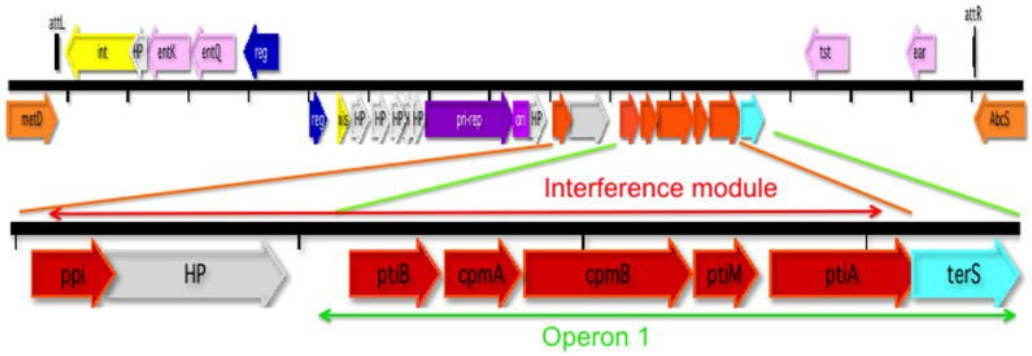

*Figure 1-4: Genome of a Staphylococcus aureus pathogenicity island. The tick marks indicate spacing at 1 kbp with the regions of operon 1 enlarged for visualisation. In orange are the flanking chromosomal genes, in yellow are the integrase and excision genes, in dark blue are the regulatory genes, in purple is the replication module, in red is the interference modules, in light blue is the terminate small subunit, in pink are the accessory genes including the toxic shock syndrome toxin 1 (*tsst*), in grey are hypothetical proteins, and in black are the att sites. Image is adapted from Figure 1 in Novick* et al. *(32)*

Transformation is the natural uptake of free DNA present in the extracellular environment and its recombination into the recipient genome (Figure 1-3c) (4, 33). The presence of DNA in the extracellular environment is due to its release from decomposing or living cells (33). If the released DNA contains genes that code for virulence factors and antibiotic resistance genes, transformation can enhance the pathogenicity of the receiving strains. In *Neisseria gonorrhoeae* transformation is a mechanism which facilitates the transfer of pathogenicity islands and contributes to its success as a pathogen (34, 35).

Overall, horizontal gene transfer allows for the acquisition of genetic material which contains genes coding for traits that can be beneficial such as increased virulence or antibiotic resistance. The newly recombined genes can then be inherited by the offspring through vertical gene transfer along with the traits already possessed by the strain or further action through mechanisms of horizontal gene transfer can help to propagate the genes.

1.1.5 Competition between bacteria

In bacteria, the competition for resources can lead to 'scrambled' and 'contest' competitions (36). In both scenarios, one strain of bacteria is favoured over its competitor either through direct or indirect methods.

Scrambled competition involves the rapid utilization of the available resources. In bacteria this involves one species depleting the shared resources before its competitor does through indirect methods (37). The production of iron scavenging siderophores by *P. aeruginosa* limits iron availability in the environment preventing its use by competitors, such as *E. coli* which require iron for its cellular processes, giving *P. aeruginosa* the competitive advantage (38).

Contest competitions involve one species interfering with its competitor by directly inhibiting its ability to grow. This can be through the production of compounds that give it the competitive advantage (37). One example of a contest competition involves T6SS in *P. aeruginosa*. The T6SS is used to transport toxins into competitor cells by piercing through the membrane of its competitor to directly inhibit their survival (39).

Within the human microbiome, many species of bacteria exist creating a diverse environment which protects the host from pathogen colonisation (40-42). It is possible for opportunistic pathogenic strains to be present, however these strains are harmless to the host under normal environmental conditions and only become pathogenic when the environment is disturbed (43). When this occurs, pathogens which have competitive traits can use this advantage to out-compete the commensal strains, allowing them to colonise and cause disease within their host (42, 44).

In general, competition between bacterial species can select for advantageous traits. These traits will improve the fitness of a strain allowing it outcompete competitors within its original niche or may even cause the strain to adapt to a new niche where it is more competitive. Therefore, species of bacteria can contain different mechanisms for competition which have been selected by their specific environment.

1.1.6 Altering gene expression

As previously discussed, mutations in genes can alter their function. If these mutations occur in regions involved in the regulation of other genes, such as in promoter regions or transcriptional regulators, the phenotypic characteristics of the strain can change. However, mutations are not necessarily required for changes in genes expression to occur as many genes are regulated through signals. This is due to the presence of complex global regulatory networks which can be influenced by the surrounding environment to change gene expression patterns. For example, in *Pseudomonas spp.* expression of genes can be altered according to the carbon source present which can affect the phenotype displayed by the cell (45, 46). Furthermore, single processes within these networks can be activated through multiple mechanisms. Within enteric bacteria the process of histidine utilisation is controlled by both nitrogen limitation and through cyclic AMP and its receptor protein CRP (47, 48). Hence, bacteria can respond to their environments without permanently changing their genome, though long-term exposure to stressors may require more permanent changes.

1.1.7 Genomic rearrangement

Bacterial species can rearrange their genomes through mechanisms resulting in inversions, translocation, duplication, and transposition of genomic regions that lead to structural changes to the bacterial chromosome. These genome rearrangements change the order of genes with the proximity to origin and terminus of replication, altering the level a gene is differentially

expressed (49). Depending on the genes that become differentially expressed, phenotypic changes can be observed in the organism. In the case of *E. coli,* genomic rearrangement of the chromosome from a strain selected for increased resistance to sodium deoxycholate showed altered sensitivity to antimicrobials which did not impact growth (50). Moreover, certain rearrangements can be associated with clinical cases, as is the case in *Helicobacter pylori¸* where specific inversions could be linked to disease state or gastric cancer (51, 52). Whilst genomic rearrangement has been detected in *P. aeruginosa* (53-55), its occurrence, effects on gene expression, and its phenotypic influence is not fully understood.

1.1.8 Codon utilisation

A codon is a series of three nucleotides which encode specific amino acids. In total there are 64 possible codon arrangements. In bacteria, three of these codons serve as stop codons to terminate protein synthesis and the other 61 correspond to one of 20 amino acids. As a result, a single amino acid can be coded for by up to six amino acids, known as redundancy. Despite being able to use numerous codon variations to encode for a singular amino acid, bacterial species show preferences over which codon they use for a particular amino acid (56). The bias seen in codon usage can be due to several reasons including optimising codon usage to correlate with the GC content of the genome and coevolution of the genome with gene copy number of tRNAs, where genes that utilise the most numerous tRNAs are more easily translated (57-59). Over time these codons become preferred due to the availability of their complementary tRNA molecule resulting in the use of these preferred codons in important and highly expressed genes (60, 61). Conversely, the use of the rarer codons, particularly in longer continuous stretches, effects the translation of the protein through ribosome pausing, ribosomal frameshifting and misincorporation of amino acids resulting in errors and/or reduced protein yields (62). Therefore, synonymous mutations that result in changes to codon utilisation can provide insight into which genes are adapted towards high or low expression levels. Furthermore, it is possible for some genes to use alternative start codons, such as GUG

and UUG, as opposed to the traditional AUG. These non-AUG start codons can effect gene expression as genes starting with non-AUG start codons have been shown to be less abundant than those starting with an AUG start codon (63).

Within *P. aeruginosa,* codon usage has been shown to favour the retention of horizontally acquired genes based on whether they use the optimal codon of the recipient strain (64). Accordingly, these genes are more likely to successfully incorporate themselves into the organisms' genomes long term. Conversely, horizontally acquired genes which do not use the optimal codons are under weaker selection and though they are able to successfully incorporate into the organisms' genomes, over time selection works against these genes (64).

Furthermore, codon usage bias has also been shown to be indicative of the environment from which an organism originates. Willenbrock *et al.* utilised two methods for determining the codon adaption index (CAI) (65): translational CAI (tCAI) and dominant CAI (dCAI) (66), to display the translational codon bias of an organism (67). From this the differences between tCAI and dCAI were used to cluster 318 bacterial strains which is displayed in Figure 1-5. The similarity in clustering did not necessarily translate according to strains found to be phylogenetic related based on sequence homology. Instead, the analysis showed that microbes from similar environmental origins clustered together, thus species with shared origins appear to have similarities in codon bias.

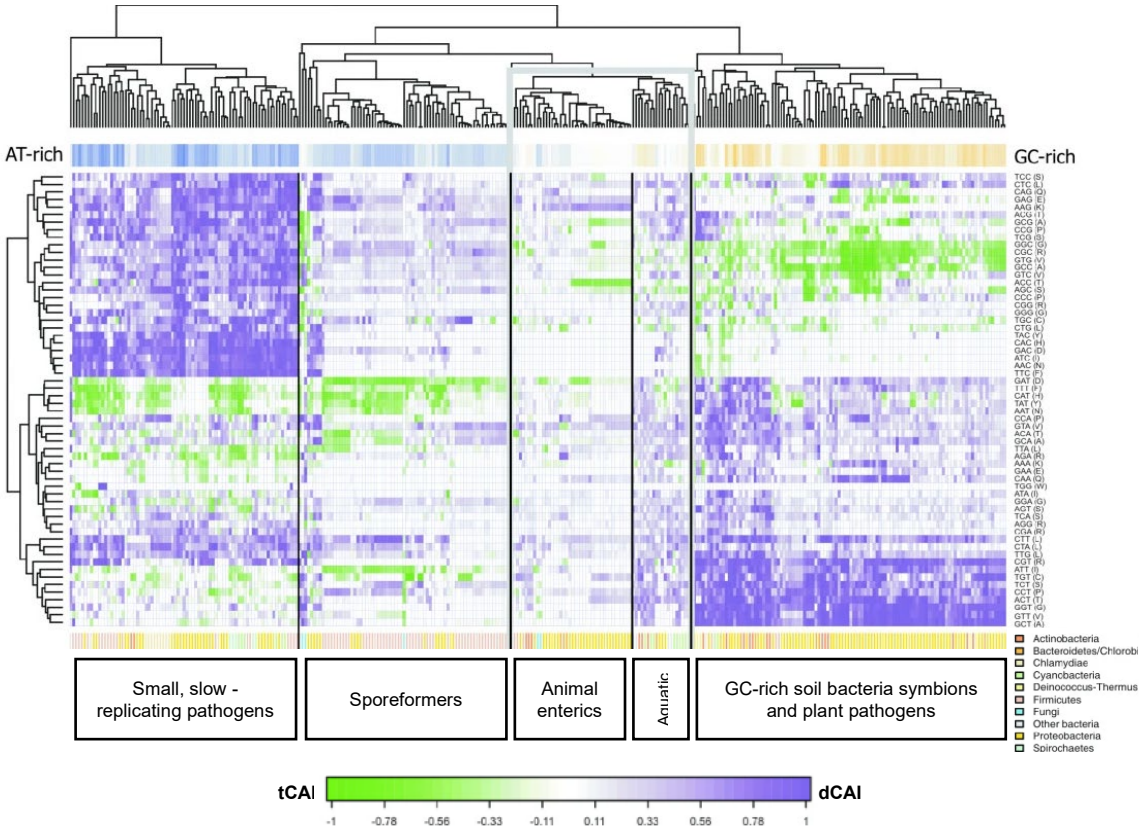

Figure 1-5: Cluster analysis of differential codon preference determined from tCAI and dCAI. Clustering is based on Euclidian distances as described in Willenbrock et al. *(67). Codons with greater preference by dCAI are in purple/blue with codons preferred by tCAI in green. GC content is indicated by the top annotations with AT rich strains coloured blue and GC rich strain coloured yellow. The bottom row annotation indicates the phylum of the strain as indicated in the key. Figure is based on Figure 2a from Willenbrock* et al. *(67).*

1.1.9 The influence of epistasis on fitness landscapes

Mutations within or between genes interact at different levels and cause various changes that alter the overall phenotype of the strain. This is defined as epistasis and is commonly seen in bacteria where it can impact the evolutionary trajectory of a strain. Within *P. aeruginosa* this can be observed through mutations to the gene encoding the β subunit of RNA polymerase, *rpoB,* that can lead to rifampicin resistance (68, 69). Whilst mutations to *rpoB* provide the strain with rifampicin resistance, it also leads to a reduction in the efficiency of RNA polymerase which reduces the fitness of the strain (70). Though reversion to wildtype *rpoB* would restore fitness levels, it would also restore susceptibility to rifampicin in the strain.

Instead, a second compensatory mutation occurs allowing the resistance to rifampicin to be retained whilst masking the cost of fitness. The compensatory mutation alone also reduces fitness, hence both mutations work reciprocally to produce a resistance phenotype that does not have a great fitness cost (70, 71).

Alterations in a bacterial genome can lead to increases or decreases in fitness which can continually change over time as part of an evolutionary trajectory to reach an optimum fitness level. Optimum fitness can be achieved through a series of mutations which can be mapped out graphically as a fitness landscape to display the genotype and fitness (Figure 1-6 and Figure 1-7).

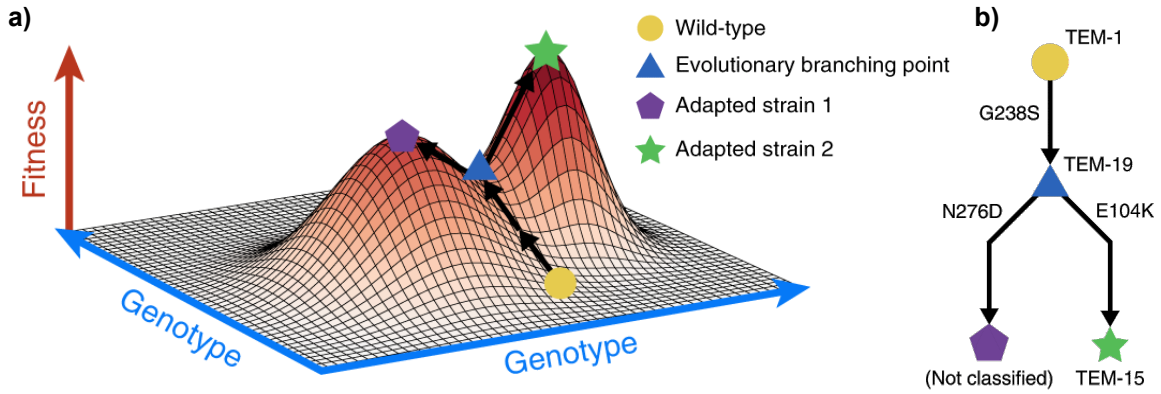

Figure 1-6: Fitness landscape model depicting the fitness of mutations in the TEM-50 gene of Escherichia coli. *Mutants strains are indicated by the shaped depicted in the key. a) Depicts the fitness landscape using the average growth rate of TEM mutant strains in cefotaxime as a measure for fitness. b) Depicts the evolutionary trajectory and mutations in TEM-1 as identified by Mira* et al. *(73). Image adapted from Figure 1 in Nichol* et al. *(72)*

The fitness landscape depicted in Figure 1-6 visually shows the trajectory of mutations in TEM-50 in context of fitness (72). The mutants present in the adapted strains provide resistance to cefotaxime and would therefore have increased fitness levels in the presence of cefotaxime. This corresponds to the peaks in Figure 1-6 which places the wildtype strain at the base of the

landscape as the strain with the lowest fitness. On the path to a resistant phenotype, the wildtype strain mutates to increase its fitness where it reaches an evolutionary branch point before a further mutation evolves the strain down one of two paths to the genotype of the adapted strains. Therefore, to reach peak fitness the strain will require two mutations. As mutations can occur in multiple points in a gene, Figure 1-7 illustrates the complexities of mutations in four different amino acids in the TEM-50 sequences which results in the production of 16 different genotypes. In this example the "1111" genotype provides the fittest configuration, however, the pathway to this genotype from the wildtype "0000" is not straightforward and the strain may incur fitness cost along the way (73).

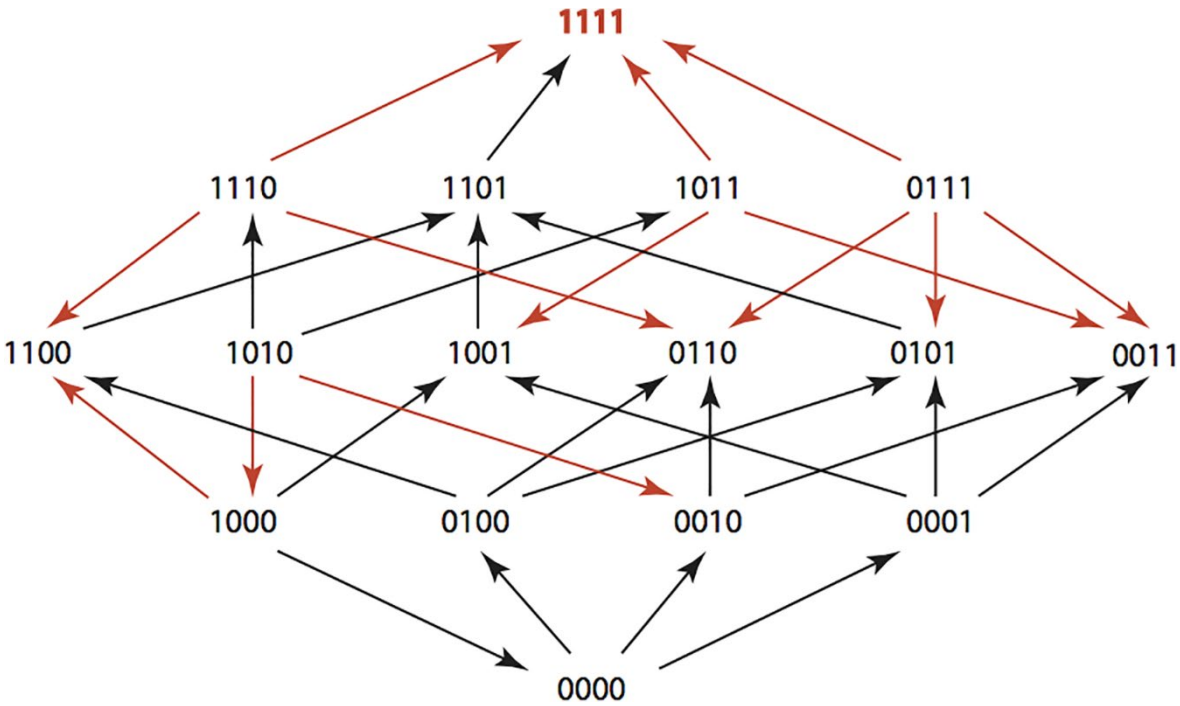

Figure 1-7: Fitness graphs connecting 16 genotypes found in TEM-50 from Escherichia coli to its adjacent genotypes. The graph depicts four possible amino acid substitutions in the TEM-50 gene with 0 indicating the unmutated wildtype and 1 indicating the substitution of an amino acid. The genotype with the highest fitness is indicated in red. Arrows show connection between two genotypes with the arrowhead pointing to the fitter genotype as determined by average growth rate in medium containing ampicillin 256 µg/ml. Red arrows indicate that the difference in growth rate between two genotypes was found to be statistically different by ANOVA with black arrows indicate no significance was found. Based on Figure 1 from Mira et al. *(73)*

1.2 *Pseudomonas aeruginosa*

As an opportunist pathogen, *P. aeruginosa* has been associated with causing infection in humans, animals, and plants and has been found both clinical and non-clinical settings (74-78). As a member of the ESKAPE group (*Enterococcus faecium, S. aureus, Klebsiella pneumoniae, Acinetobacter baumannii, P. aeruginosa* and *Enterobacter spp.*) it is a clinically important pathogen due to its ability to cause nosocomial infections in immunocompromised patients and accumulate resistance to antibiotics (79). Infections that are caused by resistant bacteria are more difficult to treat. They result in longer illness periods, prolonged hospital stays, and increased mortality which risks the lives of immunocompromised individuals (80).

It was estimated that a continued rise in antibiotic resistant infections would result in 10 million deaths a year by 2050 (81). In 2019, studies have estimated that approximately 3.57 million deaths were associated with antimicrobial resistance (AMR) and around 926 000 deaths were due to ESKAPE group pathogens (82). Thus, the inclusion of carbapenem resistant *P. aeruginosa* as a priority 1 pathogen requiring new and effective antibiotics by the World Health Organisation is understandable (83).

1.2.1 The *Pseudomonas aeruginosa* type strain

The *Pseudomonas aeruginosa* type strain, PAO1, was first isolated from a wound infection in the 1950s and was initially characterised by its biochemical characteristics (84). Later, the PAO1 was the first strain of the *P. aeruginosa* species to have its complete genome sequence published revealing the genetic characteristics of the strain (85). The sequence of PAO1 was found to be approximately 6.3 Mbp with a GC content at 66.6%. This corresponded to many open reading frames, 5570, that were detected and found to encode for a variety of regulatory genes, secretion systems, outer-membrane transporters, efflux systems, metabolic pathways,

and chemotaxis systems (85). Hence the large genome size of the strain allows the organism to encode the various mechanisms that allow it to survive and adapt in different environments.

1.2.2 *Pseudomonas aeruginosa* in the environment

P. aeruginosa has been found in a variety of environments including soil, rivers, public swimming pools, wastewater treatment plants, and healthcare settings (77, 86-91). Whilst many studies describe *P. aeruginosa* to be a natural microorganism of the soil, many of the studies looking to isolate *P. aeruginosa* from environmental sources, such as soil, have found a low prevalence ranging from 0 to 24% (86, 92-94). In particular, the prevalence of *P. aeruginosa* appears to be lower in soils that are thought to be uncontaminated by human activity in comparison to soils where there is higher human activity and are contaminated with hydrocarbons or pesticides (86, 94). For example, Crone *et al.* determined that from 136 samples taken from uncontaminated environments, only 12% were positive for *P. aeruginosa* (86). Furthermore, Vives-Flórez et al, found that from 29 non-oil contaminated environmental samples only 10.3% were found to host *P. aeruginosa* (94). Additionally, the presence of *P. aeruginosa* in environments such as hospital wastewater can facilitate the contamination of the natural environment where the effluent is disposed into a river or where sewage sludge is used as a soil fertilizer (91).

1.2.3 *Pseudomonas aeruginosa* as a clinical pathogen

As a clinical pathogen, *P. aeruginosa* has been associated with bloodstream, burn wound, ear, eye, respiratory and urinary tract infections (95-100). Additionally, in patients suffering with cystic fibrosis, *P. aeruginosa* is often found as a coloniser of the respiratory tract and is responsible for the chronic infections that increase mortality (101). This is due to the ability of *P. aeruginosa* to adapt to the cystic fibrosis environment by producing virulence factors that overcome the host defence and competition from other bacterial species (102).

As an opportunistic pathogen *P. aeruginosa* poses as a risk to those who are immunocompromised and is therefore associated with nosocomial outbreaks (103). Infections caused by the pathogen are treated with antibiotics, with the specific agent determined by local guidance and adjusted according to resistance levels. In general, quinolone antibiotics such as ciprofloxacin are often one of the first lines of treatment (104). Resistance to ciprofloxacin and other fluoroquinolone antibiotics is already described in *P. aeruginosa* due to the presence of inherited intrinsic resistance mechanisms and the ability of the organism to adapt to its environment.

1.2.3.1 Antibiotic Resistance in Pseudomonas aeruginosa

The major antibiotics used to treat *P. aeruginosa* need to be able to penetrate the cell envelope to reach their targets. In *P. aeruginosa* the outer membrane has a low permeability contributing to its innate resistance. To surpass this barrier antibiotics such as those belonging to the beta-lactam and quinolone families will enter the cell through the outer membrane porins (105). Alternatively, aminoglycosides and polymyxins are able facilitate their own uptake through lipopolysaccharides, overcoming the restrictions placed by the permeability of the outer membrane (106-108). These antibiotics then work through various modes of action (Figure 1-8).

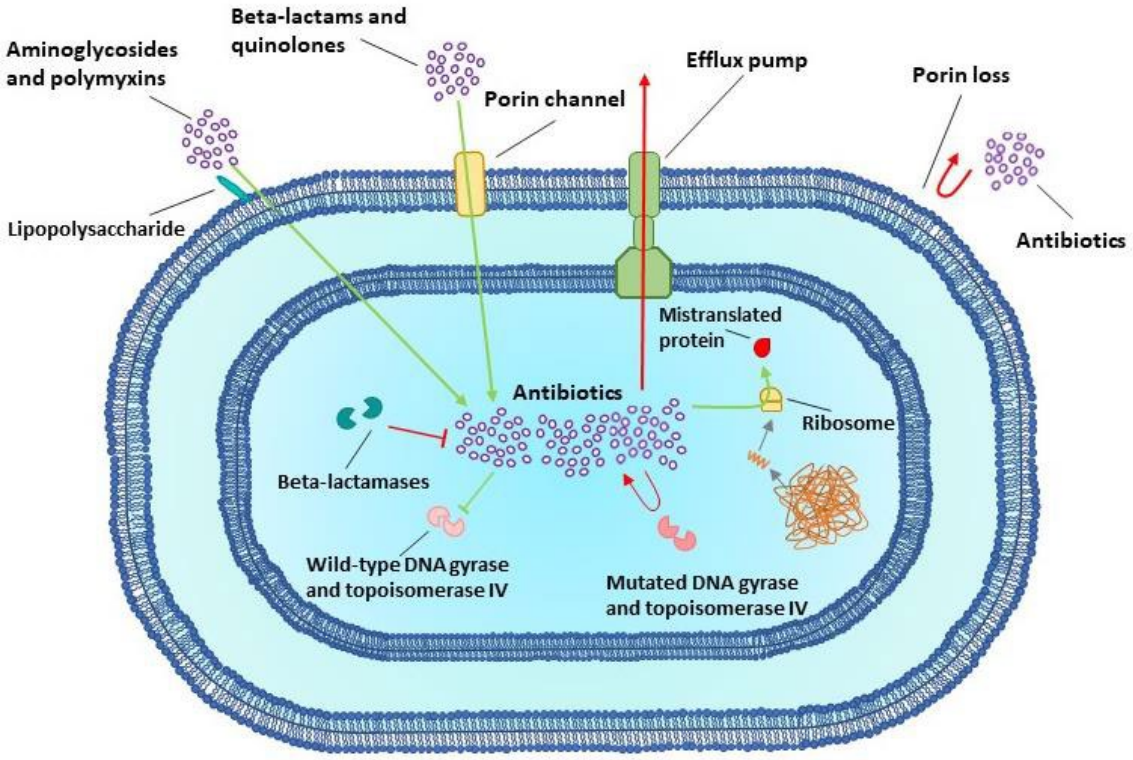

Figure 1-8: The route of entry for a selection of the antibiotics used to treat Pseudomonas aeruginosa and the resistance mechanisms towards them. Green arrows represent the entry and mode of action of the antibiotics and red arrows represent the resistance mechanisms produced towards them by P. aeruginosa.

Resistance to the antibiotics used to treat *P. aeruginosa* can be due to intrinsic, acquired, or adaptive mechanisms which will aid its survival and allow these characteristics to be inherited. It is possible for *P. aeruginosa* to accumulate multiple resistance mechanisms to express resistant phenotypes to multiple antimicrobial categories making them multidrug resistant (MDR) strains (109). The resistance of MDR strains make them more difficult to treat due to their persistence and limited treatment options that can lead to adverse clinical outcomes. The following section focuses on the resistance mechanism that are intrinsic or can be acquired through adaption to existing mechanisms.

1.2.3.1.1 Porin mediated resistance in *Pseudomonas aeruginosa*

Intrinsic resistance in *P. aeruginosa* is partially due to the low permeability of its outer membrane, which is 12-100-fold lower than *E. coli* (3). The major outer membrane porin of *P.*

aeruginosa is OprF and it is responsible for non-specific uptake of larger molecules, however it is present in limited numbers and can be expressed in closed forms that contribute to the lower permeability of the cell and thus limits the entry of antibiotics into the cell (110-112). In addition to this, clinical strains lacking OprF have been described to display antibiotic resistant phenotypes (113). However, Pumbwe *et al.* showed that a strain which lacked the OprF porin did not alter its antimicrobial phenotype when the strain was transformed with a functional *oprF* gene, suggesting that OprF loss might not be the cause of resistance in these strains (114).

OprD, a narrow outer membrane porin present in the *P. aeruginosa*, contributes to the uptake of basic amino acids into the cell (115). Additionally, the OprD porin facilitates the uptake of the carbapenem antibiotics into the *P. aeruginosa* cell (116). Mutations to the *oprD* gene can be caused by the insertion, substitution, deletion, or duplication of bases (76). This leads to the development of premature termination, amino acid substitutions, and frameshifts which thereby prevent the production of a functional OprD porin (76, 117). Without functional OprD, imipenem loses a route of entry into the *P. aeruginosa* cell resulting in increases resistance. Loss of functioning OprD has been implicated in imipenem resistant *P. aeruginosa* in clinical strains including those isolated from cystic fibrosis patients, burn infections and outbreaks in intensive care units (117-119).

1.2.3.1.2 Efflux as mechanisms of resistance in *Pseudomonas aeruginosa*

Efflux is inherent in *P. aeruginosa* and provides the bacteria with the ability to export various toxins from the cell to aid its survival. The resistance nodulation division (RND) efflux pumps are made up of three proteins that transverse the cell membrane: the RND protein, crossing the inner membrane; the membrane fusion protein, crossing the periplasmic membrane; and the outer membrane protein, crossing the outer membrane (Figure 1-9) (120). Thus, RND pumps create a passage across the cell membrane that facilitates the export of antibiotics that

enter the cell and consequently contributes to antibiotic resistance in *P. aeruginosa* (Figure 1-8) (120, 121).

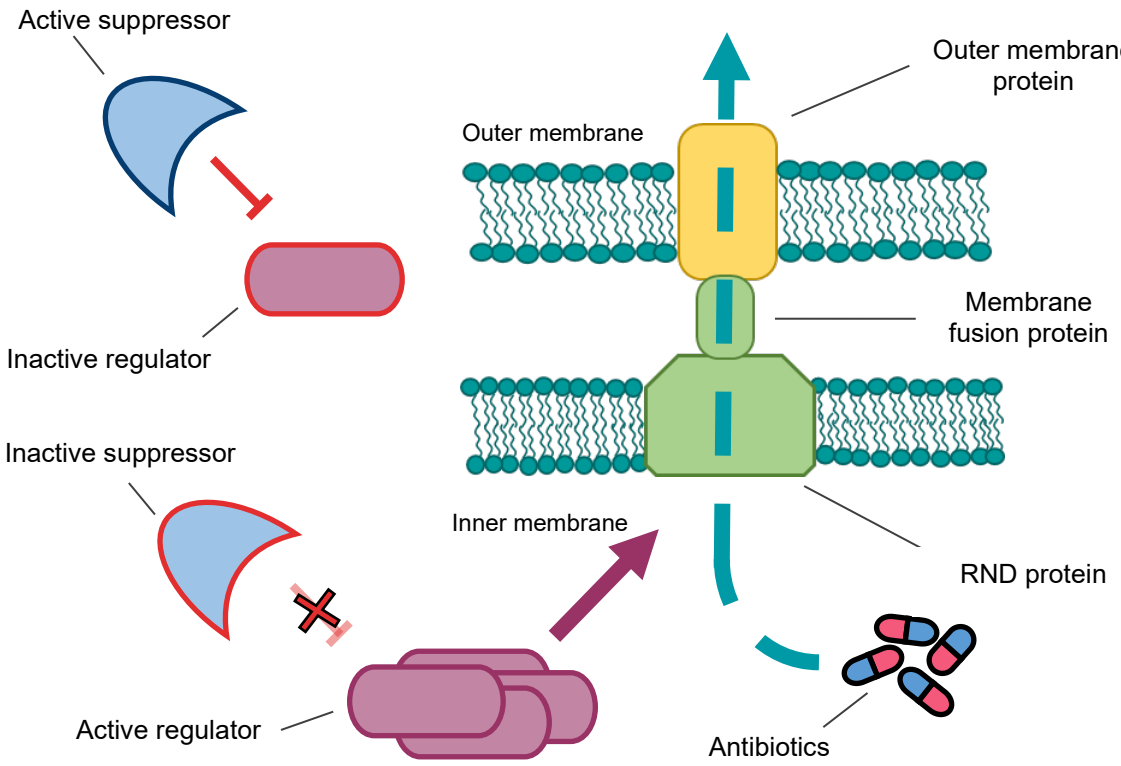

Figure 1-9: Example of a resistance nodulation division efflux pump. The control of RND efflux pump varies between individual pumps. In this example depicts an efflux pump under the control of a transcriptional suppressor and a transcriptional regulator.

1.2.3.1.3 Production of beta-lactamases by *Pseudomonas aeruginosa*

Beta-lactams, including carbapenems, contain a beta lactam ring in their structure that is vital to the mode of action. The beta-lactam ring binds to penicillin binding proteins preventing the formation of cross-links in the peptidoglycan cell wall (122). The cross-links in the peptidoglycan, which are formed by penicillin binding proteins, are important to the strength of the cell wall, without them the cell wall becomes more permeable to water leading to a weaker cell wall that is vulnerable to osmotic lysis (123).

Beta-lactamases are enzymes produced in response to beta-lactam antibiotics and work by hydrolysing the beta lactam ring structure which is characteristic of the beta lactam family. There are multiple variants of beta-lactamases which confer resistance to a wide spectrum of beta lactam antibiotics including: AmpC providing resistance to penicillins, first and second generation cephalosporins, and monobactams; extended spectrum beta-lactamases (ESBLs), such as CTX-M variants, providing resistance third and fourth generations cephalosporins, and monobactams; and carbapenemases, such as VIM variants, providing resistance to carbapenems (124-126). The genes encoding these beta-lactamases are often contained in plasmids which can be transferred through horizontal gene transfer both within and between species (127, 128).

1.2.3.1.3.1 Overexpression of AmpC

Within *P. aeruginosa* the AmpC beta-lactamase is encoded on the chromosome and is inducible by the presence of beta lactam antibiotics (129). As a result, the use of some beta-lactam antibiotics on *P. aeruginosa* can result in the expression of the intrinsic AmpC beta-lactamase (Figure 1-10a). Furthermore, mutations in AmpD and PBP4 lead to overexpression of the *ampC* gene which results in a moderate level of beta-lactam resistance (Figure 1-10b) (130-132). In addition to affecting *ampC* expression, mutations to PBP4 also leads to activation of the CreBC two component system which increases CreD expression resulting in even higher levels of resistance to beta-lactam antibiotics (Figure 1-10b). Hence, resistance mediated by the AmpC beta-lactamase can be intrinsic and adaptive in *P. aeruginosa*. Additionally, AmpC is not affected by many of the beta-lactamase inhibitors used in conjunction with beta lactams and therefore use of these combinations has little activity towards strain overexpressing AmpC (133, 134).

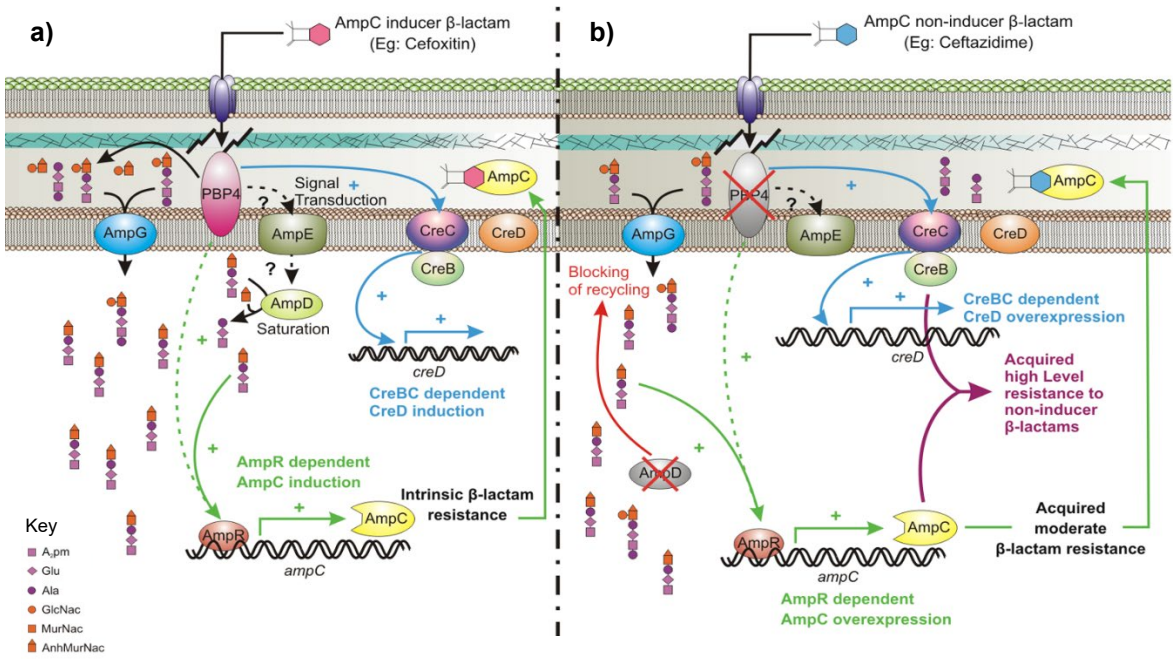

Figure 1-10: Regulation of the AmpC beta-lactamase in response to beta-lactam antibiotics. a) Shows regulation of ampC *in wildtype strains in the presence of AmpC inducing beta-lactams. In these conditions, signalling inside the cell disrupts the AmpR transcriptional regulator resulting in the expression of the AmpC beta-lactamase to generate resistance. Functional AmpD is involved in the recycling of the components that make up peptidoglycan however disruption leads to binding of its substrate to AmpR and thus expression of AmpC. b) Illustrates the influence of AmpD and PBP4 mutations on AmpC overexpression in the presence of AmpC non-inducer beta-lactams. Inactivating mutations to either AmpD or PBP4 lead to the activation of AmpR, resulting in constitutive expression and consequent moderate resistance to beta-lactams. The inactivation of PBP4 also results in the activation of CreBC which acts in conjunction with AmpC to generate high level beta-lactam resistance. The key indicates the molecules that make up peptidoglycan. The arrows illustrate pathways with a question mark (?) used to highlight pathways that need to be elucidated and a plus symbol (+) to illustrate pathways that lead to activation. Image is adapted from Figure 2 in Moya* et al.*(132).*

1.2.3.1.4 Modification to antibiotic targets in *Pseudomonas aeruginosa*

Resistance mechanisms such as porin loss and increased efflux prevent antibiotics working effectively. However, these mechanisms incur a fitness cost in terms of growth rate and virulence when compared to wild type strains in the absence of antibiotic pressure as they reduce nutrient availability and their regulation impacts other systems within the cell (135, 136).

1.2.3.1.4.1 Mutations in DNA replication machinery

The quinolone and fluroquinolone antibiotics bind to subunit A in DNA gyrase and topoisomerase IV which are both involved in the synthesis of nucleic acids (137, 138). The binding of quinolones to these enzymes blocks DNA replication and encourages DNA breaks which the bacteria will try to repair through its SOS response and DNA repair pathways. Bacterial cell death occurs when the formation of DNA breaks surpasses the attempts of the bacterial response (139).

Single nucleotide polymorphisms (SNP) in the quinolone resistance determining regions (QRDR) within the genes coding for DNA gyrase and topoisomerase IV can cause conformational changes that prevent the antibiotics from binding efficiently and therefore results in increased resistance (138, 140). Within *P. aeruginosa*, various combinations of SNPs have been identified in the quinolone resistance determining regions of the GyrA and GyrB subunits of DNA gyrase and in the ParC and ParE subunits of DNA topoisomerase IV (141-147). Mutations within these enzymes have been shown to be less costly to the cell than porin loss or increased efflux as they provide resistance to antibiotic without compromising its growth rate (148, 149). As a result, they are a more beneficial mechanism of quinolone and fluroquinolone resistance due to their selection and fitness advantage when under pressure from quinolone and fluroquinolone antibiotics.

1.2.3.1.4.2 Mutation in the ribosomal subunits

Macrolide antibiotics are not usually used to treat *P. aeruginosa* due its intrinsic outer-membrane permeability and efflux mechanisms (150). However, macrolide entry into the cell can resulting in binding to the bacterial ribosome through the large 50S subunit (151). The result of this binding leads to stalling at specific motifs in amino acid sequences that prevent bonds forming with the incoming amino acid (152). Therefore, the protein translated from a

macrolide bound ribosome is compromised and will not function correctly. Whilst this process prevents the bacteria from being able to grow, it does not result in the lysis of the cell leading to bacteriostatic effects.

In *P. aeruginosa,* exposure to macrolide antibiotics can lead to mutations within the ribosomal proteins that make up the subunits (153, 154). These mutations create ribosomes that are impervious to binding with macrolides whilst maintaining the ability to translate protein sequences. In some cases, these mutations also impose caveats on the strain by attenuating virulence traits such as motility (154). Therefore, these mutants provide *P. aeruginosa* with the ability to resist the bacteriostatic effect of macrolides with the compromise of reducing its virulence.

In addition to mutations to the large 50S subunit of the ribosome, aminoglycoside antibiotics target the 30S ribosome subunit (155). The binding of aminoglycoside antibiotics to the 30S subunit cause structural changes that alter the ribosome. As a result, the ribosome becomes impaired causing misreading errors and premature termination in the proteins they translate (156). These mistranslated proteins are unable to perform their intended roles, instead they encourage cell damage and insertion into the cell membrane contributes to cell death (157, 158).

Mutations to 16S rRNA which forms parts of the 30S ribosome subunit have been shown to cause resistance to aminoglycoside antibiotics, however in *P. aeruginosa* these mutations are uncommon (159). Instead, modifications to the 30S subunit can be achieved through the production of 16S rRNA methylase which prevents the 16S rRNA within the 30S subunit from binding with the aminoglycoside antibiotic (160, 161). This is achieved by methylation of residues located at the aminoglycoside binding sites within the 16S rRNA protein (160). As a

result, high levels of resistance towards aminoglycoside antibiotics can be detected in strains producing variants of 16S methylase (161, 162).

1.2.3.1.4.3 Lipopolysaccharide modification

The polymyxin and cationic antimicrobial peptides electrostatically interact with outer membrane lipopolysaccharide molecules and destabilises the outer membrane allowing for the uptake of antibiotics. The resulting rearrangement increases the permeability of the cell envelope leading to cell death (163). Additionally, polymyxins reduce the possibility of endotoxic shock syndrome by binding to endotoxins released by the bacteria thereby protecting the host from its affects (164).

Exposure to polymyxin and cationic antimicrobial peptides have previously been reported to result in mutations in lipopolysaccharide molecules in *P. aeruginosa* (165, 166). These mutations occur in the two-component regulatory systems that control the transcription of operons and result in the upregulation of the incorporation of 4-aminoarabinose to the lipid A component of the lipopolysaccharide molecule (166, 167). The consequence of this mutation leads to a lipopolysaccharide with a reduced negative charge. This prevents entry into the cell by decreasing the ability of polymyxin and cationic antimicrobial peptides to electrostatically interact with the lipopolysaccharide and destabilise the cell envelope (167).

1.3 Aims & Objectives

Combining whole genome sequencing (WGS) with laboratory assays can be a powerful approach to highlight the differences between pathogenic and non-pathogenic bacteria. This project aims to use WGS and phenotypic assays to identify niche adaption in *Pseudomonas aeruginosa* species and characterise the evolution to a clinical niche to explain the mechanisms responsible for the switch from environmental residents to antibiotic-resistant superbugs.

1.3.1 Hypothesis

Genotypic changes within *P. aeruginosa* result in adaption to clinical niches, through increased antibiotic resistance or virulence, which can be defined by genetic biomarkers.

1.3.2 Objectives

Specific objectives of the project are to:

1. Assess the phylogeny of strains identified as *P. aeruginosa* in conjunction with strains belonging to other *Pseudomonas* species.
2. Utilise genetic and phenotypic methods to characterise isolates of divergent *P. aeruginosa.*
3. Collect and sequence *P. aeruginosa* strains originating from clinical and environmental sources.
4. Identify biomarkers within clinical and environment lineages of *P. aeruginosa.*
5. Evolve environmental *P. aeruginosa* isolates under simulated clinical conditions to characterise the switch from the environment to a clinical setting.
6. Uncover the impact of mutations which alter tolerance to antibiotics on bacterial fitness.

Chapter 2 - Methods

2.1 Strain collection

2.1.1 In-house collection of *Pseudomonas aeruginosa* strains

A collection of 240 *P. aeruginosa* strains were present in the in-house collection where 139 originated from clinical sources and 101 originated from non-clinical environments. For the purposes of this project, a strain was defined as being isolated from a clinical source if the strain was isolated from an infection in a human. Strains found to have been isolated from sources such as animals, pipes, and water were defined as non-clinical and therefore classed as being from an environmental source. Any strains where information on the source could not be found were excluded from the project. Further information on the source location for each strain can be found in Appendix - Table 3.

2.1.2 Isolating *Pseudomonas aeruginosa* from environmental samples

Sampling sites were selected based on geographical accessibility and the basis that little human interaction is likely to have occurred at the site to find true environmental isolates of *Pseudomonas aeruginosa* which would not have been subjected to any kind of clinical exposure. Hence, sites in areas close to urban parks, heavily industrialised zones, and farmland were generally avoided due to the likely influence of human interaction and contamination from industrial or agricultural run-off. Both Figure 2-1 and Appendix - Table 6 show the location of sites where various types of environmental samples were collected. At each site sterile 50 ml falcon tubes were used to collect samples of plants (the flowers, leaves, stem, and roots from small plants, shrubs, and undergrowth) soil, leaf litter, fungi, water (from rivers, lakes, and the ocean) or marsh. The outer surface of tubes was sterilised after sample collection with 2% Chemgene HLD_4H (Chemgene™) and were transported to the laboratory. Samples were kept at

4°C and processed within 24 hours of collection where possible. In the instance immediate sample processing was not possible, samples were directly placed in a -80°C freezer upon receipt into the laboratory. Prior to sample processing, samples were slowly defrosted overnight at 4°C and then left at room temperature for one hour. All samples stored at -80°C were processed within two months from the date of collections.

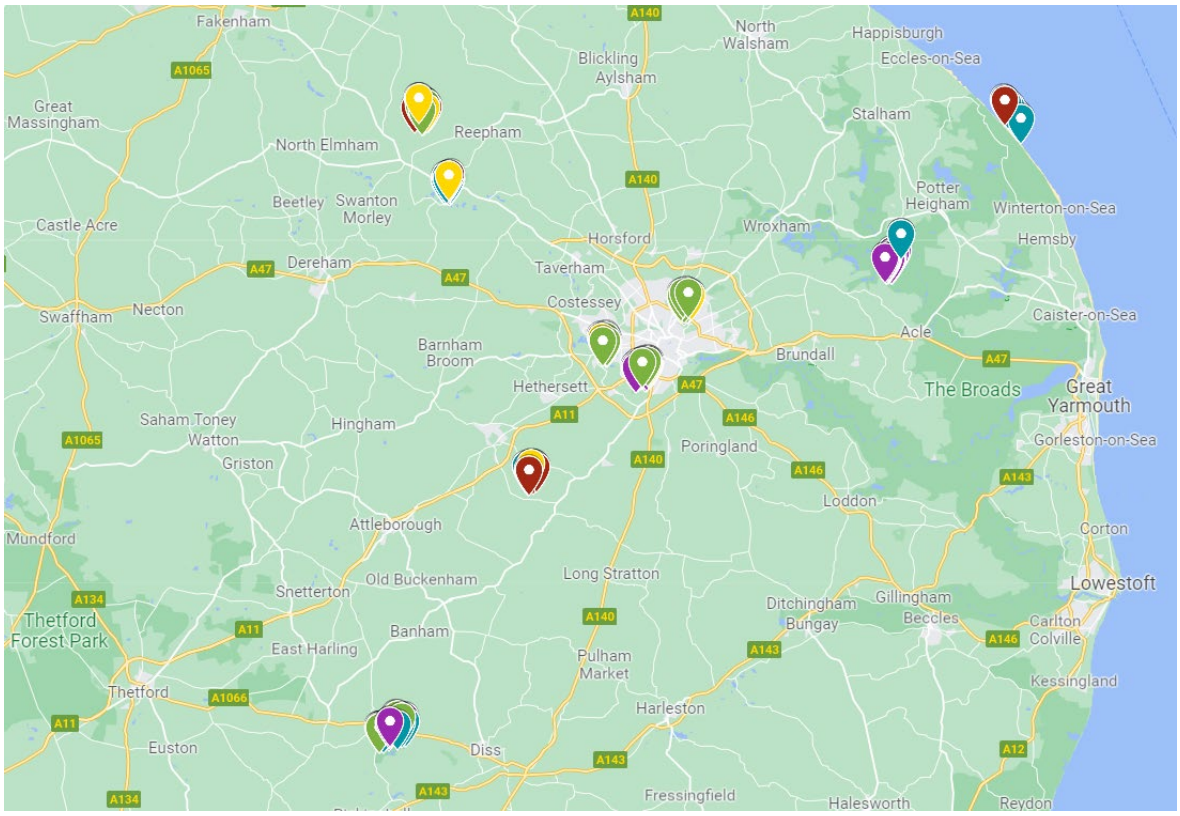

Figure 2-1: Locations of sites where environmental samples were collected. Blue markers represent water, green represents fungi and plants, purple represents fens and marshland, red represents soil, and yellow represents leaf litter. Precise coordinates for each sampling point is displayed in Appendix - Table 6

Either 1g of plant, soil, or fallen leaves samples or 1ml of water-based samples was added to 9 ml of Cetrimide broth (Sigma Aldrich) to select for the growth of *P. aeruginosa*, by inhibiting non-*P. aeruginosa* strains. Samples were incubated at 37°C for 24hrs on a 180 rpm shaker for liquid samples or a 30 rpm roller for solid samples. After centrifugation at 5,000 rcf, for 2 mins, 100µl of culture was taken from the supernatant to be spread onto Pseudomonas agar base

(Oxoid) with CN supplement (PA-CN, Oxoid) which uses cetrimide and sodium nalidixate as selective agents for *P. aeruginosa*. The supplement works as a selective agent by inhibiting the growth of Gram-positive bacteria in addition to many non-*P. aeruginosa* Gram-negative bacterial species. Cetrimide additionally encourages production of the pyocyanin pigment present in most *P. aeruginosa* strains. As pyocyanin has a visible blue-green colour, the formation of blue-green colonies indicates the presence of *P. aeruginosa.* After incubation at 37°C for 24-48 hrs, morphologically distinct colonies suspected to be *P. aeruginosa* were selected and sub-cultured onto PA-CN agar for incubation at 37°C for 24 hrs. Isolates were stored until further use at -80°C using 700 µl of an overnight culture in 10ml Luria-Bertani broth (LB, Oxoid) and 300 µl of 80% glycerol.

2.1.3 Acquisition of Environment Agency strains

Samples from 50 natural outdoor bathing sites across the United Kingdom were provided by the Environment Agency with the assistance of Louise Pearce and Christopher George (Appendix - Table 7). Water samples collected from each bathing site were first processed by the Environment Agency where 100 ml was passed through a 0.45 µm filter membrane which was placed onto PA-CN agar for 48 hrs at 37°C. Plates were stored at 4°C until transport to the laboratory. Upon arrival, streaks taken from the PA-CN agar were cultured into CN broth overnight at 37°C and then plated onto PA-CN to produces isolated colonies. Morphologically distinct colonies were then streaked on the LB agar (Oxoid) and glycerol stocks were created to store isolates at -80°C using 700 µl of an overnight culture in LB broth and 300 µl of 80% glycerol (Merck).

2.1.4 Selection of resistant mutants and sensitive revertants after chloramphenicol exposure in standard growth media

Strains reverting to a chloramphenicol sensitive phenotype through *mexS* and *mexT* were previously identified by Correia *et al*. (unpublished). Spontaneous chloramphenicol-resistant strains were generated by first spreading a selection of strains onto Tryptic Soy Agar (TSA, Sigma-Aldrich) plates supplemented with 100, 200, and 400 μg/ml of chloramphenicol and then incubated at 37°C overnight. As no breakpoint for chloramphenicol resistance is defined for *P. aeruginosa,* a range of concentrations: 100, 200, and 400 μg/ml, was used to ensure the mutational window was covered. Colonies that grew on the chloramphenicol supplemented plates were suspected of having developed spontaneous resistance. These colonies were then streaked onto TSA containing 400 μg/ml chloramphenicol alongside its parent strain and incubated overnight at 37°C to confirm if strains were able to tolerate a high concentration of chloramphenicol and could therefore be considered true resistant mutants. The true resistant mutants were then used to inoculate 1 ml of Brain Heart Infusion (BHI) broth, a nutrient rich growth medium, or SSM9PR broth (1x M9 salts, Sigma-Aldrich; 2mM MgSO4 Sigma-Aldrich; 0.1mM $CaCl_2$, Sigma-Aldrich; 1% glucose, Sigma-Aldrich; 1% casamino acids, Sigma-Aldrich; 1mM thiamine HCl, Sigma-Aldrich; and 0.05mM nicotinic acid, Sigma-Aldrich), a defined minimal growth medium. Cultures were passaged six times over 2.5 weeks by using 10 μl of culture to inoculate 1 ml of fresh BHI or SSM9PR broth at room temperature or 37°C. Both a rich and minimal growth medium was used to determine if nutrient availability during passages would affect the ability of strain to revert. The final passages were plated on a general growth medium, TSA, and incubated at 37°C overnight after which single colonies were identified by replica plating on TSA with and without 400 μg/ml of chloramphenicol where strains with reduced growth on chloramphenicol agar were harvested. Following isolation, the chloramphenicol-resistant mutants and chloramphenicol-sensitive revertants underwent minimum inhibitory concentration (MIC) testing along with their respective parent to confirm the MICs for the strains (Section 2.5.3).

Mutations in *mexS* and *mexT* were confirmed by extracting the DNA of chloramphenicol-resistant mutants, chloramphenicol-sensitive revertants, and their respective parents by using 1 ml of overnight LB broth culture as input for the GeneJet Genomic DNA Purification system (ThermoFisher, UK). Sequencing was performed at the Quadram Institute as described in Section 2.2.2, and assembled as described in Section 2.2.3. Changes in *mexS* and *mexT* were confirmed using BLAST (168) by taking the *mexS* and *mexT* nucleotide sequences from *P. aeruginosa* UCBPP-PA14 (GCF_000014625.1) to create a custom database.

2.1.5 Identification of *Pseudomonas aeruginosa*

2.1.5.1 Gram staining and oxidase test

A single colony was selected from overnight growth on LB agar at 37°C and suspended in sterile distilled water. Suspensions were heat fixed at 50°C on microscopic slides until the suspensions were dried. Crystal violet (Pro-Lab Diagnostics) was used to stain the slides for 30-60 sec and washed with water before the dye was fixed with iodine (Pro-Lab Diagnostics) for 30-60 secs. Grams differentiator (Pro-Lab Diagnostics) was used to wash away the crystal violet before Safranin (Pro-Lab Diagnostics) was added for 60-90 secs to dye the cells where the crystal violet was washed away. Slides were viewed under the Olympus BX40 Clinical Microscope with a GXCAM HiCHrome MET camera using the x100 objective to identify the Grams status and shape of bacterial cells.

Oxidase strips (Microgen) were used to confirm oxidase activity in strains. A single colony from an overnight culture on LB agar incubated at 37°C was spread onto an oxidase strip, a colour change from clear-white to blue-purple indicates the ability to oxidise cytochrome C and thus an oxidase-positive strain.

2.1.5.2 Molecular identification of Pseudomonas aeruginosa

Strains confirmed as oxidase positive Gram-negative bacilli were subjected to PCR to confirm the identification of *P. aeruginosa* using the *gyrB* and *ecfX* genes as described in Table 2-1. Template DNA was produced by suspending cells from an overnight growth on LB agar in 500 µl sterile distilled water and heating them at 95°C for 10 mins to lyse cells. Lysates were then centrifuged at 17,000 rcf for 1 min and 300 µl of the supernatant was transferred to a sterile tube for use as the template DNA. PCRs were performed for each target using a reaction mix comprising of 12.5 µl MyTaq Red mix (Bioline), 1.25 µl of forward primer (10µM), 1.25 µl of reverse primer (10 µM), 9 µl nuclease free water (Invitrogen) and 1 µl template DNA. To act as a control each PCR conducted included a reaction containing 1 µl of template DNA from the *P. aeruginosa* PAO1 strain (GCF_000006765.1) for a positive control and 1 µl of NFW in place of a DNA template for a negative control.

Table 2-1: Primers for identification of Pseudomonas aeruginosa

Primer	*Oligonucleotide sequence 5' -3'*	*Annealing temperature (°C)*	*Reference*
ECF1	ATGGATGAGCGCTTCCGTG	58	(169)
ECF2	TCATCCTTCGCCTCCCTG		
GyrPA-398	CCTGACCATCCGTCGCCACAAC	66	(170)
GyrPA-620	CGCAGCAGGATGCCGACGCC		

The PCRs were performed on the Veriti Thermo cycler (Applied Biosystems) with the following conditions: initial denaturation at 95°C for 5 min; 35 cycles at 95°C for 45 secs, 45 secs at the appropriate annealing temperature (Table 2-1), and 72°C for 45 secs; and a final elongation at 72°C for 5 min. Gel electrophoresis at 100 volts for 1 hour was used to separate PCR products on a 2% agarose gel (Fisher Bioreagents) made with 1X TAE Buffer and stained with a 1X concentration of GelRed® (Millipore).

2.1.5.3 Curation of **Pseudomonas aeruginosa** *genome sequences from repositories*

To expand upon the number of genomes within the project, sequences were downloaded from the Pseudomonas Genome Database (171) and NCBI Genbank(172). Metadata was used to determine the isolation source as either clinical or non-clinical according to the definitions defined in Section 2.1.1. If the isolation source of the sequence could not be clearly determined to be either clinical or non-clinical the sequence was excluded from the project.

Sequences were downloaded from the online databases as contigs, scaffolds, and complete genomes. Scaffolds and complete genomes containing gaps were converted into contigs with the split.scaffolds.to.contigs.pl script (https://github.com/MadsAlbertsen/miscperlscripts/) with the minimum length of contigs set to 200 bp. To ensure sequence quality was universal amongst the entire genome collection used in the project, sequences were analysed in Quast v5.0.2 (173). Sequences were only included in the project if they met the selection criteria described in Section 2.2.3. Due to large proportion of isolates originating from cystic fibrosis infections, isolates whose origins could be attributed to cystic fibrosis were randomly selected in Microsoft Excel to ensure the number of strains isolated from cystic fibrosis patients was proportional to the number isolated from respiratory infections not related to cystic fibrosis. This was performed by using the RAND function to first assign a random real number greater than or equal to 0 and less than 1 to each cystic fibrosis isolate, ordering these numerically from smallest to largest, and then taking the first 427 strains to approximately match the number of respiratory isolates.

2.1.6 Identification of duplicate strains from the database

To avoid the inclusion of duplicate strains metadata was checked ensuring only the most recent version was used. Additionally, to avoid multiple examples of the same clone being included in the dataset, clonally linked isolates were identified as strains having a single nucleotide

difference (SNP) difference <30, as determined by snp-dists v0.8.2 (174), the same BioProject identifier, and from the same niche (clinical or environmental) were removed. For each group of clonally linked genomes identified in this manner, one genome was retained with the duplicates removed. See Appendix III for python scripts used to remove clonally linked strains.

2.1.7 Strains used in the comparison of PA7-like strains

The cultures of strains found to be part of the PA7-like group acquired for phenotypic testing are described in Appendix - Table 1. The following isolates were obtained through BEI Resources, NIAID, NIH: *Pseudomonas aeruginosa*, Strain MRSN 3705, NR-51542*; Pseudomonas aeruginosa*, Strain MRSN 6241, NR-51550; and *Pseudomonas aeruginosa*, Strain MRSN 3705, NR-51542. These strains are part of the *Pseudomonas aeruginosa* Diversity Panel provided by the Multidrug-Resistant Organism Repository and Surveillance Network (MRSN) at the Walter Reed Army Institute of Research (WRAIR), Silver Spring, MD, USA. The LMG 5031 isolate was obtained from the BCCM/LMG Bacteria Collection, the PA7 (DSZM 24068) isolate was obtained from the Leibniz Institute's DSMZ collection, and the ATCC 9027 strain was obtained as a Culti-Loop™ from Thermo Scientific. These cultures were obtained with the assistance of Mylène Robert, Ina Attée, Sophie Nozick, Alan R. Hauser, Stephanie Lewis, Bernadette Blanc, and Alex van Belkum.

To compare the PA7-like strains identified in the study to closely related strains a selection of well characterised *P. aeruginosa* reference strains were used for comparisons (Appendix - Table 2). Additionally, strains belonging to other *Pseudomonas* species were identified using the Type Strain Genome Server (TYGS) which uses the 16S rRNA gene sequence to identify strains within the TYGS database closely related to the PA7-like strains that were input into the programme (175). These strains are described in Appendix - Table 2 along with their accession number and an indication of the nomenclature status according to the List of

Prokaryotic names with Standing in Nomenclature (LPSN) database (accessed: 5th December 2022) (176).

2.2 Extraction and sequencing of genomic DNA

2.2.1 Purification of genomic DNA

Whole genome sequencing was performed for strains from the in-house collection using overnight cultures were set up for strains in 5ml LB broth and incubated with shaking at 180 rpm at 37°C. Genomic DNA was extracted with the Promega Wizard® Genomic DNA purification kit using 1ml of the overnight culture. The following adaptions were made to the Gram-negative protocol to ensure successful isolation of the genomic DNA: all centrifugation steps were performed at 17,000 x G with the length of time increased to 5 mins; the protein precipitation solution was cooled in ice before its addition to the RNAase-treated cell lysate; and purified DNA was rehydrated in 100 µl nuclease free water (NFW).

The quality of the purified DNA was checked using 2 µl on the Nanodrop Spectrophotometer 2000 (Thermo Scientific) and the quantity was confirmed using 2 µl of DNA with the Qubit™ dsDNA BR Assay Kit (Invitrogen) with the Qubit™ fluorometer (Invitrogen). Purified DNA was diluted to 5 ng/ml in NFW for library preparation with the quantity confirmed using the Qubit™ HS DNA kit (Invitrogen).

2.2.2 Sequencing of genomic DNA

Preparation of genomic libraries for sequencing was performed using the Illumina DNA Prep Kit (Illumina). Following this, sequencing was performed using the NextSeq 500 Mid Output kit (Illumina) on the Illumina NexSseq500 instrument (Illumina) following the recommended denaturation and loading recommendations which included a 1% PhiX spike (Illumina). Library preparation and sequencing was performed by the core sequencing service at the Quadram Institute for Biosciences (Norwich, UK).

2.2.3 Assembly and annotation of raw sequencing reads

Illumina adapters were trimmed from the raw sequencing reads with Trimmotatic v0.39(177) with the headcrop, leading, and trailing parameters set to 20; a sliding window of 4:20; and the minimum length of sequences set to 36. The quality of trimmed sequencing reads was then assessed with FastQC v0.11.9 (178). Trimmed reads were then input into SPAdes v3.14.0 (179) for *de novo* genome assembly with the generated assemblies filtered with bbmap v37.28 (180) to remove contigs < 200bp in length. Final assemblies were then annotated using Prokka v1.14.6 (181) using an annotation file generated with genomes from the Pseudomonas Genome Database (171) to first annotate from (accessed 23rd April 2021). The "compliant" feature was switched on to force genbank/ENA/DDJB compliance and the "usegenus" option was set to "Pseudomonas" to use genus-specific BLAST databases to annotate proteins which were not labelled using the custom annotation file. Annotations were quality checked using Quast v5.0.2 (173), with sequences showing a contig N50 ≥50,000-bp or the number of contigs to be ≤300 were included in the strain collection for the project. Sequences not fitting the selection criteria were re-extracted and re-sequenced as described.

2.2.4 Confirmation of species identification

The species of the cultured isolates was identified from the final genome assemblies with Kraken2 v2.1.1(182) using the bacterial database (accessed 7th January 2021). Strains suspected of containing contaminants due to the presence of multiple contigs identifying as different species including *P. aeruginosa* were cultured on the selective PA-CN agar overnight at 37°C and purified to be re-extracted and re-sequenced as described in Sections 2.2.1 and 2.2.2. Additionally, NCBI BLAST v2.10.0+ (168) was used to query genome assemblies with the 16S rRNA nucleotide sequence from the *P. aeruginosa* type strain PAO1.

2.2.5 Multi-locus sequence typing and identification of antimicrobial resistance genes

Ariba v2.14.6 (183) was used to identify the multi-locus sequence type by utilising the PubMLST scheme (184) for *P. aeruginosa.* AMR gene presence was identified with Ariba using the Comprehensive Antibiotics Resistance Database (185) (CARD, accessed 10th August 2021). As the input of Ariba requires sequencing reads which were not available for all strains included in the project the genome assemblies for all strains were transformed into sequencing reads using randomreads.sh script from bbmap. The parameters of the scripts were set to produce 850,000 paired-end reads without errors per assembly that were 300 bp in length. With the assumption that a *P. aeruginosa* genome is approximately 6.5 Mbp in length, this would equate to a coverage of 39.23 using the following Equation 1 where C is the coverage, L is the read length, N is the number of reads and G is the genome length.

Equation 1: Lander-Waterman equation (186) to determine sequencing coverage.

$$C = \frac{\mathrm{LN}}{G}$$

2.3 Speciating *Pseudomonas aeruginosa*

2.3.1 Core genome alignment

Annotated sequences were input into Panaroo v1.2.8 (187) to determine the number of core genes defined in this study as genes present in >99% of sequences. The alignment option was selected to generate a core gene alignment using mafft v7.487(188) which was then input into snp-sites v2.5.1(189) to create a filtered core gene alignment based on single nucleotide polymorphisms (SNPs). A phylogenetic tree of the core SNP alignment was generated in as described in Section2.3.4.

2.3.1.1 Analysis of the core genome alignment

Statistical analysis on the core genome alignment was performed with PopGenome v2.6.1(190). The core genome alignment was first broken down into 100,000bp blocks using the SeqIO module in python 3.8. The blocks were then recombined into one alignment in PopGenome where pairwise comparisons between the nucleotide diversity (D_{XY}) and gene flow (F_{ST}) were calculated. Heatmaps of the statistics were visualised in R v4.0.0 (191) using heatmap3 v1.19 (192).

2.3.2 Robust clustering

Robust clustering of strains was achieved using the ribosomal snakemake workflow (github.com/LCrossman/ribosomal_snakemake) that extracts and aligns the 16 ribosomal proteins described by Hug *et al.* which is then used to create a phylogenetic tree through FastTree v2.1.11 (193, 194). As input for the workflow the protein sequences of 16 ribosomal proteins were taken from the PAO1 type strain (GCF_000006765.1) (Appendix - Table 4).

2.3.3 Clustering from the sequence alignments

Hierarchical clustering was performed over five levels with the R v4.0.0 (191) based programme FastBaps v1.0.6 (195) using "optimise.symetric" as the Dirichlet prior hyperparameter. The cluster obtained were then used to annotate phylogenetic trees where specified.

2.3.4 Generation of phylogenetic trees

Phylogenetic trees were created for nucleotide alignments using FastTree v2.1.11 (193) using the generalised time reversible model for nucleotide evolution and gamma likelihoods to scale branches. Resulting phylogenetic trees were visualised with the Interactive Tree Of Life (iTOL)(196).

2.3.5 Average nucleotide identity

The average nucleotide identity (ANI) was used to determine the similarity of nucleotides between the assemblies and the genome of the *P. aeruginosa* type strain PAO1 (GCF_000006765.1) with FastANI v1.33 (85, 197). Additionally, the ANI was used to determine similarity between each of the core lineages by taking the mean average of ANI scores found between genome assemblies belonging to the lineage and comparing these between lineages.

2.3.6 16S rRNA phylogeny and Digital DNA-DNA hybridisation

Digital DNA:DNA hybridisation (dDDH) was used on strains with <95% ANI to confirm their species identification against type and reference strains on the TYGS database (175). Assemblies found to have less than the species cut-off, 95% for ANI and 70% for dDDH (198), were removed from the alignments and considered to be a species other than *P. aeruginosa*. TYGS also identified the 16S rRNA sequence present in each strain which was used to generate

a minimum evolution phylogenetic tree based on SSU rRNA distances with branch support from FASTME v2.1.6.1(199) inferred using 100 pseudo-bootstrap replicates(200). To check for the presence multiple 16S rRNA copies, Barrnap v0.9 (201) was used to reveal the number of 16S rRNA copies which were present in the PA7-like strains.

2.3.7 Sourmash

Sourmash v4.3.0 (202) was used to generate genomic signatures containing MinHash sketches with *k*-mer sizes of 31 and 51. Sketches of the same *k*-mer size were compared against each other using the estimated Jaccard index to assess the similarity. The resulting matrix was visualised in R v4.0.0 using heatmap3 v1.19(192).

2.3.8 BRIG

Genomic comparisons were generated and visualised using the BLAST Ring Image Generator (BRIG) v0.95 (203). Comparisons were made using the nucleotide sequence of the PA7-like strains against both the PAO1 (GCF_000006765.1) and PA7 (GCF_000017205.1) genomic sequence with the average GC content of the query strain also visualised as one of the rings.

2.3.9 Carbon Utilisation

2.3.9.1 Phenotypic microarray

Growth using various carbon substrates (204) was measured using the PM1 microplate on the OmniLog® PM System (Biolog). A selection of 11 PA7-like strains and 23 strains representing the remainder of the *P. aeruginosa* core genome phylogeny (Figure 3-5) were grown on BUG+B agar (Biolog) overnight at 37°C. Cell suspensions were prepared following the protocol outlined in "PM Procedure for *E.coli* and other GN Bacteria" (204) using the IF-0 (Biolog)

inoculating fluid to achieve 42% transmittance on the Biolog Turbidimeter. The suspension was diluting as specified in IF-0 with redox dye mix A (Biolog) with 100 µl of the diluted inoculum added to each well of the PM1 plates. Plates were incubated in the OmniLog at 37°C with absorbance reading taken at 590 nm every 15 minutes for 48 hours. The experiment was replicated once resulting in two replicates per strain.

Growth curves were generated in ggplot2 v3.3.5 (205), by plotting the mean absorbance at 590 nm against time for the PA7-like strains (n = 22) and *P. aeruginosa* strains (n = 46) with error bars representing the 95% confidence interval. The area under the curve was calculated for the PA7-like and *P. aeruginosa* groups using GrowthCurver v0.3.1 (206). To establish if there was a difference in area between the two groups across the various substrates a Kruskal-Wallis test was performed using rstatix v0.7.0 (207). Specific substrates with a significant difference ($p \leq 0.05$) between the are under the curve for PA7-like and *P. aeruginosa* groups were identified by Mann-Whitney *U* tests on the area under the curve.

2.3.9.2 Analysis of pathways associated to significant substrates

Substrates where a difference in growth between the PA7-like and *P. aeruginosa* strains was found were input into BioCyc (208) to reveal pathways in PAO1 (GCF_000006765.1) and PA7 (GCF_000017205.1) in which they participate. Pathways involved in the consumption of the substrates were isolated to reveal the genes which facilitate them. These genes were then compared between the strains to determine their presence. Those absent in one strain were inspected against the countering strain using their nucleotide sequences and BLAST to confirm the gene absence was genuine and not due to annotation of the genome. Strains with BLAST identities ≤90% or with no matches were recorded as genes with potential involvement in the difference in growth seen between PA7-like and *P. aeruginosa* groups.

2.3.9.3 Alignment of the pyoverdine gene-containing regions

To align selected genes involved in pyoverdine type I biosynthesis the *pvdD, pvdI*, and *pvdJ* genes of PAO1 (GCF_000006765.1) were extracted and aligned to the corresponding region in PA7 (GCF_000017205.1)using the progressiveMauve v2.4.0 algorithm (209). This was repeated for the genes involved in pyoverdine type II biosynthesis using the *pvdI(2)* and *pvdJ(2)* genes from *P. aeruginosa* NCTC 12903 (GCF_900636755.1) and the corresponding regions from PA7. The alignments were viewed in Mauve (210) or MView (211).

2.4 Analysis of the *Pseudomonas aeruginosa* genome

2.4.1 Core gene alignment of *Pseudomonas aeruginosa* strains

Panaroo v1.2.8 (187) was used to identify the pangenome of *P. aeruginosa* strains excluding the members of the PA7-like group. A core SNP alignment was produced using these strains as described in Section 2.3.1 with a clustering of the SNP alignment and phylogenetic inference performed as described in Section 2.3.3 and Section 2.3.4.

2.4.2 Statistical association to niche

Fishers exact tests were calculated using the Fisher exact probability calculator (212) by comparing the clinical and environmental strain distribution of the entire dataset against the distribution apparent in the core groups determined by hierachial clustering of the core SNP alignment. Individual strains were determined to be clinical or environmental based on their source of isolation (Appendix - Table 3) with clonally linked strain counted once (Section 2.1.7). The resulting *p*-values were adjusted using the Benjmaini-Hochberg correction (213). Core groups with a significant difference ($p \leq 0.05$) in their distribution of clinical and environmental isolates were determined to be associated to either a clinical or environmental niche.

2.4.3 Association of genetic markers with core lineages

2.4.3.1 Pyseer

Pyseer v1.3.10 (214) was used to assess gene and SNP association to specific niches. To determine gene association, the gene presence and absence output from Panaroo v1.2.8 (187) was used as input into Pyseer. The gene presence and absence dataset was filtered to only include one representative of clonally linked strains (described in Section 2.1.7) from the same

environment. Level 1 FastBaps clusters, identified in the core genome alignment, was used to classify the "lineage" of the strain with its "trait" being determined as clinical or environmental based on its source of isolation (Appendix - Table 3). A linear mixed model of fixed and random effects was used and fitted from the similarity of the core SNP phylogeny determined by Section 2.4.1. A pairwise distance matrix of genomic sketches was generated using Sourmash in order to determine the lineage effect. The "min-AF" and "max-AF" parameters were applied at 0.05 and 0.95 respectively to adjust the proportion of samples required to contain the gene for it to be included in the analysis. The resulting output was filtered by the "lrt-pvalue" which is the *p*-value of association adjusted for population structure to determine significant variants ($p \leq 1.00 \times 10^{-6}$).

To identify SNP association, the parameters of the programme were set as described for gene association however a variant call format (vcf) file was used as the input in place of the gene presence and absence file. The vcf file was produced by generating synthetic reads (Section 2.2.5) to the nucleotide sequence of the PAO1 type strain using snippy v4.6.0 (215) to create individual vcf files which were then merged into a single vcf file using the vcfmerge script from bcftools v1.15.1 (216).

2.4.4 Analysis of the accessory genome

2.4.4.1 Mandrake

The gene presence and absence as determined by Panaroo v1.2.8 (187) was used as input into Mandrake v1.2.2 (217). Accessory distances were calculated using the "sketches" option which uses Sketchlib v2.1.1 (218) to create a sketch database from the fasta sequence files. The HDBSCAN clustering to calculated spatial clustering was "turned-on" in order to determine clusters based on the accessory genome of the dataset. The resulting files produced by

Mandrake were visualised in Microreact (219) with metadata indicating the core group, accessory group, and the percentage of clinical isolates in each group onto the plots.

2.4.5 Determination of minimum inhibitory conditions

The minimum inhibitory concentration (MIC) of a range of antibiotics (Table 2-2) for the evolved strains along with the respective parent and revertant strains was determined by adjusting the OD_{600} of an overnight culture in Mueller-Hinton Broth (MHB, Millipore) to 0.08-0.1. The adjusted culture was further diluted 1:100 and 75 µl was used to inoculate 75 µl of MHB supplemented with the relevant antibiotic doubling in concentration across a sterile clear flat-bottomed 96-well polystyrene plate (Corning® CLS3370, Greiner M3061, or Nunc® P7491) to cover the MIC range described in Table 2-2. To act as a control for growth, 75 µl of the diluted culture was inoculated into 75 µl of MHB with no antibiotic. As a negative control, 75 µl of NFW was added to 75 µl of MHB. The *P. aeruginosa* ATCC 27853 was used as a control for antibiotic concentrations. Plates were incubated with the lid at 37°C for 16-18 hrs without shaking.

After incubation at 37°C for 16-18 hrs, MICs were recorded at the doubling dilution at which there was no visible growth. This was confirmed by adding 45 µl of 0.22µm filter sterilised 0.015% resazurin sodium salt (Sigma-Aldrich) in sterile distilled water to each well and incubated for 2 hours at 37°C. Resazurin sodium salt changes from blue to pink/purple when in the presence of growing cells and thus the MICs were recorded at the first doubling dilution in which no colour change was detected. The experiment was performed three times to generate three replicates.

Table 2-2: Dilution range for antibiotics used in determining MICs

Antibiotic	***Company***	***MIC range (µg/ml)***
Piperacillin (PIP)	Sigma-Aldrich	0.5-256
Piperacillin + Tazobactam (PIP/TAZ)*	Sigma-Aldrich/Sigma-Aldrich	0.5-256
Ceftazidime (CAZ)	Merck	0.25-128
Ceftazidime + Avibactam (CAZ/AVI)*	Merck/MedChemExpress	0.25-128
Aztreonam (AZT)	Merck	0.5-256
Imipenem (IMP)	Sigma-Aldrich	0.125-64
Meropenem (MEM)	MedChemExpress	0.25-128
Ciprofloxacin (CIP)	Sigma Aldrich	0.008-4
Tobramycin (TOB)	Sigma-Aldrich	0.008-4
Chloramphenicol (CHL)	Sigma-Aldrich	1-512

**For antibiotic/inhibitor combinations the concentration of inhibitor (TAZ and AVI) was kept constant at 4 µg/ml across the dilution series*

2.5 Evolution from the environment to a clinical niche

2.5.1 Assessing the absence of *mexS* and *mexT* genes

To confirm the absence of *mexS* and *mexT* genes, raw sequencing reads from revertants and their respective mutant and parent strains were mapped to the PAO1 genome PAO1 (GCF_000006765.1) using the BWA v0.7.17 (220) aligner. Aligned files were sorted and indexed with Samtools v1.16.1 (216) and then visualised in the Integrated Genome Browser (IGB) (221) to confirm the length of the deletion covering the *mexS* and *mexT* region and the other genes affected by the mutation.

2.5.2 Selection of human plasma concentration

Three environmental strains (PA63, PA232, and PA2629) of *Pseudomonas aeruginosa* were grown in Mueller-Hinton Broth (MHB), overnight, diluted to an OD_{600} 0.08-0.1. 1µl of diluted strains were used to inoculate 200 µl of MHB supplemented with 0.38% sodium citrate (Sigma Aldrich) and sterile human plasma ranging from 0% to 100% (TCS Biosciences). Strains were incubated at 37°C in the FLUOstar Omegaplate reader (BMG Labtech) overnight with shaking at 200 rpm and absorbance readings taken at 600 nm every 5 mins. Growth curves were generated in R v4.0.0 using the ggplot2 v3.3.5 (205) package to plot the arithmetic mean with error bars shown as the 95% confidence intervals based on 4 replicates from 2 independent experiments containing 2 replicates each. Statistical analysis on growth curves was performed in R v4.0.0 using a two-way repeated measure ANOVA followed by a one-way ANOVA and pairwise t-test from the rstatix v0.7.0 package (207).

2.5.3 Evolution of strains to clinical conditions

Environmental strains were cultured in MHB supplemented with 10% human plasma and 0.38% sodium citrate (MHB + 10% plasma) for 48 hrs at 37°C whilst shaking at 200 rpm, with

five replicates per strain. After 48 hrs, replicates were passaged by using 100 µl of culture to inoculate fresh MHB + 10% plasma with either CHL (8 µg/ml) or CIP (0.008 µg/ml) and then incubated for 48 hrs at 37°C with shaking at 200 rpm. The passages were repeated ten times for CHL and 20 times for CIP, with the antibiotic concentration doubling at each passage to a final concentration of 4096 µg/ml or until there was no visible growth. At each passage, 1 ml of culture was kept and stored in a cryovial at -80°C. To act as a control, three replicates per strain were passaged in MHB + 10% plasma with no antibiotic. An illustration of this experiment is displayed in Figure 2-2.

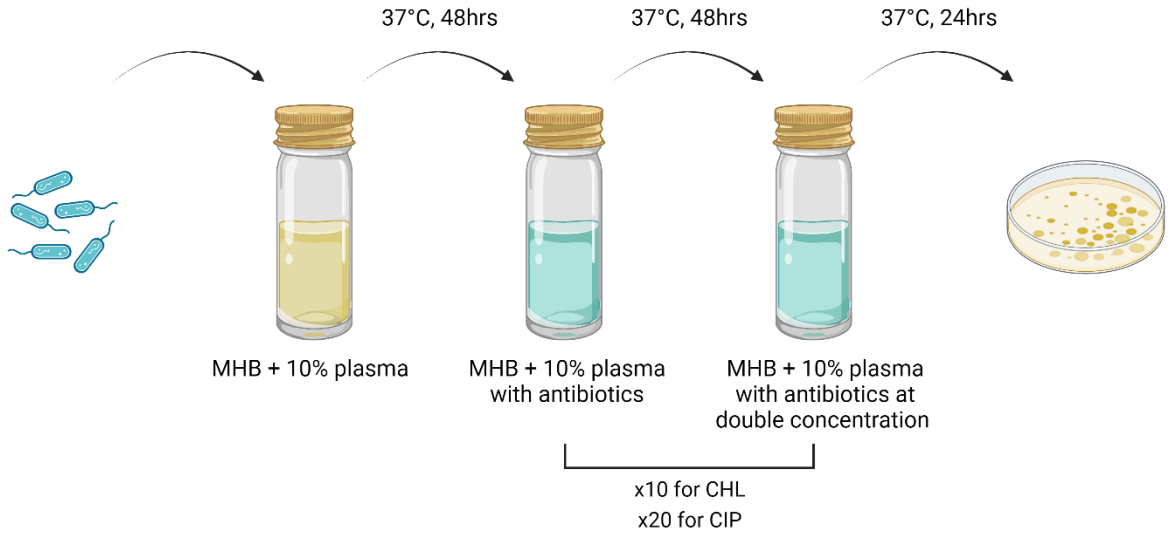

Figure 2-2: Illustration of the experiment to adapt environmental strains towards a clinical niche. Image created with BioRender.com.

After the final passage, 100 µl was spread onto Mueller-Hinton agar (MHA, Millipore) and incubated at 37°C overnight. For each replicate, morphologically distinct colonies were cultured in MHB at 37°C overnight and stored at -80°C in 20% glycerol for further use. The MIC in MHB + 10% plasma for each of the morphologically distinct evolved strains was determined using the method described in Section 2.4.5 for the antibiotics at ranges described in Table 2-3 alongside the controls.

Table 2-3: MIC ranges for evolved strains

Antibiotic	*Company*	*MIC range (µg/ml)*
Chloramphenicol (CHL)	Sigma-Aldrich	2-1024
Ciprofloxacin (CIP)	Sigma-Aldrich	0.25-128
Imipenem (IMP)	Sigma-Aldrich	0.125-64

2.5.4 Reversion of evolved strains to a sensitive phenotype

Evolved strains showing increased MICs to the antibiotics they were evolved in were passaged in MHB + 10% plasma with no additional antibiotics with each passage occurred after a 48 hr incubation at 37°C. After ten passages, strains were plated onto MHA + 10% plasma and incubated for 24 hrs, morphologically distinct colonies were isolated and replica plated onto MHA +10% plasma with and without antibiotic. This was either CIP 0.008 µg/ml or CHL 8 µg/ml depending on the antibiotic the strain was initially evolved in to confirm reversion to a more sensitive phenotype. Isolates with growth on antibiotic free agar and no growth on the antibiotics supplemented media were considered revertants and confirmed as such by MIC testing as described in Section 2.4.5 using the antibiotics and ranges described in Table 2-3. An illustration of this experiment is displayed in Figure 2-3.

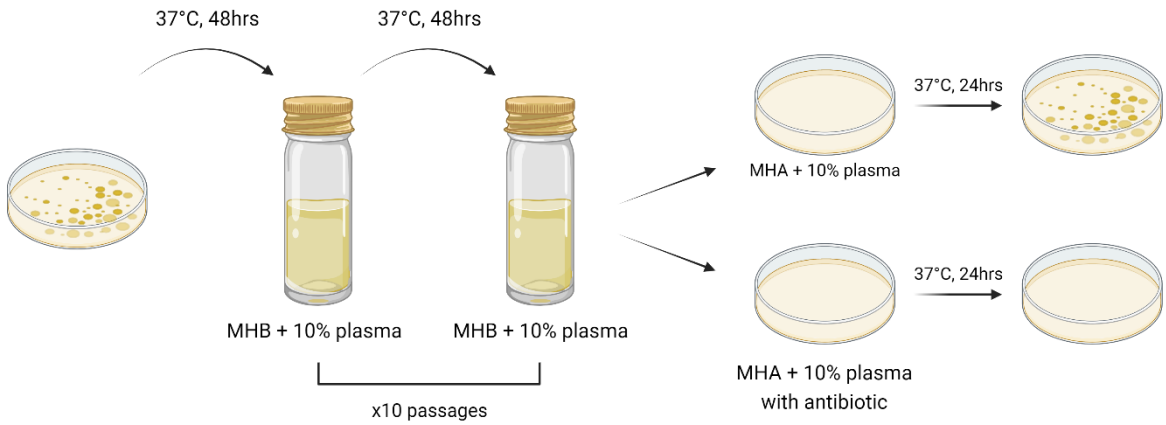

Figure 2-3: Illustration of the experiment to revert resistant strains back to a more susceptible phenotype. Image created with BioRender.com.

2.5.5 Identification of mutations

Mutations in the antibiotic evolved strains and revertants were detected using Snippy v4.6.0 (215) to reveal small insertions, deletions, and substitutions and Breseq v0.37.0 (222) to confirm the small mutations and reveal larger mutations. To check for the presence of large deletions that would not be picked up using the previously listed programmes, sequencing reads of the antibiotic evolved, revertant, and control strains were mapped to an assembly of the respective parent strain using the BWA v0.7.17 aligner (220). Aligned files were sorted and indexed with Samtools v1.16.1 (216) which was then used to determine the coverage depth at each position which was then visualised in blocks of 10,000 bp using the ggplot2 v3.3.5 module (205).

2.5.6 Visualisation of protein structure

The protein structure of CmrA (A0A0H2ZA95) was obtained from UniProt (223) using the AlphaFold (224) predicted structure from the PA14 sequence (GCF_000014625.1). The structure was visualised using protein imager (225) and are annotated with the mutations identified in snippy v4.6.0 (215) and Breseq v0.37.0 (222).

2.5.7 Comparison of bacterial growth

2.5.7.1 Generation of bacterial growth curves

To determine bacterial fitness, growth curves were conducted for each set of parent, mutant, and revertant strains in the media of which the reversion occurred. This was either BHI, SSM9PR, or MHB + 10% plasma broth. Strains were initially cultured overnight at 37°C in the relevant broth to condition strains to the media. The density of the overnight culture was adjusted to OD_{600} 00.08-0.1 and further diluted 1:20 to create an inoculum containing approximately 5×10^6 cfu/ml. 20 µl of the final inoculum was then added to five wells of a

sterile clear flat-bottomed 96-well polystyrene plate (Corning® CLS3370, Greiner M3061, or Nunc® P7491) containing 180µl of broth and five wells containing 180 µl broth supplemented with a concentration of chloramphenicol or ciprofloxacin two doubling dilutions below the lowest MIC detected for the tested strains in each broth. The inner wells of the 96 well plate was used where possible to avoid condensation interfering with the readings. The plate was incubated at 37°C with shaking at 100rpm at the beginning of each cycle on the FLUOstar Omega plate reader (BMG Labtech). Absorbance readings at a wavelength of 600 nm were taken every 5 minutes over the course of 24-36 hrs and the type of 96-well plate used was input into the programme to adjust for any variation caused by using different plates. To act as a blank, 20µl of NFW was used to inoculate five wells of media and five wells of media supplemented with antibiotic. The average absorbance reading of blank wells at each timepoint and media condition was calculated and taken away from the absorbance reading at the corresponding timepoint and media condition.

Growth curves were plotted using ggplot2 v3.3.5 (205) R v4.0.0 (191) using the average OD_{600} up to 16 hrs to cover the exponential phase of growth. Error bars are shown as 95% confidence intervals based on ten replicates generated across two independent experiments each containing five replicates.

2.5.7.2 Analysis of bacterial growth

The GrowthCurver v0.3.1(206) package in R v4.0.0 (191) to calculate growth rate and area under the experimental curve from 0 to 1000 mins. Relative fitness was calculated using the bacterial growth rate as a proxy for each strain. The growth rate for replicate mutant and revertant strains was divided the average growth rate of the parent strain in the same condition. Mann-Whitney *U* tests were performed with rstatix v0.7.0 (207) to compare relative fitness and area under the curve with P-values adjusted using the Benjamini-Hochberg method.

Chapter 3 - Speciating *Pseudomonas aeruginosa*

3.1 Introduction

3.1.1 Identifying bacterial species

Bacterial identification was initially based on phenotypic characterisation. For instance, *P. aeruginosa* strains could be described as facultative aerobes that are glucose and lactose non-fermenting; catalase, citrate, and oxidase positive; rod-shaped Gram-negative staining organisms with a polar flagellum that can produce blue and green pigments (226). Over time the ability to identify bacteria has developed alongside genomic sequencing which has allowed for the incorporation of the entire genetic background of the species.

3.1.1.1 Speciating bacteria using 16S ribosomal RNA

16S rRNA was first proposed as a method to determine the phylogenetic relationships between bacterial strains (227). The nature of the gene in its conservation of function and presence across bacterial species made this gene advantageous for this purpose. Due to sequence divergence over time, the gene was shown to be able to differentiate between bacterial species and became a method used in the speciation of bacteria (227). As a result, the 16S rRNA sequence of a strain is required as part of the description of a new species. Despite this, the method is limited in its abilities to fully differentiate between bacterial species due to its low resolution from focussing on a single highly conserved gene (228).

3.1.1.2 DNA-DNA hybridisation

DNA-DNA hybridisation (DDH) is a method used to compare two bacterial species by annealing fragmented DNA of an unknown strain to the fragmented DNA of a known species to create

hybrid DNA (229). The stability of the hybridised DNA fragments is measured and strains showing >70% similarity to one another are considered the same species (230). The process of creating hybrid DNA is long and difficult to reproduce leading to the method being flawed and prone to errors (229). Additionally, as the method relies on the physical comparison between two strains there are no universal databases that can be used for unanimous calling. Nevertheless, the method itself has much higher resolution than 16S rRNA for speciating bacteria as it encompasses the whole genome as opposed to a singular gene (229, 231).

3.1.1.3 Average nucleotide identity

The average nucleotide identity (ANI) measures the similarity between two genomic sequences and is used as a more precise *in silico* alternative to DDH (232-234). Additionally, the method overcomes the limitations caused by identification using 16S rRNA by expanding beyond a single gene allowing it to fully differentiate between species with closely related 16S rRNA (232). ANI was initially limited by its reliance on using completed genomes to generate comparisons, however programmes have been developed to allow draft genomes to be compared accurately (197).

3.1.1.4 Robust clustering

Phylogenetic analysis can provide useful insight into the classification of species. Hug *et al.* described a new method for uncovering the tree of life (Figure 3-1) (194). The process involves the analysis of 16 ribosomal proteins that are conserved throughout all Archaea, Bacteria and Eukarya. Therefore, it allows for the generation of a phylogenetic tree across all species. It also has the advantage of a higher resolution than phylogenies created using 16S rRNA, multilocus sequence typing (MLST), or multilocus sequence alignment (MLSA) phylogenies which rely on fewer genes. Moreover, it avoids the use of genes with different functions that would create errors leading to the production of a more refined phylogeny. Consequently, novel bacteria

species can be classified utilising this method (235). For the purposes of this thesis this method is referred to as robust clustering.

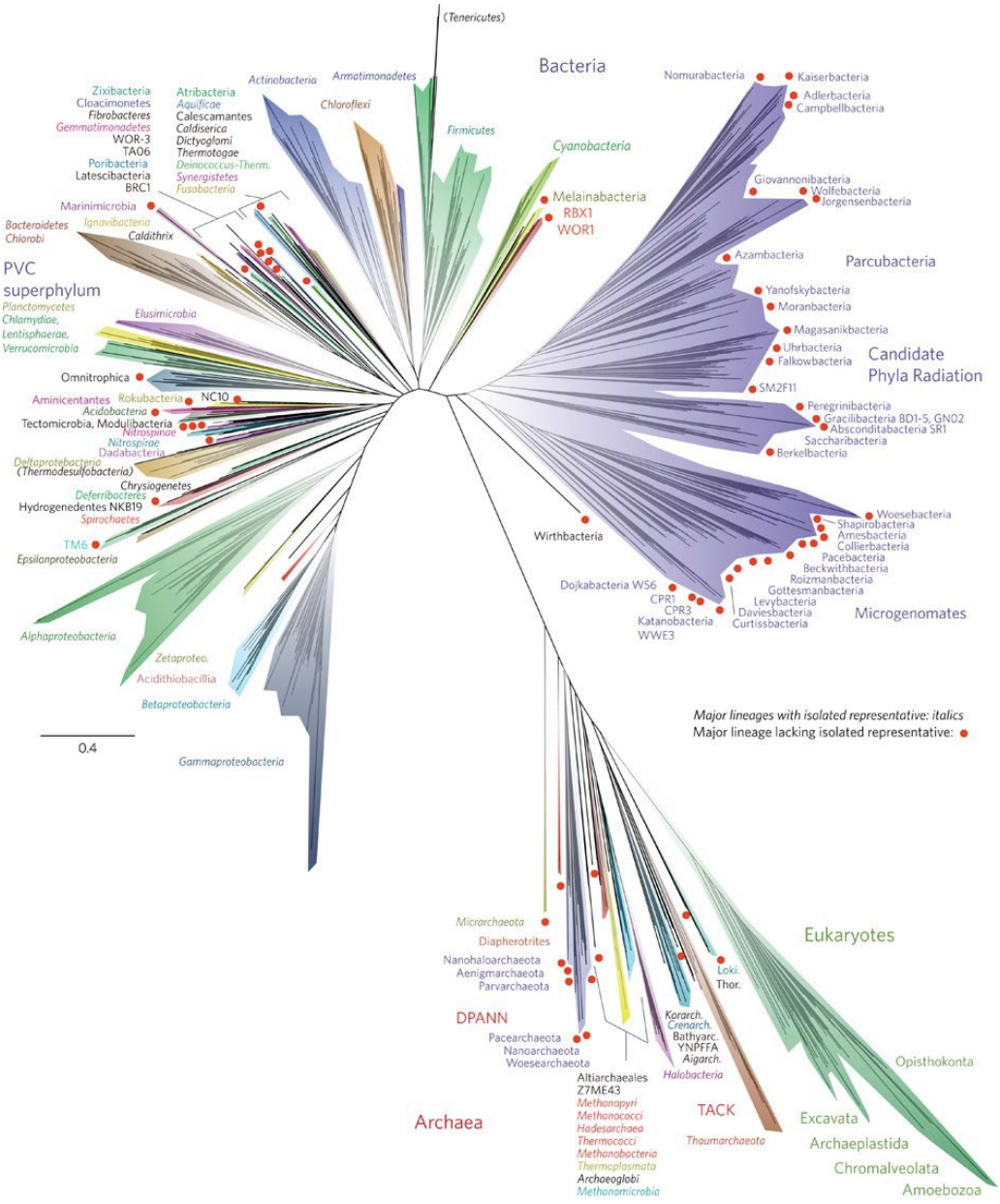

Figure 3-1: The new tree of life. The tree is a maximum likelihood tree created from an alignment of 16 ribosomal protein sequences from various Archaea, Bacteria, and Eukarya species. Well-characterises lineage named and coloured to differentiate the lineages. Image is taken from Hug et al. *(194)*

3.1.2 *Pseudomonas aeruginosa* taxonomy

When it comes to classifying bacteria there are guidelines stipulated by the International Code of Nomenclature of Prokaryotes (ICNP) that need to be followed for the nomenclature to be

valid (236). *P. aeruginosa* is classified as a valid name and was first described by Gessard in 1882 who noted the presence of blue and green colouration on bandages (237). Subsequently, the species was classified as belonging to the *Pseudomonas* genus, which derives from the Greek words *pseudo* meaning "false" and *monas* meaning "single unit" with the species name designated *aeruginosa* derived from the Latin translation of *aerūgō* to rusted copper (238-240). The organism itself is a single cell and thus the designation of *Pseudomonas* is thought to have derived from resemblance to the *Monas* genus. The genus name *Pseudomonas* was initially used to encompass all Gram-negative rod-shaped aerobic bacilli with polar flagella. However, the discovery of 16S rRNA to taxonomically classify bacteria resulted in the genus being divided (226, 241). This also allowed for the differentiation at species level, however this not always applicable for all bacteria (228).

3.1.2.1 Changes to species level classification in **Pseudomonas**

With the ability to use the genomic sequence of bacteria to speciate strains, existing nomenclature has been adjusted accordingly. The correct nomenclature is given in the List of Prokaryotic names with Standing in Nomenclature (LPSN) (176). As previously mentioned, 16S rRNA can fail to correctly identify species, hence DDH can be utilised to solve this issue. However, this method also comes with its own caveats. Thus, Lalucat *et al.* utilised a MLSA scheme consisting of four housekeeping genes (*16S rRNA, gyrB, rpoB,* and *rpoD*), genome-to-genome distance calculations (GGDC), and ANI to delineate species (198, 242, 243). The result of this was the reclassification of species that had previously been classified as separate species into a singular species. For example, *Pseudomonas citronellolis* and *Pseudomonas humi* were reclassified as the same species under the name *P. citronellolis; Pseudomonas nitroreducens* and *Pseudomonas nitrireducens* were reclassified as *P. nitroreducens; and Pseudomonas meliae, Pseudomonas amygdali, Pseudomonas savastanoi,* and *Pseudomonas ficuserectae* were reclassified under *P. amygdali* (242). Reasoning for the incorrect classification of these strains varied from a lack of sequencing technologies at the time the "novel" strain was discovered,

unavailability of the type strain sequence as it had yet to be described and thus the "novel" sequence had no comparator, and a lack of bioinformatics programmes to identify the similarities between the "novel" and recognised type strain (242). The names of species that fall under this type of reclassification are considered heterotypic synonyms with a single name selected to be the correct name for the species (176).

In addition to the merging of previously separate species into a singular species, strains originally characterised as belonging to the same species have also been separated into their own individual groups. This was the case in a study by Morimoto *et al.* where strains originally classified as *Pseudomonas fluorescens* and *Pseudomonas putida* were shown not to meet the species boundaries for ANI, considered to be ≥95%, and a digital version of DDH (dDDH), considered to be ≥70% (175, 197, 244). Specifically, the strains originally identified as *P. fluorescens* were reclassified as *Pseudomonas kilonensis* and *Pseudomonas brassicacearum;* and strains originally identified as *P. putida* were reclassified as *Pseudomonas alloputida, Pseudomonas asiatica, Pseudomonas juntendi, Pseudomonas monteilii,* and *Pseudomonas mosselii*. Hence, it is possible for strains that have previously been identified as one species to be reclassified as a separate species when they do not fit the criteria of the species they were originally named as.

3.1.3 Exclusion of select *Pseudomonas aeruginosa* strains in phylogenetic studies

When analysing the core genome of a species it is important to ensure that all strains included in the study are of high quality and are correctly identified to prevent errors in the naming of core genes. A previous study on the *P. aeruginosa* pan-genome by Freschi *et al.* displayed a distantly related group of *P. aeruginosa* strains (143). This group has previously been described in studies assessing the *P. aeruginosa* core genome where it was shown to be diverge from the main group of *P. aeruginosa* strains (146, 245-248). Strains within the group include

the *P. aeruginosa* PA7 strain (249) and are found to have ANI values ranging from 93-94% when compared to the other *P. aeruginosa* groups (143, 244). As the ANI values were <95%, which is considered the species boundary, it provoked the question as to whether these strains belong to the *P. aeruginosa* species (197). Due to this phenomenon this divergent group of isolates has been excluded in pangenome analyses of the *P. aeruginosa* species (250, 251) or even used as an outgroup (252).

3.1.4 *Pseudomonas aeruginosa* PA7

The *P. aeruginosa* PA7 strain was originally isolated from a non-respiratory infection in Argentina due to its unique resistance pattern. The complete genome sequence of the strain was published in 2010 by Roy *et al*. where it was described as a taxonomical outlier (249). This was due to housekeeping genes showing divergence to other well characterised *P. aeruginosa* strains which included the PAO1 type strain. Out of the seven housekeeping genes used in MLST, only two showed a high nucleotide identity (97-99%) with the remaining five displaying lower identities (86-94%) (249). Furthermore, the number of predicted proteins in PA7 which share similarity to a selection of other *P. aeruginosa* strains is 4,890 (Figure 3-2). In comparison, the number of predicted proteins unique to PA7 is 1,008, which is greater than the number of unique predicted proteins in any of the *P. aeruginosa* strains it was compared with (Figure 3-2). Despite the evidence pointing towards PA7 being an outlier, Roy et al. found that the similarity in the ribosomal RNA genes and other genes involved in protein synthesis placed the strain close to other *P. aeruginosa* strains (249). Hence, the PA7 strain and its PA7-like relatives are routinely classified into the *P. aeruginosa* species.

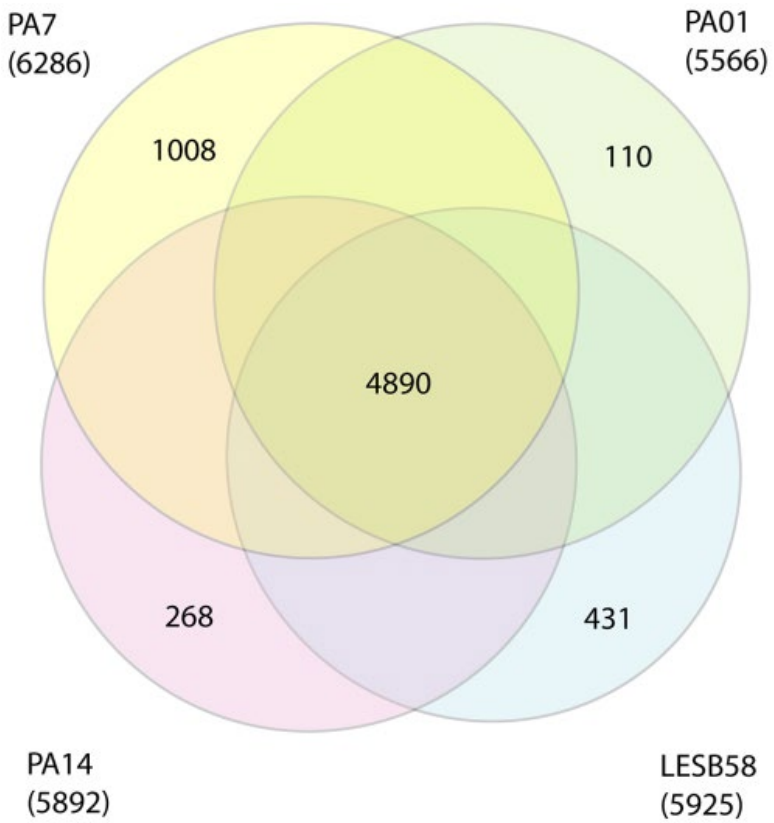

Figure 3-2: Comparison of gene present in Pseudomonas aeruginosa *strains. The Venn diagram shows the number of predicted proteins from the PAO1, PA14, LESB58, and PA7 which share similarity. The total number of predicted proteins found in each genome is indicated in brackets under the strain name. Image is taken from Figure 2 from Roy* et al*. (249)*

3.1.4.1 Gene association within PA7-like strains

Comparison of the genome sequences of *P. aeruginosa* strains and other PA7-like strains has indicated that the *cat* gene, conferring resistance to chloramphenicol through a chloramphenicol acetyltransferase, was only present in PA7-like strains suggesting the gene was likely acquired by this group (143). The *exoU* and *exoS* genes, which encode effector proteins secreted by the type III secretion system, were described as absent in the PA7 strain and later discovered to be absent in all PA7-like strains (248, 249). Additionally, the OprA porin that forms part of the MexXY-OprA/OprM efflux pump was present in a small number of divergent *P. aeruginosa* strains in addition to the PA7-like strains. Due to the presence of a small portion of the *oprA* gene being found in other *P. aeruginosa* strains it is presumed that *oprA* expression was lost from an ancestral *P. aeruginosa* strain following the divergence OprA

positive strains (143, 253). Hence, previous literature has been able to identify discrepancies in gene presence and absence between PA7-like and *P. aeruginosa* strains.

3.1.5 Chapter aims

Given that PA7-like strains have previously been removed from pan genome analyses of *P. aeruginosa*, this chapter aims to further characterise the inclusion of the PA7-like strains as part of the *P. aeruginosa* species. The specific objectives covered are as followed:

1. Assess the phylogeny of strains identified as *P. aeruginosa* in conjunction with strains belonging to other *Pseudomonas* species.
2. Utilise genetic and phenotypic methods to characterise groups of divergent *P. aeruginosa* strains.

3.2 Results

3.2.1 Phylogenetic analysis of the *Pseudomonas* genus

3.2.1.1 16S rRNA of the Pseudomonas *species*

Comparison of 16S rRNA is the method that has historically distinguished the difference between bacterial species. A Type Strain Genome Sever (TYGS) (175) generated phylogeny based on the 16S rRNA of 29 *Pseudomonas spp.* in addition to five strains identified as *P. aeruginosa*, including the *P. aeruginosa* PA7 strain, groups all the *P. aeruginosa* strains together in a well-supported monophyletic clade with a bootstrap of 1 (Figure 3-3). The *P. aeruginosa* PA7 strain is considered a genomic outlier within the *P. aeruginosa* species and often branches away from the main group of *P. aeruginosa* strains in phylogenetic studies but this is not evident when using 16S rRNA data (143, 146, 249). 16 strains with similar genetic profiles to PA7 were identified with Kraken2 which used a k-mer based approach to compare genome sequences to the Kraken2 bacteria database of strains (182). BLAST results of these PA7-like strains against the 16S rRNA nucleotide sequence of *P. aeruginosa* PAO1 showed 99-100% identity between the strains and thus, if solely considering the 16S rRNA, support the inclusion of the strains into the *P. aeruginosa* species (Table 3-1). It should be noted that some stains were found to have multiple copies of the 16S rRNA gene, however BLAST analysis showed the copies to have 100% identity to each other (Table 3-1). Phylogenetic analysis of the 16S rRNA of PA7-like strains and 25 other *Pseudomonas spp.* places the PA7-like strains in a monophyletic clade together with sequences of the *P. aeruginosa* reference strain DSM 50071 (PAO1) supported with a bootstrap of 1.00 (Figure 3-4).

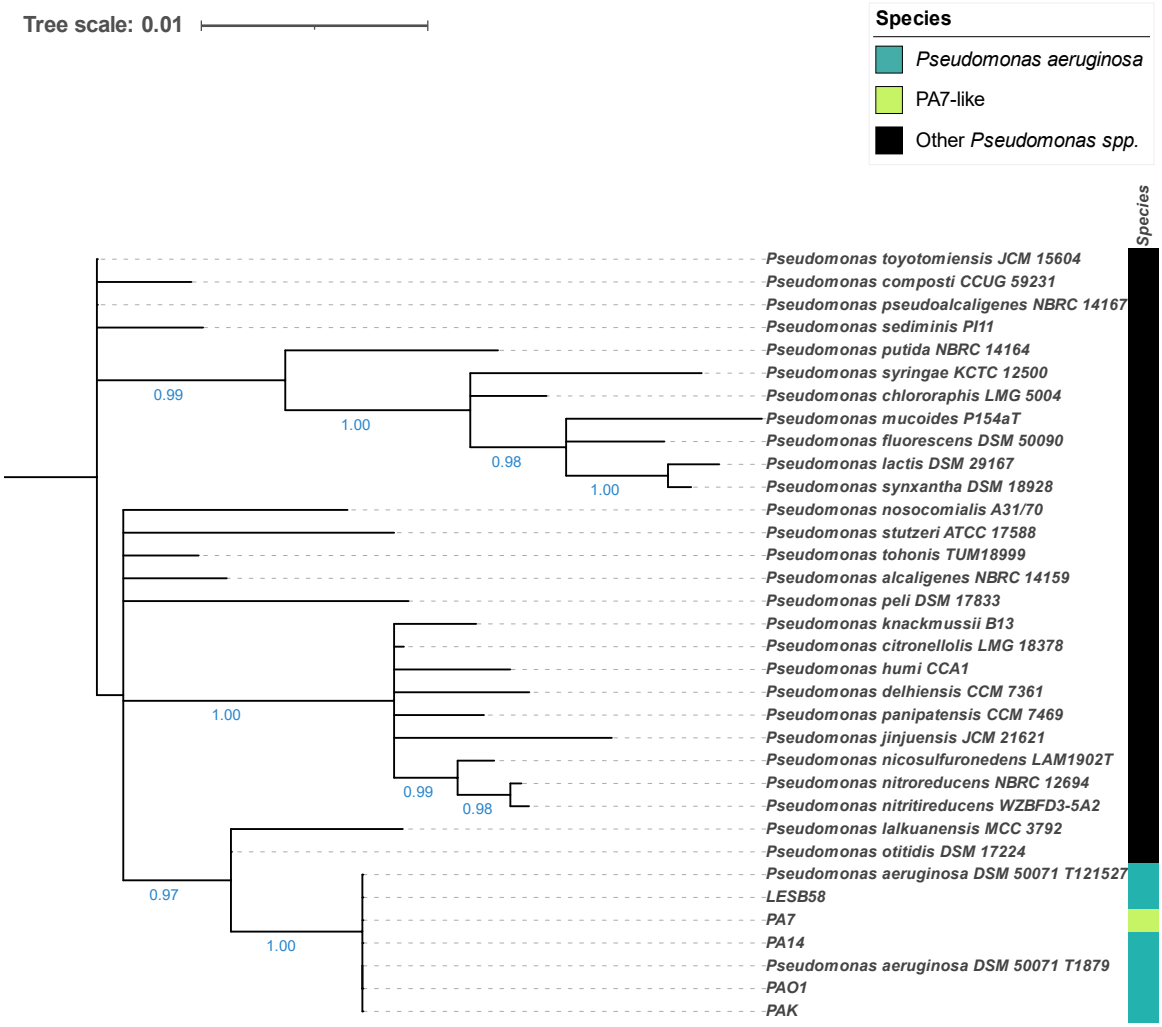

Figure 3-3: Minimum evolution tree displaying the 16S rRNA phylogeny of 34 Pseudomonas strains. The tree is rooted at the midpoint with bootstrap values, determined by 100 bootstrap replicates, indicated along the branches. Nodes with bootstrap values <0.95 have been collapsed. Branch lengths are scaled by Genome BLAST Distance Phylogeny (GBDP) (175) and annotations indicate the bacterial species.

*Table 3-1: BLAST results of PA7-like strains against the 16S rRNA sequences from Pseudomonas aeruginosa PAO1**

Strain	Copies	Expect Value	Identity (%)
PA259	1	0.0	100
PA580	1	0.0	99
PA628	1	0.0	99
PA828	1	0.0	100
PA868	1	0.0	100
PA964	1	0.0	100
PA1129	3**	0.0	100
PA1130	1	0.0	100
PA1145	4**	0.0	100
PA1646	1	0.0	100
PA1780	1	0.0	100
PA1794	1	0.0	99
PA1802	1	0.0	100
PA2045	4**	0.0	100
PA2078	1	0.0	100
PA2541	1	0.0	100
PA2548	1	0.0	100

* *BLAST matches shorter in length than the query sequence are excluded from the table.*

** *PA1129, PA1130, and PA2045 were shown to contain multiple copies of the 16S rRNA gene by Barrnap v0.9 (201) however all copies were found to have Expect values of 0.0 and identities of 100%.*

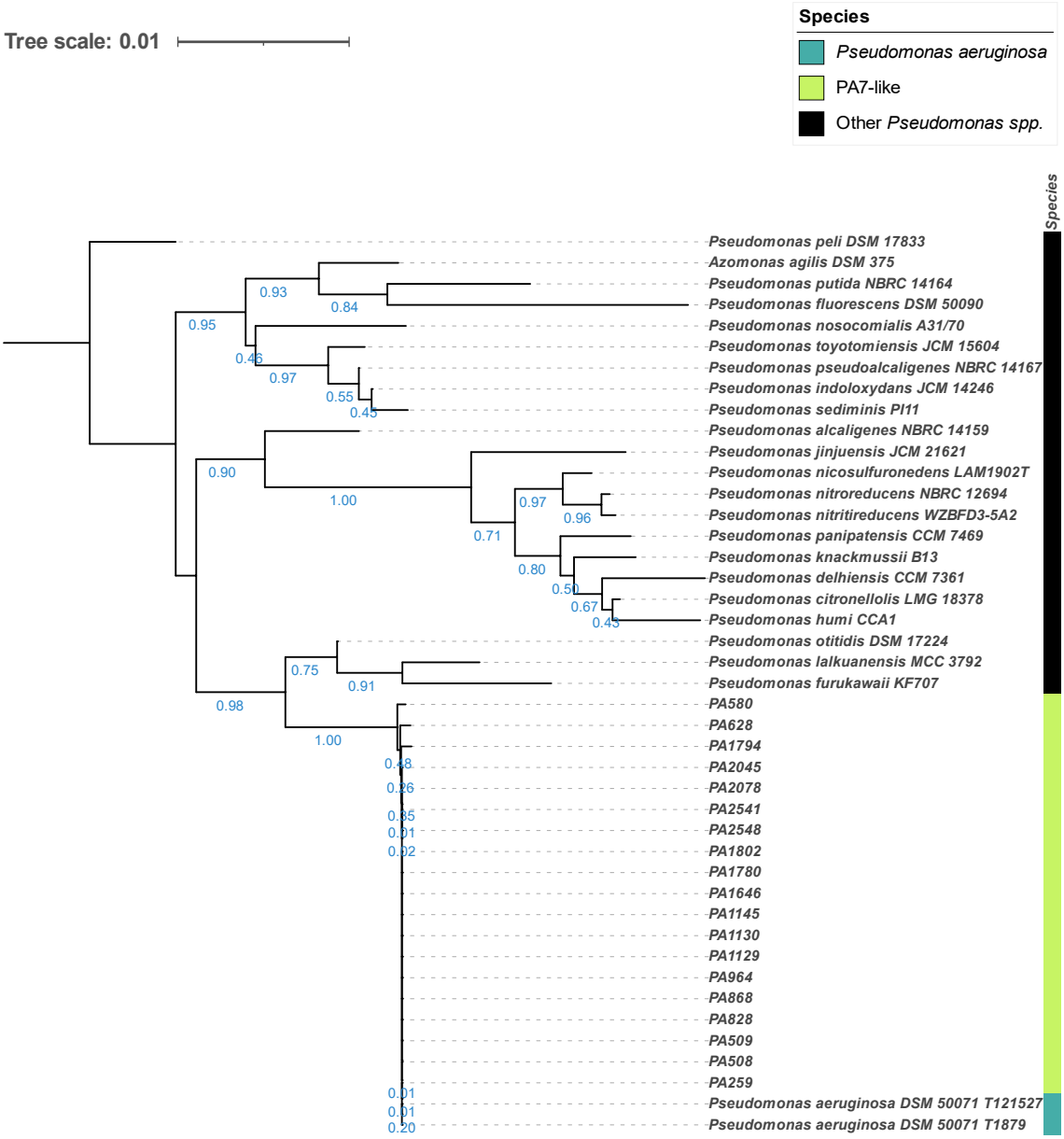

Figure 3-4: Minimum evolution tree displaying the 16S rRNA phylogeny of Pseudomonas strains including 19 PA7-like strains. The tree is rooted at the midpoint with bootstrap values, determined by 100 bootstrap replicates, indicated along branches, nodes with bootstrap values <0.95 have been collapsed. The tree is scaled by GBDP (175) and annotations indicate the bacterial species.

Whilst the other *Pseudomonas spp.* form their own leaves within the 16S rRNA phylogenies depicted in Figure 3-3 and Figure 3-4, some of the species are not validly published with individual species names by the ICNP (236). For example, *Pseudomonas indoloxydans* and *Pseudomonas sediminis* are not validly published species names under the ICNP and do not appear to be a synonym for another species. Some of the species' names have been found to be

synonyms of previously classified species. Of the strain included in Figure 3-3 and Figure 3-4, *Pseudomonas humi* is considered a heterotypic synonym of *Pseudomonas citronellolis*, *Pseudomonas nitritireducens* is a heterotypic synonym of *Pseudomonas nitroreducens,* and *Pseudomonas pseudoalcaligenes* is a heterotypic synonym of *Pseudomonas oleovorans* (not included in the 16S rRNA phylogeny). Thus, these species are considered the same species as their respective heterotypic synonym by the ICNP. Additionally, *Pseudomonas nosocomialis* is a homotypic synonym of the orphaned species *Stutzerimonas nosocomialis* and thus is not considered part of the Pseudomonas genus by the ICNP.

For the heterotypic synonyms the 16S rRNA sequences were not identical with Figure 3-3 showing branch lengths of 0.005559 for *P. citronellolis* and *P. humi* and 0.001312 for *P. nitrireducens* and *P. nitroreducens* despite being considered the same species. Furthermore, smaller branch lengths between different species with validly published names, *P. lactis* and *P. synxantha* = 0.003284, *P. citronellolis* and *P. knackmussi* = 0.00405532, and *P. citronellolis* and *P. panipatensis* = 0.00440241, were seen than the branch length between *P. citronellolis* and *P. humi*. Therefore, identification based on the 16S rRNA gene is problematic and cannot be solely relied on to provide an accurate species identification as they are defined by the ICNP.

3.2.1.2 Robust clustering to speciate the **Pseudomonas** *genus*

16S rRNA sequencing can be a useful method for classifying bacteria due to its universal presence across bacterial genomes (227), however, its reliance on using a single gene to identify species is limiting (228). Therefore, we used a nucleotide alignment of 16 ribosomal proteins, as described by Hug *et al.* (194), to group *Pseudomonas spp.* producing robust clusters (RC) with Fastbaps based on a Dirichlet process mixture model. (195) This method identifies clusters at multiple levels by merging clusters at each level though Bayesian hypothesis testing. At RC level 1, the highest level of clustering, five groups were identified within the ribosomal

protein alignment (Figure 3-5). As with the 16S rRNA phylogeny, *P. aeruginosa* PA7 clusters together with the *P. aeruginosa* strains at level 1, however it forms its own separate branch within the cluster that is supported by a bootstrap of 1.00. At RC level 2, the groups identified at RC level 1 are sub-divide into 10 smaller groups that begin to separate some of the *Pseudomonas spp.* into their own species clusters. Though some species remain part of the same group at RC level 2 (e.g. *P. syringae* and *P. fluorescens*), the clustering identifies the PA7 strain as its own cluster separate from the other *P. aeruginosa* strains (Figure 3-5).

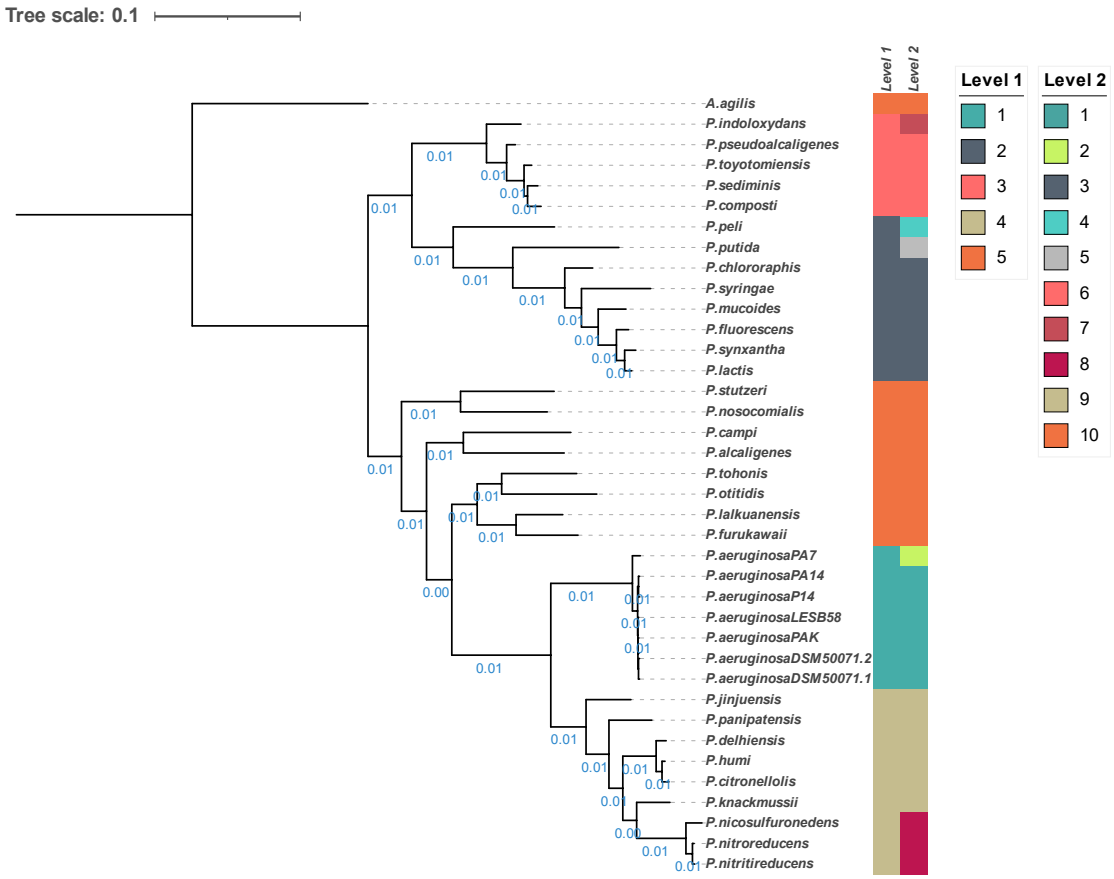

Figure 3-5: Maximum-likelihood phylogenetic tree based on the alignment of 16 ribosomal proteins. Bootstrap values, calculated by 100 bootstrap replicates, are displayed across branches and those with bootstrap support <0.95 have been collapsed. The tree, constructed with a generalised time-reversible model (GTR) and Gamma20 likelihoods, has been rooted at the midpoint. The scale bar represents the substitutions per site.

In contrast to the phylogeny generated from the 16S rRNA gene, strains that have been characterised as the same species were found to have a closer relationship when considering the RC phylogeny. For instance, *P. nitrireducens* and *P. nitroreducens* have a branch length of 0.00261, and *P. citronellolis* and *P. humi* a branch length of 0.00684 which is 3.4 and 1.3 times smaller than the branch length separating PA7 and the *P. aeruginosa* species node (0.00897). Additionally, the branch length between species which have been classified as separate but had small variations in their 16S rRNA, were longer than seen between the PA7 and other *P. aeruginosa* strains (*P. lactis* and *P. synxantha,* 0.0126; *P. citronellolis* and *P. knackmussi,* 0.0546; and *P. citronellolis* and *P. panipatensis,* 0.0612). Moreover, these lengths were similar or greater than seen between strains which displayed greater 16S rRNA branch lengths (*P. pseudoalcaligenes* and *P. indoloxydans,* 0.0436; *P. humi* and *P. delhiensis,* 0.0130; and *P. dehliensis* and *P. citronellolis,* 0.0157). Thus, the RC based on the 16 ribosomal proteins described by Hug *et al.* provides a more representative phylogeny of the nomenclature as specified by the ICNP, except for PA7 which is classified within the *P. aeruginosa* species (236).

3.2.1.3 Robust clustering of the **Pseudomonas aeruginosa** *species*

To investigate if RC could be used to identify clusters within the *P. aeruginosa* species, the nucleotide sequences of 16 ribosomal proteins for 2,405 *P. aeruginosa* strains was aligned and input into Fastbaps (195) to identify RC groups across multiple levels. Clustering of the alignment identified 13 groups at RC level 1 and is visualised as a phylogenetic tree in Figure 3-6. The fourth RC group identified at level 1 was shown to contain the same 17 strains that were identified as PA7-like. Like the PA7 strain in RC analysis of the *Pseudomonas* genus (Figure 3-5), the PA7-like strains formed their own group, RC 4, which was separate from the other *P. aeruginosa* strains. This group formed a monophyletic clade with a branch length of 0.00650 supported with a bootstrap of 1.00. In comparison, the next longest branch, which was supported by a bootstrap of 1.00, had a length of 0.00107. The other 12 RC groups did not show similar levels of divergence as the PA7-like strains, instead they had shorter branch lengths

indicating high similarity within the non-PA7-like *P. aeruginosa* strains. Thus, the RC alignment was not able to clearly define clusters within the *P. aeruginosa* species except for the PA7-like strains which grouped into their own well supported cluster.

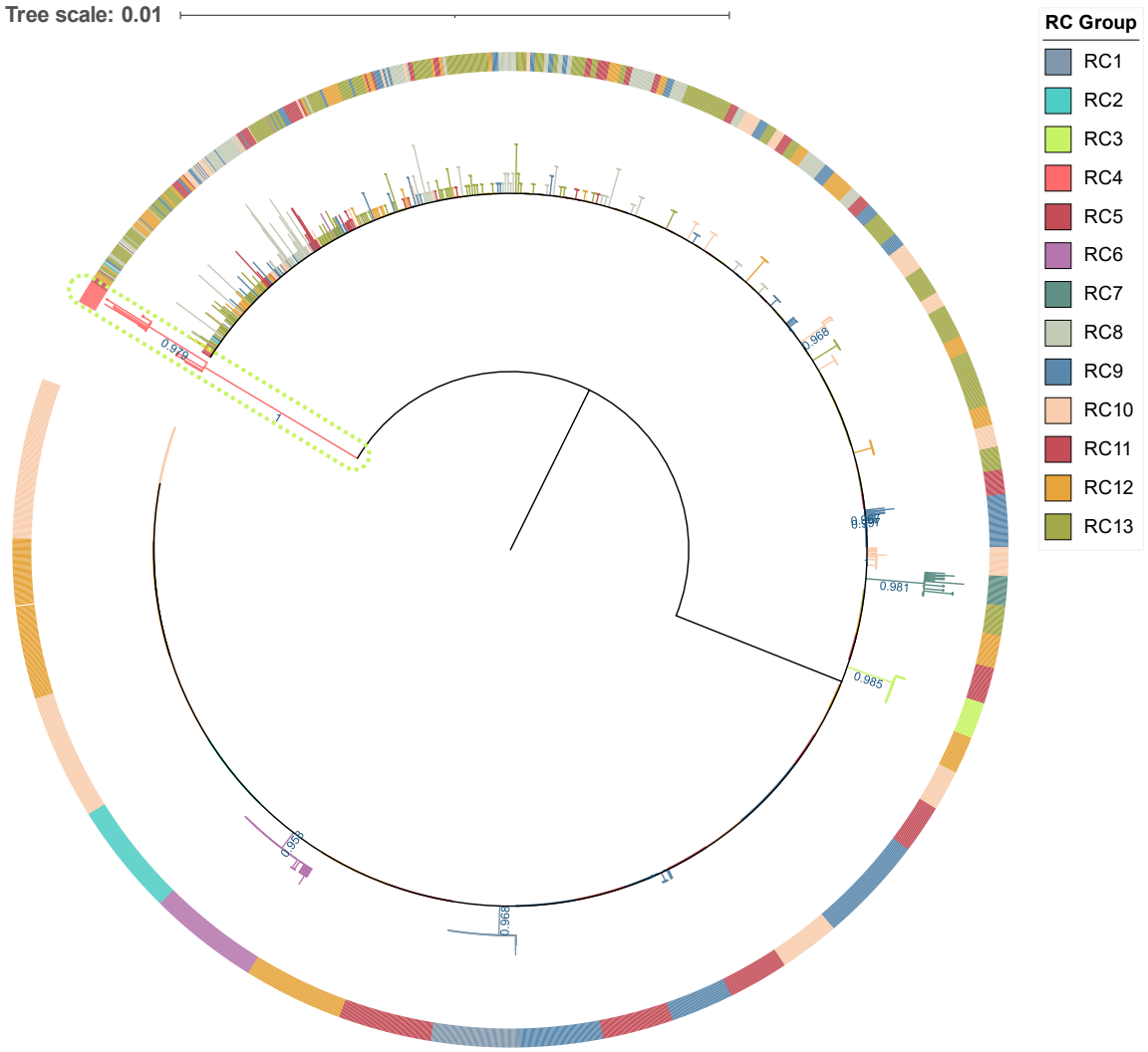

Figure 3-6: Maximum-likelihood tree of 16 ribosomal proteins used for robust clustering of the Pseudomonas aeruginosa species. Bootstraps are determined via 100 bootstrap replicates, with branches with <0.95 support collapsed for visualisation. The tree is constructed with FastTree using GTR and Gamma20 likelihoods with and RC clusters are annotated along the rim of the tree. The scale bar represents substitutions per site. The branch encompassing the PA7-like strains is highlighted with a light green dashed line.

3.2.1.4 Core genome alignment of **Pseudomonas aeruginosa** *and the PA7-like strains*

To analyse the population structure within *P. aeruginosa*, we analysed the core genome defined here as genes present in ≥99% of strains analysed. Panaroo v1.2.8 (187) was used on a set of 2,632 strains of *P. aeruginosa,* described in Appendix - Table 3. A total of 39,637 genes were identified in the *P. aeruginosa* pangenome with 4,283 of these genes found to present in 99% of the genome and therefore considered the core genome. An alignment of these core genes was made with mafft v7.487 (188) and filtered to retain only the polymorphic sites with snp-sites v2.5.1 (189) to produce the core SNP tree depicted in Figure 3-7.

Clustering of the core gene alignment with the FastBaps v1.0.6 algorithm (195) using the core genome SNP alignment identified the presence of 19 clusters at Level 1. As with the RC tree of *P. aeruginosa* strains visualised in Figure 3-6, a diverging branch was identified containing a cluster of strain named Core5. This diverging cluster, consisting of the 17 PA7-like strains and the PA7 strain, were found in RC4 (Figure 3-6). The branch length separating the Core5 group was 0.70338 and was supported with a bootstrap of 1. In comparison, the second longest branch, also supported by a bootstrap of 1 was found to have a branch length of 0.09576. Hence, core SNP analysis from our set of *P. aeruginosa* strains concurred with previous studies on the *P. aeruginosa* core genome that the PA7-like strains were genomic outliers within the *P. aeruginosa* core genome (143, 146, 250, 254).

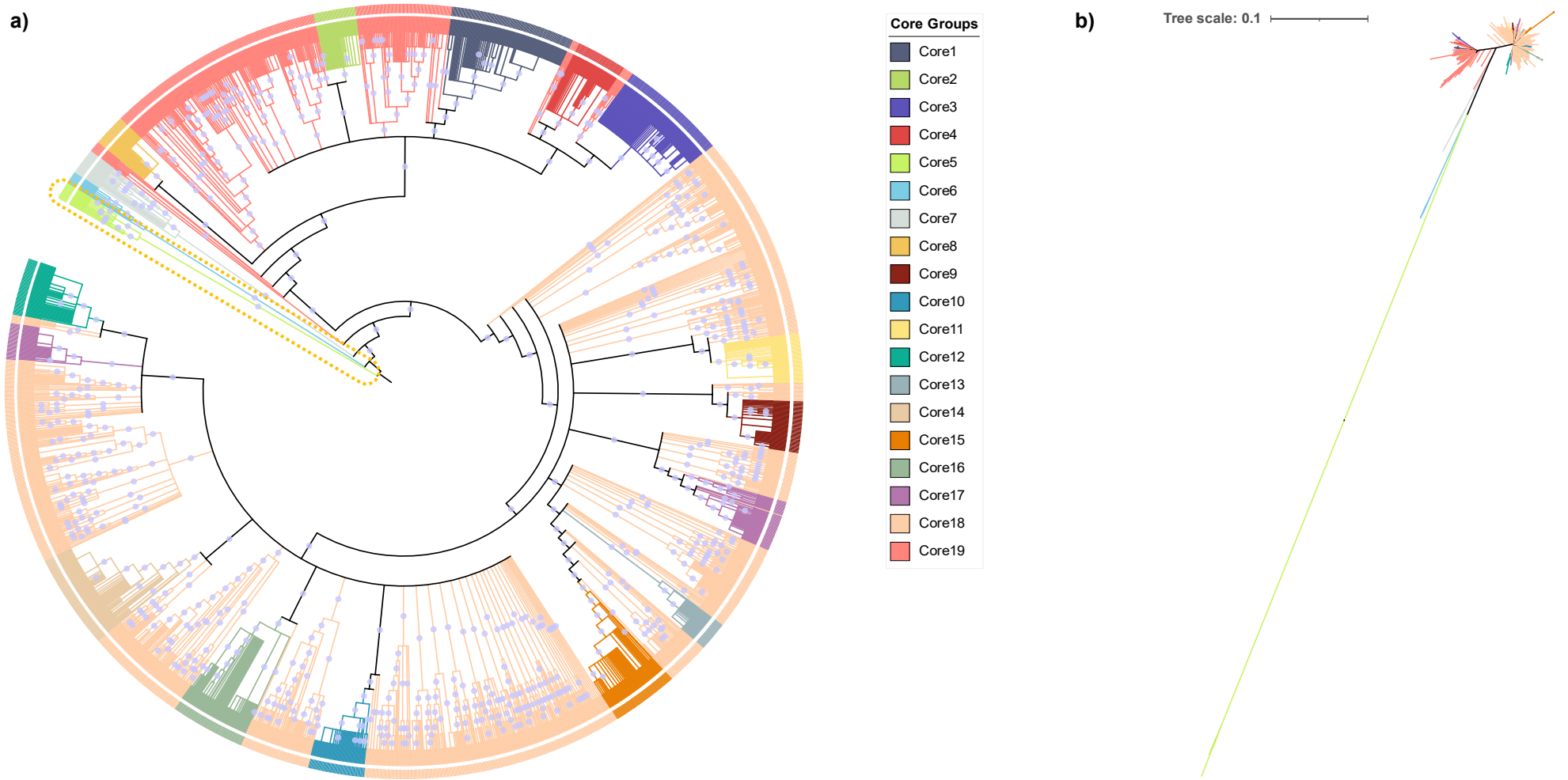

Figure 3-7: Maximum-likelihood tree of the core SNPs present in Pseudomonas aeruginosa. The tree is constructed with FastTree using GTR and Gamma20 likelihoods with 100 bootstrap replicates. Bootstraps values ≥0.95 are depicted by ● on the circular tree (a) which has been rooted at the midpoint with the PA7-like strains circled in orange. Branch lengths are shown on the unrooted tree (b) with the scale bar representing substitutions per site. Colours on both trees represent the FastBaps clusters found at Level 1.

3.2.1.4.1 Geneflow

The Hudson fixation index (F_{ST}) is a measure that can identify gene flow between two sub-populations (255). At an F_{ST} of 0 no differentiation is identified and thus indicates high gene flow between the two populations, while at an F_{ST} of 1 the converse is inferred. The F_{ST} between sub-populations of *P. aeruginosa* identified from the core genome was calculated using PopGenome (190) and is displayed in Figure 3-8.

From the core genome phylogeny depicted in Figure 3-7, the largest clusters were Core 18 and Core 19, both of which contained smaller clusters within the clades they formed on the phylogenetic tree. Both Core 18 and Core 19 showed high levels of gene flow with the smaller core groups identified. Each of these smaller groups were more isolated from one another and showed higher F_{ST} values indicating there was less gene flow amongst these smaller groups. An exception within the smaller core groups was Core 17 which was split across two clades that were both encompassed by Core 18 and showed lower F_{ST} values with Core 18 and smaller clusters that were closely related according to the core gene phylogeny. Another exception was Core 5, the PA7-like containing group, Core 6, and Core7 which were both isolated from the main cluster of strains in the core genome phylogeny. All these groups showed high F_{ST} values across a smaller range, 0.903 to 0.952 for Core 5, 0.805 to 0.927 for Core 6, and 0.672 to 0.919 for Core 7 when compared against the other core groups, suggesting they were more genetically closed off (Figure 3-8).

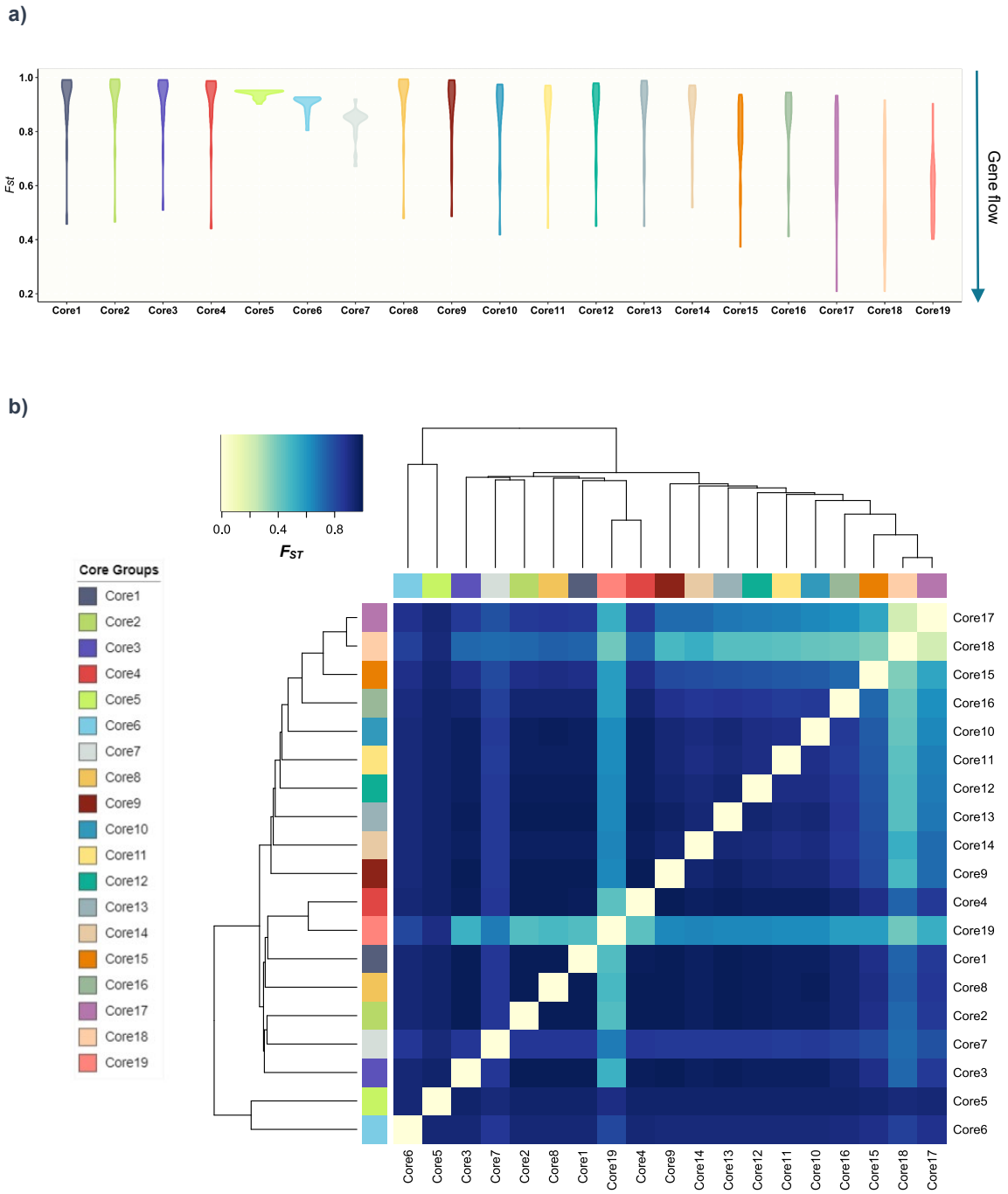

Figure 3-8: Gene flow (F_{ST}) *between core groups of* Pseudomonas aeruginosa *including the PA7-like group. a) Depicts a violin plot of* F_{ST} *values shared between a single core group and the other groups. b) Shows the* F_{ST} *pairwise comparisons between the core group which are annotated along the edges of the heatmap. The dendrogram is drawn by assessing the similarity of the* F_{ST} *values contained in the matrix. Raw data of the heatmap is provided in Appendix - Table* 25.

3.2.1.4.2 Nucleotide divergence

Absolute nucleotide divergence (D_{xy}) measures the average number of nucleotide substitutions per site between populations to infer the diversity between the two populations (256). Using the groups generated by clustering of the core genome illustrated in Figure 3-7, the D_{xy} was calculated for *P. aeruginosa* using the core genome alignment and is visualised in Figure 3-9. The group displaying the greatest divergence from the other core groups was Core 5, the group containing the PA7-like strains. Hence, the D_{xy} values concurred with the core genome phylogeny in Figure 3-7 and signified the divergence of this PA7-like strain containing group from the larger cluster of *P. aeruginosa* strains. Following this divergence were the Core 6 and Core 7 groups, which also exhibited large D_{xy} values (Figure 3-9) and diverging branches in the core genome phylogeny (Figure 3-7). However, the divergence seen was not as great or as clustered together as the divergence displayed by the Core 5 PA7-like group when compared to the other groups.

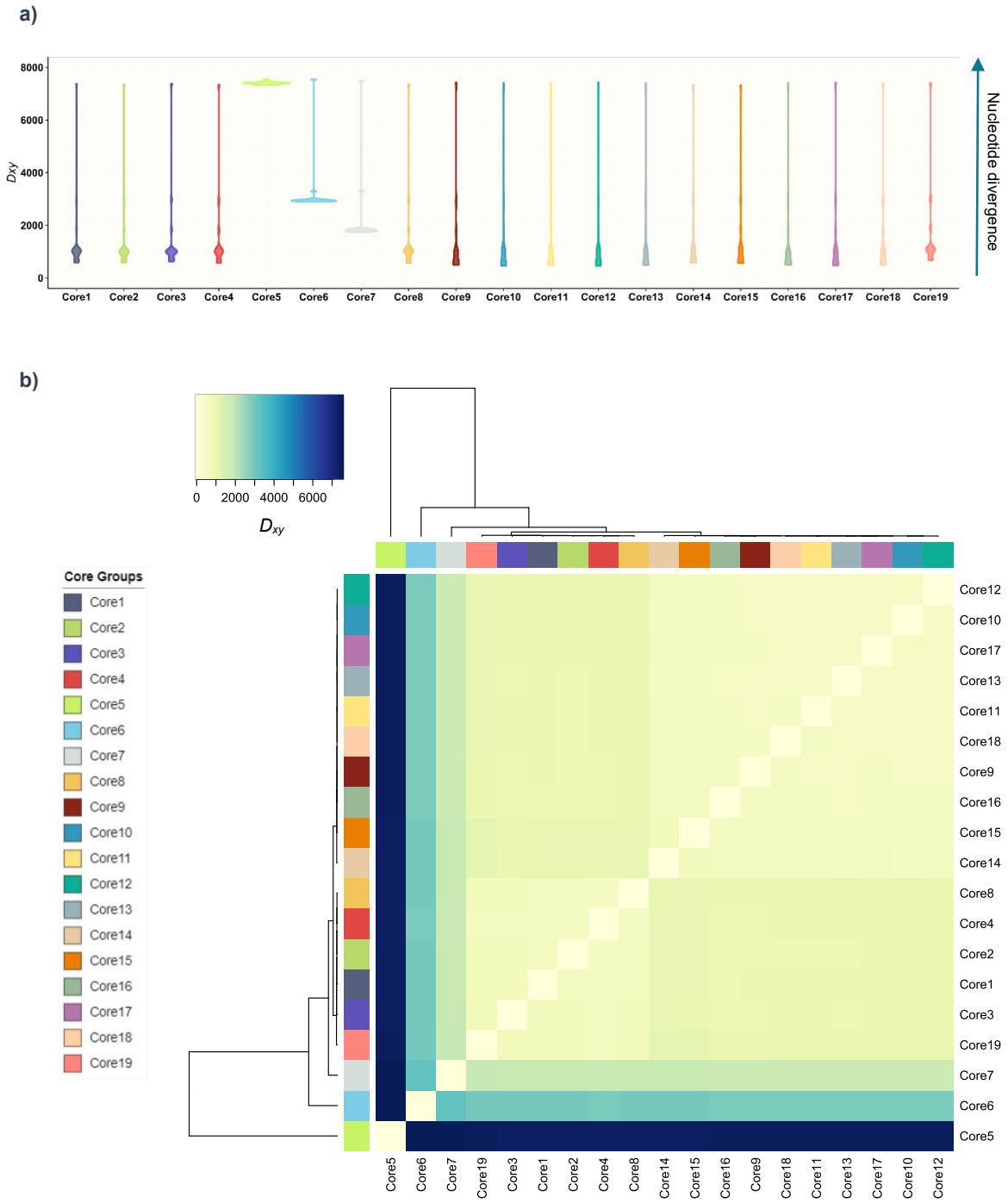

Figure 3-9: Absolute nucleotide divergence (D_{xy}) *between core groups of* Pseudomonas aeruginosa *including the PA7-like group. a) Depicts a violin plot of* D_{xy} *values shared between the named core group and the other groups. b) Shows the individual* D_{xy} *pairwise comparisons between the core groups which are annotated along the edges of the heatmap. The dendrogram is drawn by assessing the similarity of the* D_{xy} *values contained in the matrix. Raw data of the heatmap is provided in Appendix - Table 26.*

3.2.2 Genomic analysis of the PA7-like strains

3.2.2.1 Average nucleotide identity of PA7-like cluster

Average nucleotide identity (ANI) is a method used to compare two sequences and measure the similarity between the nucleotides. ANI values between the PA7-like strains and closely related *Pseudomonas* species identified through TYGS, are displayed in Figure 3-10.

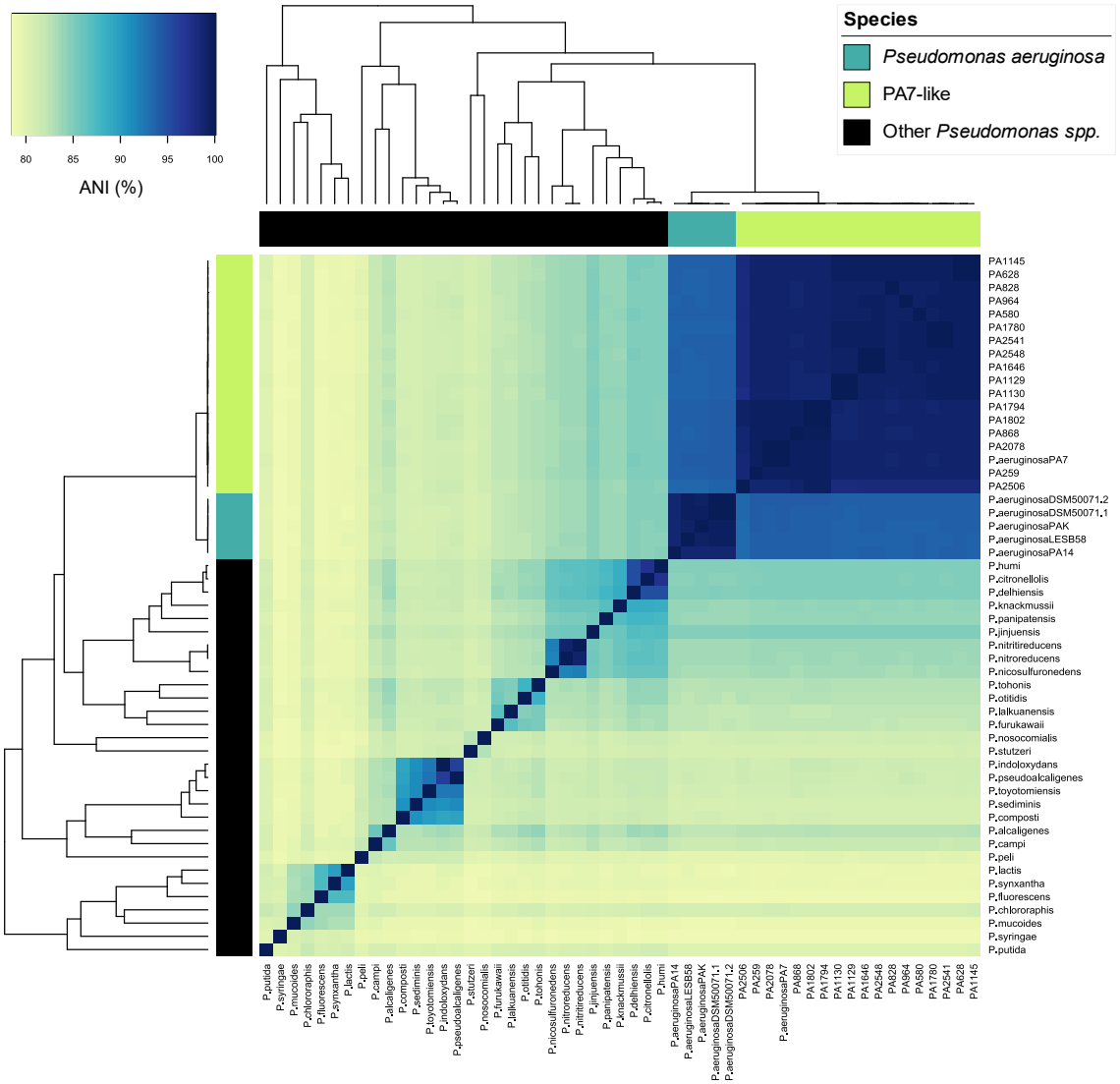

Figure 3-10: Average nucleotide identity of PA7-like strains with Pseudomonas *spp. The heatmap depicts the ANI values as percentages with annotations along the rows and columns representing species. The dendrogram is based on the similarity of the ANI values. Raw data of the heatmap is provided in Appendix - Table 27.*

Within the PA7-like group of strains ANI values show there is high similarity between PA7-like genomes (97.8-100%) and, when compared to other Pseudomonas species, the PA7-like genomes have the highest similarity with *P. aeruginosa*. However, ANI values between PA7-like and *P. aeruginosa* strains were below 95%, ranging from 93.4-94.1% (Figure 3-10). Whilst the ANI value between PA7 and *P. aeruginosa* did not appear to support their current nomenclature, the ANI value between the species with heterotypic synonyms was within the ≥95% cut-off that is used to define strains belonging to the same species (*P. nitritireducens* and *P. nitroreducens*, ANI = 98.96%; *P. citronellolis* and *P. humi,* ANI= 97.17%) (197). Also showing ANI values within the same species boundary were *P. pseudoalcaligenes* and *P. indoloxydans,* ANI = 96.31%; *P. humi* and *P. delhiensis,* ANI = 95.13%; and *P. dehliensis* and *P. citronellolis*, ANI = 95.07%. Between the previously mentioned strains with close relationships within the 16S rRNA phylogeny the ANI values were as followed: *P. lactis* and *P. synxantha* = 89.90%, *P. citronellolis* and *P. knackmussi* = 88.84%, and *P. citronellolis* and *P. panipatensis* = 87.78% agreeing with their distinction as separate species. Therefore, like the RC phylogeny, the ANI values classified the PA7-like strains outside the *P. aeruginosa* species.

3.2.2.2 Comparison of MinHash sketches

Sourmash (202) uses MinHash sketches to create genomic signatures that can be compared to calculate the Jaccard similarity index between genomes using a scale between 0 and 1, with 1 being the highest degree of similarity. A matrix showing the similarity between the MinHash generated signatures based on a *k*-mer size of 31 is depicted in Figure 3-11. Within the PA7-like strains the similarity ranges from 0.460-0.986, however when comparing the PA7-like strains to *P. aeruginosa* strains the similarity between the two groups ranges from 0.113-0.143. Whilst a cut-off for the species threshold has not been identified for the Jaccard index calculated through Sourmash, some species of Pseudomonas showed closer relationships with each other than seen between the PA7-like strains and *P. aeruginosa*, (*P. indoloxydans* and *P. pseudoalcaligenes* = 0.299; *P. delhiensis* and *P. humi* = 0.781; and *P. citronellolis* and *P. dehliensis*

= 0.567). The strains with close relationships in terms of their 16S rRNA phylogeny showed less similarity in their Jaccard index (*P. lactis* and *P. synxantha* = 0.0378, *P. citronellolis* and *P. knackmussi* = 0.0299, and *P. citronellolis* and *P. panipatensis* = 0.0264) than seen between the strains considered to be from the same species (*P. nitritireducens* and *P. nitroreducens* = 0.604; *P. citronellolis* and *P. humi* = 0.300), as would be expected by strains belonging to separate species. Consequently, the relationship of these strains revealed by the comparison of MinHash sketches is more in accordance with the ANI and RC phylogeny than it is with the 16S rRNA generated phylogeny.

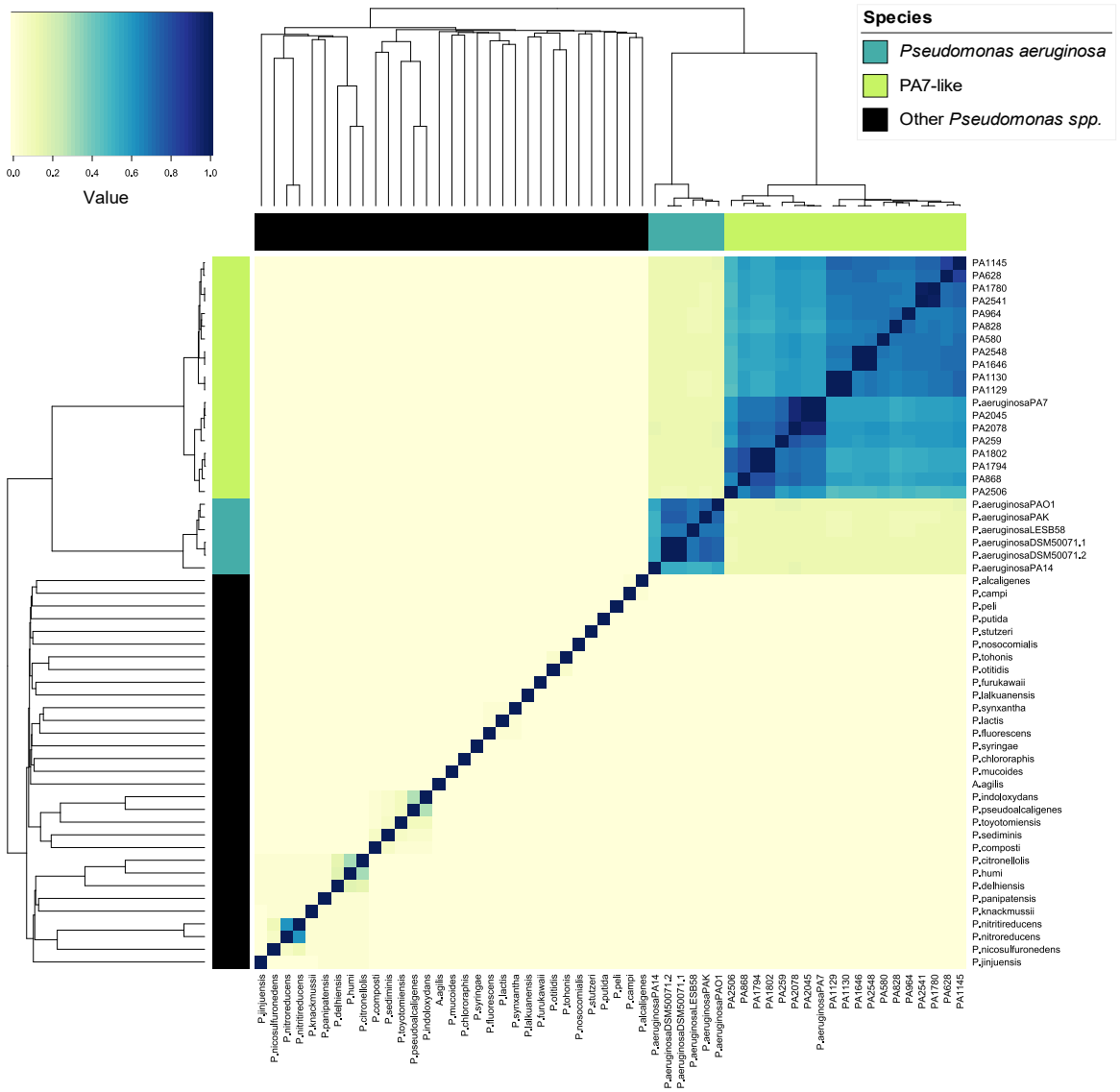

Figure 3-11: Jaccard similarity index of genomic signatures of PA7-like and Pseudomonas spp. *based on a k-mer size of 31. The dendrogram is based on the similarity of the heatmap which visualises a matrix of Jaccard similarity index values between strains. Annotations alongside the rows and columns indicate the species. Raw data of the heatmap is provided in Appendix - Table* 28.

3.2.2.3 Digital DNA-DNA hybridisation

DNA-DNA hybridisation (DDH) is a method used to determine the relationship between two strains, by mixing the DNA of two strain to create hybrid sequences and then using the melting temperatures of the hybrid DNA to assess similarity. TYGS used the theory of DDH and sequencing data to generate pairwise comparisons of digital-DDH (dDDH) to assess the similarity between two sets of genome sequences (175). Figure 3-12 shows a heatmap

depicting pairwise comparisons between a selection of *P. aeruginosa* strains and closely related *Pseudomonas spp.* that were identified by TYGS.

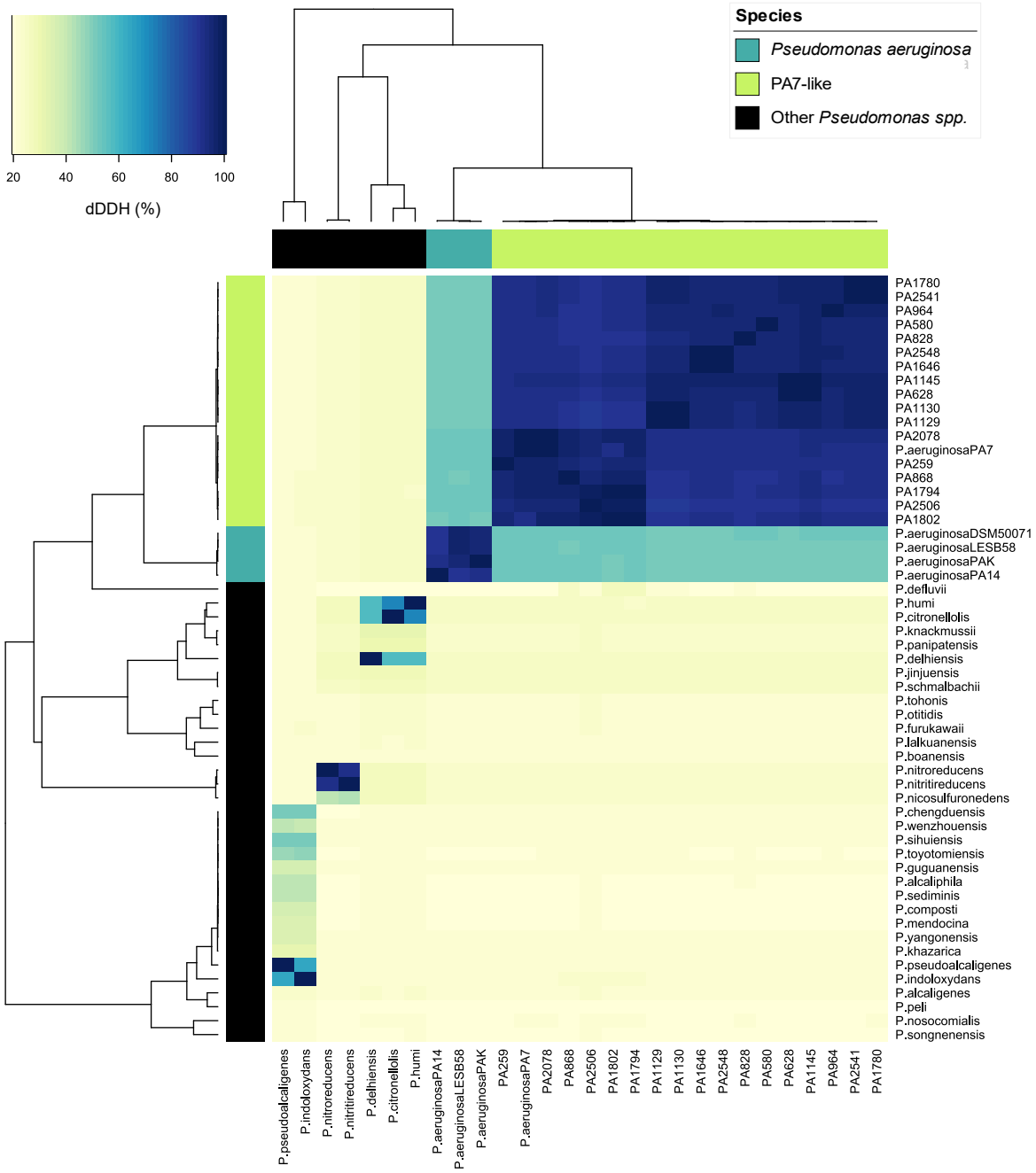

Figure 3-12: Pairwise digital DNA-DNA hybridisation (dDDH) of Pseudomonas *strains. The dDDH values were determined using TYGS with the dendrogram determined by the dissimilarity of the dDDH matrix. Raw data of the heatmap is provided in Appendix - Table* 31.

In DDH, species which show ≥70% similarity with each other are considered the same species, this cut-off value is also applied to dDDH (175, 230). The PA7 strain had dDDH values ranging from 52.5-53% when compared to other *P. aeruginosa* strains. These were the highest dDDH values identified between PA7 and other species. However, as the dDDH value was below the

species cut-off it suggests that while PA7 is most like *P. aeruginosa* it does not belong within it. Likewise, the PA7-like strains were also found to have dDDH values <70% (Figure 3-12) when compared to *Pseudomonas spp.* following the observance seen in the ANI values of PA7-like strain and *Pseudomonas spp.* (Figure 3-10).

For the non-*P. aeruginosa* Pseudomonas species, the dDDH values for the strains were only ≥70% between *P. nitritireducens* and *P. nitroreducens* (dDDH = 90.5%) and *P. humi* and *P. citronellolis* (dDDH = 72.8%) supporting their classification as the same species. Of the remaining non-*P. aeruginosa* strains, the dDDH values were <70%, supporting the classification of these species as separate. Whilst the dDDH values of some strains were <70% and enough to be considered distinct species (*P. humi* and *P. delhiensis,* dDDH = 57.2%; and *P. dehliensis* and *P. citronellolis*, dDDH = 57.4%) their values were still greater than those seen between PA7-like strains and *P. aeruginosa* (51-2-53.1%).

3.2.2.4 Visualisation of the PA7-like genomes

The differences seen between the PA7-like and *P. aeruginosa* strains have shown the two groups do not fit the characteristics on strains belonging to the same species. To ensure the differences seen in the output of the Sourmash (Figure 3-11) and dDDH (Figure 3-12) programmes, which consider gaps present in the sequences, were not due to large scale insertion or deletion BRIG was used to visualise BLAST identities. PA7-like strains were compared against the PAO1 type strain, (Figure 3-13) and the converse was applied to visualise PAO1 and the PA7-like strains against PA7 (Figure 3-14).

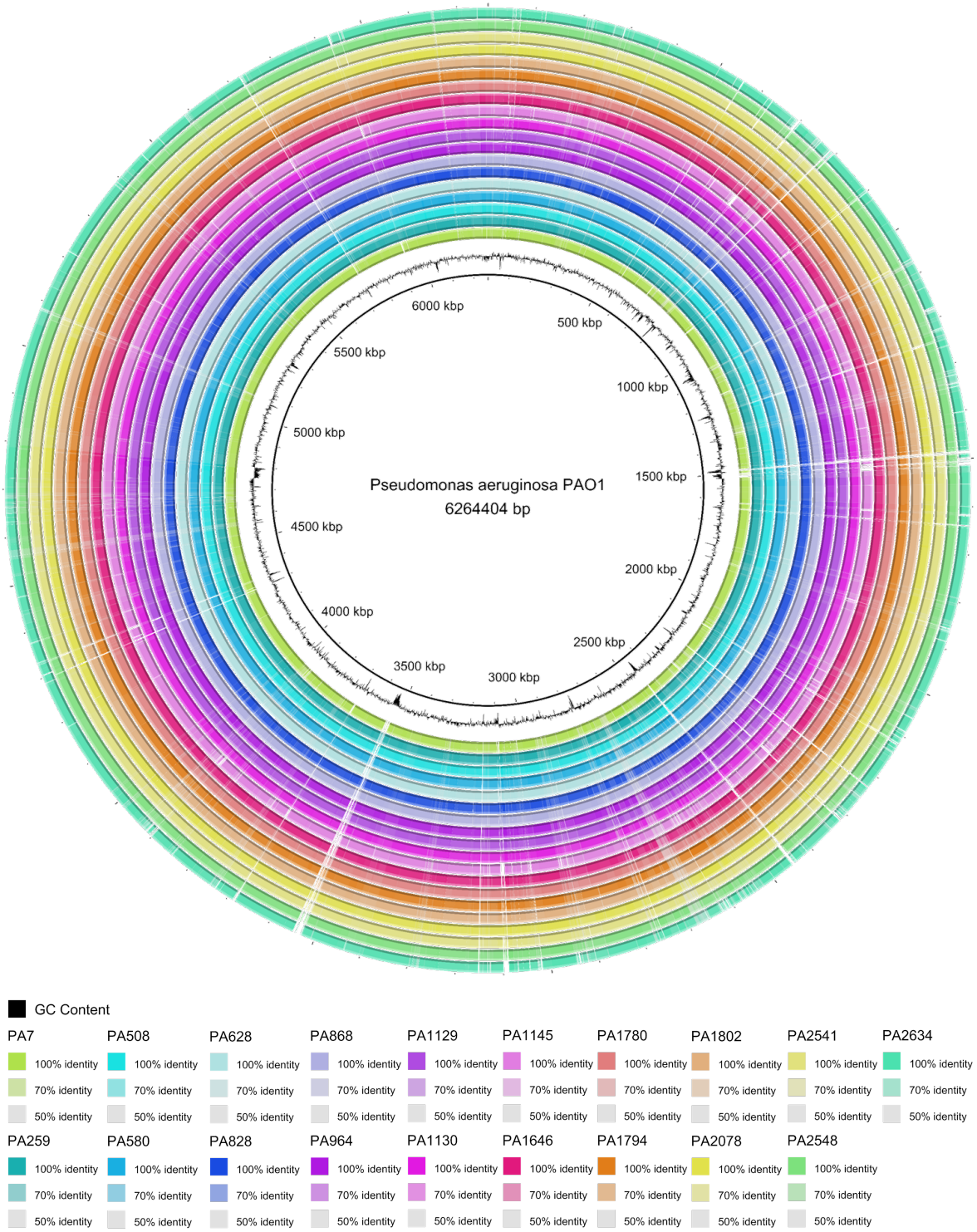

Figure 3-13: BRIG diagram of the Pseudomonas aeruginosa *PAO1 strain compared against PA7-like strains. The inner ring depicts the GC content of the PAO1 genome centred at the median with increases extending outwards. The remaining ring illustrates comparisons between the PA7-like strains and PAO1 strain. The PA7 strain, highlighted in green, and the PA7-like strains, highlighted in various colours, are shaded as described according to the BLAST identities against the PAO1 genome.*

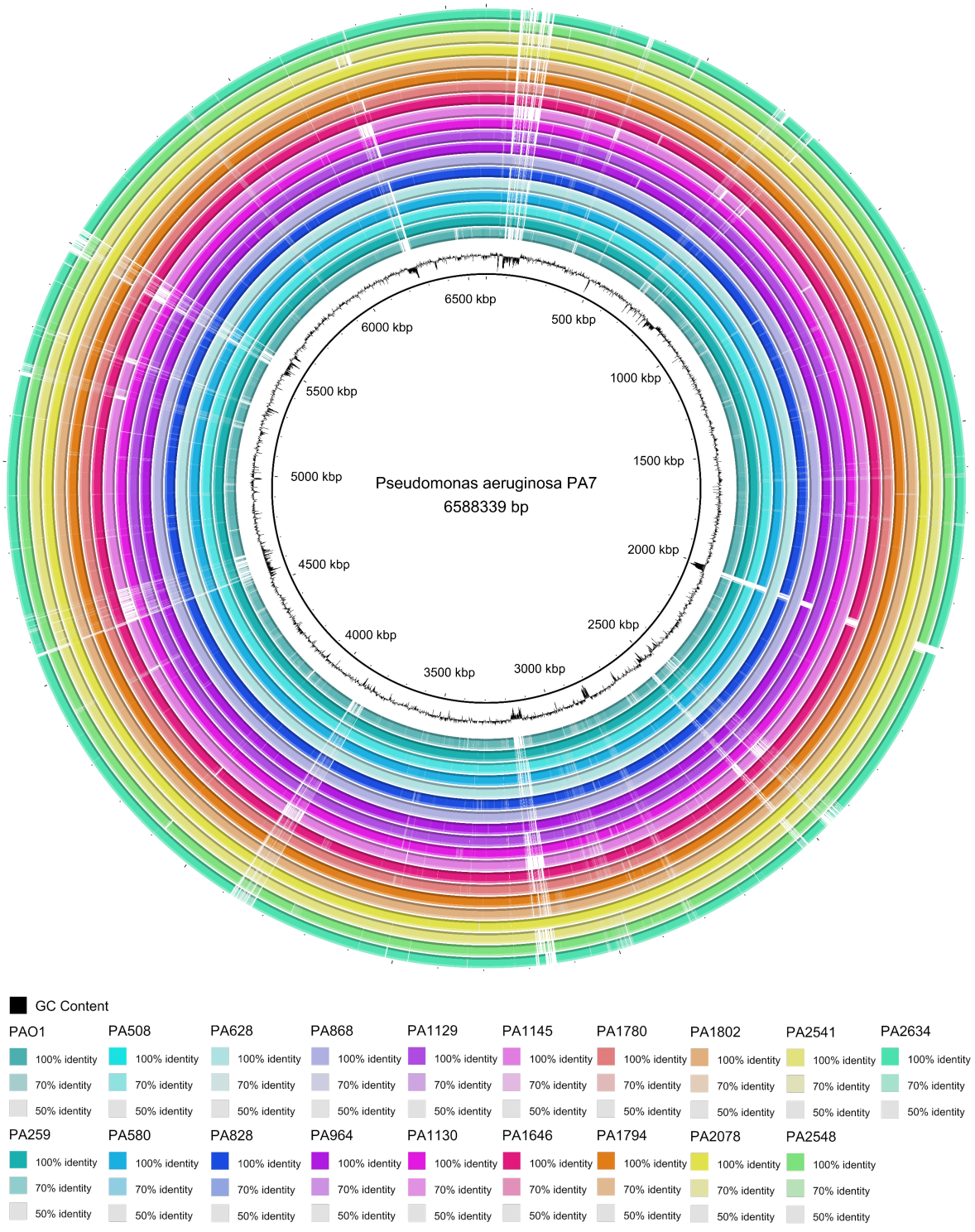

Figure 3-14: BRIG diagram of the Pseudomonas aeruginosa *PA7 strain compared against the PAO1 type strain and PA7-like strains. The inner ring depicts the GC content of the PA7 genome centred at the median with increases extending outwards. The next ring, highlighted in teal, illustrates the comparison between the PA7 strain and PAO1 with the PA7-like strains coloured as described in the legend. Rings are shaded according to the BLAST identity between the strain and PA7 genome.*

BLAST analysis using the PAO1 strain as a reference, shows gaps within the PA7 strain suggestive of either multiple deletions within PA7 or insertions within PAO1 (Figure 3-13). The gaps seen in PA7 were also present across the PA7-like strains and correlated to regions where the GC content diverged from the median. Due to this deviation in the GC content, it is likely for the gaps to be due to insertions within the PAO1 genome. Comparison of PAO1 with PA7 as the reference also showed similar results with gaps within the PAO1 genome These gaps were seen across some of the PA7-like strains but were not universal among the PA7-like group. As with the PAO1 strain, these gaps coincided with changes in the GC content. This suggests a history of insertions in the PA7-like group after the divergence of the PA7-like strains either through the dissemination of insertions into some but not all the PA7-like strains, or by deletions in some strains following divergence.

Evidence of multiple insertion and deletion events were visible between the PAO1 and PA7-like strains across their respective genomes. These events were not commonly present amongst the PA7-like strains and the events which appeared universal to the group did not collate to correspond to the differences seen in comparisons of the genomic signatures (Figure 3-11). Thus, the genetic differences resulting in the divergence of the PA7-like strains is unlikely to be the result of an *P. aeruginosa* strain with insertion and/or deletion to its genome.

3.2.3 Phenotypic characterisation of the PA7-like cluster

3.2.3.1 Comparison of carbon utilisation

Carbon utilisation of PA7-like and *P. aeruginosa* strains was compared using the PM1 microplate on the OmniLog® system over a 48-hour period. Cellular respiration was measured through a redox reaction with absorbance at 590 nm. The growth curves using the absorbance readings of PA7-like and *P. aeruginosa* strains across varying carbon sources is depicted in Figure 3-15.

A Kruskal-Wallis test confirmed that there was a difference ($\chi^2(191) = 5215.4$, $p \leq 0.00000001$) between the growth of PA7-like and *P. aeruginosa* strains across the various difference substrates. When comparing the growth using the area under the curve of the PA7-like and *P. aeruginosa* strains in each individual substrate, five were found to show a difference ($p \leq 0.05$) in growth between the two groups (Figure 3-16). These substrates were D-Alanine (A09, PA: *Mdn* = 3500.74, *IQR* = 5030.12; PA7-like: *Mdn* = 6151.35, *IQR* = 4836.92; Mann-Whitney test *U* = 343, *p* = 0.032), Glycerol (B03, PA = 7424.97, *IQR* = 1315.55; PA7-like: *Mdn* = 6648.02, *IQR* = 1459.88; Mann-Whitney test *U* = 767, *p* ≤ 0.001), L-Serine (G03, PA: *Mdn* = 560.82, *IQR* = 2587.12; PA7-like: *Mdn* = 3033.24, *IQR* 2695.70; Mann-Whitney test *U* = 279.5, *p* = 0.003), Mono Methyl Succinate (G09, PA: *Mdn* = 1817.48, *IQR* = 3392.05; PA7-like: *Mdn* = 4631.29, *IQR* = 4210.99; Mann-Whitney test *U* = 236, *p* ≤ 0.001), and Pyruvic Acid (H08, PA: *Mdn* = 3859.70, *IQR* = 4862.59; PA7-like: *Mdn* = 6586.10, *IQR* = 3199.60; Mann-Whitney test *U* = 354, *p* = 0.047).

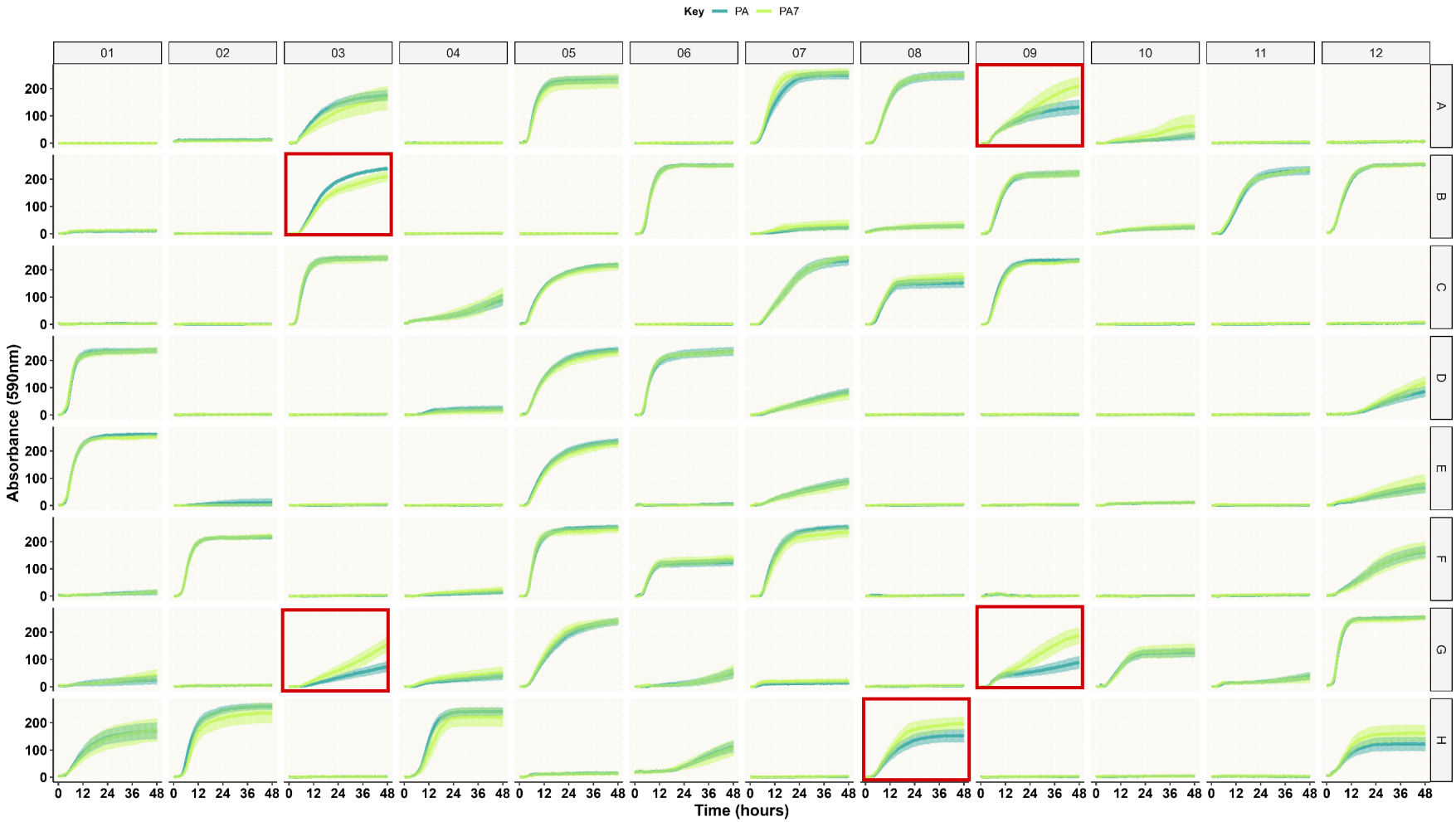

Figure 3-15: Absorbance at 590 nm of PA7-like and Pseudomonas aeruginosa *(PA) over 48 hours. Absorbance is plotted as the average mean of either PA7-like (n = 11) or PA (n=23) with each individual strain replicated twice for a n= 22 for PA7-like and n = 46 for PA strains. Error bars represent the 95% confidence interval (CI) of the mean and highlighted in red are substrates with a significant difference (*p ≤ *0.05) in area under the curve between the PA7-like and PA groups determined by a Mann-Whitney* U *test. For key matching position to substrate see Table* 3-2.

Table 3-2: Substrates contained within the Biolog PM1 plate for carbon utilisation.

Position	Substrate	Position	Substrate
A01	Negative Control	*E01*	L-Glutamine
A02	L-Arabinose	*E02*	m-Tartaric Acid
A03	N-Acetyl-D-Glucosamine	*E03*	D-Glucose-1-Phosphate
A04	D-Saccharic Acid	*E04*	D-Fructose-6-Phosphate
A05	Succinic Acid	*E05*	Tween 80
A06	D-Galactose	*E06*	α-Hydroxy Glutaric Acid-γ-Lactone
A07	L-Aspartic Acid	*E07*	α-Hydroxy Butyric Acid
A08	L-Proline	*E08*	ß-Methyl-D-Glucoside
A09	**D-Alanine**	*E09*	Adonitol
A10	D-Trehalose	*E10*	Maltotriose
A11	D-Mannose	*E11*	2-Deoxy Adenosine
A12	Dulcitol	*E12*	Adenosine
B01	D-Serine	*F01*	Glycyl-L-Aspartic Acid
B02	D-Sorbitol	*F02*	Citric Acid
B03	**Glycerol**	*F03*	myo-Inositol
B04	L-Fucose	*F04*	D-Threonine
B05	D-Glucuronic Acid	*F05*	Fumaric Acid
B06	D-Gluconic Acid	*F06*	Bromo Succinic Acid
B07	D,L-α-Glycerol-Phosphate	*F07*	Propionic Acid
B08	D-Xylose	*F08*	Mucic Acid
B09	L-Lactic Acid	*F09*	Glycolic Acid
B10	Formic Acid	*F10*	Glyoxylic Acid
B11	D-Mannitol	*F11*	D-Cellobiose
B12	L-Glutamic Acid	*F12*	Inosine
C01	D-Glucose-6-Phosphate	*G01*	Glycyl-L-Glutamic Acid
C02	D-Galactonic Acid-γ-Lactone	*G02*	Tricarballylic Acid
C03	D,L-Malic Acid	***G03***	**L-Serine**
C04	D-Ribose	*G04*	L-Threonine
C05	Tween 20	*G05*	L-Alanine
C06	L-Rhamnose	*G06*	L-Alanyl-Glycine
C07	D-Fructose	*G07*	Acetoacetic Acid
C08	Acetic Acid	*G08*	N-Acetyl-ß-D-Mannosamine
C09	α-D-Glucose	***G09***	**Mono Methyl Succinate**
C10	Maltose	*G10*	Methyl Pyruvate
C11	D-Melibiose	*G11*	D-Malic Acid
C12	Thymidine	*G12*	L-Malic Acid
D01	L-Asparagine	*H01*	Glycyl-L-Proline
D02	D-Aspartic Acid	*H02*	p-Hydroxy Phenyl Acetic Acid
D03	D-Glucosaminic Acid	*H03*	m-Hydroxy Phenyl Acetic Acid
D04	1,2-Propanediol	*H04*	Tyramine
D05	Tween 40	*H05*	D-Psicose
D06	α-Keto-Glutaric Acid	*H06*	L-Lyxose
D07	α-Keto-Butyric Acid	*H07*	Glucuronamide
D08	α-Methyl-D-Galactoside	***H08***	**Pyruvic Acid**
D09	α-D-Lactose	*H09*	L-Galactonic Acid-γ-Lactone
D10	Lactulose	*H10*	D-Galacturonic Acid
D11	Sucrose	*H11*	Phenylethylamine
D12	Uridine	*H12*	2-Aminoethanol

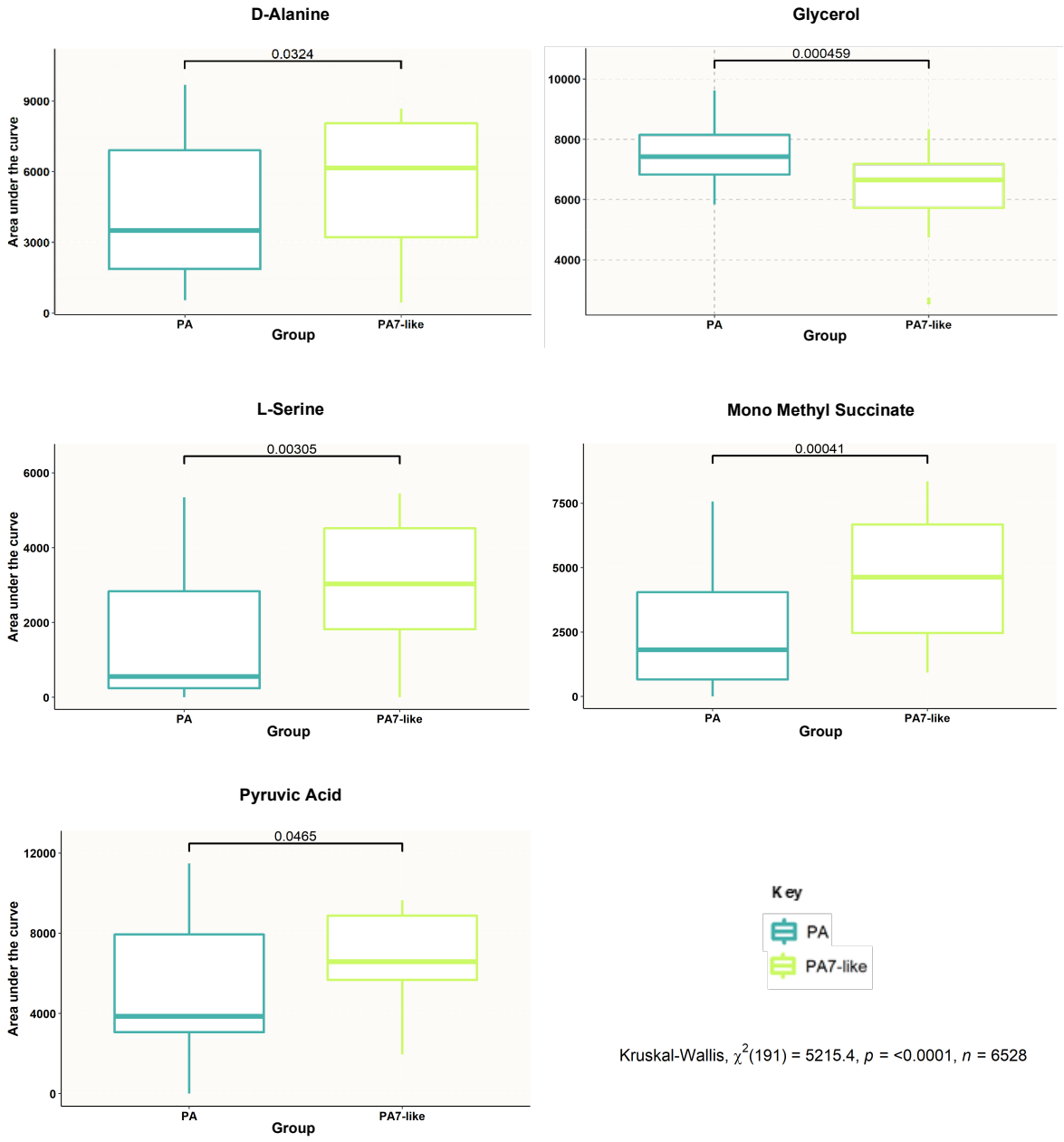

Figure 3-16: Substrates with a significant difference in area under the curve between PA7-like strains and Pseudomonas aeruginosa *(PA) strains. Significance (p ≤ 0.05) between PA7-like (n = 11, with two replicates per strain) and PA (n = 23, with two replicates per strain) was established by Mann-Whitney U tests.*

From the substrates showing different growth patterns between PA7-like and *P. aeruginosa,* metabolic pathways involving their consumption were identified for both the PAO1 (GCF_000006765.1) and PA7 (GCF_000017205.1) strain using BioCyc (257), (258). As mono methyl succinate is not a compound contained in the PAO1 or PA7 database, succinate was

used in its place. The genes involved in these pathways were compared to assess whether they were universally present in both strains. In cases where genes were only identified in once strain, BLAST was used to determine the presence of orthologous genes (168). Genes confirmed to be solely present in one strain with no orthologs identified are shown in Table 3-3 with genes showing orthologs with ≤90% identity according to BLAST shown in Table 3-4.

Table 3-3: Genes present in Pseudomonas aeruginosa *PAO1 involved in metabolic pathways involving the consumption of substrates producing different growth patterns between the PA7 and PAO1.*

Substrate	***Strain***	***Gene***	***Gene product***	***Pathways that consume the compound***
Pyruvate	*PAO1*	*lpd3*	dihydrolipoamide dehydrogenase	▪ pyruvate decarboxylation to acetyl CoA I
Pyruvate	*PAO1*	*PA1217*	2-isopropylmalate synthase	▪ superpathway of branched chain amino acid biosynthesis
L-serine	*PAO1*	*PA2104*	cysteine synthase	▪ L-cysteine biosynthesis I
Pyruvate	*PAO1*	*PA2683*	serine/threonine dehydratase	▪ L-isoleucine biosynthesis I (from threonine) ▪ superpathway of branched chain amino acid biosynthesis ▪ L-serine degradation
L-serine	*PAO1*	*pvdD*	pyoverdine synthetase D	▪ pyoverdine I biosynthesis
L-serine	*PAO1*	*pvdJ*	pyoverdine biosynthesis protein PvdJ	▪ pyoverdine I biosynthesis

From the genes involved in the consumption of the substrates revealed to produce different patterns of growth between PA7-like and *P. aeruginosa* strains, six were unique to PAO1 (Table 3-3). While no genes were unique to PA7, eight genes were detected in PA7 and/or PAO1 with orthologous genes with ≤90% BLAST identity in the alternate strain (Table 3-4). Across these genes, six were found to be involved in pyoverdine I biosynthesis, therefore this pathway was further investigated.

Table 3-4: Genes with orthologous matches in metabolic pathways involving the consumption of substrates producing different growth patterns between PA7 and PAO1.

Substrate	PAO1 gene*	PAO1 product	PAO1 gene length	PA7 gene*	Gene product	PA7 gene length	BLAST identity (%)	BLAST expect value	PAO1 pathway consuming substrate	PA7 pathways consuming substrate
L-serine	***PA2531***	pyoverdine aminotransferase	1125 bp	*PSPA7_RS12930*	pyridoxal phosphate-dependent aminotransferase	1122 bp	88	0.00	▪ pyoverdine I biosynthesis ▪ L-histidine biosynthesis	▪ not described
L-serine	***pvdA***	L-ornithine N5-oxygenase	1332 bp	*PSPA7_RS13680*	SidA/IucD/PvdA family monooxygenase	1332 bp	83	0.00	▪ pyoverdine I biosynthesis	▪ not described
L-serine	***pvdE***	pyoverdine biosynthesis protein PvdE	1650 bp	*PSPA7_RS13625*	cyclic peptide export ABC transporter	1653 bp	72	2.00×10^{-128}	▪ pyoverdine I biosynthesis	▪ not described
L-serine	***pvdF****	pyoverdine synthetase F	828 bp	***PSPA7_RS13630****	pyoverdine synthetase F	828 bp	83	0.00	▪ pyoverdine I biosynthesis	▪ pyoverdine I biosynthesis
Succinate	*PA1883*	NADH-quinone oxidoreductase subunit A	399 bp	***ndhC***	NADH-quinone oxidoreductase subunit A	399 bp	89	6.00×10^{-134}	▪ NADH to cytochrome bo oxidase electron transfer I	▪ aerobic respiration I (cytochrome c)
Pyruvate	*PA0851*	hypothetical protein	963 bp	***PSPA7_RS22205***	threonine dehydratase	963 bp	90	0.00	▪ not described	▪ L-isoleucine biosynthesis I (from threonine) ▪ superpathway of branched chain amino acid biosynthesis
Succinate	*cioB*	cyanide	1008 bp	***cydB***	cytochrome d ubiquinol	1005 bp	86	0.0	▪ not described	▪ succinate to cytochrome bd

		insensitive terminal oxidase			oxidase subunit II					oxidase electron transfer
Succinate	*cioA*	cyanide insensitive terminal oxidase	1467 bp	***PSPA7_RS14855***	cytochrome ubiquinol oxidase subunit I	1443 bp	88	0.0	▪ not described	▪ succinate to cytochrome bd oxidase electron transfer ▪ succinate to cytochrome bo oxidase electron transfer

** Highlighted in bold are the genes found involved in the consumption of the substrates in the respective strain labelled in the heading of the column. The corresponding gene was identified through a BLAST search using the highlighted gene.*

*** Genes* pvdF *and* PSPA7_RS13630 *were both identified in their respective strains however had BLAST identities ≤90%.*

3.2.3.1.1 Pyoverdine I biosynthesis

Pyoverdine is a fluorescent pigment produced by *P. aeruginosa* which acts as a siderophore to aid the bacterium with iron acquisition and virulence (259-260). Once synthesised, pyoverdine is exported out of the cell where it binds ferric iron (Fe^{3+}) to form a pyoverdine-Fe^{3+} complex. Specific transporters on the outer membrane, FpvA and FpvB, recognise the pyoverdine-Fe^{3+} complex and facilitate its uptake into the cell (259). Additionally, the interaction of the pyoverdine-Fe^{3+} complex with the transporters activates signalling pathways that lead to the production of virulence factors, such as the cytotoxic endotoxin A (259). A *P. aeruginosa* strain can synthesise one of three different pyoverdine structures each encoded by different gene structures, with PA7 containing the sequence for pyoverdine type II, previously described in ATCC 27853 (NCTC 12903), as opposed to the type I sequence found in PAO1 (Figure 3-17, Figure 3-18) (249, 259-261). As previously mentioned, six genes identified in PAO1 involved in pyoverdine biosynthesis either had no corresponding gene or had an identity ≤90% to its corresponding gene in PA7. This variation is characteristic of the gene structure seen between the synthesis of type I and II pyoverdine (261). Figure 3-17 shows the pyoverdine I biosynthesis pathway with the genes involved highlighted, as no pathway was available for pyoverdine II biosynthesis, the gene structure present in PA7 was compared to the pyoverdine I biosynthesis pathway present in PAO1.

Of the substrates identified as having different patterns in growth, L-serine was the only substrate involved in the pyoverdine I biosynthesis pathway, where the non-ribosomal peptide synthetase, PvdI, combines two L-serine molecules with L-arginine and N5-formyl-N5-hydroxy-L-ornithine as part of the process to produce ferribactin, a precursor to pyoverdine I. The production of ferribactin also involves PvdD, PvdJ, and PvdL, which together with PvdI forms ferribactin synthase. The *pvdI* gene sequences from PAO1 was used as the query to identify the gene in PA7 via a BLAST search. The outcome of the search covered only 81% of the query sequences and showed a 93% identity within this region. The *pvdL* gene was present

in its full format in PA7, showing 97% identity with 100% of the PAO1 query sequence covered. Conversely, alignment of the region containing the other two genes, *pvdD* and *pvdJ,* in addition to the *pvdI* gene in PAO1, showed the region mapped to two genes in PA7 *pvdJ(2)* and *pvdI(2)*(Figure 3-18a). The genes found in PA7 did not cover the full length of the sequence seen in PAO1 nor was there high identity between the genes from the two strains (Figure 3-18a). Instead, alignment of the regions containing these genes showed some similarity to one another however the order of the matches were rearranged with the PA7 *pvdJ(2)* gene showing similarity to a portion of *pvdD* and *pvdI* from PAO1 and the PA7 *pvdI(2)* gene sharing similarity to portions of the *pvdJ* and *pvdI* genes from PAO1 (Figure 3-18b). As shown in Figure 3-18a, the rearrangement of the genes appeared to occur as blocks with the end of *pvdD,* all of *pvdJ* and the beginning of *pvdI* PAO1 genes being swapped with a middle portion of the PAO1 *pvdI* gene to create the gene structure seen in PA7. Additionally, the rearrangement showed varying gaps between the regions sharing similarity implying multiple insertion and/or deletion events had occurred in addition to a rearrangement of the sequence. Furthermore, orthologs for the PAO1 genes were present in the PA7 strain, though some had low identities ≤90% (*pvdA, pvdF, pvdP, pvdE,* and *PA2531*) and did not cover the full query sequence (Figure 3-17).

A BLAST analysis of the protein sequence of the *pvdI(2)* gene between PA7 and ATCC 27853 (NCTC 12903) showed 100% coverage of the query with 96.5% identity and an E-value of 0.0 with the *pvdJ(2)* genes showing 100% coverage of the query with 96.7% identity and an E-value of 0.0 (Figure 3-18b). Though, PA7 shared similarity to the gene structure of ATCC 27853 (NCTC 12903), there were variations in the protein sequence of PvdI(2) and PvdJ(2), thus it is unclear if the pyoverdine II biosynthesis pathway present in PA7 is functional (Appendix - Alignment 2).

To summarise, variations in pyoverdine biosynthesis were present between PAO1, which contains the gene structure for pyoverdine type I and PA7, which contained the gene structure

for pyoverdine type II. Between the PA7-like and *P. aeruginosa* groups, area under the curve was greater for the PA7-like group when L-serine utilisation was analysed (Figure 3-16). Therefore, it is possible that the two gene structures have varying effects producing the differences seen in area under the curve, however further analysis to determine the pyoverdine gene structures and its effects on fitness in all PA7-like and *P. aeruginosa* strains is required as no studies on this topic could be identified. Additionally, the pyoverdine II biosynthesis pathways requires characterisation to fully elucidate and compare the differences that exist between the two pyoverdine types.

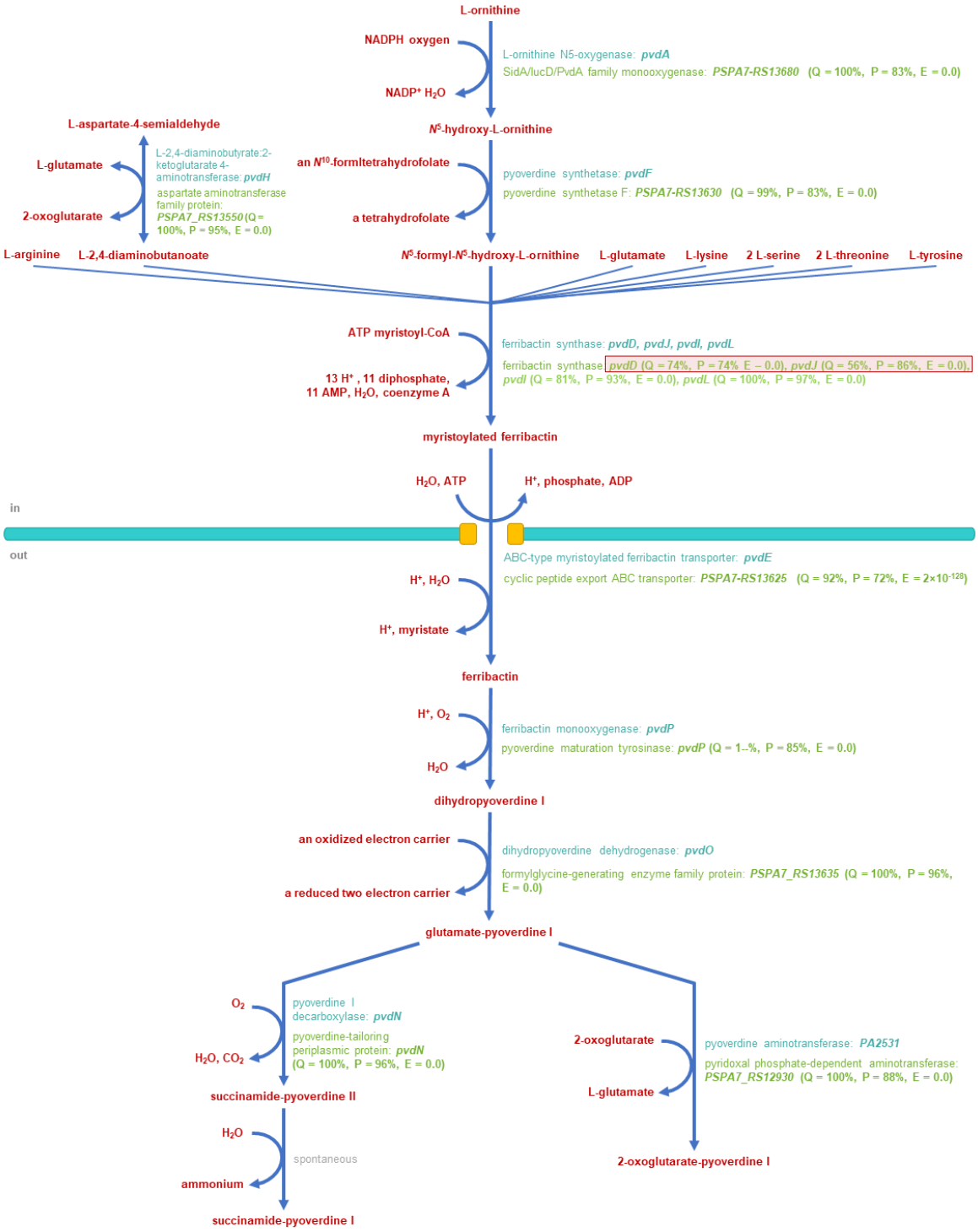

Figure 3-17: Pyoverdine I biosynthesis pathway. The pathway is annotated with the genes and their products highlighted in teal if present in PAO1. Gene sequences from PAO1 were put through a BLAST search to determine the closest match present in PA7 and are highlighted in green. BLAST results are depicted on the figure (Q = query coverage, P = percentage identity and E = E-value). The genes highlighted in the red box were identified as a single conjoined gene in PA7, however have been depicted as separate to display the result of the BLAST search. Image is based on the MetaCyc PWY-6409 pathway (257).

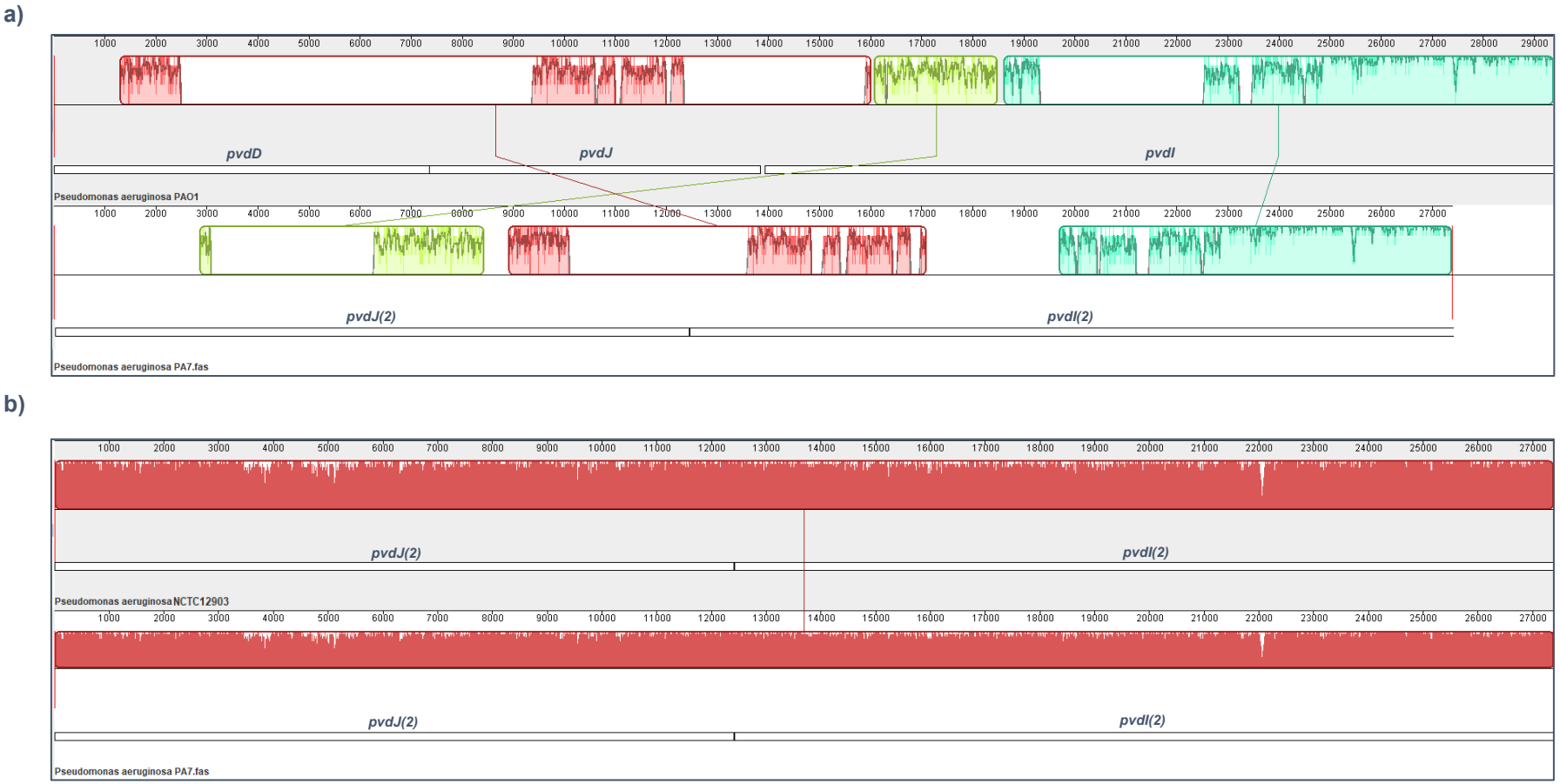

Figure 3-18: Alignment generated with progressiveMauve of the sequence region containing the pvdD, pvdJ, *and* pvdI *genes in* Pseudomonas aeruginosa*. a) Shows the alignment of PA7 using the PAO1 genes as a reference. b) Shows the alignment of the same region in PA7 using NCTC 12903 as a reference. Locally collinear blocks containing homologous regions are outlined with a similarity profile between the two sequences represented inside. Related blocks coloured accordingly and are connected by the lines between the alignment.*

3.2.3.2 Comparison of antibiotic profiles

3.2.3.2.1 Minimum inhibitory concentration

P. aeruginosa is known for its intrinsic, adaptive, and acquired mechanisms providing resistance to antibiotics. To assess whether these mechanisms were similar between PA7-like and *P. aeruginosa* strains, the MIC of ten antibiotics and antibiotic inhibitor combinations was determined for 12 PA7-like strains and 23 *P. aeruginosa* strains as described in section 2.4.5. Antimicrobial sensitivity testing was performed for both the PA7-like and *P.* aeruginosa strains to investigate if there were any resistance patterns associated with either group. Table 3-5 displays the MIC results of the PA7-like and *P. aeruginosa* strains for a spectrum of antibiotics. Despite resistance to piperacillin, piperacillin and tazobactam, ceftazidime, aztreonam, and ciprofloxacin being prevalent in the PA7-like strains no clear patterns of resistance unique to either group was observed. However, when considering the values of the MICs, the PA7-like strains tended to cover a broader range including higher concentrations for all antibiotics tested except ceftazidime and avibactam, meropenem, and chloramphenicol (Figure 3-19). The resistance seen in some of the PA7-like strains was not seen in the environmental PA7-like strain, hence the MICs observed in these PA7-like strains may have been due to exposure to a clinical environment and not characteristic of the PA7-like strains. Additionally, Mann-Whitney U tests comparing the MICs of clinically isolated PA7-like and *P. aeruginosa* strains for each antibiotic revealed there was no difference (AZT: $p = 0.464$, CAZ: $p = 0.267$, CAZ/AVI: $p = 0.546$, CHL: $p = 0.701$, CIP: $p = 0.377$, IMP: $p = 0.154$, MEM: $p = 0.885$, PIP: $p = 0.520$, PIP/TAZ: $p = 0.429$, TOB: $p = 0.298$) between the two groups (Table 3-6). This analysis was performed on only the strains isolated from clinical environments to avoid bias created by the PA7-like group containing one environmental strain in comparison to the 11 found in the *P. aeruginosa* group. Overall, the phenotypic data collected did not show any differences in the antimicrobial resistance profiles of PA7-like and *P. aeruginosa* strains, however this is possibly due to the small dataset as there is only a small number of PA7-like strains available. Therefore, the

genomes of these strain were analysed further to see if there were any difference in the AMR genes contained between the two groups (Section 3.2.3.2.2).

Table 3-5: Minimum inhibitory concentrations of PA7-like and Pseudomonas aeruginosa *strains. MLST sequence types were identified with ARIBA and MIC, reported as µg/ml, coloured according to the resistance (R) and sensitive (S) breakpoints as described by EUCAST*.*

Project ID	Group	Source	MLST**	PIP	PIP/TAZ	CAZ	CAZ/AVI	AZT	IMP	MEM	CIP	TOB	CHL
PA9	PA	Clinical	244	4	4	0.5	1	2	0.125	≤0.25	1	0.5	32
PA47	PA	Clinical	17	8	16	2	2	16	4	1	1	2	256
PA54	PA	Clinical	977	8	4	2	2	8	2	≤0.25	0.125	2	64
PA63	PA	Environmental	253	4	4	1	2	4	2	0.5	0.125	2	32
PA64	PA	Environmental	357	2	2	0.5	0.5	1	2	≤0.25	0.125	2	64
PA91	PA	Environmental	27	4	4	2	1	4	4	≤0.25	0.06	2	128
PA97	PA	Environmental	395	8	4	2	1	2	4	0.5	0.125	1	128
PA119	PA	Clinical	446	2	4	0.5	0.5	≤0.5	2	≤0.25	0.125	2	64
PA130	PA	Clinical	1591	4	4	2	1	4	4	≤0.25	0.125	2	64
PA135	PA	Clinical	136	4	4	1	1	4	2	≤0.25	0.25	2	128
PA150	PA	Environmental	252	64	16	4	2	8	4	0.5	0.125	2	128
PA232	PA	Environmental	195	4	4	1	1	1	4	0.5	0.125	2	128
PA245	PA	Clinical	1632	8	8	2	1	8	2	1	0.25	1	128
PA264	PA	Clinical	235	256	256	>128	128	>256	16	8	>4	>4	>512
PA270	PA	Environmental	1228	4	2	2	1	4	8	1	0.25	2	128
PA2583	PA	Clinical	274	8	8	4	4	2	4	8	0.5	0.25	128
PA2621	PA	Environmental	253	4	8	1	1	2	8	0.5	0.125	2	64
PA2625	PA	Environmental	179	8	4	1	1	4	2	≤0.25	0.06	2	64
PA2629	PA	Environmental	1233	4	8	2	2	4	8	0.5	0.25	2	64

PA2632	PA	Environmental	1328	8	8	2	1	4	4	0.5	0.125	2	128
PA2448 (PA14)	PA	Clinical	591	4	4	2	2	4	0.25	≤0.25	0.125	2	64
PA2204 (PAO1)	PA	Clinical	549	4	4	1	1	2	4	0.5	0.125	2	8
PA1305 (PAK)	PA	Clinical	693	4	4	2	2	2	0.5	≤0.25	0.125	2	64
PA259	PA7-like	Clinical	**	128	128	16	1	32	16	2	4	2	64
PA508	PA7-like	Clinical	2230	2	2	0.5	1	1	4	≤0.25	0.125	1	64
PA1129	PA7-like	Clinical	2028	≤0.5	≤0.5	1	1	≤0.5	0.5	≤0.25	0.06	2	64
PA1646	PA7-like	Environmental	**	4	4	2	1	2	2	≤0.25	0.06	2	32
PA1780	PA7-like	Clinical	2031	256	128	16	1	64	2	≤0.25	2	1	64
PA1794	PA7-like	Clinical	3043	256	256	>128	4	128	16	4	2	>4	128
PA1802	PA7-like	Clinical	3043	256	256	>128	8	256	32	4	2	>4	128
PA2078	PA7-like	Clinical	1195	256	256	16	1	32	2	≤0.25	>4	2	32
PA2541	PA7-like	Clinical	2031	2	1	1	0.5	≤0.5	2	≤0.25	0.125	2	32
PA2634	PA7-like	Clinical	2211	2	4	1	1	2	8	0.5	0.06	2	64
PA2045 (PA7)	PA7-like	Clinical	1195	256	256	64	2	128	4	0.5	>4	>4	512

** Piperacillin (PIP): R = >16 mg/L, S = ≤0.001 mg/L; Piperacillin and Tazobactam (PIP/TAZ): R = >16 mg/L, S = ≤0.001 mg/L; Ceftazidime (CAZ): R = >8 mg/L, S = ≤0.001 mg/L; Ceftazidime and Avibactam (CAZ/AVI): R = >8 mg/L, S = ≤8 mg/L; Aztreonam (AZT): R = >16 mg/L, S = ≤ 0.001 mg/L; Imipenem (IMP): R = >4 mg/L, S = ≤0.001 mg/L; Meropenem (MEM): R = >8 mg/L, S = ≤2 mg/L; Ciprofloxacin (CIP): R = >0.5 mg/L, S = ≤0.001 mg/L; Tobramycin (TOB): R = >2 mg/L, S = ≤2 mg/L; Chloramphenicol (CHL): no breakpoints are described*

*** One or more loci were unidentifiable from sequencing data, thus sequence type was indeterminable*

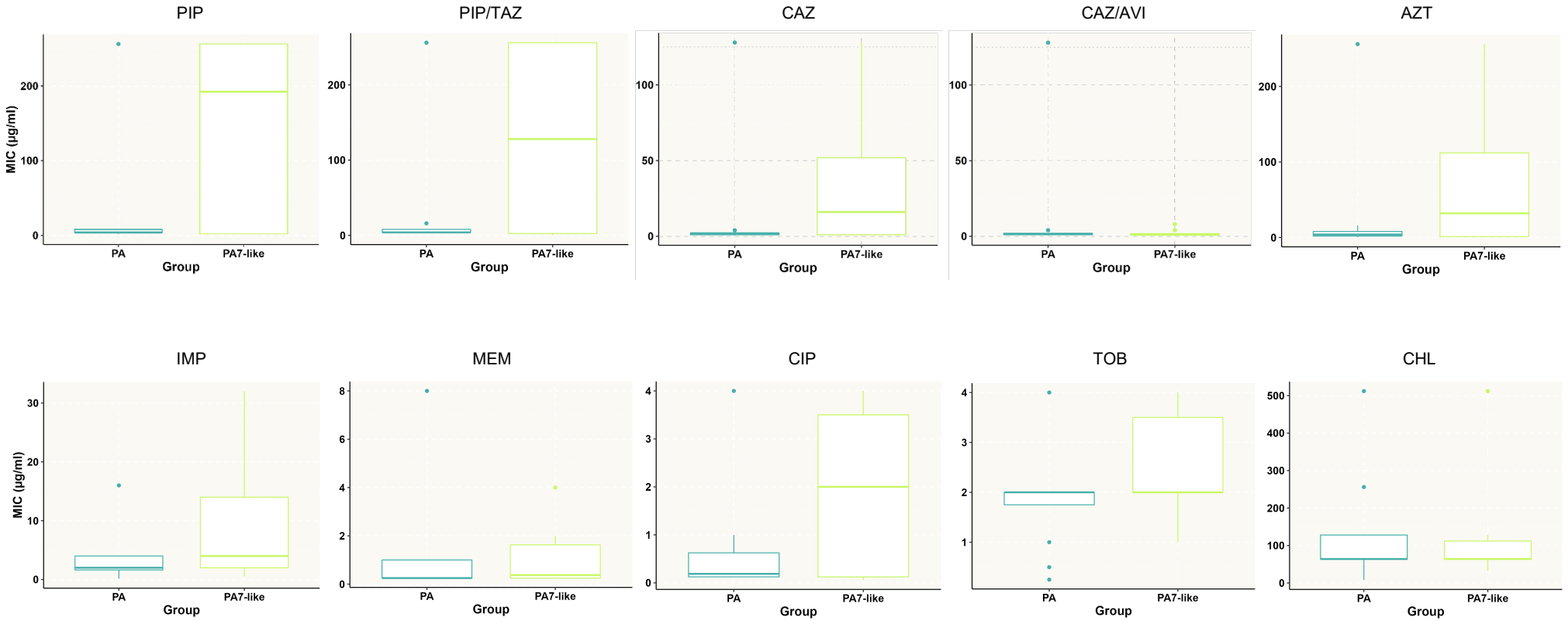

Figure 3-19: Minimum inhibitory concentration (µg/ml) of clinical Pseudomonas aeruginosa *(n = 12) and PA7-like (n = 10) strains. Mann-Whitney* U *tests were performed between the two groups (Table* 3-6*) where the difference between the MIC values between the two groups was not found to be significant (*p ≤ *0.05).*

Table 3-6: Mann-Whitney U *test results comparing minimum inhibitory concentrations between clinically isolated* Pseudomonas aeruginosa *and PA7-like strains.*

Antibiotic	Group	Mdn	IQR	U	p
PIP	PA	4	4	50	0.520
	PA7-like	192	254		
PIP/TAZ	PA	4	4	48	0.429
	PA7-like	128	253.5		
CAZ	PA	2	1	43	0.267
	PA7-like	16	51		
CAZ/AVI	PA	1.5	1	69	0.546
	PA7-like	1	0.75		
AZT	PA	4	6	48.5	0.464
	PA7-like	32	110.75		
IMP	PA	2	2.375	38.5	0.154
	PA7-like	4	12		
MEM	PA	0.25	0.75	57.5	0.885
	PA7-like	0.375	1.375		
CIP	PA	0.188	0.5	46.5	0.377
	PA7-like	2	3.375		
TOB	PA	2	0.25	45.5	0.298
	PA7-like	2	1.5		
CHL	PA	64	64	66	0.701
	PA7-like	64	48		

3.2.3.2.2 Genes associated with antimicrobial resistance

74 resistance genes were identified in PA7-like and *P. aeruginosa* strains using the ARIBA programme (183) to find matches in the Comprehensive Antibiotic Resistance Database (CARD). Figure 3-20 depicts the summary of the ARIBA results indicating the state of the variant of the named gene involved in resistance. Genes were either absent from the assembly, present in a complete state, fragmented into smaller sequences across more than one contig, interrupted due the presence of the gene in a single contig in a discontiguous format, or partial where the full gene sequence was not discovered in the assembly. The tree in Figure 3-20 is based on the state of the genes identified in the strains and shows the PA7-like and *P. aeruginosa* groups to be contained in separate monophyletic clades. Furthermore, the PA7-like strains did not carry *armR*, *fosA, oxa-50, nfxB, mexM, mexP* and *opmE* genes in addition to absence or partial presence of the *aph(3'), mexC, parS,* and *catB7* genes. Additionally, the *oprJ*,

mexN, and *mexY* genes were interrupted and/or partial across all of the PA7-like strains. These absences/interruptions/partial absences seen in these genes were mostly unique to the PA7-like strains apart from *armR,* which was absent in one of the *P. aeruginosa* strains; *fosA* and *opmE,* which were present in an interrupted format in one *P. aeruginosa* strain; *catB7*, which was absent or interrupted in four *P. aeruginosa* strains; and *mexY* which was interrupted in two *P. aeruginosa* strains*.* The *oprD* gene was also fully or partially absent in most of the PA7-like strains, however this was not unique to the group due to the absence and interruption of the gene in three *P. aeruginosa* strains*.* No genes solely present in PA7-like strains were identified, the gene closest to this was *oprA* which was only present in one *P. aeruginosa* strain and so was predominantly identified in PA7-like strains.

Overall, the differences seen between the 17 genes present or absent between the two groups (*aph(3')*, *armR, fosA, mexC, mexZ, oxa-50, oprA, oprJ, parS, catB7, nfxB, mexM, mexN, mexP, mexY, opmE,* and *oprD*) were mostly in genes connected to membrane permeability. Thus, it appears there are difference in the proteins controlling the permeability of the membrane in *P. aeruginosa* and PA7-like strains. Though a significant difference was not observed between the PA7-like and *P. aeruginosa* strains in terms of their MIC. The variation in resistance profiles seen against some of antibiotic and antibiotic inhibitor concentrations (piperacillin, piperacillin and tazobactam, ceftazidime, aztreonam, and ciprofloxacin) may be linked to the genetic difference described in this section, however further work is required to confirm if this is the case. As only a selection of *P. aeruginosa* strains were included for this section of work, it is unclear if the difference seen between the PA7-like and *P. aeruginosa* strain will translate across the entire species. Additionally, the PA7-like strains presented in this study are mostly from clinical sources (Table 3-5) and the presence and absence of certain resistance genes may be due to selection under clinical conditions.

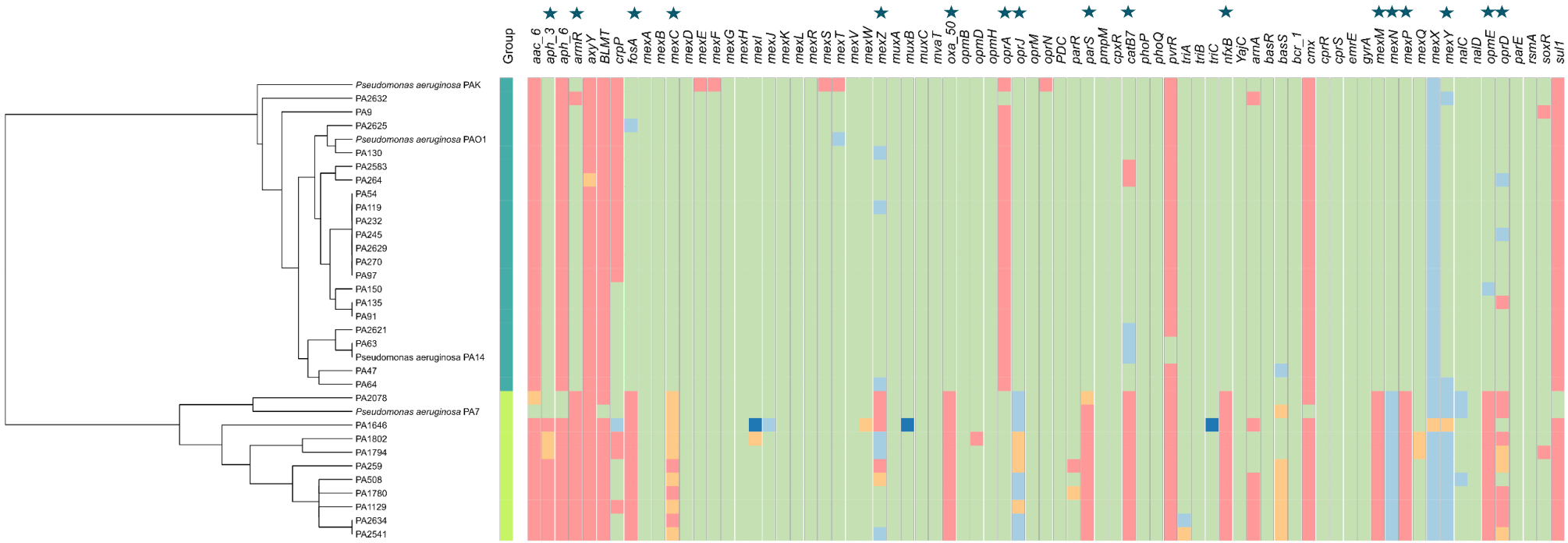

Figure 3-20: Summary of resistance genes identified in Pseudomonas aeruginosa *and PA7-like strains. The tree is based on the state of resistance genes contained by the strains and identified using the CARD database. The first annotation column is coloured according to the group the strain belongs to with bright green representing PA7-like and teal for* P. aeruginosa. *The following columns are annotated according to the assembly state of the variant contained by the strain with red if there was no assembly for the gene, pale green if the gene was present, dark blue for a fragmented assembly, light blue for an interrupted assembly, and orange for a partial assembly of the gene. A star (★) indicates the 17 genes where differences in the state of resistance genes contained by* P. aeruginosa *and PA7-like strains were observed. Image created with Phandango (434).*

3.3 Discussion

The taxonomical outlier PA7 and related strains are often removed from studies on the *P. aeruginosa* pangenome due to the diversity between their genome sequences. Hence, the goal of this chapter was to characterise the inclusion of the PA7-like strain within the *P. aeruginosa* species.

During the writing of this thesis a selection of PA7-like strains were re-classified under the names *Pseudomonas paraeruginosa*; the specific isolates which have been renamed are indicated in Appendix - Table 1 and are correct according to NCBI Taxonomy (accessed 2nd August 2023) (262-264). The type strain for *P. paraeruginosa* species is ATCC 9027 which is included in this study under the project ID of PA508 (262, 263). The species description of *P. paraeruginosa* indicates that the distinction from *P. aeruginosa* can be achieved based on whole genome comparisons using ANI, average amino acid identity (AAI), and dDDH, as well as by the presence of specific proteins, however phenotypic variation within the species is less apparent (262, 263). Considering this reclassification, the remaining PA7-like strains, are likely members of the *P. paraeruginosa* species. To maintain context in this thesis, the PA7-like strains, defined here as strain belonging to the Core5 group, will continue to be referred to as "PA7-like". Hence, this term will include strains taxonomically reclassified as *P. paraeruginosa*.

3.3.1 Phylogenetics based on 16S rRNA disagree with taxonomical nomenclature

Within the 16S rRNA sequence of PA7-like strains there is a high similarity with other *P. aeruginosa* strains including PAO1, the type strain for the species (Figure 3-4) (262, 263). The similarity is what initially resulted in PA7 being declared part of the *P. aeruginosa* species despite also being classed as an outlier (249). This is something that would be expected of strains belonging to the same species, such as *P. nitrireducens* and *P. nitroreducens* which are

considered heterotypic synonyms of each other and therefore considered the same species. Thus, it would be expected for these two strains to have shown similar levels of relatedness as the PA7-like and *P. aeruginosa* strains. However, the 16S rRNA phylogeny created in this study showed the two to be more distant than the PA7-like strain and *P. aeruginosa.* It is due to this difference in 16S rRNA and other genotypic, chemotaxonomic, and phenotypic data that caused the two species to be considered separate until *P. nitritireducens* was reclassified as a heterotypic synonym of *P. nitroreducens* in the ICNP due to the similarity in a 4-gene (16S rRNA, *gyrB, rpoB,* and *rpoD*) multilocus sequence analysis (242, 265). Additionally, *P. lactis* and *P. synxantha* appeared to be more closely related in terms of their 16S rRNA than *P. citronellolis and P. humi* despite the characterisation of *P. lactis* and *P. synxantha* as separate species in nomenclature. This highlights the flaws that can be present in identification based solely on 16S rRNA due to its reliance on a single gene, which can have multiple copies in a single strain. Hence, identification using solely this method should be taken cautiously.

To alleviates these discrepancies, this study used robust clustering based on the 16 ribosomal protein genes described by Hug *et al.* that were used to create a larger alignment to supplement the analysis of the 16S rRNA phylogeny. In contrast to the 16S rRNA phylogeny, the robust clustering method showed greater dissimilarity between PA7-like and *P. aeruginosa* strains. Consequently, this supported the recent reclassification of some of PA7-like strains included in this study as *P. paraeruginosa* (262, 263). Furthermore, the dissimilarity between *P. nitrireducens* and *P. nitroreducens* was found to be smaller and more akin to strains from the same species whereas *P. lactis* and *P. synxantha,* showed a greater diversity in robust clustering as would be expected from strains from separate species. Hence, the two methods conflict over the level of diversity found between both strains classified as the same species and strains classified as separate species.

3.3.2 Whole genome sequencing to resolve *Pseudomonas aeruginosa* speciation

Resolving discrepancies in bacterial identification can be achieved using whole genome analyses which provide a higher resolution due to their use of the whole genome. To characterise the genetic difference between the PA7-like strains against *P. aeruginosa*, the core genomes of 2,632 strains identified as *P. aeruginosa* was determined. The core genome consisted of 4,283 genes representing approximately a ninth of the total number of genes present in the pangenome. Both the core SNP and robust clustering phylogeny showed PA7-like group of strains (Core5) to be divergent from the rest of the *P. aeruginosa* strains (Figure 3-7). This correlated with previous studies that have generated a core genome phylogeny of *P. aeruginosa* (143, 146, 251).

To further characterise this divergence, this study utilised the ANI between strains, Jaccard similarity index of genomic sketches via Sourmash, and dDDH to determine the differences between strains. Both the ANI and dDDH have fixed cut-off values for determining whether strains belong to the same species which is set at ≥95% and ≥70% respectively. When comparing the core groups with ANI (Figure 3-10) and dDDH (Figure 3-12), the divergent PA7-like group is unable meet the set thresholds for determining members of the same species. This confirms the results described by Rudra *et al.* which also showed that PA7-like strains displayed were below the suggested cut-offs for species boundaries (262, 263). The inability to meet these species-determining thresholds has previously led to the re-assignment of strains initially identified as *P. fluorescens* and *P. putida* to other *Pseudomonas* species with which they shared greater similarity (244). If considering these metrics to determine species identification, the PA7-like strain do not meet characteristics of a *P. aeruginosa* strain. Additionally, the comparison of the genomic sketches of the PA7-like and *P. aeruginosa* strains through Sourmash was consistently low (Figure 3-11). Whilst no value is set to reveal the species cut-off through this method, the values between the PA7-like and *P. aeruginosa* were below those seen between species that are currently classified as separate. Therefore, all three

metrics used to compare the genomic sequences of PA7-like and *P. aeruginosa* strains agreed that the PA7-like genomes do not share high enough similarity to be part of *P. aeruginosa* or any other known species and thus appear to represent their own species. Hence, these results further support the reclassification of some PA7-like strain as *P. paraeruginosa* groups and suggests that all PA7-like should be classified as members of this species (262, 263). To a lesser extent the Core6 and Core7 groups also showed divergence with respect to the core SNP phylogeny, however this did not translate across to the robust clustering phylogeny. Despite also showing divergence, the Core6 and Core7 groups did meet the species thresholds and therefore their inclusion in the *P. aeruginosa* is indisputable and as such should remain part of *P. aeruginosa* species.

Gene flow between the core groups showed PA7-like strains to be more closed off from the other groups (Figure 3-8). Additionally, the nucleotide diversity seen between the PA7-like group with other *P. aeruginosa* core groups clearly demonstrates the separation of these strains at the nucleotide level (Figure 3-9). The level of divergence seen in these strains could potentially be explained by insertions and/or deletions between the PA7-like group and the other *P. aeruginosa* strains. However, BRIG diagrams comparing PA7-like strain to PAO1 (Figure 3-13 and Figure 3-14) showed little evidence that this was the case. Instead, it indicated the presence multiple small insertion and/or deletions had occurred within the PA7-like strains after the divergence of the PA7-like group. Moreover, most of the divergence observed between the PA7-like strains and *P. aeruginosa* could be linked polymorphisms in the genomes as evident in comparisons of the D_{xy}, ANI, Jaccard similarity index between genomic sketches, and dDDH values. Thus, it unlikely that PA7-like group of strains represent a group of *P. aeruginosa* strains which lost or gained a portion of its genome. Instead, the PA7-like groups of strains and the *P. aeruginosa* group of strains represent two groups which evolved away from each other over the course of numerous mutations.

3.3.3 Pyoverdine variation between *Pseudomonas aeruginosa* and PA7-like strains

Comparison of the genomic sequences of PA7-like and *P. aeruginosa* strains showed clear differences between the two and so the phenotypic characteristics of these strains was also investigated. Five carbon substrates showed differences in the area under the curve between groups of *P. aeruginosa* and PA7-like strains. The substrates in question were D-alanine, glycerol, L-serine, mono methyl succinate, and pyruvic acid (Figure 3-16). These substrates are involved in numerous pathways including amino acid metabolism, aerobic respiration, and electron transport, all of which can affect growth of the bacterium. Comparison of the affected pathways between PAO1 and PA7 implicated the genes involved in pyoverdine I biosynthesis as a potential pathway that may differ between the two strains. Whilst PAO1 produces pyoverdine type I, PA7 produces pyoverdine type II and therefore does not utilise the same pathways as the PAO1 strain (249). The majority of research on pyoverdine biosynthesis is focused on pyoverdine type I and so it is difficult to ascertain how the different pathways influences the organism. The structure of pyoverdine type I and type II are distinctive from one another however, the molecules are both involved in iron chelation despite the structural differences (260). Strains that produce pyoverdine type II have been shown to be susceptible to killing by pyocin S3 whereas strains producing pyoverdine type I are resistant (266). As pyocin S3 is a bacteriocin, it has cytotoxic effects on target cells through its DNase activity (267). Due to the ability of pyocin S3 to utilise the receptor for iron-bound pyoverdine type II (ferripyoverdine) to enter the cell, *P. aeruginosa* strains which produce pyoverdine type II are vulnerable to the effects of pyocin S3 (266). Therefore, the production of different pyoverdine types can influence bacterial survival in competitive environments. Though PAO1 and PA7 produce pyoverdine type I and type II respectively, it is unclear if and what type of pyoverdine is produced by all the strains in the *P. aeruginosa* groups and PA7-like groups in this study. Hence further work is required to fully understand whether the variation between the *P. aeruginosa* and PA7-like strains can be linked to the type of pyoverdine produced.

3.3.4 Resistance profiles between *Pseudomonas aeruginosa* and PA7-like strains

Observable differences were seen in the MIC profiles between the *P. aeruginosa* and PA7-like strains, but these were not found to be significant nor were they found to be universal to either group. When first reported, the PA7 strain was described as highly resistant to cephalosporins, monobactams, and fluroquinolones, resistant to piperacillin, carbenicillin, levofloxacin, and chloramphenicol, and sensitive to carbapenems (249). In general, half of the PA7-like strains showed a broader range of resistance across antibiotic classes whereas the *P. aeruginosa* strains mostly had lower resistance levels across the antibiotic classes (Figure 3-19). The resistance seen in the PA7-like strains included piperacillin, ceftazidime, aztreonam, and ciprofloxacin in a similar pattern to the PA7 strain. The addition of beta-lactam inhibitors to the beta-lactam antibiotics resulted in resistance being upheld in the piperacillin and tazobactam combination. In contrast, strains were found to be susceptible to the ceftazidime and avibactam combination indicating the presence of a beta-lactamases that are susceptible to avibactam. Genes encoding a beta-lactamase were not detected in the PA7-like strains by ARIBA, however this is possibly due to the absence of some resistance genes in the CARD database (Figure 3-20). Beta-lactamases are not uncommon in *P. aeruginosa,* with AmpC being chromosomally encoded in *P. aeruginosa.* Strains containing certain AmpC genotypes have previously shown susceptibility to the ceftazidime and avibactam combination due to the inhibitive binding of avibactam to AmpC (268). Presently, it is unclear if the resistance patterns observed in the PA7-like strains are connected to any AmpC genotype or another beta-lactamases. Whilst the MIC results appear to suggest that PA7-like strains appear to be more resistant, the *P. aeruginosa* strains used as comparators consisted of an even split between clinical and environmental strains. As environmental strains of *P. aeruginosa* are less likely to be exposed to antibiotic pressure than clinical strains it can be expected for this group of strains to have lower MICs than the PA7-like groups of strains which mostly contained clinical isolates (Table 3-5).

AMR related genes contained by the *P. aeruginosa* and PA7-like isolates showed that some of the AMR genes present in the *P. aeruginosa* group were either absent or disrupted in many of the PA7-like strains (Figure 3-20). Most of these genes involved components of efflux pumps and porins which are positioned in the outer membrane. Therefore, it suggests that some of the differences that exist between the *P. aeruginosa* and PA7-like strains is due to variation in their outer membranes. It is possible that this variation could translate to differences in membrane permeability thus providing an explanation for the slight difference in MIC profiles seen against piperacillin, piperacillin and tazobactam, ceftazidime, aztreonam, and ciprofloxacin, however further work is required to confirm any difference in membrane permeability.

In terms of AMR genes identified that were not localised to the outer membrane, the *oxa-50* gene was only present in the *P. aeruginosa* group and absent in the PA7-like strains. The *oxa-50* gene is a chromosomally encoded beta-lactamase that confers a narrow spectrum of resistance to certain beta-lactams such as ampicillin, piperacillin, and imipenem (269). The *oxa-50* gene, including members of the OXA-50 family, is often described as intrinsic to the species having been found in all strains in studies comparing the genomic profiles of *P. aeruginosa* strains which excluded members of the PA7-like group (252, 270-272). In contrast, a study of 32 *P. aeruginosa* isolates by Petrova *et al.* found only three isolates to be positive for *oxa-50* (273). Similarly, Grupper *et al.* found the *oxa-50* gene to be present in 40 out of 47 isolates (274). Whilst this would imply that *oxa-50* is not intrinsic to the *P. aeruginosa* species, identification of the *oxa-50* gene was performed in both studies using the Acuitas Resistome Tes (OpGen, USA), a method that uses microfluidic PCR to detect 46 different resistance genes and their variants in Gram-negative bacteria. Additionally, the method of species identification was not described by Grubber *et al.* and was performed by Petrova *et al.* using phenotypic methods that are unable reveal if the isolates were part of the PA7-like group or the other divergent major clades (273-275). The studies by Babouee Flury *et al.,* Eladawy *et al*., Gómez-

Martínez *et al.* and Subedi *et al.* utilised whole genome sequencing to characterise the strain included in their studies and so create a more accurate identification of the species and *oxa-50* gene variants present. Overall, the results of this study agree with Babouee Flury *et al.,* Eladawy *et al.*, Gómez-Martínez *et al.* and Subedi *et al.* in that the *oxa-50* gene, including genetics variants, is intrinsic to the *P. aeruginosa* species when PA7-like strains are excluded (252, 270-272)

The complete genome sequence of the PA7 strain showed the presence of the *catB7* gene which confers resistance to chloramphenicol (249). In this study, *catB7* was found in all but four strains belonging to the *P. aeruginosa* group and none of the PA7-like strains which included the PA7 strain (Figure 3-20). Whilst this was an unexpected result for the PA7 stains, inspection of the CARD database referenced by ARIBA confirmed the *catB7* genotype contained by the PA7 strain was not present (accessed 2nd July 2023) (185). Therefore, it is possible the absence of *catB7* in PA7-like strains is due to its absence from the database. Nevertheless, this does indicate that *catB7* present in the *P. aeruginosa* groups is unlike any gene present in the PA7 strain and the rest of the PA7-like group. As such, it's possible that PA7-like groups of strains contain a variant of *catB7* that is unique to the group. Further investigation is required to confirm whether the *catB7* variant contained by PA7 is also present in all the other PA7-like strains.

3.3.5 Robust clustering in resolving species discrepancies

For the non-*P. aeruginosa* strains included in these analyses, the similarities seen in the ANI, Sourmash sketches, and dDDH between strains reclassified as the same species (*P. nitrireducens* and *P. nitroreducens,* and *P. humi* and *P. citronellolis),* are characteristic of strains belonging to the same species (Figure 3-10, Figure 3-11, and Figure 3-12). Additionally, the phylogeny created through robust clustering (Figure 3-5) also found these strains to be closer

to each other than the phylogeny of the 16S rRNA phylogeny (Figure 3-3). Therefore, these analyses were more supportive of the recent reclassification of these strains than analysis based on the 16S rRNA sequence alone (176, 242).

When considering the 16S rRNA phylogeny (Figure 3-3) some strains showed greater similarity to one another than *P. citronellolis* and *P. humi* which are considered to be the same species (*P. lactis* and *P. synxantha, P. citronellolis* and *P. knackmussi,* and *P. citronellolis* and *P. panipatensis*). Given this, it might be expected for these strains to also be reclassified as members of the same species. However, the metrics comparing the genomic sequences of these strains confirmed they were their own separate species (Figure 3-10, Figure 3-11, and Figure 3-12). This was also in agreement with the phylogeny produced by robust clustering which showed the strains to have a greater distance to one another than seen in *P. citronellolis* and *P. humi* (Figure 3-5). Hence, the phylogeny created by 16S rRNA places strains in positions that are questionable when considering whole genome sequence analyses. In comparison, the more refined and higher resolution phylogeny created by robust clustering of the 16 ribosomal proteins agreed with whole genome analyses and produced a more reliable method for species delineation (194).

Some strains showed greater diversity in their 16S rRNA phylogeny (*P. pseudoalcaligenes* and *P. indoloxydans, P. humi* and *P. delhiensis,* and *P. dehliensis* and *P. citronellolis*) than seen between known species classified as separate. This would be expected of strains classified as separate species however, their ANI values suggested these strains met the threshold for being members of the same species. This was also evident in their genomic sketches which showed the Jaccard similarity index to be close or greater than the reclassified species *P. nitritireducens* and *P. nitroreducens,* and *P. citronellolis* and *P. humi*. However, the dDDH values were below the threshold to even be members of the same subspecies. Additionally, the phylogeny created through robust clustering did not show support for the strains being reclassified as members

of the same species. Whilst the robust clustering methods does not have a set threshold for determining species, the distance seen in between these strains was far greater than those considered the same. Hence, the methods used in this study disagreed over whether these strains should be classified as the same species. The reasons for this are currently unclear however, it may involve the presence of MGEs common between the strains that may skew of methods that compare the whole genomic sequences such as ANI, Jaccard similarity index of genomic sketches, and dDDH. Additionally, methods that rely on 16SrRNA are subject to errors due to ability of 16S rRNA to be horizontal transferred between bacterial species and the presence of multiple copies of the gene that can vary within the species (276-279). In these cases, it is more appropriate to utilise methods that are less likely to be affected by recombinant DNA and copy number variation and to continue to treat the strains as member of separate species as implied by robust clustering. These methods generally involve use of the whole genome sequence. The advent of new sequencing technologies and development of low cost high-throughput methods make speciation via the whole genomic sequence more accessible and should therefore be taken advantage of where possible to avoid incorrect identification.

Chapter 4 - Niche adaption in *Pseudomonas aeruginosa*

4.1 Introduction

As described in Section 1.2.2, *P. aeruginosa* has been isolated from environmental sources and is consequently described as an environmental microbe. Despite this, the isolation rate of *P. aeruginosa* from environmental samples uncontaminated by humans is low, suggesting the organism is more actively present in environments with human activity (86). Nevertheless, *P. aeruginosa* can be isolated from both clinical and environmental settings. The characteristics of these two settings are extremely diverse and thus *P. aeruginosa* must display great adaptability to survive in both niches.

4.1.1 Whole genome sequencing of *Pseudomonas aeruginosa*

Whole genome sequencing of *P. aeruginosa* allows for the identification of the bacterial pangenome which can be divided into the core genes, present in all strains, and the accessory genes, present in only some. Recently, the *P. aeruginosa* pan genome was defined by Freschi *et al.* and was constructed from 1,311 isolates (143). It was found to have 665 core genes, defined as genes present in all strains; 26,420 flexible genes, defined as genes present in more than one but not all strains; and 27,187 unique genes, defined as genes present in only one strain. Thus, the total number of genes present in the pangenome was 54,272 indicating the *P. aeruginosa* core genome represents <1% of the pangenome. The core genome itself was found to consist of housekeeping genes alongside genes with unknown functions whilst the accessory genome consists of genes involved in secondary metabolism, intracellular trafficking, secretion and MGEs (143). Phylogenetic analysis of the SNPs present in the core genome uncovered the presence of two larger and three smaller groups of *P. aeruginosa* expanding on the number of

groups described previously (Figure 4-1). In some cases, strains were located in the border between groups though this was due to the transfer of MGEs (143).

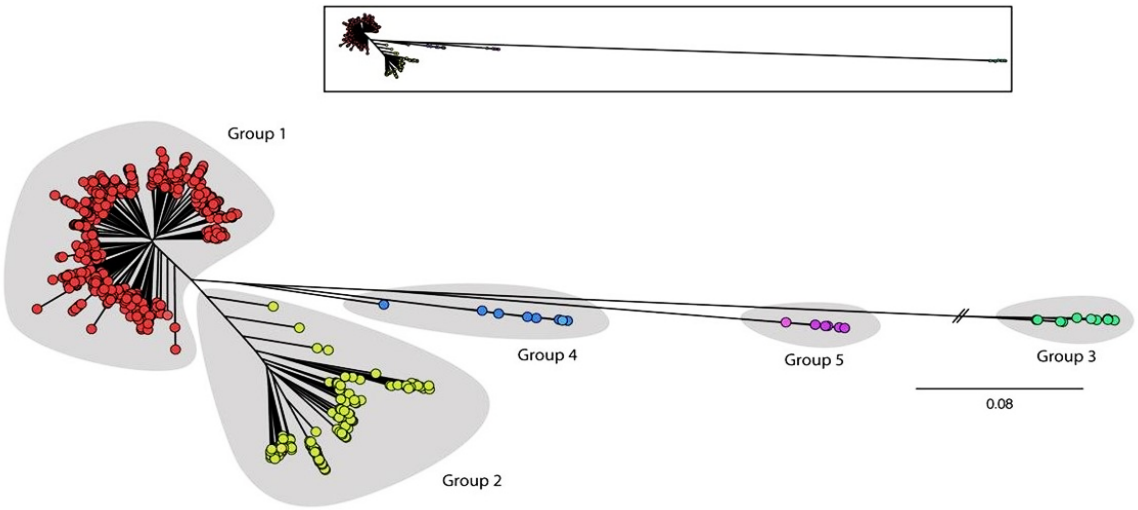

Figure 4-1: Phylogenetic tree of Pseudomonas aeruginosa *groups based on SNPs in the core genome. The core genome was defined as genes present in 100% of strains resulting in the alignment being determined from 55,664 SNPs from 448 core genes without paralog ambiguities. The tree is constructed with maximum-likelihoods using FastTree and a GTR model and 1000 bootstraps. The phylogeny is divided into five groups that are outlined in grey with specific group indicated by the colour red for Group 1, yellow for Group 2, green for Group 3, blue for Group 4, and purple for Group 5. The branch length, scaled by substitutions per site, of Group 3 is shortened for the purposes of the main tree due to its length which is illustrated in the smaller tree. Image is adapted from Figure 2 by Freschi* et al.*(143).*

4.1.1.1 Diversity between core phylogenetic groups

Analysis of the core phylogenetic groups by Botelho *et al.* has shown the strains belonging to the different phylogenetic groups illustrated in Figure 4-1 have diversity between them. In particular, strains in Group 2 were shown to have larger genomes than strains from Group 1 as well as strains from Group 4 and Group 5 which were combined in the study (251). This was regardless of whether regions of genome plasticity were masked. Consequently, the larger genome size was attributed to the larger accessory genome of Group 2 and an absence of CRISPR-Cas systems (251). The diversity between groups also extended to AMR genes and defensive CRISPR-CAS systems which were overrepresent in regions of plasticity in both Group 1 and Group 2 (251).

4.1.2 Clinical and environmental lineages in *Pseudomonas aeruginosa*

Previous work performed by Dean *et al.* produced a phylogeny based on an alignment of the seven genes involved in the *P. aeruginosa* MLST scheme (*acsA, aroE, guaA, mutL, nuoD, ppsA,* and *trpE*), overlayed with an annotation showing the presence of clinical or environmental isolates in each clade (Dean and Wain, unpublished). The study revealed that certain clades within the phylogeny showed a bias for containing isolates from a clinical or environmental origin. Therefore, it was hypothesised more detailed phylogenetic analysis would be able to reveal lineages associated with a specific niche.

Previously, it has been shown that clinical isolates from the same phylogenetic clade can cause different types of infection in geographically distant settings (252). The isolates in question were sourced from cystic fibrosis and keratitis infections in India and Australia. With respect to the core genome phylogeny these isolates were spread across the two major groups, Group 1 and Group 2 described by Freschi *et al.* and are depicted in Figure 4-2 (252). The isolates found to be part of phylogenetic Group 2 included one Australian and all seven of the Indian keratitis isolates with the remaining Australian nine cystic fibrosis and five keratitis isolates found in Group 1 (Figure 4-2)(252). In terms of linking the phylogenetic differences between the strains to phenotypic differences, the Indian keratitis isolates were found to have a greater resistance profile, however it is possible this was influenced by the less regulated use of antibiotics as opposed to having a phylogenetic link (252). Overall, this suggest that genetic diversity exists between strains isolated from different sources.

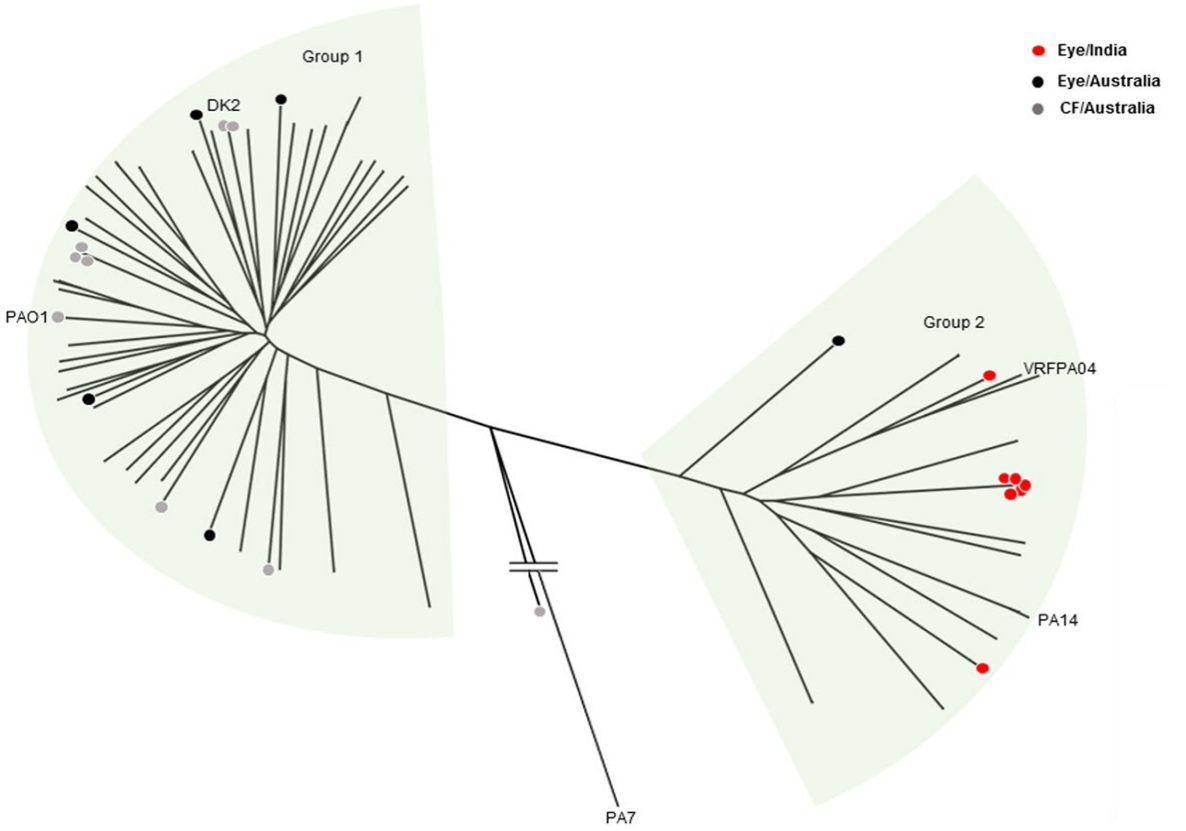

Figure 4-2: Maximum likelihood tree based on the alignment of SNPs in the core genome of 82 Pseudomonas aeruginosa. *Isolates are annotated with coloured circles to represent the origin of the strain as indicated in the key. The positions of some* P. aeruginosa *reference strains are also annotated for the purposes of visualisation (VRFPA04, UCBPP-PA14, PAO1, and DK2). Image is adapted from Figure 2 from Subedi* et al. *(252)*

Another study by Gómez-Martínez *et al.* analysed the difference between isolates from urine, sputum and environmental samples (270). Phylogenetic trees created from the core gene SNPs and from the sequences of the MLST genes showed the formation of small clades predominantly containing isolates from clinical (sputum and urine) or environmental settings (Figure 4-3). Figure 4-4 depicts the presence or absence of resistance genes in the 65 isolates included in the study. The presence of AMR genes in the environmental *P. aeruginosa* was lower than the isolates obtained from sputum and urine samples. This is something that could be expected of isolates that are less likely to be exposed to antimicrobials. In addition, the occurrence of MGEs, which are often associated with the carriage of AMR genes, was lower in the environmental strains. Therefore, this indicates the presence of observable genetic

differences between clinical and environmental strains through phylogenies based on core SNPs and MLST sequences in addition to the presence and absence of AMR genes.

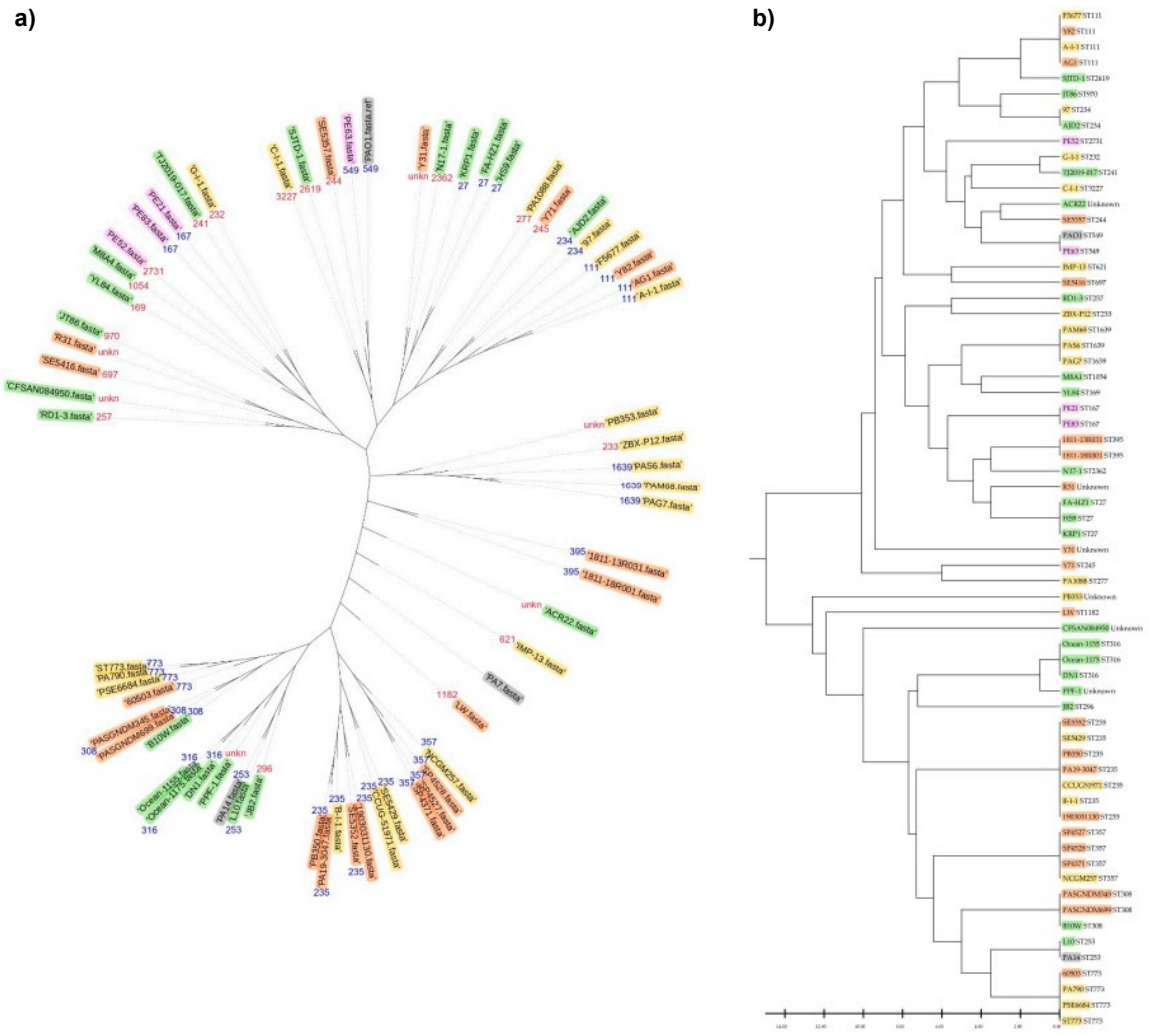

Figure 4-3: Phylogenetic trees of clinical and environmental strains of Pseudomonas aeruginosa. *Trees were created from 65* P. aeruginosa *strains with a) formed using SNPs present in the core genomes and b) formed from the concatenation of the seven genes involved in the* P. aeruginosa *MLST scheme (*acsA, aroE, guaA, mutL, nuoD, ppsA, *and* trpE*). The core SNP phylogeny is created with maximum-likelihoods and is unrooted. MLST types are indicated next to the strain name in a) by the red and blue text. The MLST dendrogram in b) is created using MEGA v 11.0.10 with the unweighted pair group method with arithmetic mean (UPGMA) algorithm and linkage distances are indicated on the scale at the bottom. Strain names are coloured according to the source of isolation: yellow for urine samples not from Mexican hospitals, orange for sputum samples not from Mexican hospitals, green for environmental samples, pink for urine or sputum isolates obtained from Mexican hospitals, and grey for reference strains. Figure is based on both Figure S4 and Figure S5 from Gómez-Martínez* et al. *(270).*

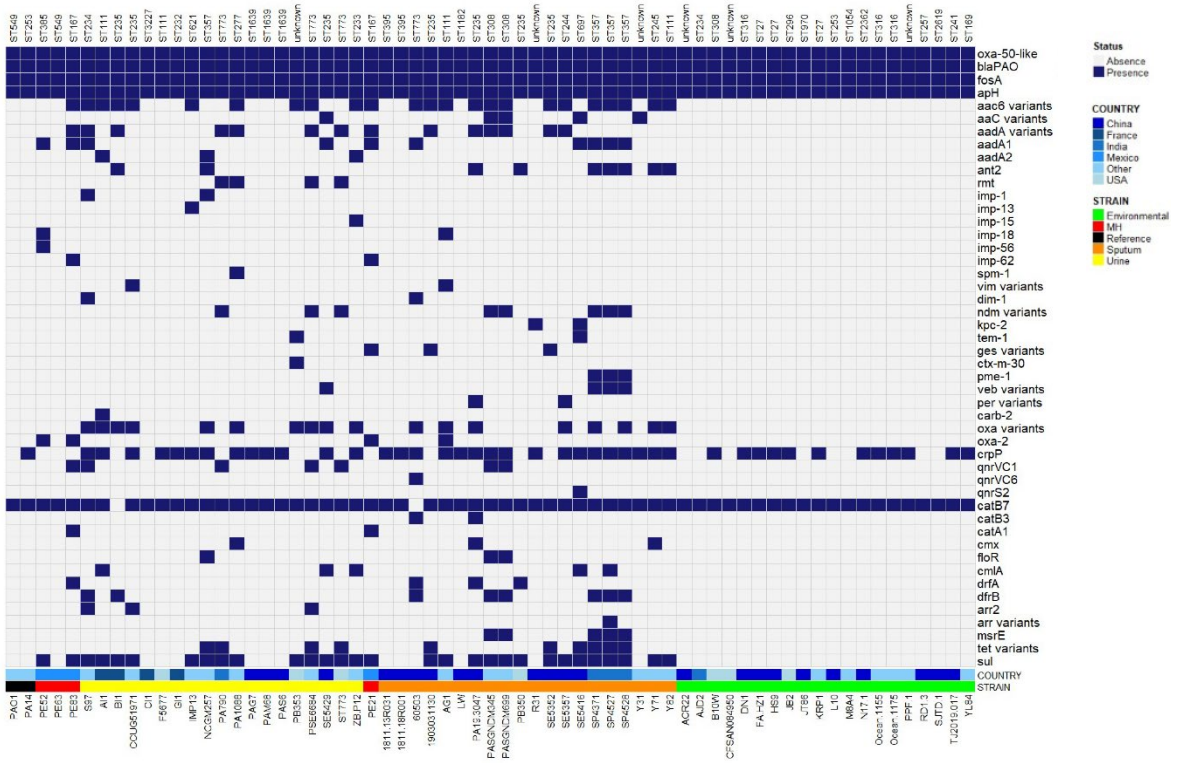

Figure 4-4: Presence and absence of resistance genes in Pseudomonas aeruginosa *isolates from urine, sputum, and environmental isolates. The image is based on 47 resistance genes detected from 65* P. aeruginosa *isolates with the* P. aeruginosa *PAO1 and PA14 strains used as a reference. Gene presence is indicated by a dark blue annotation and grey for gene absence. The country of origin is also indicated by varying shades of blue as indicated in the key and the isolation source is annotated green for environmental origins, red for urine or sputum isolates from Mexican hospitals (MH), black for reference strains, orange for sputum isolates not from Mexican hospitals, and yellow for urine isolates not from Mexican hospitals. Figure is adapted from Figure 3 in Gómez-Martínez* et al. *(270).*

4.1.3 Biomarkers of *Pseudomonas aeruginosa* of niche adaption

Biomarkers represent measurable characteristics present in an organism that can allow for it to be identified. This can include gene presence/absence, SNPs, proteins, metabolic products, and codon preference that are unique to the strain requiring identification. As different niches require specific characteristics to survive it is possible that the factors responsible for these characteristics could act as biomarkers which would in turn allow for the identification of the niche that a strain originated from.

4.1.3.1 Genes as biomarkers

4.1.3.1.1 ExoU and ExoS

The type III secretion system is responsible for the secretion of exotoxins, including ExoU and ExoS, which can affect the virulence of a strain during an infection. The ExoU and ExoS exotoxins are respectively associated with the cytotoxic and invasive characteristics seen in *P. aeruginosa* (248, 280). ExoU is a phospholipase enzyme whose activity disrupts the cell membranes of its human host leading to rapid cell death (281). ExoS is an enzyme with both RhoGAPase and ADP ribosylation activity which result in cell rounding and apoptosis within human hosts (282).

In *P. aeruginosa* distinct groups can be characterised by the production of either ExoU or ExoS as the two exotoxins are rarely encoded together or not at all (76, 248, 251). Specifically, *exoS* is overrepresented in Group 2 and *exoU* is overrepresented in Group 1 of the major clades described in Figure 4-1 by Freschi *et al.* (143, 248). This can be seen in *P. aeruginosa* isolated from various sources where the presence of invasive ExoS-producing strains is dominant over cytotoxic ExoU-producing strains (76, 246, 248, 252, 283). In particular, the occurrence of ExoS is higher within environmental isolates and is thought to be less important within a clinical niche where its production appears to be associated only with certain infection sites such as burn wounds and the urinary tract (284). Furthermore, a study by Woflgang *et al.* found that it was possible for a recombination event to occur in ExoS-producing strains which will lead to the deletion of *exoS* (285). As ExoU-producing strains lack the *exoS* gene it is possible that the acquisition of *exoU* may be responsible for the deletion of *exoS* (285). The presence of *exoU* and *exoS* has also been associated with infections by Gómez-Martínez *et al.* where *exoU* was predominantly found in isolates from sputum and *exoS* was predominantly found in isolates from urine (270). Hence, the presence of *exoU* and *exoS* may indicate which of the major groups, as defined by Freschi *et al.*, a strain originates from in addition to its source of isolation (Figure 4-1) (143).

4.1.3.1.2 O12 serotype

A study by Thrane *et al.* found the O12 serotype of *P. aeruginosa*, which has been associated with multi drug resistance, to cluster in core phylogeny Group1 and Group3 (146). Within Group 1, the O12 serotype strains clustered with a strain from the O4 serotype. Analysis of this O4 serotype strain and the O12 serotype strains, implied that a "serotype island" encoding the gene cluster associated with the O12 serotype was likely to have been transferred to an O4 serotype strain which switched to presenting an O12 serotype (146). This "serotype island" was also found to encode the *gyrA C248T* allele which can confer resistance to fluroquinolone antibiotics in O12 serotype strains (146, 148). The ability to switch serotype may possibly allow strains to evade the host immune system and in the case of serotype O12 lead to enhanced resistance (146).

4.1.3.2 Codon utilisation in adapting to a niche

In most cases changing the nucleotide in the third position of a codon does not result in an amino acid change. However, changes in codon utilisation can be indicators of selection where more optimal codons, which are more translationally efficient, are prevalent in highly expressed genes (56, 286). Table 4-1 shows codon usage in highly expressed genes in PAO1 as relative synonymous codon usage (RSCU) (287). Furthermore, codon utilisation can also be reflective of the environment an organism is growing in with low nitrogen environments producing strains whose codon usage is skewed in favour of those comprised of the adenine and thymine/uracil nucleotides which have lower nitrogen requirements (288).

Table 4-1: Codon usage in highly expressed genes from Pseudomonas aeruginosa *PAO1. Based on Table 2 from Grockock* et al. *(287).*

Amino Acid	Codon*	Number of codons	RSCU	Amino acid	Codon*	Number of codons	RSCU
Phe	UUU	13	0.10	*Ser*	UCU*	21	0.30
	UUC*	244	1.90		UCC*	205	2.92
Leu	UUA	2	0.02		UCA	0	0.00
	UUG	9	0.09		UCG	68	0.97
	CUU	11	0.11		AGU	10	0.14
	CUC	64	0.65		AGC	117	1.67
	CUA	4	0.04	*Pro*	CCU*	24	0.36
	CUG*	501	5.09		CCC	41	0.61
Ile	AUU	44	0.32		CCA	5	0.07
	AUC*	363	2.68		CCG*	200	2.96
	AUA	0	0.00	*Thr*	ACU*	69	0.62
Met	AUG	180	–		ACC*	362	3.28
Val	GUU*	173	0.91		ACA	3	0.03
	GUC	288	1.52		ACG	8	0.07
	GUA*	101	0.53	*Ala*	GCU*	257	1.16
	GUG	196	1.03		GCC	415	1.88
Tyr	UAU	17	0.20		GCA	70	0.32
	UAC*	153	1.80		GCG	141	0.64
His	CAU	22	0.34	*Trp*	UGG	31	–
	CAG*	107	1.66	*Arg*	CGU*	322	3.42
Gln	CAA	52	0.32		CGC	232	2.46
	CAG	278	1.68		CGA	2	0.02
Asn	AAU	37	0.23		CGG	7	0.07
	AAC*	283	1.77		AGA	2	0.02
Lys	AAA	139	0.47		AGG	0	0.00
	AAG	454	1.53	*Gly*	GGU*	270	1.50
Asp	GAU	104	0.53		GGC	435	2.41
	GAC	292	1.47		GGA	4	0.02
Glu	GAA*	299	1.14		GGG	13	0.07
	GAG	227	0.86	*Stop*	UGA	13	0.78
Cys	UGU	2	0.08		UAA	36	2.16
	UGC*	49	1.92		UAG	1	0.06

** Indicates optimal codons*

4.1.4 Chapter aims

Considering the ability of *P. aeruginosa* to adapt to both clinical and environmental niches, the aims for this chapter were to assess the depth of niche adaption in the *P. aeruginosa* core genome and to use this information to reveal lineages with a greater association towards a clinical or environment niche. Once obtained, biomarkers indicating association to a niche can then be identified. The specific objectives to be covered in this chapter are:

1. Collect and sequence *P. aeruginosa* strains originating from clinical and environmental sources.
2. Identify biomarkers within clinical and environment lineages of *P. aeruginosa.*

4.2 Results

4.2.1 Isolation of *Pseudomonas aeruginosa* from the environment

4.2.1.1 Isolation from environmental samples sourced across Norfolk

Across 10 sites surrounding Norwich, 177 samples were obtained from environmental sources and their distribution across each site is shown in Table 4-2. Each sample underwent enrichment and selection to obtain *P. aeruginosa* isolates as described in Section 2.1.2. Growth on the *P. aeruginosa* selective medium PA-CN was seen in cultures from 113 of the sampling sites. For each site, morphologically distinct colonies were isolated resulting in the collection of 248 suspected *P. aeruginosa* isolates (Appendix - Table 6). Oxidase and Gram staining showed 138 of the suspected *P. aeruginosa* isolates to be oxidase positive Gram-negative bacilli (Appendix - Table 6) and thus crude DNA from these strains was extracted as described in Section 2.1.5.2 for PCR identification.

Table 4-2: Distribution of environmental samples obtained across sites

Site	Fungi	Leaf litter	Marsh	Plants	Soil	Water	Total
Danby Woods	0	1	0	1	13	0	15
Foxely Woods	0	6	0	5	12	1	24
Horsey Gap	0	0	0	0	1	7	8
Lower Wood	0	2	0	1	8	1	12
Marston Marsh	0	0	7	1	3	4	15
Mousehold Heath	0	6	0	6	7	1	20
Redgrave and Lopham Fen	2	0	23	2	0	6	33
Sparham Pools	0	1	0	0	4	11	16
University Broads	0	4	0	4	6	0	14
Upton Broad and Marshes	0	0	18	0	0	2	20
Total	2	20	48	20	54	33	177

To confirm the identity of suspected *P. aeruginosa* isolates, two simplex PCRs were performed targeting the *ecfX* and *gyrB* genes as these have previously been shown to be effective in identifying *P. aeruginosa* from environmental samples (169). One oxidase positive Gram-negative bacillus (LWR011.2), isolated from a plant sample in Lower wood, showed the presence of the expected bands at 528bp and 222bp respectively for the *ecfX* and *gyrB* genes. The other 137 oxidase positive Gram-negative bacilli isolates showed no bands at the appropriate target and so were considered a species other than *P. aeruginosa*. Figure 4-5 and Figure 4-6 show examples of the PCR products on 2% agarose gel. Thus, the genomic DNA from LWR011.2 was extracted and sequenced along with seven other strains testing negative as *P. aeruginosa* by PCR to confirm the identity of these strains as non-*P. aeruginosa*. After trimming, raw reads were input into Kraken2 confirming the identity of LWR011.2 as *P. aeruginosa* and the non-*P. aeruginosa* strains as other species (Table 4-3).

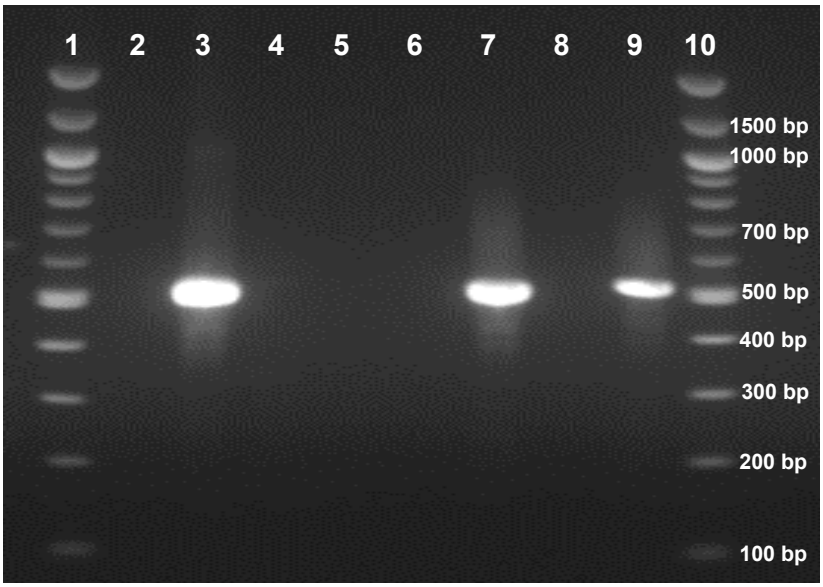

Figure 4-5: Products from a PCR targeting the ecfX gene in environmental isolates visualised on a 2% agarose gel. Lanes 1 to 10 represent the following: 100 bp ladder, LWR010.1, LWR011.2, LWR012.1, HG003.1, HG003.2, 15TB0901, negative control, positive control, 100 bp ladder.

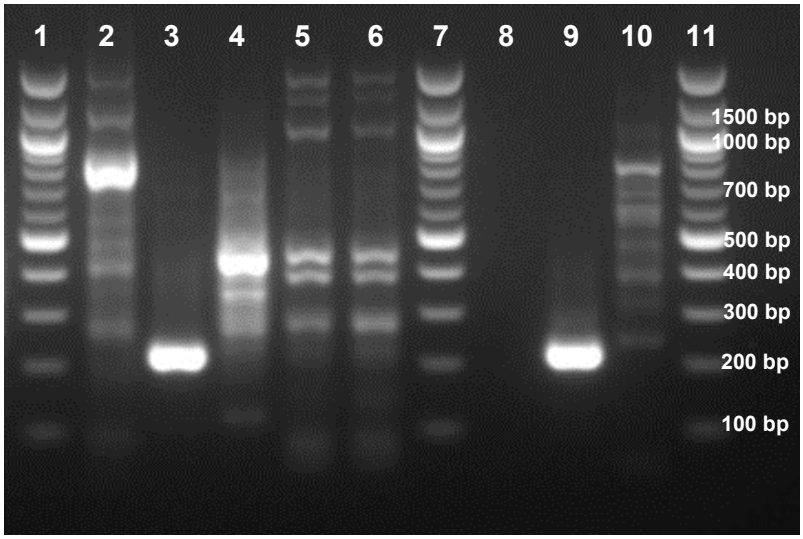

Figure 4-6: Products from the PCR targeting the gyrB gene in environmental isolates visualised on a 2% agarose gel. Lanes 1 to 11 represent the following: 100 bp ladder, LWR010.1, LWR011.2, LWR012.1, HG003.1, HG003.2, 100 bp ladder, negative control, PAO1 positive control, MH009.1, 100 bp ladder.

Table 4-3: Identity of environmental isolates by whole genome sequencing. Sequencing ID is reported according to the species match identified by Kraken2.

Isolate number	Oxidase	Gram Stain	Sequencing ID
ENV009.1	+	Gram negative bacilli	*Pseudomonas synxantha*
FW023.2	+	Gram negative bacilli	*Pseudomonas putida*
LWR011.2	+	Gram negative bacilli	*Pseudomonas aeruginosa*
MH009.1	+	Gram negative bacilli	*Pseudomonas putida*
MH018.1	-	Gram negative bacilli	*Escherichia sp. E4742*
MM008.1	+	Gram negative bacilli	*Pseudomonas putida*
MM009.1	+	Gram negative bacilli	*Pseudomonas sp.* Leaf58
RLF024.1	+	Gram negative bacilli	*Pseudomonas sp.* CCOS 191

4.2.1.2 Isolation of strains from natural bathing sites

The Environment Agency provided 50 additional samples taken from natural bathing sites across England (Figure 4-7) which resulted in the isolation of 191 morphologically distinctive strains with the ability to grow on PA-CN selective agar (Appendix - Table 7). Following PCR, 17 of the isolates showed the presence of bands for both the *ecfX* and *gyrB* targets and therefore

the genomic DNA was purified and sequenced. Raw reads were input into Kraken2 to confirm the species identity, where all 17 isolates, sourced from 13 different sites, were confirmed as *P. aeruginosa.*

Figure 4-7: Sites where environmental samples positive for Pseudomonas aeruginosa were collected. One site, Lower Wood was part of in-house sampling and the remaining 13 were for samples obtained from the Environment Agency.

4.2.2 The *Pseudomonas aeruginosa* pangenome

Previous studies using a phylogeny created from an alignment of MLST genes have produced clades with clinical or environmental associations (Dean and Wain, unpublished). To assess whether these associations could be detected using the core genome, a dataset of 2,611 *P. aeruginosa* strains was curated. This dataset excluded the PA7-like strains as analyses of their

genomes showed they did not fit the criteria to be considered the same species as the other *P. aeruginosa* strains (Chapter 3). The core genome was identified with Panaroo which found 4,482 genes to be contained in the core genome (13.0% of the pangenome), defined in this study as genes present in ≥ 99% of strains. The rest of the pangenome consisted of 668 soft core genes present in 95 – 99% strains, 1,343 shell genes present in 15 – 95%, and 32,347 cloud genes present in 0 – 15% of strains; together these genes form the accessory genome and totalled 34,358 genes.

4.2.2.1 Alignment of the core genes

The core genes were aligned through Panaroo using Mafft as the aligner. Due to the size of the core gene alignment, single nucleotide polymorphisms (SNPs) were filtered out of the alignment with SNP-sites, and this core SNP alignment was then used to estimate a phylogenetic tree using FastTree (Figure 4-8). Hierarchical clustering of the core SNP alignment is displayed in Figure 4-8a and was performed using FastBaps.

Level 1 clustering revealed the presence of 23 clusters which were taken as the core groups for this analysis. As with the previous core SNP alignment which included the PA7-like strains (Figure 3-7), two groups showed a large divergence from the main cluster of *P. aeruginosa* strains. These groups were Core9, correlating to Core6 in Figure 3-7, and Core7, correlating to Core7 in Figure 3-7, which had branch lengths of 0.25611 and 0.09321 respectively separating them from the nodes connecting to the other *P. aeruginosa* strains. Despite this divergence, whole genome analysis of the strains showed the two groups to fit the criteria of the *P. aeruginosa* species (Chapter 3) and thus were included in further analysis.

The largest core group identified was Core19 consisting of 953 strains, including the *P. aeruginosa* PAO1 and PAK strains. The Core19 group encompassed 11 smaller groups (Core10,

Core11, Core12, Core13, Core14, Core15, Core16, Core17, Core20, Core22, and Core23) which showed enough variation in the alignment to be considered distinctive groups within the larger Core19 cluster. As with Core19, the next largest group, Core21 consisting of 220 strains, also encompassed other small core groups though in this case it was for eight groups (Core1, Core2, Core3, Core4, Core5, Core6, Core8, and Core18). Both the Core19 and Core21 groups were found on opposing sides of the core phylogeny (Figure 4-8) and correspond to Group 1 and Group 2 in the phylogeny described by Freschi et al (Figure 4-1) (143). The Core7 and Core9 groups correspond to the Group 4 and Group 5 clades respectively Figure 4-1.

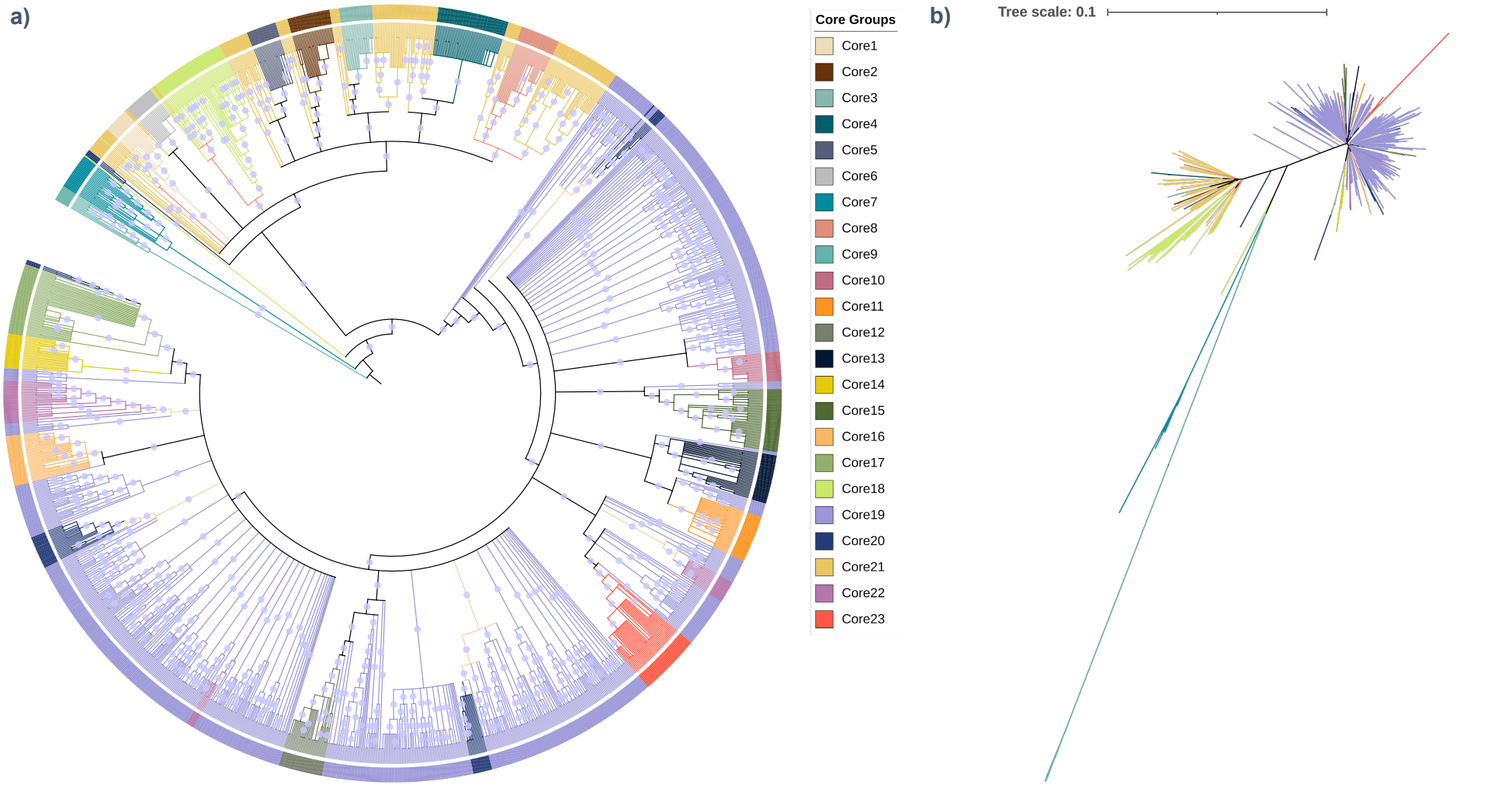

Figure 4-8: Maximum-likelihood tree of the core SNPs present in Pseudomonas aeruginosa. The tree is constructed with FastTree using GTR and Gamma20 likelihoods with 100 bootstrap replicates. Bootstraps values ≥0.95 are depicted by ● on the circular tree (a) which has been rooted at the midpoint of the longest branch (lengths not depicted). Branch lengths are shown on the unrooted tree (b) with the scale bar representing substitutions per site. Colours on both trees represent the FastBaps (195) clusters found at Level 1.

High-risk clones of *P. aeruginosa* can be identified using the MLST scheme by Curran *et al.* (289). Figure 4-9 depicts ten MLST types identified as the top high-risk clones due to their prevalence, spread, and their AMR profile (290) in addition to well characterised reference strains.

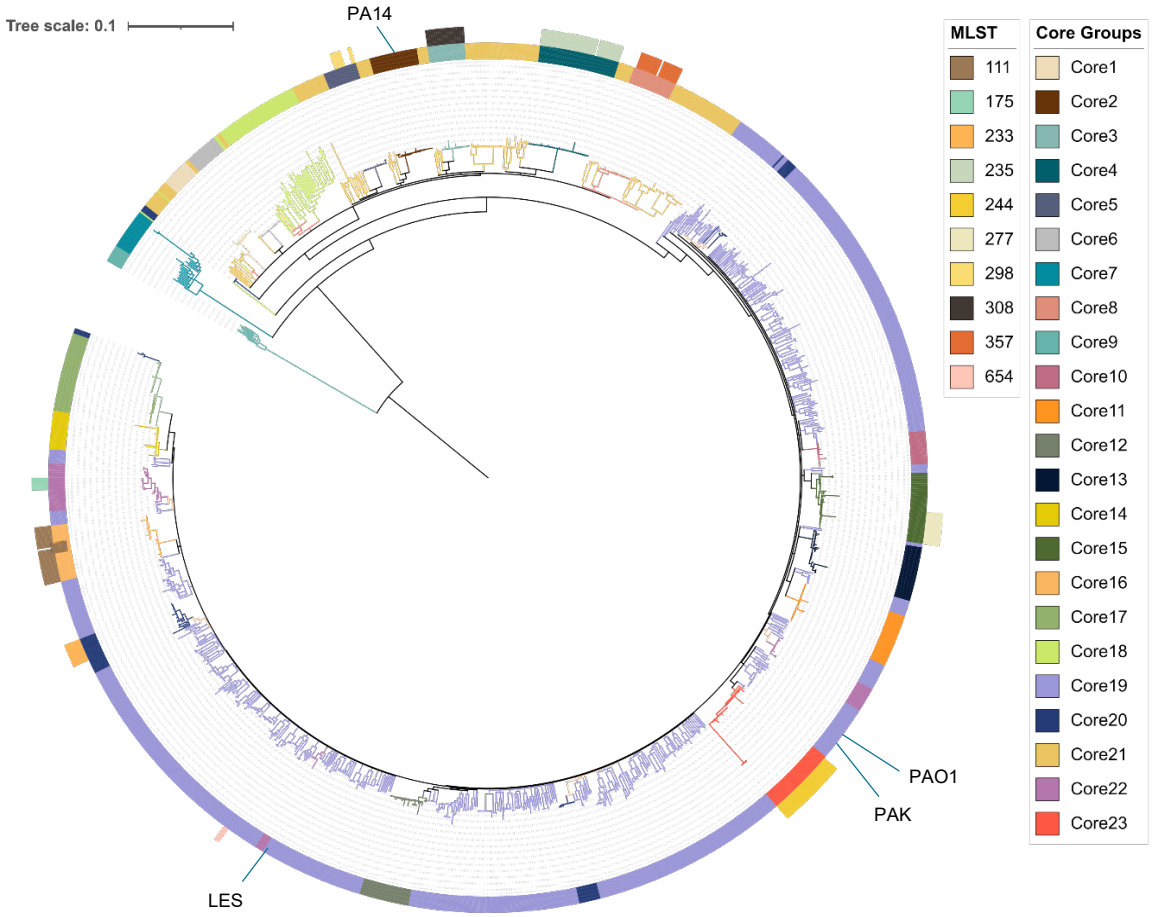

Figure 4-9: Location of epidemic lineages in the Pseudomonas aeruginosa *core genome phylogeny. Phylogenetic tree is a maximum-likelihood tree created using an alignment of core SNPs present in* P. aeruginosa. *The tree is constructed with FastTree using GTR and Gamma20 likelihoods with 100 bootstrap replicates. Branches with < 0.95 support have been collapsed with the tree rooted at the midpoint of the longest branch. Branch lengths were scaled by substitutions per site. The inner ring is coloured to annotate the core groups determined by Level 1 hierarchical clustering using FastBaps with branches coloured if all strains in the clade belong to the same core group. The MLSTs of strain from ten high-risk clones identified in Curran et al. (289) are annotated on the outer ring with the PAO1, PA14, and PAK reference strains labelled in addition to the PA1617 strain, labelled here as LES, which is part of the lineage of the Liverpool Epidemic Strain (LES).*

The ten MLST types identified as being epidemic high-risk clones (ST111, ST175, ST233, ST235, ST244, ST277, ST298, ST308, ST357, and ST654) were spread across the *P. aeruginosa* core SNP phylogeny (289, 290). Two of these MLST types were contained to their own core groups (ST308 to Core3 and ST111 to Core16) with ST235 also confined to the Core4 group in additional to a strain whose MLST type was not determinable (Appendix - Table 3). The Core5, Core8, and Core23 groups were almost confined to one MLST type, ST298, ST357 and ST244 respectively, however contained representatives from one or two other MLST types (Core5 also contained ST446, Core8 also contained ST2592 and ST3396, and Core23 also contained ST1227) (Appendix - Table 3). However, in all but one case these were single locus variants of the dominant ST, except for ST3369 which is a double locus variant of ST357. The remaining MLST types from high-risk clones (ST175, ST233, ST277, and ST654) were found in core groups that included multiple other MLST types. The high-risk MLST types were spread across the core SNP phylogeny and not confined to a specific clade.

4.2.2.2 Analysis of the core genome alignment

4.2.2.2.1 Gene flow

To assess gene flow between the core groups generated after the removal of the PA7-like strains, pairwise F_{ST} values between each of the groups was calculated using PopGenome (255). Figure 4-10 depicts the distribution of F_{ST} values between each core group against all other groups (a), and (b) shows the individual pairwise comparisons between each group as a heatmap. Low gene flow, an F_{ST} close to 1, was seen between both the Core7 and Core9 groups when compared to the other groups. Both the Core7 and Core9 groups had long branch lengths from the main cluster of strains (0.083 and 0.246) in the core SNP phylogeny (Figure 4-8) which combined with the low levels of gene flow with the other groups suggest that these two groups are more genetically isolated from the main cluster of *P. aeruginosa.* Whilst the remaining core groups mainly showed high F_{ST} values with the other core groups, they also showed low F_{ST} values (≤0.6) with at least two other groups. Most notable were the Core18,

Core19, Core20, Core21 and Core22 groups which showed high levels of gene flow amongst them. In particular, the highest levels of gene flow in these groups were seen in the core groups located within the same major clade, this being Group 1 for Core18 and Core21, and Group2 for Core19, Core20 and Core22. These groups represent some of the larger core groups which were spread across the core SNP phylogeny shown in Figure 4-8 and suggests that these core groups experienced greater levels of recombination. This is possibly why the FastBaps algorithm was unable to fully differentiate these larger overlapping core groups into distinctive individual groups and instead kept them as larger groups which surrounded the smaller more distinct core groups that did not experience similar levels of recombination.

To investigate the extent at which these larger groups influence gene flow within and between Group 1 and Group 2 Mann-Whitney *U* tests were performed on the pairwise F_{ST} values seen in the core groups linked to the two major clades (Figure 4-11). This study showed the levels of gene flow were greater in Group 1 than Group 2 regardless of whether the overlapping core groups are included in the comparison (Including all core groups within Group 1: *Mdn* = 0.754, *IQR* 0.394; Including all core groups within Group 2: *Mdn* = 0.955, *IQR* 0.441; Mann-Whitney test *U* = 695, *p* = 0.001. Excluding overlapping core groups within Group 1: *Mdn* = 0.860, *IQR* = 0.153; Excluding overlapping core groups within Group 2: Mdn = 0.983, IQR 0.029; Mann-Whitney test U = 6, $p \leq 0.001$) (Table 4-4 and Appendix - Table 8). Within Group 1 the removal of Core19, Core20 and Core22 increases the median F_{ST} by 0.106 (Table 4-4). As an F_{ST} of 1.00 represent no gene flow this indicates that 43.1% of the gene flow observed within Group 1 is due to the inclusion of these core groups in Group 1. In Group 2, the difference in including and excluding the Core18 and Core21 is 0.028, whilst this is a small difference it represents 62.2% of the gene flow observed in Group 2 when these core groups are included (Table 4-4). Between Group 1 and Group 2, removing the overlapping groups, Core18, Core19, Core20, Core21, and Core22, results in a difference of 0.032 which correlated to 48.5% of the gene flow observed (Table 4-4). Additionally, the removal of the overlapping core groups reduces the variation,

observable by the smaller interquartile ranges, in gene flow identified both within and between Group 1 and Group 2 (Table 4-4).

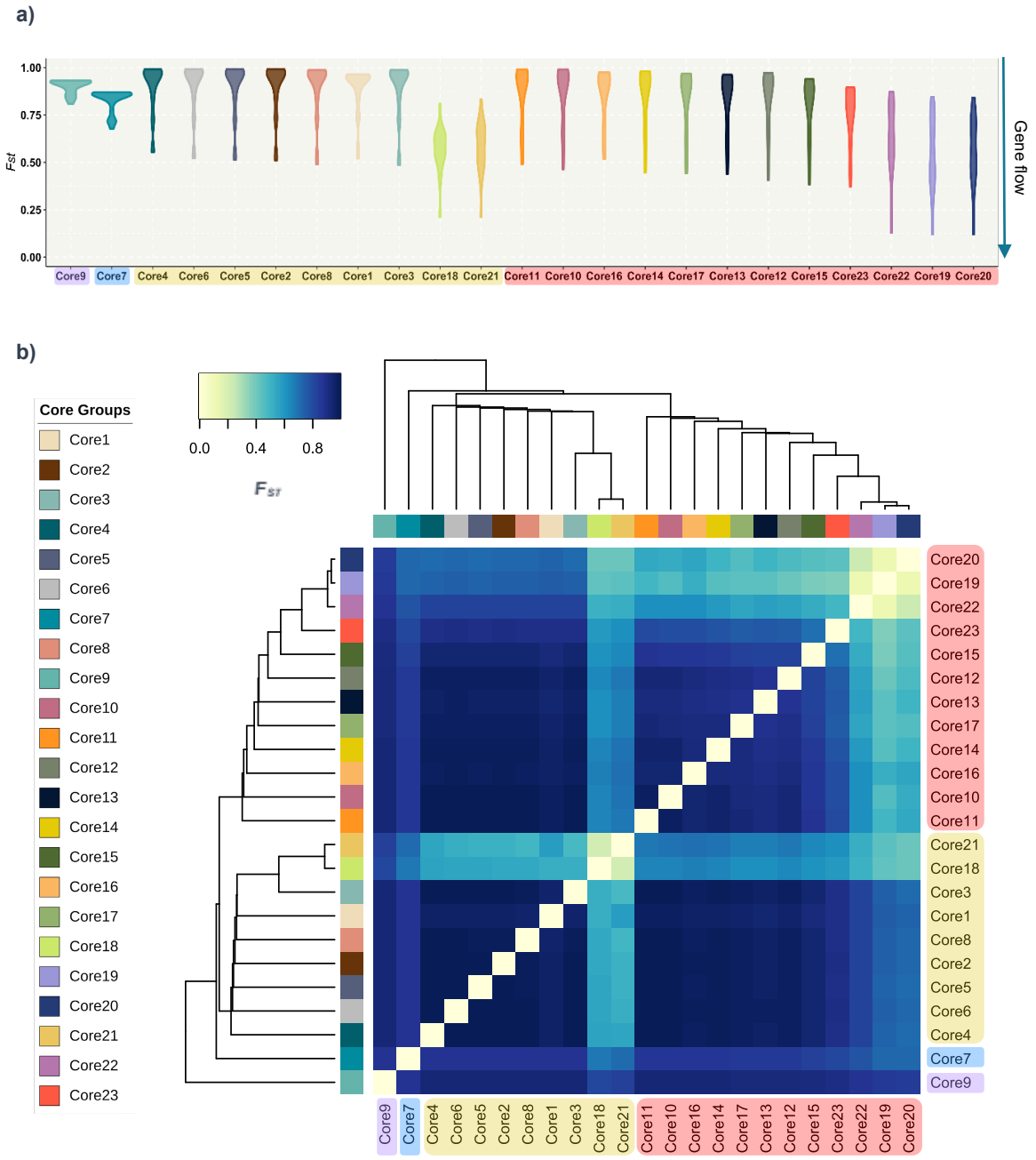

Figure 4-10: Gene flow (F_{ST}) *between core groups of* Pseudomonas aeruginosa. *a) Depicts a violin plot of* F_{ST} *values shared between the core groups. b) Shows the* F_{ST} *pairwise comparisons between the core group which are annotated along the edges of the heatmap. The dendrogram is drawn by assessing the similarity of the* F_{ST} *values contained in the matrix. Core groups are shaded according to the major clade as defined by Freschi* et al. *that the group belongs to: Red for Group 1 , Yellow for Group 2, Blue for Group 3, and Purple for Group 5 (143). Raw data for the heatmap is displayed in Appendix - Table 33.*

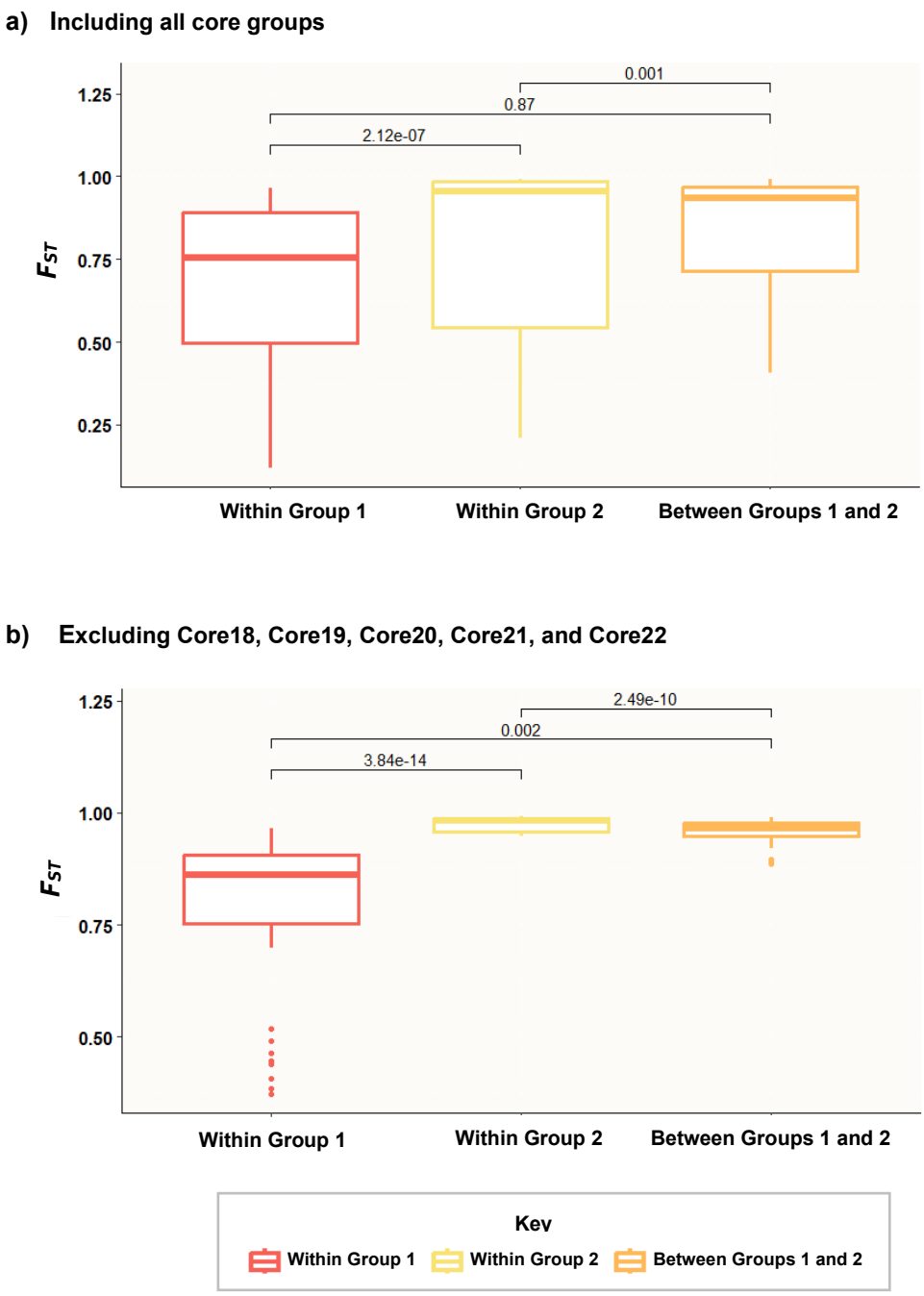

Figure 4-11: Gene flow (F_{ST}) *between the two major clades of* Pseudomonas aeruginosa. *a) Shows the* F_{ST} *values seen within and between the core groups belonging to the Group 1 and Group 2 clades described by Freschi* et al. *b) Depicts the* F_{ST} *values seen between the core groups belonging to Group 1 and Group 2 excluding the Core18, Core19, Core20, Core21, and Core22. Mann-Whitney U tests were performed to compare the difference between* F_{ST} *values between each set with the* p*-values annotated in the brackets above the boxplots.*

Table 4-4: Median and Interquartile ranges of pairwise F_{ST} *values observed within and between Group 1 and Group 2*

Group	Including all core groups		Excluding overlapping core groups	
	Mdn	IQR	Mdn	IQR
Within Group 1	0.754	0.394	0.860	0.153
Within Group 2	0.955	0.441	0.983	0.029
Between Groups 1 and 2	0.934	0.254	0.966	0.029

4.2.2.2.2 Nucleotide divergence

To provide an indication of nucleotide divergence, the number of nucleotide substitutions per site between the core groups, the D_{xy} value, was calculated with PopGenome (256). As seen in the core SNP phylogeny (Figure 4-8), the Core7 and Core9 groups showed the most divergence in terms of the pairwise D_{xy} values (Figure 4-12). Unlike the other core groups, the divergence seen in the Core7 and Core9 groups was constant across all the other groups indicating these two groups were less like the rest of the *P. aeruginosa* lineages (Figure 4-12b), consistent with the core SNP phylogeny. The remaining core groups showed lower levels of divergence with each other except when compared to Core7 and Core9. While all these groups showed less divergence, two blocks could be seen amongst these groups suggesting that whilst these groups were more similar to one another there was still a divide. The groups present in each of these divisions also corresponded to the two larger monophyletic clades that were described by Freschi *et al.* in Figure 4-1. This supports the concept that there are higher levels of similarity between certain *P. aeruginosa* core lineages.

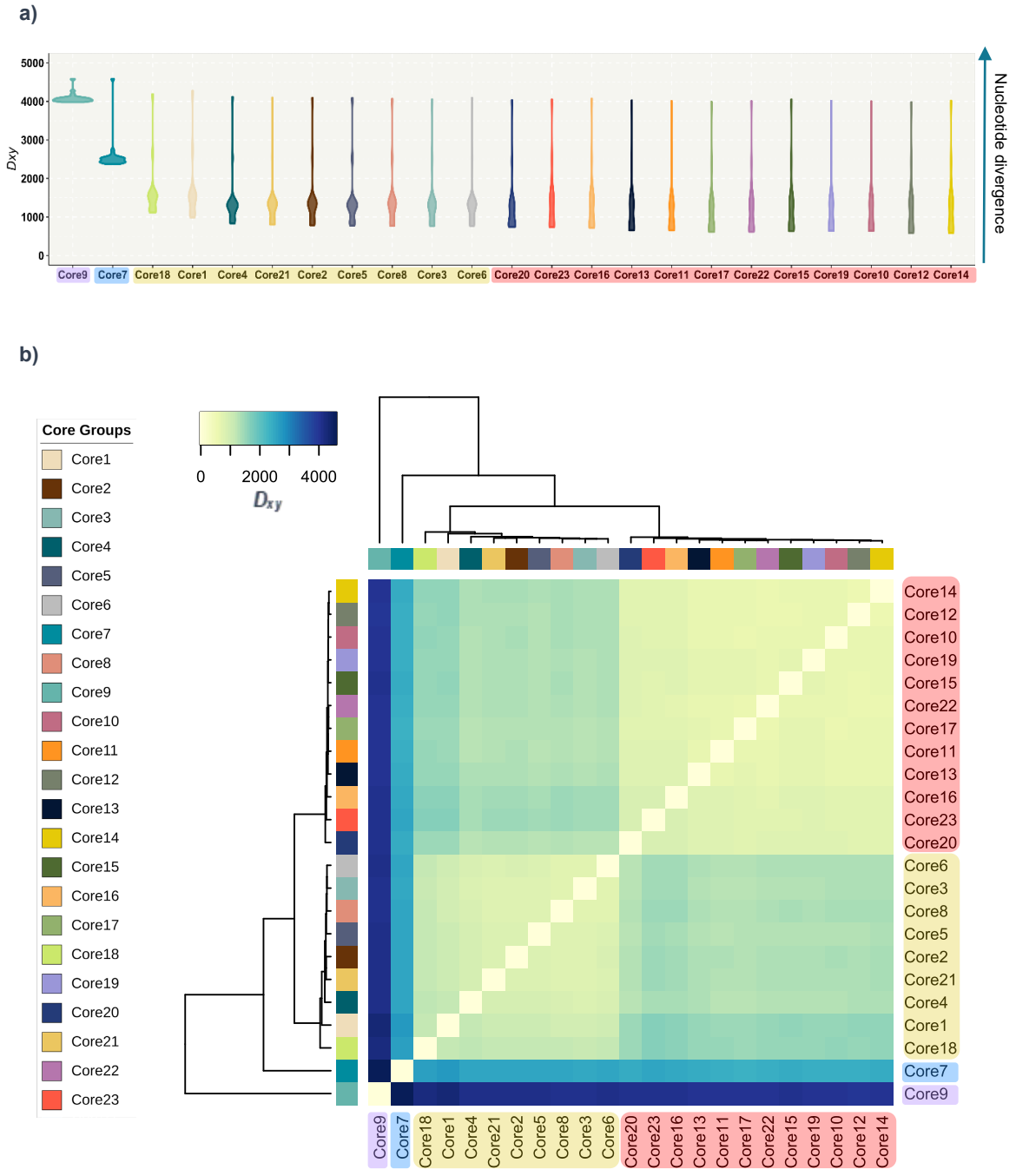

Figure 4-12: Absolute nucleotide divergence (D_{xy}) *between core groups of* Pseudomonas aeruginosa. *a) Depicts a violin plot of* D_{xy} *values shared between the named core group and the other groups. b) Shows the individual* D_{xy} *pairwise comparisons between the core groups which are annotated along the edges of the heatmap. The dendrogram is drawn by assessing the similarity of the* D_{xy} *values contained in the matrix. Core groups are shaded according to the major clade as defined by Freschi* et al. *that the group belongs to: Red for Group 1 , Yellow for Group 2, Blue for Group 3, and Purple for Group 5 (143). Raw data for the heatmap is displayed with Appendix - Table 32.*

4.2.3 Identification of niche specific clades

To assess the presence of niche adaption using the *P. aeruginosa* core genome, individual strains were marked as belonging to a clinical or environmental niche to determine the presence of clinical strains in each of the core groups (Table 4-5). In total, 2,611 strains were included in the study with 1,874 being clinical isolates and 737 being environmental isolates. Sequences available in online repositories can be clonally linked to one another, for example by multiple strains being from the same hospital outbreak. Therefore, strains from the same BioProject identifier that were clonally linked (<30 SNPs apart) and from the same niche (clinical or environmental) were only counted once by randomly selecting a single strain for inclusion to reduce bias in the data. This brought the total number of clinical strains to 1,089 and the total number of environmental strains to 408 (Table 4-5).

Table 4-5: Source of isolation for Pseudomonas aeruginosa *strains*

	Source type	No. isolates	No. isolates after removal of clonally linked strains
Clinical	Abscess/skin/ulcer/wound infections	167	118
	Bacteraemia	216	137
	Body fluid	9	5
	Bone and joints	5	3
	Burn	42	30
	Cancer	30	16
	Cystic fibrosis	427	200
	Ear	12	8
	Eye	74	63
	Gastrointestinal	21	14
	Genital tract	5	4
	Intra-abdominal tract	128	65
	Nosocomial infections	3	1
	Respiratory tract	410	249
	Typhoid fever	16	6
	Unknown clinical origin	81	32
	Urinary tract	228	138
Environmental	Algae	2	2
	Clinical environment: Dental, Hospital	106	24
	Farm environment	8	5
	Food	6	5
	Home environment	18	13
	Hydrocarbon contamination	19	7
	Industrial	60	12
	Lab	3	3
	Other environmental source	69	38
	Plants	31	26
	Sewage/wastewater	9	9
	Soil: Manure, Rocks, Sand	62	41
	Water: Lakes, Oceans, Ponds, Puddles, Rivers	202	136
	Water: Swimming Pool	42	12
	Various animal species	100	75

4.2.3.1 Distribution of isolation source across the core phylogeny

To assess whether any of the core groups were associated with a particular source of *P. aeruginosa,* the individual source types of the five largest groups after removal of clonally linked isolates were overlayed on top of the core SNP phylogeny and are displayed for clinical isolates in Figure 4-13 and environmental isolates in Figure 4-14.

The largest source of isolation seen in this dataset after discounting clonally linked isolates was respiratory infections (249) not thought to have originated from cystic fibrosis (Table 4-5). This was followed by isolates from infections in cystic fibrosis patients (200). Due to the involvement of *P. aeruginosa* in cystic fibrosis lung infections and the substantial body of work in this area, the high proportion of isolates from cystic fibrosis patients was not a surprising find. As shown in Figure 4-13, the five largest clinical source types were spread across the core SNP phylogeny.

With regards to the environmental sources, the largest group of strains were the isolates from water which came to a total of 244 strains, including 42 isolates from swimming pools (Table 4-5). The next largest environmental source seen in the dataset were the strains isolated from clinical environments (106), however once isolates from clonally linked isolates was removed the group became smaller and consisted of 24 isolates. As with the distribution of clinical source, the environmental sources were dispersed across the core SNP phylogeny and were not associated with specific clades within the tree (Figure 4-14).

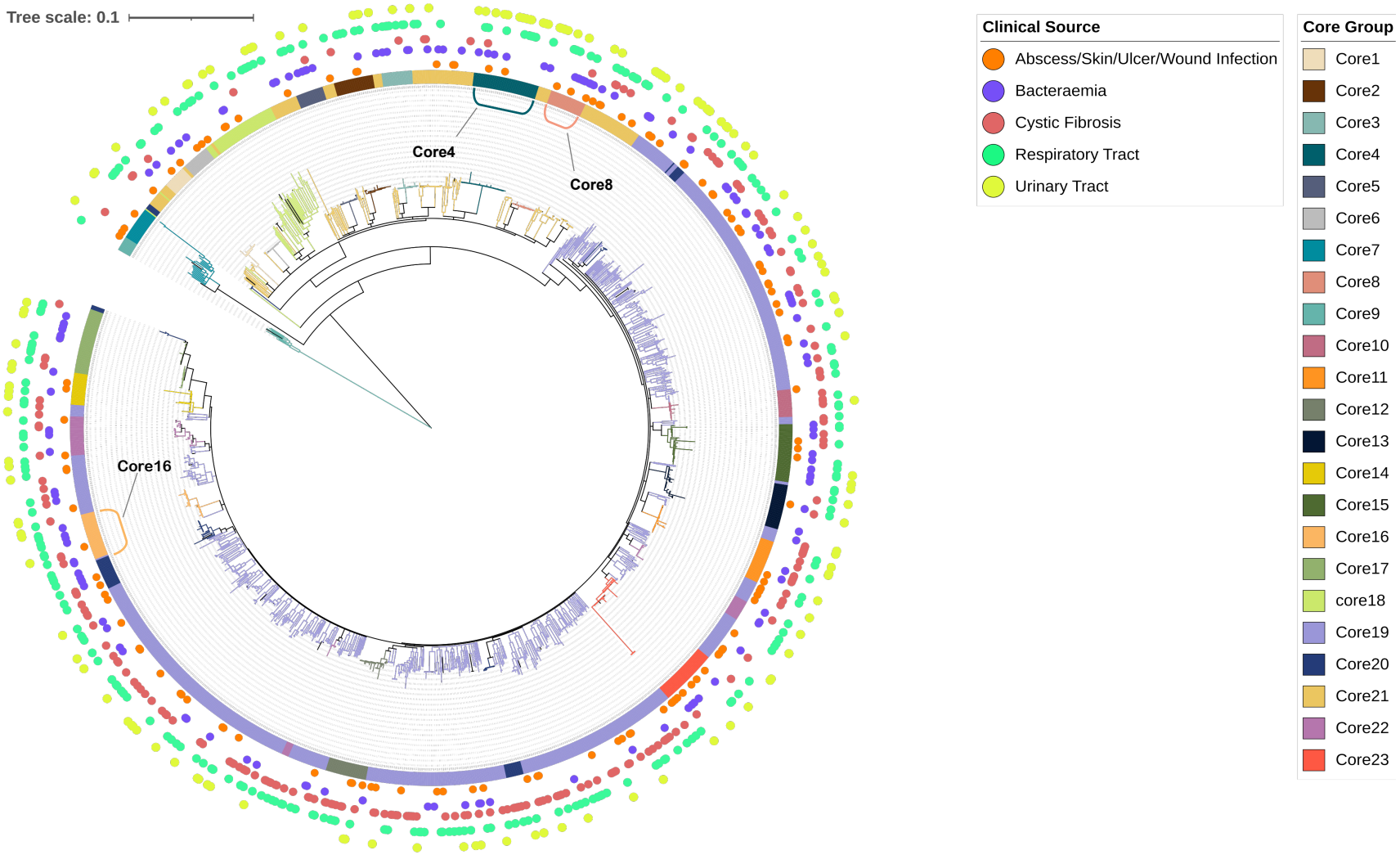

Figure 4-13: Distribution of clinical sources across the core SNP phylogeny. The phylogeny is displayed as a maximum likelihood tree and is rooted at the mid-point of the longest branch. The innermost ring depicts the core group of the strain with the clinical source of the strain depicted subsequently, only the five largest source types after the removal of clonally linked strains are shown.

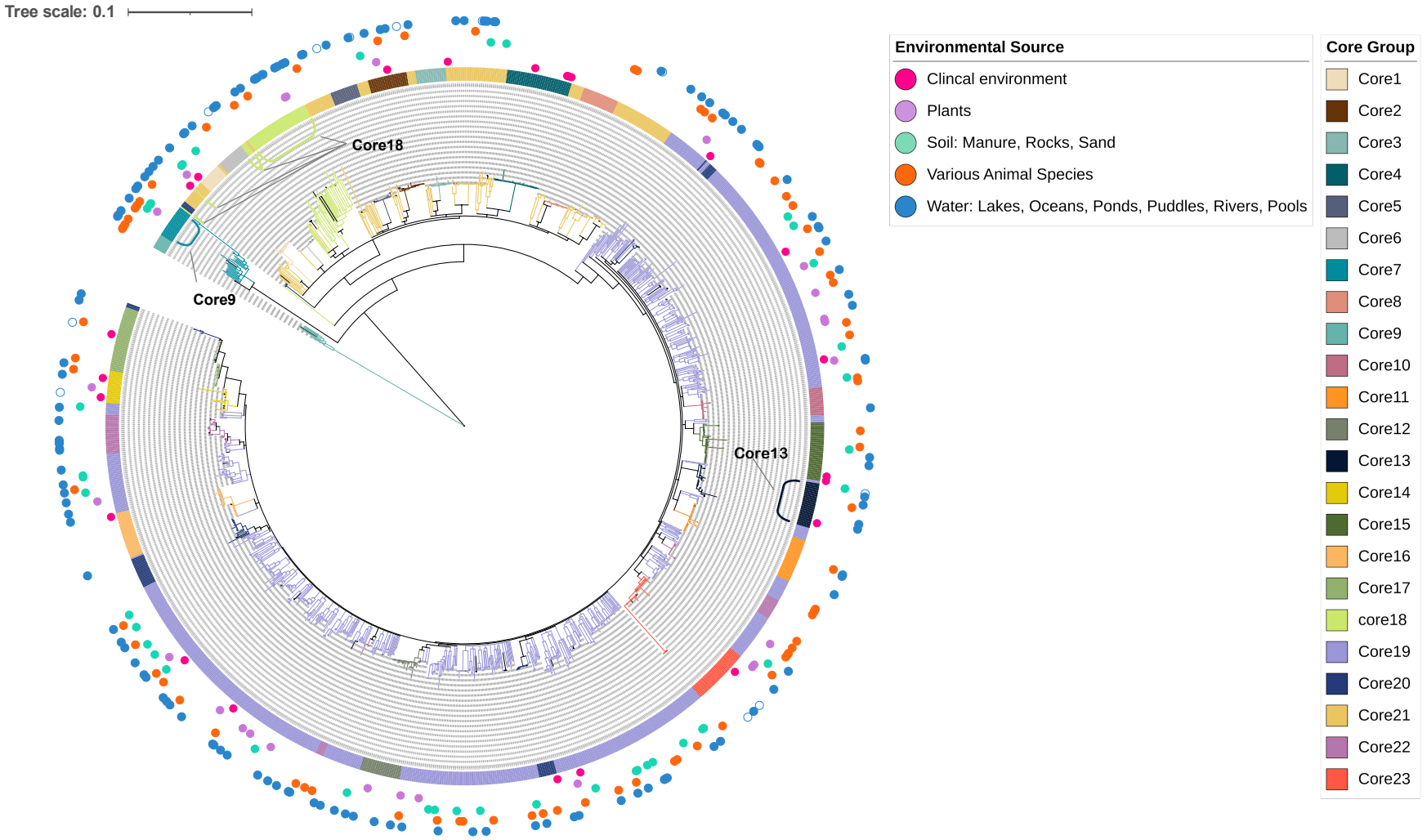

Figure 4-14: Distribution of environmental sources across the core SNP phylogeny. The phylogeny is displayed as a maximum likelihood tree and is rooted at the mid-point of the longest branch. The innermost ring depicts the core group of the strain with the environmental source of the strain depicted subsequently, only the five largest source types after the removal of clonally linked strains are shown. Isolates from swimming pools have been grouped with water for the purposes of the diagram and are depicted as unfilled circles.

4.2.3.2 Niche bias in core lineages

A fisher's exact test was used to compare the distribution of clinical and environmental strains in each group against the entire dataset to detect groups with an association with a particular niche (Table 4-6). Overall, the total dataset was shown to contain 72.3% clinical strains, when assessed against the 23 core groups, three groups were shown to have a greater association to an environmental niche (Core9 = 30.0%, Fisher's exact test p = 0.035 0.05; Core13 = 38.7%, Fisher's exact test p = 0.003; and Core 18 = 51.9%, Fisher's exact test, p = 0.027) and one group was shown to show a greater association towards a clinical niche (Core8 = 96%, Fisher's exact test = 0.043), though it consisted of only ten strains. These groups were distributed across the core SNP phylogeny (Figure 4-15) indicating the association towards either a clinical or environmental niche was not specific to certain areas of the phylogeny and instead were dispersed across the phylogeny. In addition to the Fisher's test, a Wald's test was performed using pyseer v1.3.10 to look at associations of the core groups with clinical or environmental niches (214). When considering the significant p-values ($p \leq 0.05$) for the Wald's test, the Core4, Core8, and Core16 groups showed an association ($p \leq 0.05$) to a clinical niche and the Core9, Core13, and Core18 groups showed an association ($p \leq 0.05$) to an environmental niche. Hence, these six groups were studied further to identify genetic markers of niche adaption.

*Table 4-6: Fisher's exact test and Wald's test comparing the distribution of clinical and environmental strains across the core groups. Resulting p-values were calculated after the removal of clonally linked strains and adjusted using the Benjamini-Hochberg correction with significant p-values ($p \leq 0.05$) indicated in **bold**.*

Core group	Number of isolates	Percentage of clinical isolates	Fisher's test adjusted p-value	Wald's test statistic	Wald's test p-value
Core1	16	62.50	0.655	0.917	0.359
Core2	27	62.96	0.492	1.142	0.253
Core3	21	90.48	0.239	1.720	0.086
Core4	45	88.89	0.073	2.349	**0.019**
Core5	19	78.95	0.963	0.608	0.543
Core6	19	73.68	1.095	0.092	0.926
Core7	23	56.52	0.228	1.724	0.085
Core8	25	96.00	**0.043**	2.168	**0.030**
Core9	10	30.00	**0.035**	2.662	**0.008**
Core10	19	68.42	0.707	0.425	0.671
Core11	30	86.67	0.253	1.674	0.094
Core12	28	85.71	0.290	1.514	0.130
Core13	31	38.71	**0.003**	3.957	**0.000**
Core14	22	68.18	0.857	0.483	0.629
Core15	40	82.50	0.398	1.386	0.166
Core16	32	90.63	0.096	2.144	**0.032**
Core17	45	75.56	0.942	0.429	0.668
Core18	52	51.92	**0.027**	3.321	**0.001**
Core19	715	71.33	0.732	1.177	0.239
Core20	47	85.11	0.217	1.888	0.059
Core21	146	72.60	1.045	0.041	0.967
Core22	46	73.91	1.000	0.181	0.857
Core23	39	79.49	0.713	0.953	0.341

To examine the association of isolation sources within the core groups, a Fisher's exact test and Wald's test were performed on the distribution of isolates in each core group against the distribution in the entire dataset for each of the five largest clinical and five largest environmental sources (Table 4-7). For the five largest clinical sources the distribution in core groups amongst strains from abscess/skin/ulcer/wound infections, bacteraemia infections, cystic fibrosis patients, respiratory tract infections, and urinary tract infections showed associations with at least one core group (Table 4-7). Of these core groups, only three showed

significant association with an isolation source in both the Fisher's exact test and Wald's test: Core4 to urinary tract infections (Fisher's exact test, $p \leq 0.001$; Wald's test, $p \leq 0.001$), Core8 to bacteraemia infections (Fisher's exact test, $p = 0.007$; Wald's test, $p \leq 0.001$). Both of these core groups predominantly contained specific MLST types (Core4 with ST235 and Core8 with ST357) representing epidemic high-risk clones (Figure 4-15) and were also found to be more biased toward a clinical niche when the isolation sources were accounted for (Figure 4-15).

From the five largest environmental sources (clinical environments, plants, soil, animals, and water), only two were found to be associated with specific core groups in both the Fisher's exact and Wald's tests (Table 4-7). These were Core9, which was associated with strains isolated from animals (Fisher's exact test, $p = 0.023$; Wald's test, $p \leq 0.001$), and Core18 which was associated with isolates from water (Fisher's exact test, $p = 0.046$; Wald's test, $p = 0.001$), which were both found to be associated with an environmental niche (Table 4-7). Neither of these groups were associated with any MLST types from epidemic high-risk clones which could be expected of strains not associated with a clinical niche (Figure 4-15). The Core9 group is made up of ten isolates and so only a few strains from an environmental source would be needed to skew the group. Additionally, the Core9 group represents a cluster of strains that also shows divergence from the main cluster of strains in the core SNP phylogeny depicted in Figure 4-8 whilst still being members of the *P. aeruginosa* species.

Table 4-7: Fisher's exact test and Wald-s test comparing the distribution of isolates from across core groups from specified sources. Table is a subset showing the results found to be significant by either test (p ≤ 0.05), the full table is displayed in the appendix (Appendix - Table 9). P-values were calculated after the removal of clonally linked strains and adjusted using the Benjamini-Hochberg correction.

Source*	Core Group**	Number of isolates in core group	Percentage of isolates in source	Percentage of isolates not in source	Fisher's test adjusted p-value	Wald's test statistic	Wald's test p-value
Abscess/Skin/Tissue/Ulcer/Wound	Core23	39	17.95	82.05	0.506	2.28	**0.023**
Bacteraemia	Core5	19	31.58	68.42	0.070	3.10	**0.002**
	Core8*	25	36.00	64.00	**0.007**	4.16	**3.17×10^{-5}**
	Core15	40	22.50	77.50	0.079	2.83	**0.005**
	Core19	715	6.43	93.57	0.183	3.44	**0.001**
Cystic Fibrosis	Core11	30	33.33	66.67	0.058	3.07	**0.002**
	Core12	28	28.57	71.43	0.169	2.30	**0.021**
	Core18*	52	1.92	98.08	0.075	2.07	**0.038**
	Core19	715	18.18	81.82	0.058	5.15	**0.000**
	Core21	146	6.16	93.84	0.075	2.60	**0.009**
Respiratory Tract	Core3	21	38.10	61.90	0.265	2.53	**0.012**
	Core16*	32	31.25	68.75	0.399	2.18	**0.029**
Urinary Tract	Core4*	45	28.89	71.11	**0.000**	4.27	**1.92×10^{-5}**
	Core14	22	22.73	77.27	0.564	2.10	**0.035**
Clinical environment: Dental, Hospital	Core4*	45	8.89	91.11	0.184	3.41	**0.001**
	Core14	22	9.09	90.91	0.609	2.44	**0.014**
	Core19	715	0.70	99.30	0.828	2.50	**0.012**
Plants	Core19	715	2.52	97.48	1.000	2.14	**0.032**
Soil: Manure, Rocks, Sand	Core1	16	12.50	87.50	0.564	2.15	**0.031**
	Core7	23	13.04	86.96	0.564	2.71	**0.007**
	Core19	715	4.20	95.80	0.564	3.15	**0.002**
Various Animals Species	Core9*	10	40.00	60.00	**0.023**	3.94	**0.000**
	Core19	715	6.85	93.15	0.843	3.06	**0.002**
Water: Lakes, Oceans, Ponds, Puddles, Rivers, Swimming Pools	Core9*	10	30.00	70.00	0.368	2.12	**0.034**
	Core18*	52	25.00	75.00	**0.046**	3.39	**0.001**

**Sources highlighted in red indicate a clinical origin and source highlighted in green indicate an environmental origin.*

***Indicates core groups found to be associated with a clinical or environmental niche.*

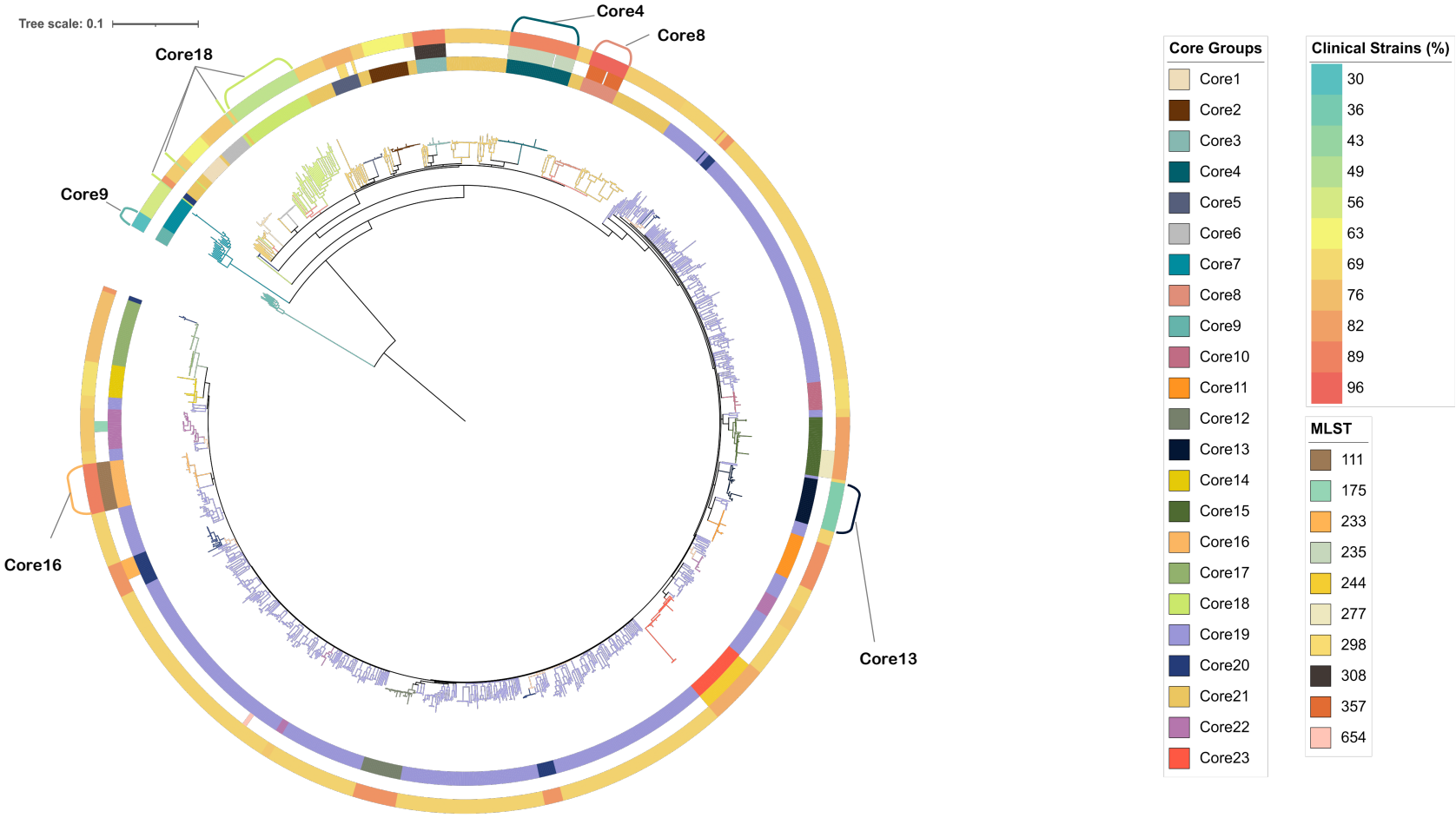

Figure 4-15: Maximum likelihood tree based on the core SNP alignment showing the presence of clinical isolates in each group. The tree is constructed with FastTree using GTR and Gamma20 likelihoods with 100 bootstrap replicates. Branches with < 0.95 support have been collapsed with the tree rooted at the midpoint of the longest branch which were scaled by substitutions per site. Clonally linked isolates have been pruned from the tree. The inner ring shows the core groups, the central ring shows the epidemic high-risk clones, and the outer ring displays the percentage of clinical isolates contained by a core group.

4.2.3.3 Antimicrobial resistance in environmental isolates

Treatment of *P. aeruginosa* involves the use of various antibiotics depending on the type of infections and guidelines in the local area. In general, fluoroquinolones such as ciprofloxacin are often used due to its activity against the organism (104). The MICs for various antibiotics from a range of families was determined for 103 environmental isolates of *P. aeruginosa* present in the in-house collection. The MIC values obtained are described in Table 4-8 along with information on isolate MLST ST and source of isolation.

The most common MLST types seen across the environmental isolates are ST252, ST253, and ST395 (Table 4-8). Many of the isolates from ST252 were isolated from other environmental sources which included showers and sinks. ST253 was predominantly isolated from water environments and ST395 from clinical environments. These MLST types did not correspond to any of the ten MLST types identified as being epidemic high-risk clones (ST111, ST175, ST233, ST235, ST244, ST277, ST298, ST308, ST357, and ST654) (290).

In terms of the MICs seen across the environmental isolates, most strains were found to be susceptible or within the susceptible, increased exposure range of all the antibiotics tested as defined by EUCAST (291)(Table 4-8). Exceptions to this were seen in strains PA149, PA150, PA155, and PA2632, towards some of the beta-lactam antibiotics: piperacillin and ceftazidime and their beta-lactam inhibitor combinations piperacillin/tazobactam and ceftazidime/avibactam. These MICs were only slightly above the resistance breakpoints described by EUCAST (291). For the carbapenem antibiotics, imipenem and meropenem, resistance towards imipenem was seen in 14 of the isolates. However, the isolates from animals and food had been specifically collected due to their resistance towards imipenem and thus the resistance in these nine strains was expected. Resistance was also seen to the monobactam aztreonam in four strains PA141, PA152, PA159 and PA2632 from various environmental sources.

In general, most of the strains showed little resistance towards the antibiotics tested. In the few cases where resistance was seen, the strain was only found to be resistant to one or two of the antimicrobial categories. Thus, based on the antibiotics tested, no strain was considered multidrug-resistant, defined as resistance to more than one antimicrobial agent to three or more antimicrobial categories (109). As these isolates were obtained from environmental sources, the likelihood of exposure towards the antibiotics tested is low. Thus, it is not surprising for there to be low levels of resistance amongst these strains.

Table 4-8: Minimum inhibitory concentrations of environmental Pseudomonas aeruginosa *isolates. MLST sequence types were identified with ARIBA and MIC, reported as µg/ml, coloured according to the resistance (R) and sensitive (S) breakpoints as described by EUCAST*.*

Project ID	Isolation Source	MLST**	PIP	PIP/TAZ	CAZ	CAZ/AVI	AZT	IMP	MEM	CIP	TOB	CHL
PA2	Home environment	298	8	8	1	2	4	1	1	0.125	0.5	128
PA3	Home environment	1990	4	4	2	2	8	8	2	0.06	0.25	64
PA154	Home environment	252	8	8	2	2	16	1	≤0.25	0.125	0.5	128
PA155	Home environment	252	16	32	4	4	8	1	0.5	0.25	0.5	64
PA155	Home environment	252	8	8	2	2	4	8	2	0.25	0.5	128
PA151	Lab	252	8	8	2	2	16	2	0.25	0.125	0.5	128
PA152	Lab	252	16	16	4	4	32	2	0.5	0.125	0.5	128
PA153	Lab	3514	16	8	2	2	4	2	0.5	0.125	0.5	128
PA92	Clinical environment: Dental, Hospital	395	4	4	2	1	2	2	≤0.25	0.125	0.5	128
PA93	Clinical environment: Dental, Hospital	395	4	4	2	1	4	2	≤0.25	0.06	1	128
PA94	Clinical environment: Dental, Hospital	395	4	4	2	1	2	2	≤0.25	0.06	0.5	128
PA95	Clinical environment: Dental, Hospital	395	4	4	2	1	2	2	≤0.25	0.06	1	128
PA96	Clinical environment: Dental, Hospital	395	4	4	2	2	2	2	≤0.25	0.06	1	128
PA96	Clinical environment: Dental, Hospital	395	4	2	2	1	2	2	≤0.25	0.125	1	64
PA98	Clinical environment: Dental, Hospital	395	2	4	1	1	4	2	≤0.25	0.06	0.5	64
PA99	Clinical environment: Dental, Hospital	395	4	4	2	1	2	4	0.5	0.125	0.5	64
PA100	Clinical environment: Dental, Hospital	395	8	4	1	1	2	2	≤0.25	0.06	1	64
PA101	Clinical environment: Dental, Hospital	395	4	4	1	2	2	2	0.5	0.06	1	64
PA102	Clinical environment: Dental, Hospital	395	8	4	2	1	2	2	≤0.25	0.125	1	64
PA103	Clinical environment: Dental, Hospital	395	4	2	1	1	2	2	≤0.25	0.06	1	64
PA104	Clinical environment: Dental, Hospital	395	4	2	1	2	2	2	≤0.25	0.06	1	64

PA105	Clinical environment: Dental, Hospital	395	2	4	1	2	2	4	≤0.25	0.125	1	64
PA107	Clinical environment: Dental, Hospital	395	4	4	1	1	2	2	0.5	0.125	1	64
PA108	Clinical environment: Dental, Hospital	395	4	4	1	2	2	2	≤0.25	0.06	1	64
PA60	Other environmental source	3514	4	4	1	1	2	1	0.5	0.125	0.5	64
PA61	Other environmental source	252	16	4	2	2	2	4	2	0.5	0.125	128
PA63	Other environmental source	253	8	8	1	2	8	1	≤0.25	0.06	0.25	64
PA64	Other environmental source	357	4	4	1	1	2	0.5	0.5	0.06	0.5	64
PA139	Other environmental source	252	8	8	2	4	8	2	0.5	0.06	0.5	64
PA140	Other environmental source	252	8	8	4	4	8	2	1	0.125	0.5	128
PA141	Other environmental source	252	8	8	4	4	32	1	1	0.125	1	128
PA142	Other environmental source	252	8	8	4	4	8	2	0.5	0.125	0.5	128
PA143	Other environmental source	3514	16	16	2	2	16	2	0.5	0.06	1	128
PA144	Other environmental source	252	16	16	4	4	16	2	0.5	0.25	1	128
PA145	Other environmental source	252	8	8	2	2	4	2	1	0.125	0.5	64
PA146	Other environmental source	252	8	8	2	2	4	2	0.5	0.06	0.5	128
PA147	Other environmental source	2465	8	8	2	4	16	1	1	0.125	0.5	128
PA148	Other environmental source	252	8	8	2	2	8	1	0.5	0.06	0.5	128
PA149	Other environmental source	252	32	32	16	4	16	2	0.5	0.25	1	128
PA150	Other environmental source	252	64	32	16	4	4	2	1	0.125	0.5	128
PA156	Other environmental source	252	8	8	2	4	8	2	0.5	0.125	0.5	256
PA157	Other environmental source	252	8	8	2	2	4	2	1	0.25	0.5	128
PA158	Other environmental source	252	8	8	2	4	8	4	≤0.25	0.125	0.5	128
PA159	Other environmental source	252	8	8	4	4	32	2	0.5	0.125	0.5	128
PA160	Swimming Pool	309	16	16	2	2	16	4	0.5	0.25	1	256
PA161	Swimming Pool	395	4	8	2	2	4	4	0.5	0.125	1	256

PA162	Swimming Pool	667	4	4	1	1	4	4	≤0.25	0.125	1	32
PA163	Swimming Pool	253	4	4	1	1	4	4	≤0.25	0.125	1	64
PA164	Swimming Pool	667	2	2	1	1	2	4	≤0.25	0.25	0.5	32
PA165	Swimming Pool	253	4	4	1	1	4	2	≤0.25	0.125	1	64
PA166	Swimming Pool	1248	4	4	1	2	4	4	≤0.25	0.06	1	64
PA167	Swimming Pool	252	8	8	2	2	4	8	≤0.25	0.06	1	128
PA168	Swimming Pool	1248	4	4	2	1	4	4	≤0.25	0.125	1	32
PA169	Swimming Pool	395	4	2	2	1	2	2	≤0.25	0.125	1	128
PA170	Swimming Pool	179	2	2	1	0.5	2	4	≤0.25	0.06	1	64
PA171	Swimming Pool	395	4	4	2	2	2	2	0.5	0.06	1	128
PA172	Swimming Pool	179	2	2	1	1	2	4	≤0.25	0.125	1	64
PA173	Swimming Pool	253	4	8	1	1	4	4	0.5	0.125	1	64
PA174	Swimming Pool	253	4	4	1	2	4	1	0.5	0.125	1	64
PA175	Swimming Pool	313	4	8	2	1	4	4	≤0.25	0.06	1	64
PA176	Swimming Pool	395	2	1	0.5	≤0.25	≤0.5	2	≤0.25	0.06	0.5	64
PA177	Swimming Pool	244	8	8	2	1	4	4	0.5	0.125	1	128
PA178	Swimming Pool	244	4	4	1	0.5	2	2	≤0.25	0.125	0.5	64
PA179	Swimming Pool	253	8	4	1	1	4	2	≤0.25	0.125	1	128
PA180	Swimming Pool	253	4	4	2	2	4	1	0.5	0.125	1	64
PA181	Swimming Pool	244	4	4	1	1	1	2	≤0.25	0.06	0.5	64
PA182	Swimming Pool	253	4	2	1	1	2	2	≤0.25	0.125	1	64
PA183	Swimming Pool	253	4	4	1	1	4	2	0.5	0.25	1	128
PA184	Swimming Pool	252	16	8	4	2	8	4	≤0.25	0.06	1	128
PA185	Swimming Pool	253	4	4	1	1	4	0.5	0.5	0.125	1	128
PA189	Swimming Pool	560	8	8	2	2	8	4	≤0.25	0.125	1	64

PA205	Food	389	4	4	1	2	4	1	0.5	0.06	0.5	64
PA206	Food	1228	4	8	2	2	8	2	0.5	0.125	0.125	128
PA207	Food	**	8	8	2	2	8	16	4	0.125	0.5	128
PA208	Food	1228	4	4	2	2	8	1	0.5	0.125	0.5	128
PA209	Food	1228	4	4	2	2	4	1	1	0.125	0.5	128
PA210	Food	**	8	8	2	2	8	16	4	0.125	0.5	64
PA232	Plants	195	4	4	1	2	8	4	0.5	0.06	0.25	64
PA265	Animal	**	8	8	2	2	8	16	4	0.25	0.5	64
PA266	Animal	**	4	8	2	2	8	16	4	0.125	0.5	64
PA267	Animal	**	8	8	2	2	8	16	4	0.125	0.5	128
PA268	Animal	**	8	8	2	2	8	8	4	0.125	0.5	64
PA269	Animal	**	8	8	2	4	16	16	4	0.125	0.5	64
PA270	Animal	1228	4	4	2	2	8	2	1	0.125	1	128
PA271	Animal	**	8	8	2	2	8	16	4	0.125	0.5	64
PA272	Animal	**	8	8	2	2	8	8	4	0.125	0.5	64
PA2617	Water: Lakes, Oceans, Ponds, Puddles, Rivers	244	4	8	1	2	8	0.5	0.5	0.06	0.5	64
PA2618	Water: Lakes, Oceans, Ponds, Puddles, Rivers	244	4	4	1	2	8	0.5	0.5	0.06	0.5	64
PA2619	Water: Lakes, Oceans, Ponds, Puddles, Rivers	244	4	4	1	2	4	2	1	0.125	0.5	64
PA2620	Water: Lakes, Oceans, Ponds, Puddles, Rivers	253	4	4	1	2	4	8	2	0.06	0.25	64
PA2621	Water: Lakes, Oceans, Ponds, Puddles, Rivers	253	4	8	1	2	2	8	4	0.06	0.25	64
PA2622	Water: Lakes, Oceans, Ponds, Puddles, Rivers	253	8	8	2	2	2	1	0.5	0.06	0.25	64
PA2623	Water: Lakes, Oceans, Ponds, Puddles, Rivers	253	8	4	2	2	2	1	0.5	0.125	0.25	64
PA2624	Water: Lakes, Oceans, Ponds, Puddles, Rivers	698	8	8	1	4	2	4	2	0.03	0.5	64
PA2625	Water: Lakes, Oceans, Ponds, Puddles, Rivers	179	16	8	2	2	2	2	1	0.03	0.5	64
PA2626	Water: Lakes, Oceans, Ponds, Puddles, Rivers	439	8	8	2	4	4	2	1	0.125	0.5	64

PA2627	Water: Lakes, Oceans, Ponds, Puddles, Rivers	847	8	8	2	4	4	2	4	0.125	0.5	64
PA2628	Water: Lakes, Oceans, Ponds, Puddles, Rivers	179	4	4	1	2	4	4	1	0.06	0.5	64
PA2629	Water: Lakes, Oceans, Ponds, Puddles, Rivers	1233	8	8	2	2	2	2	1	0.06	0.5	64
PA2630	Water: Lakes, Oceans, Ponds, Puddles, Rivers	485	8	8	2	2	8	2	≤0.25	0.125	0.5	64
PA2631	Water: Lakes, Oceans, Ponds, Puddles, Rivers	1226	8	8	2	2	8	1	≤0.25	0.125	0.5	128
PA2632	Water: Lakes, Oceans, Ponds, Puddles, Rivers	1328	32	16	4	8	32	2	≤0.25	0.125	1	128
PA2633	Water: Lakes, Oceans, Ponds, Puddles, Rivers	882	8	8	2	2	8	1	1	0.125	0.5	128

** Piperacillin (PIP): R = >16 mg/L, S = ≤0.001 mg/L; Piperacillin and Tazobactam (PIP/TAZ): R = >16 mg/L, S = ≤0.001 mg/L; Ceftazidime (CAZ): R = >8 mg/L, S = ≤0.001 mg/L; Ceftazidime and Avibactam (CAZ/AVI): R = >8 mg/L, S = ≤8 mg/L; Aztreonam (AZT): R = >16 mg/L, S = ≤ 0.001 mg/L; Imipenem (IMP): R = >4 mg/L, S = ≤0.001 mg/L; Meropenem (MEM): R = >8 mg/L, S = ≤2 mg/L; Ciprofloxacin (CIP): R = >0.5 mg/L, S = ≤0.001 mg/L; Tobramycin (TOB): R = >2 mg/L, S = ≤2 mg/L; Chloramphenicol (CHL): no breakpoints are described*

*** One or more loci were unidentifiable from sequencing data, thus sequence type was indeterminable*

4.2.4 Genetic markers of niche adaption

4.2.4.1 Association with isolation source

The genetic complement of a strain provides it with the means to survive in a given niche. Therefore, strain genotype, including both gene presence or absence and allelic variation, could be associated with the niche the bacterium was isolated from. Considering this, strains were characterised as belonging to a clinical or environmental niche based on their source of isolation. Strains found to be clonally linked were removed to keep only one copy resulting in 1,089 (72.7%) clinical strains and 408 (27.3%) environmental strains in the dataset. Metadata concerning the genetic characteristic of these strains was input into Pyseer to identify markers which would connect these strains to their isolation source.

4.2.4.1.1 Markers identified using gene presence and absence

Taking the gene presence and absence found in the *P. aeruginosa* pangenome, Pyseer identified 3,331 genes associated with either a clinical or environmental niche with four of these genes showing a significant association ($p \leq 1.00 \times 10^{-6}$) (Table 4-9). Based on the lrt p-value, the *group_16294* gene was shown to have the greatest association with a niche with a total of 153 strains found to contain the gene (Table 4-9). The distribution of strains containing this gene was found to be split 66.6% from a clinical niche and 33.3% from an environmental niche. When comparing this to the distribution of the overall dataset the gene appeared to be skewed in the direction of an environmental niche. The gene identified encoded glutamine synthetase which catalyses the production of glutamate and ammonia to glutamine and plays a key role in nitrogen metabolism (292).

The second highest association based on gene presence and absence was seen for *group_14964* (Table 4-9). The distribution of strains containing this gene was split 67.2% towards a clinical niche and 32.8% towards an environmental niche. Therefore, when compared to the number

of clinical and environmental strains in the whole dataset, the distribution of strains containing the variant was skewed toward an association with the environmental niche. The amino acid sequence of the *group_14964* gene appeared to match *oprD* in the PAO1 type strain, however this was only partially as a portion of the sequence at the C-terminal end of the gene was missing (Figure 4-16). Additionally, multiple SNPs were present in the regions coding for external loops which help to form the overall protein structure of the porin (76). Thus, it is likely that *group_14964* encodes a non-functional OprD-like porin.

The remining genes found to show an association were *group_14040* and *intI1* which were seen in 77 and 529 strains respectively (Table 4-9). The distribution of strains containing the *group_14040* variant was divided 69,9% clinical to 30.1% environmental and the distribution in *intI1* was split 92.3% toward a clinical niche and 7.7% to an environmental niche. Therefore, the *group_14040* gene, which encoded a hypothetical protein, showed a distribution skewed towards a clinical niche. However further characterisation of the gene is required to ascertain the functions of its product and therefore its influence in niche adaption. The *intI1* gene appeared to have a greater association to a clinical niche identified encodes an integrase IntI1.

Overall, four genes were identified with a skew towards either a clinical or environmental niche based on the gene presence and absence. Three of the genes were skewed in the direction of environmental niche and had links to nitrogen metabolism, cell permeability, and the transfer of genetic elements. All of these have the potential to provide advantages in a niche however the extent of this advantage is currently unclear.

Table 4-9: Genes with a significant association toward a clinical or environmental niche. Significance (p ≤ 1.00 × 10^{-6}) was determined using the lrt p-value identified using Pyseer with the number of strains containing the gene also described. The clinical and environmental percentage is calculated as the number of strains from a clinical or environmental niche which contain the gene against the total number of strains that contain the gene.

Gene	p-value	Clinical (%)	Environment (%)	Core1	Core2	Core3	Core4	Core5	Core6	Core7	Core8	Core9	Core10	Core11	Core12	Core13	Core14	Core15	Core16	Core17	Core18	Core19	Core20	Core21	Core22	Core23	Total number of strains
group_16294	1.04×10^{-10}	62.1	37.9	7	3	6	14	7	4	10	5	2	6	8	5	12	5	4	11	15	11	243	14	49	20	9	470
group_14964 – oprD	8.58×10^{-8}	95.3	4.7	0	1	0	2	3	1	0	2	0	2	3	2	2	2	0	4	2	2	60	4	8	5	0	106
group_14040-hypothetical protein	3.83×10^{-7}	69.9	30.1	8	26	15	35	15	14	15	21	10	15	26	17	24	20	33	31	41	46	515	37	119	33	39	1156
intI1	4.85×10^{-7}	92.3	7.7	4	6	7	31	0	2	2	14	0	2	2	0	0	5	13	14	7	2	34	15	17	10	7	195

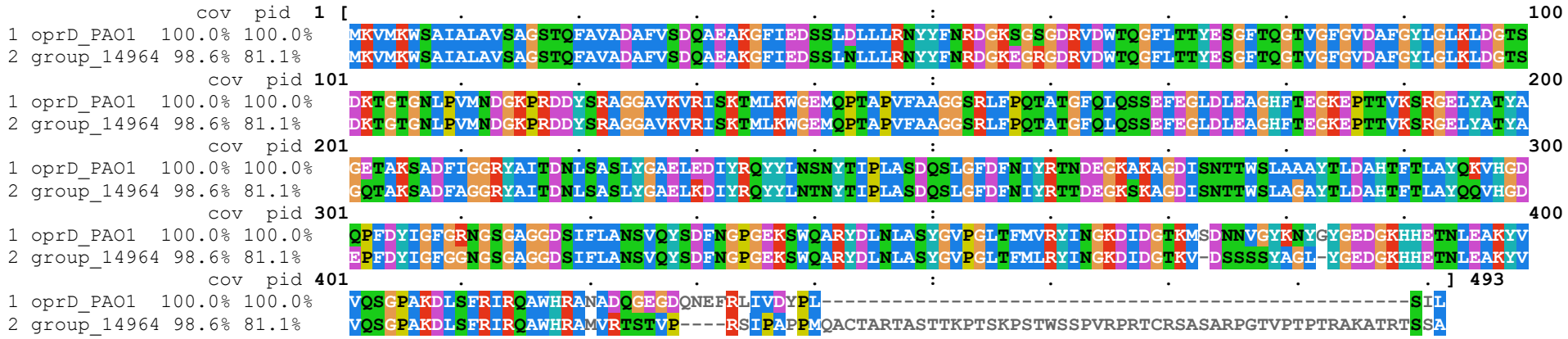

Figure 4-16: Amino acid alignment of the oprD *gene in PAO1 with the* group_14964 – oprD *variant. Amino acids are aligned with Mafft (188) and coloured according to amino acid physiochemical property (Blue = hydrophobic, Red = Positive charge, Magenta = Negative charge, Green = Polar, Pink = Cysteines, Orange = Glycines, Yellow = Prolines, Cyan = Aromatic, and White = Unconserved).*

4.2.4.1.2 Markers identified using single nucleotide polymorphisms

When considering SNPs present amongst clinical and environmental niches 86,685 were identified when looking at SNPs called against the PAO1 strain, four of these were shown to have significant *p*-values making them SNPs of interest (Table 4-10 and Figure 4-17).

The SNP showing the greatest association resulted in a synonymous mutation in *gyrA* which encodes the DNA gyrase subunit A (Table 4-10). The SNP was present 93% of clinical and 7% of environmental strains from a total of 298 strains containing the SNP, indicating the SNP was more prevalent in a clinical niche. Mutations in *gyrA* at position 83 (Thr83Ile) have previously been shown to induce resistant phenotypes, however the SNP identified was synonymous (293). Therefore, the function of the DNA gyrase subunit A is unlikely to be altered and cause a resistant phenotype. Furthermore, the mutation resulted in the codon used to code for threonine to change from ACG to ACA. Instead of this change altering the codon used to one that is more or less optimal than its predecessor, it brought the codon one step closer to one coding for isoleucine (AUA) (Table 4-1).

The second and third most significant SNPs corresponded to the 166 bp intergenic region located between the *birA* and *PA2204_04417* in the PAO1 genome (Table 4-10). The SNPs were distributed amongst the clinical and environmental strains 66.6% to 33.4% and 68% to 32% respectively. Thus, both SNPs showed a greater skew to an environmental niche. The *PA2204_04417* gene, which is downstream of the intergenic region, encodes the 5S rRNA protein. Together, 5S rRNA, 23S rRNA, and 16S rRNA form the bacterial ribosome which is required for protein synthesis.

Table 4-10: SNPs with a significant association toward a clinical or environmental niche. Significance (p ≤ 1.00 × 10^{-6}) was determined using the lrt p-value identified using Pyseer with the number of strains containing the gene also described. The clinical and environmental percentage is calculated as the number of strains from a clinical or environmental niche which contain the SNP against the total number of strains that contain the SNP. SNPs were identified using the PAO1 type strain as a reference for calling and have been underlined in the table.

Gene (position)**	Mutation	Reference	Query*	Effect*	p-value	Clinical (%)	Environment (%)	Core1	Core2	Core3	Core4	Core5	Core6	Core7	Core8	Core9	Core10	Core11	Core12	Core13	Core14	Core15	Core16	Core17	Core18	Core19	Core20	Core21	Core22	Core23	Total number of strains
gyrA ← (3558951)	Thr83Thr	AC<u>G</u>	AC<u>A</u>	Synonymous	1.42 ×10^{-13}	93.0	7.0	4	2	12	33	4	3	3	20	0	4	4	3	1	3	18	22	9	3	75	19	34	13	9	298
birA ← / ← 5SrRNA (4788503)		T	C	Intergenic	2.23 ×10^{-12}	66.6	33.4	11	19	16	0	16	15	13	19	10	14	26	21	23	15	32	18	40	25	424	33	90	37	2	919
birA ← / ← 5SrRNA (4788526)		A	G	Intergenic	3.10 ×10^{-9}	68.0	32.0	10	19	15	35	16	14	0	18	7	14	24	21	23	15	31	18	38	41	390	29	93	33	2	906
thrB → / ← nrdJb (6188038)		C	G	Intergenic	1.37 ×10^{-7}	70.1	29.9	12	22	17	37	18	15	9	25	4	19	0	22	30	18	0	26	44	27	580	45	118	37	39	1164

** Indicates whether the codon is optimal*

***Arrows indicate the direction of the gene and the position of the SNP relative to the PAO1 reference strain is displayed in parentheses.*

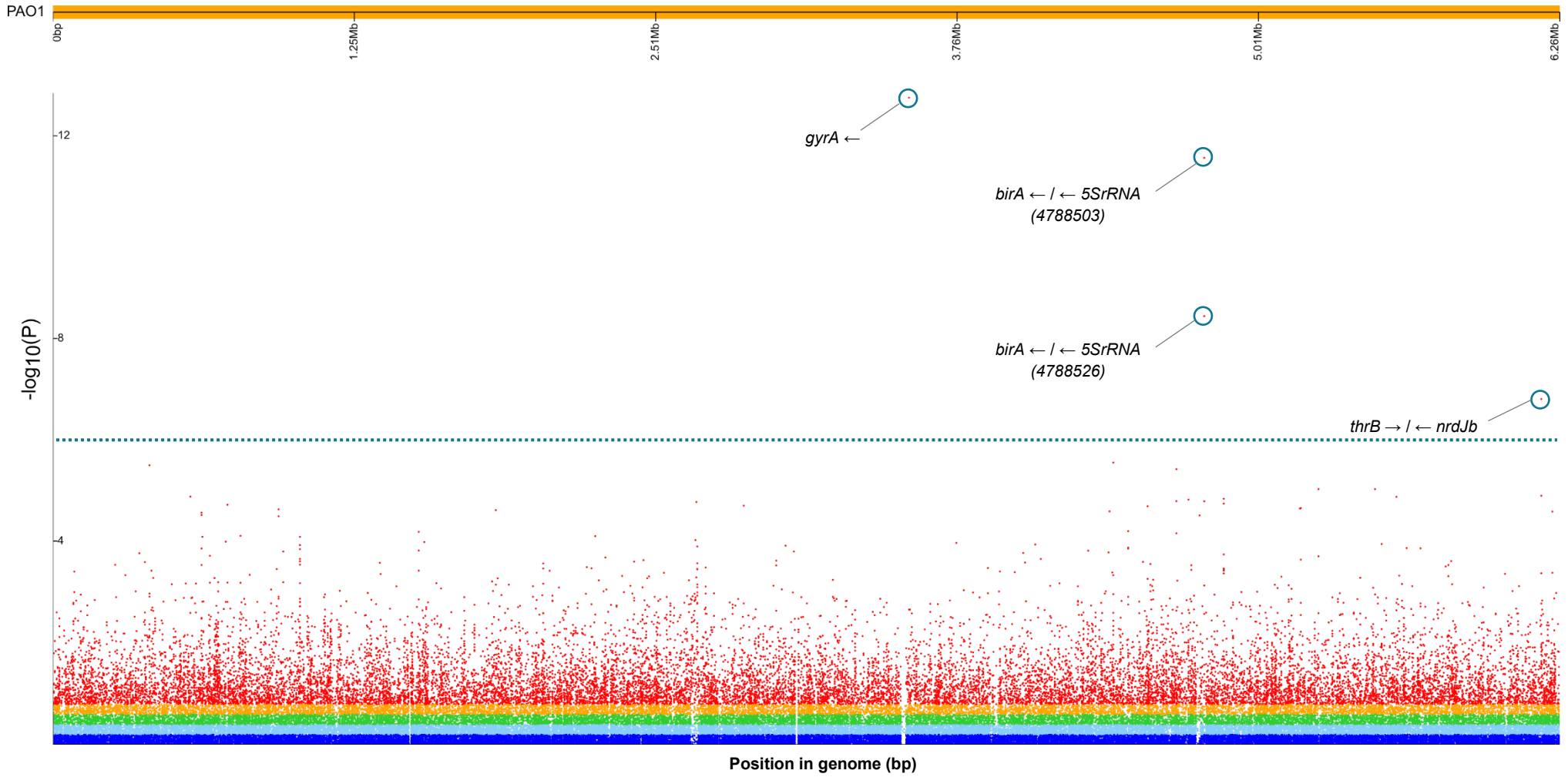

Figure 4-17: Manhattan plot of SNPs against the PAO1 type strain identified using the isolation source. The y-axis depicts -log10(P) where P is the lrt-pvalue identified using Pyseer (214). The dashed blue line indicates the point at which the p*-value is 1.00 × 10^{-6} and annotated with the gene or region effected by the SNP. Image is visualised in Phandango (434).*

The remaining SNP identified was also found in an intergenic region that was 289 bp long and located in between the *thrB* and *nrdJb* genes (Table 4-10). Of all the SNPs identified with a significant association towards a niche, this SNP was identified in 1,164 strains making it the most prevalent SNP with a significant association to niche. The distribution amongst the strains containing it was divided 70.1% to a clinical niche and 29.9% to an environmental niche indicating it was slightly skewed towards a clinical niche. The *thrB* and *nrdJb* genes found either side of the intergenic region containing the SNP encode for a homoserine kinase (ThrB) and the class II (cobalamin-dependent) ribonucleotide reductase subunit (NrdJb) respectively. As both genes are read in the direction of the intergenic region the SNP is located downstream of both genes.

To summarise, four SNPs, called against the PAO1 type strain, were identified in *P. aeruginosa* pangenome with an association towards a niche. Though these SNPs were found to be significant, they were not universally present in all the strains and nor were they found in all the clinical or environmental niches. Hence none of the SNPs identified were able to serve as a general biomarker to indicate whether an individual strain originated from a clinical or environmental niche. However, the fact that an association was seen in at least a portion of the strains indicates that some SNPs may indicate adaptation to clinical or environmental niches.

4.2.4.2 Association with niche-specific lineages

Each of the core groups contain a mixture of clinical and environmental strains, however determining whether an isolate truly originates from a clinical or environmental source is complex. As a result, this can mask or amplify the signals from biomarkers that are representative of adaption to a niche. To overcome this, the core groups showing associations towards clinical and environmental niches (Table 4-6) were isolated from the dataset in order to identify biomarkers in the niche-specific lineages without the noise of the other core groups without clinical or environmental associations. This smaller subset contained 102 strains

belonging to a clinical group and 93 strains belonging to an environmental group. This was then input into Pyseer to determine the genetic markers of strains which align to either a clinical or environmental lineage.

4.2.4.2.1 Markers identified from gene presence and absence

Using the genes present and absent in strains belonging to clinically or environmentally associated lineages, 2,918 genes of interest were identified, with five determined to be statistically significant ($p \leq 1.00 \times 10^{-6}$) (Table 4-11). Two of the genes identified, *group_8633* and *group_12273* were hypothetical proteins with no described function. Both genes showed a higher prevalence in clinical lineages with 97.5% of strains containing *group_8633* and 94.1% of strains containing *group_12273* being from clinical lineages. In both cases two strains from environmental lineages were also found to contain the genes. Within the clinical lineages, the genes identified were not found universally across the clinically associated core groups, with *group_8633* found only in Core4 and Core16, and *group_12273* found solely in Core16.

The remaining genes identified were: *group_8976*, a cysteine hydrolase; *group_16540*, and MFS transporter; and *group_12508*, a transcriptional regulator. Each gene was present in all Core4, Core13, and Core16 strains. As Core4 and Core16 were found to be clinical lineages, the distribution of strains containing the genes was skewed towards the clinical lineages and split 71.3% clinical and 28.7% environmental. The products of the genes were a cysteine hydrolase encoded by *group_8976*, a major facilitator superfamily (MFS) transporter encoded by *group_16540*, and a GntR family transcriptional regulator encoded by *group_12508.*

Overall, the five genes identified all showed an association in the direction of the clinical lineages. However, the genes identified were not present across all the clinical core groups. This was mainly due to the Core8 group which did not contain any of the genes identified.

Additionally, the genes were all present in at least one of the environmental core groups. Hence, the genes identified were not required by *P. aeruginosa* for adaption to a clinical niche nor were they unique to a niche.

Table 4-11: Genes with a significant association within niche specific clades. Significance ($p \leq 1.00 \times 10^{-6}$) was determined using the lrt p-value identified using Pyseer with the number of strains containing the gene also described. The clinical and environmental percentage is calculated as the number of strains from a clinical or environmental lineage containing the gene against the total number of strains containing the gene. Core groups are highlighted red if belonging to a clinical niche and green if belonging to an environmental lineage.

Gene	Product	p-value	Clinical (%)	Environment (%)	Core4	Core8	Core16	Core9	Core13	Core18	Total number of strains
group_8633	Hypothetical protein	3.43×10^{-10}	97.5	2.5	45	0	32	1	0	1	79
group_8976	Cysteine hydrolase	1.39×10^{-9}	71.3	28.7	45	0	32	0	31	0	108
group_16540	MFS transporter	1.39×10^{-9}	71.3	28.7	45	0	32	0	31	0	108
group_12508	GntR family transcriptional regulator	1.39×10^{-9}	71.3	28.7	45	0	32	0	31	0	108
group_12273	Hypothetical protein	3.35×10^{-8}	94.1	5.9	0	0	32	0	0	2	34

4.2.4.2.2 Markers identified using single nucleotide polymorphisms

Based on SNPs called against the PAO1 type strain, 1,294 SNPS were identified as showing significance with either a clinical or environmental lineage (Table 4-12). Due to the large number of SNPs identified (1,294), only SNPs where $p \leq 1.00 \times 10^{-20}$ were taken forward for further analysis. The dashed yellow line in Figure 4-18 represents the point at which $p = 1.00 \times 10^{-20}$.

Table 4-12: The 13 SNPs with the greatest significant association to a niche specific clade. Significance ($p \leq 1.00 \times 10^{-6}$) was determined using the lrt p-value identified using Pyseer with the number of strains containing the gene also described. The clinical and environmental percentage is calculated as the number of strains from a clinical or environmental lineage that contain the SNP against the total number of strains containing the SNP. SNPs were identified using the PAO1 type strain as a reference for calling and are underlined in the table.

Gene (position)**	Mutation	Reference codon*	Query codon*	Effect	p-value	Clinical (%)	Environment (%)	Core4	Core8	Core16	Core9	Core13	Core18	Total number of strains
PA_02698 → (2961328)	Glu46Glu	GA<u>G</u>	GA<u>A</u>*	Synonymous	1.13×10^{-40}	35.2	64.8	45	0	0	0	31	52	128
PA_04157 ← (4510007)	Pro257Pro	CC<u>G</u>*	CC<u>A</u>	Synonymous	3.06×10^{-35}	87.5	12.5	45	25	0	10	0	0	80
ccmB → (1603008)	Glu44Glu	GA<u>G</u>	GA<u>A</u>*	Synonymous	7.87×10^{-31}	23.1	76.9	0	25	0	0	31	52	108
PA_03444 → (3728929)	Arg230Arg	CG<u>U</u>*	CG<u>C</u>	Synonymous	7.87×10^{-31}	23.1	76.9	0	25	0	0	31	52	108
cntI ← (5427504)	Asp61Asp	GA<u>C</u>	GA<u>U</u>	Synonymous	7.87×10^{-31}	88.5	11.5	45	0	32	10	0	0	87
PA_02980 ← (3231002)	Gln57Gln	CA<u>G</u>	CA<u>A</u>	Synonymous	6.49×10^{-24}	96.6	3.4	0	25	32	0	0	2	59
PA_00279 ← (308052)	Pro347Pro	CC<u>A</u>	CC<u>G</u>*	Synonymous	1.58×10^{-23}	86.4	13.6	45	25	0	10	0	1	81
PA_04640 ← (5029352)	Ala299Ala	GC<u>U</u>*	GC<u>C</u>	Synonymous	1.58×10^{-23}	86.4	13.6	45	25	0	10	0	1	81
rmd ← (6144163)	Thr277Ala	<u>A</u>CC*	<u>G</u>CC	Missense	1.58×10^{-23}	86.4	13.6	45	25	0	10	0	1	81

pcaH → *(175357)*	Thr195Thr	ACC*	ACU	Synonymous	1.82×10^{-22}	96.6	3.4	0	25	32	0	0	2	59
PA_05700 → *(6206318)*	Ser9Ser	UCC*	UCU*	Synonymous	1.02×10^{-21}	96.6	3.4	0	25	32	0	0	2	59
trxA ← *(5900398)*	Leu100Leu	CUG*	UUG	Synonymous	1.65×10^{-21}	90.5	9.5	0	25	32	0	0	6	63
fdhD → *(5832440)*	Gly180Glu	GGG	GAG	Missense	2.59×10^{-21}	81.4	18.6	0	25	32	10	0	3	70

** Indicates whether the codon is optimal*

***Arrows indicate the direction of the gene and the position of the SNP relative to the PAO1 reference strain is displayed in parentheses.*

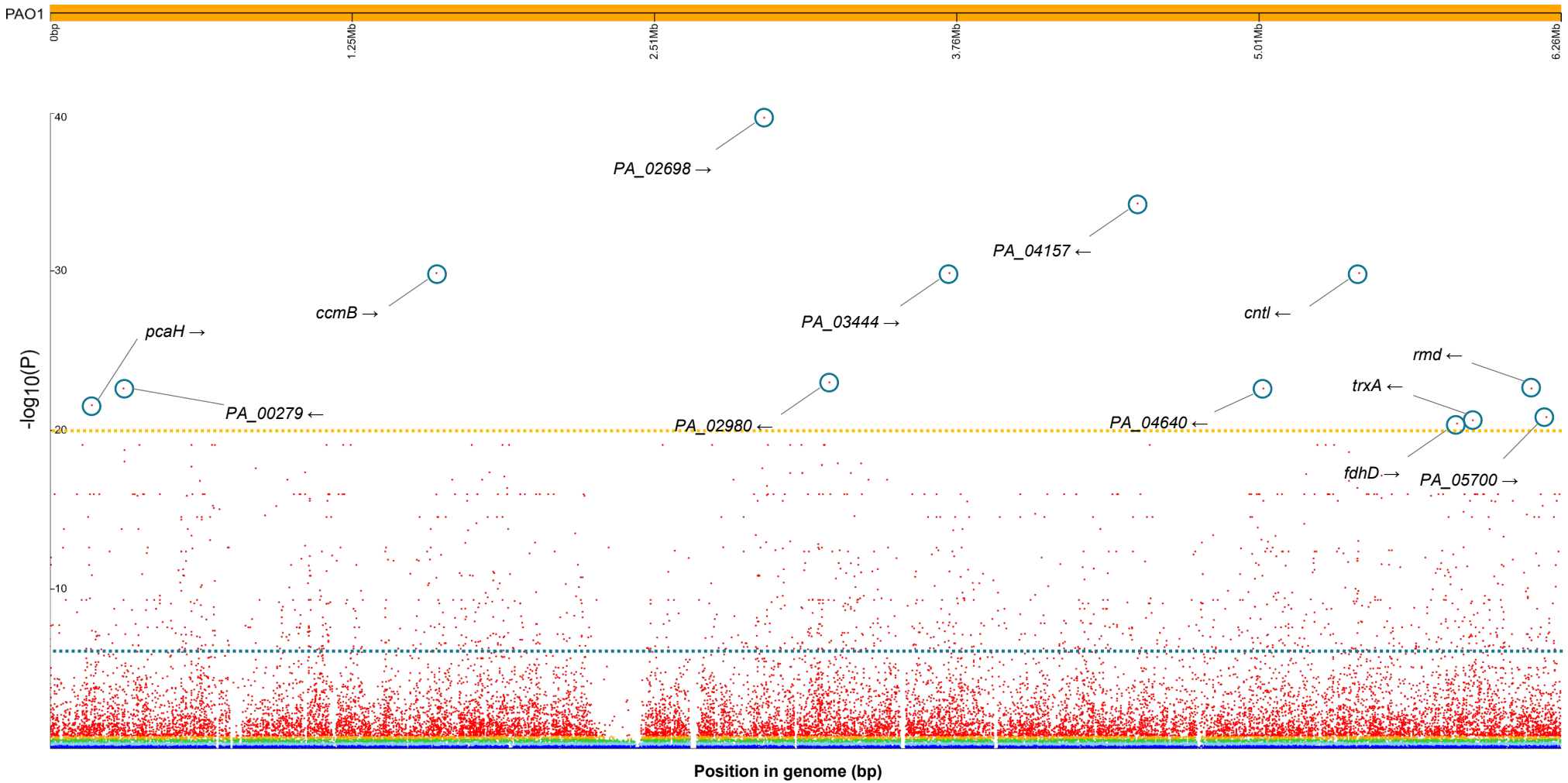

Figure 4-18: Plot of SNPs against the PAO1 type strain identified using clinical and environment lineages. The y-axis depicts -log10(P) where P is the lrt-pvalue identified using Pyseer (214). The dashed blue line indicates the point at which the p-value is 1.00×10^{-6} and the dashed yellow line indicates when the p-value is 1.00×10^{-20}. The genes effected by the SNP are circled and annotated with the gene name. Image is visualised in Phandango (434).

As depicted in Figure 4-18, 13 of the SNPs identified had a p-value above the yellow line ($p \leq 1.00 \times 10^{-20}$) and are listed in Table 4-12. When considering the effect of these SNPs only two were found to cause missense mutations that alter the resulting transcribed product (Table 4-12). These SNPs were found in the *rmd* and *fdhD* genes which encode GDP-4-keto-6-deoxy-D-mannose reductase and formate dehydrogenase accessory protein FdhD. The remaining 11 SNPs all resulted in synonymous mutations (Table 4-12). Whilst these SNPs did not necessarily alter the amino acid, changes were seen in the codon used. In some cases, the optimal codons were affected which could alter translational efficiency, gene expression, and potentially the protein function.

The SNP showing the greatest association with a niche was detected at Glu46Glu in the *PA_02698* gene which encodes an arginyltransferase. Of the strains containing the SNP, 64.8% belonged to environmental core groups and thus linking the SNP to an environmental lineage. All strains present in the Core4, Core13, and Core18 groups contained the SNP with strains in the other groups not containing the SNP at all. However, the SNP resulted in a synonymous change and the function of the gene was likely unchanged. Whilst the function of the gene appears unchanged, the codon used at amino acid position 46 coding for glutamic acid changed to GAA, which is the more optimal codon for the amino acid (Table 4-1).

The SNP resulting in the Pro257Pro mutation was identified in *PA_04157* which encodes a protein kinase. Of the strains containing the SNP, the bias was skewed towards the clinical lineages with 87.5% of strains containing the SNP being linked to clinical core groups. Specifically, the core groups containing the SNP were Core4, Core8, Core9. Therefore, the association of the SNP in significant core groups was focussed to two clinical core groups and one environmental group. The specific SNP resulted in a synonymous mutation that is unlikely to affect the overall structure of the protein kinase, however the codon for proline changed from the more optimal CCG to the less optimal CCA (Table 4-1).

The SNPs seen in *ccmB* and *PA_03444*, were present in all strains belonging to Core8, Core13, and Core16. The genes encoded for a heme exporter protein CcmB and a metal dependent hydrolase respectively. As both Core 13 and Core18 were associated with an environmental niche the overall distribution between strains was skewed 76.9% in the direction of an environmental niche. Hence, the SNPs seen in *ccmB* and *PA_03444* appeared to identify some environmental lineages with the caveat of also being able to identity one of the clinical core groups. Both SNPs resulted in synonymous changes in the protein however *ccmB* changed the codon coding for glutamic acid from a less optimal GAG to a more optimal GAA and *PA_03444* changed from the more optimal CGU to the less optimal CGC codon for arginine (Table 4-1).

The SNP present in the *cntl* gene encoding pseudopaline biosynthesis protein CntL was found in 88.5% of strains belonging to the clinical group which contained the SNP. Though associated with a clinical lineage the SNP was only present in the Core4 and Core16 clinical groups with the Core8 group not showing any presence of the SNP. In addition to the Core4 and Core16 clinical group, the SNP was also present in all strains from the Core9 group. Thus, the SNP was present in all the same strains as the SNP present in *PA_04157.* The SNP itself resulted in a synonymous change at position 230 of the amino acid sequence. The amino acid at this position was aspartic acid which has no preferred codon and so it could not be determined if the mutations had any benefit to the strains containing it (Table 4-1).

The SNP in *PA_02980*, which encodes a LysR family transcriptional regulator, was present in all strains belonging to the clinical groups Core8 and Core16 with an additional two SNPs present in Core18 skewing the distribution 96.6% in the direction of a clinical niche. It should be noted that while an association with a clinical niche was seen, only 55.9% of strains belonging to a clinical group contained the SNPs. Hence the SNP does not appear to be a marker of all clinical strains. As with the SNP seen in the *cntl* gene, the amino acid effected by the SNP,

glutamine, had no preferred codon and so it is unclear if the SNP alters fitness in the strain (Table 4-1).

The next three SNPs detected in the *PA_00279*, *PA_04640,* and *rmd* genes were associated with the clinical niche with 86.4% of strains containing the SNP belonging to clinical groups. The genes encode an MFS transporter, a HAMP domain-containing histidine kinase, and a GDP-4-keto-6-deoxy-D-mannose reductase. As with the SNPs identified in *PA_04157* and *cntl,* the SNPs seen in the genes were present in all strains from the Core4, Core8, and Core9 groups. In contrast to *PA_04157* and *cntl,* one strain from the Core18 group was also found to contain the three SNPs described. Both the *PA_00279* and *PA_04640* genes developed synonymous mutations which resulted in changes to the codon used. In *PA_00279*, the amino acid effected was proline, and the change in the codon moved in the direction of the more optimal codon (from CCA to CCG) (Table 4-1). In contrast, the *PA_04640* gene showed the reverse where the synonymous mutation changed the alanine codon from one that was more optimal to one that is less (Table 4-1). In the case of the SNP present in *rmd,* the resulting effect of this SNP was a missense mutation leading to Thr277Ala change (Table 4-12). Figure 4-19 illustrates the mutation in terms of an amino acid alignment between the sequence present in the PAO1 type strain and the PA64 belonging to Core8.

The SNPs identified in the *pcaH* and *PA_05700* were present in all strains that were part of the clinical Core8 and Core16 groups (Table 4-12). Additionally, two strains belonging to the environmental group Core18 were found for each SNP though these were not found to be the same strains. This brought the overall distribution of strains containing the SNP to skew towards a clinical niche with 96.6% of the strain belonging to a clinical group. This distribution was similar to the one seen in the SNP present in *PA_02980*. Hence, as with the SNP in *PA_02980*, the SNPs seen here were associated with only two of the clinical lineages but could not fully identify all strains belonging to the clinical group. The amino acid effected by the SNP in *pcaH*

was threonine which experienced a change from a more to less optimal codon (Table 4-1). The SNP in the *PA_05700* gene corresponded to a codon for serine, the mutation resulting in a change from UCC to UCU, both of which are considered optimal (Table 4-1). Therefore, it unclear if the change in codon provided any benefit to the strain.

The next SNP identified generated a synonymous mutation in the *trxA* gene. Like the previous SNPs seen in *PA_02980, pcaH,* and *PA_05700*, this SNP was found in all Core8 and Core16 groups, however in contrast to the previously mentioned SNPs, this SNP was present in six strains belonging to Core18. Hence, the overall distribution of this SNP in the strains which contain it is skewed 90.5% towards the clinical niche. This SNP was not able to identify all strains belonging to a clinical lineage despite its association with the niche. The amino acid effected in the *trxA* gene was leucine whose codon changed from the more optimal CUG codon to the less optimal UUG (Table 4-1).

Finally, the SNP seen in *fdhD* was associated with a clinical niche with 81.4% of strains containing the SNP belonging to a clinical group. As with the previously mentioned SNPs in *PA_02980*, *pcaH*, *PA_05700*, and *trxA*, the SNP was present in all strains belonging to the clinical Core8 and Core16 groups. Furthermore, the SNP was also present in all strains belonging to the environmental Core9 group as well as three strains belonging to the Core18 group. Hence the SNP was seen across multiple core groups regardless of whether the group was clinical or environmental, however the skew was in favour of the clinical niche. This SNP altered the amino acid sequence resulting in Gly180Glu mutation which is depicted in Figure 4-20.

Overall, for each SNP associated with a clinical niche, at least one clinically-associated core group did not contain the SNP. This was also seen for SNPs associated with an environmental niche. Furthermore, the SNPs showing association with a clinical niche were also identified in strains associated with an environmental niche and the converse was also true for SNPs

associated with an environmental niche. Hence, none of the SNPs identified represented all strains belonging to a clinical or environmental core group. Instead, the SNPs represent skews towards certain genetically-related strains in certain core groups. Most of the SNPs identified resulted in synonymous mutations. As many of these synonymous mutations resulted in changes to the codon expressed it is possible that selection is occurring in terms of the codons used. Therefore, it is possible these SNPs represents the selection of codons which may indicate the codon preferences by clinical and environmental *P. aeruginosa* strains, however further analysis of the effects caused by the synonymous codon changes is required.

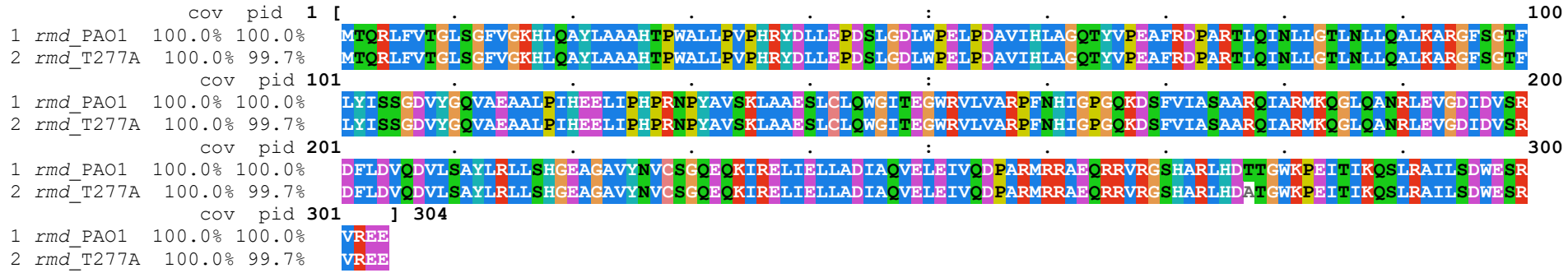

Figure 4-19: Alignment of the rmd *gene in PAO1 with the* rmd *gene contained in the Core8 strain, PA64. Alignment was generated with Mafft (188)and amino acid are coloured according to their physiochemical property. (Blue = hydrophobic, Red = Positive charge, Magenta = Negative charge, Green = Polar, Pink = Cysteines, Orange = Glycines, Yellow = Prolines, Cyan = Aromatic, and White = Unconserved).*

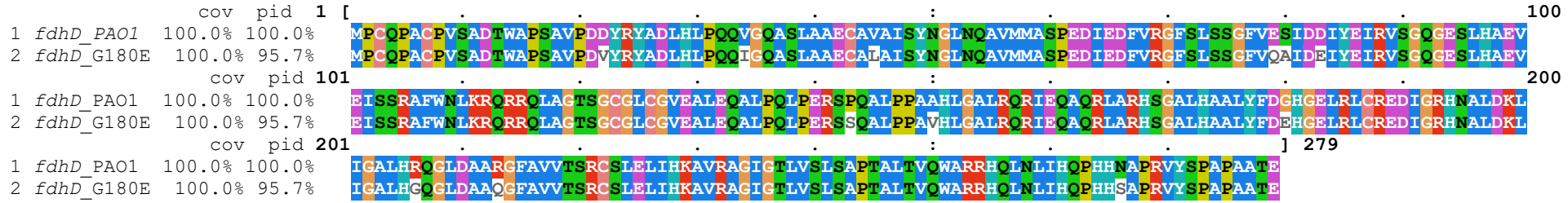

Figure 4-20: Alignment of the fdfD *gene in PAO1 with the* fdhD *gene contained in the Core8 strain, PA64. Alignment was generated with Mafft (188)and amino acid are coloured according to their physiochemical property. (Blue = hydrophobic, Red = Positive charge, Magenta = Negative charge, Green = Polar, Pink = Cysteines, Orange = Glycines, Yellow = Prolines, Cyan = Aromatic, and White = Unconserved).*

4.2.5 Niche adaption within the accessory genome

To assess the prevalence of niche adaption beyond the core lineages, Mandrake (217) was used to analyse the accessory genomes, which represents around 97.0% of the *P. aeruginosa* pangenome. The gene presence and absence output from Panaroo was used alongside genomic sketches of the strains to visualise spatial clustering of strains based on the accessory genes. From this, 103 clusters were identified and assigned numbers as accessory groups (Table 4-13). There were far more accessory groups than the clustering of the core genome in Section 4.2.2.2 which produced 23 core groups. As shown in Figure 4-21, some core groups were linked with multiple accessory groups, while other core groups were almost exclusively linked with a single accessory group, and some accessory groups were linked with multiple core groups. In some instances, the multiple core groups contained by an accessory group were spread across the core SNP phylogeny (Figure 4-8) displaying the ability of the accessory genome to bring strains closer together in term of their overall genetic compliment. This was particularly evident in the largest accessory group, Accessory102, which was comprised of core groups belonging to both the Group 1 (Core10, Core13, Core15, Core16, Core19, Core22, and Core23) and Group 2 (Core1, Core8, Core18, and Core21) major clades (Figure 4-1).

In contrast to the distribution of clinical strains across the core groups, the distributions of clinical strains across the accessory groups found only one accessory group, Accessory47(Fisher's exact test, $p = 0.038$), to have a significant association ($p \leq 0.05$) with a clinical niche once the *p*-values were corrected (Table 4-13). Accessory47 consisted of 36 strains with 22 being from the clinically associated Core8 and the remaining 14 strains were from the Core21 group which showed no association toward a niche (Table 4-6). Both Core8 and Core21 were part of the larger Group 2 clade (Figure 4-1) and so the accessory clustering appeared to group strains from similar core backgrounds in this instance (Figure 4-8). The Core8 group was also found to be associated with bacteraemia infections (Table 4-7) and so, association with bacteraemia infections in Accessory47 was also tested. This confirmed that

Accessory47 also had an association with strains from bacteraemia infections when compared against the distribution of bacteraemia isolates in the entire dataset (Fisher's exact test, $p \leq 0.001$). Despite not containing all the isolates in Core8, the predominant MLST type in Accessory47 was also ST 357 though this was localised to all but two of the isolates that were from Core8 (Appendix - Table 3). The remaining two isolates of Core8 contained within Accessory47 were ST 2592 and ST 3396, which were respectively single locus variants and double locus variants of ST 357. The remaining isolates belonged to other MLST types: ST 532, ST 773, and ST 1971 were not associated with any of the other epidemic high-risk clones (Appendix - Table 3). No other accessory groups were found to be associated with a niche due to the large number of clusters found which each contained a small number of strains.

Table 4-13: Fishers exact test comparing the proportion of clinical and environmental strains in each accessory group against the entire dataset. P-*values have been adjusted using the Benjamini-Hochberg correction with significant p-values (p ≤ 0.05) indicated in* ***bold****.*

Accessory group	Number of isolates	Percentage of clinical isolates	Adjusted p-value	Accessory group	Number of isolates	Percentage of clinical isolates	Adjusted p-value
Acessory1	10	30.00	0.318	*Acessory53*	7	71.43	1.000
Acessory2	21	66.67	0.928	*Acessory54*	22	50.00	0.238
Acessory3	7	71.43	1.088	*Acessory55*	2	0.00	0.385
Acessory4	14	85.71	1.103	*Acessory56*	2	50.00	0.991
Acessory5	48	77.08	0.941	*Acessory57*	3	100.00	0.990
Acessory6	43	88.37	0.231	*Acessory58*	5	80.00	1.000
Acessory7	4	75.00	1.000	*Acessory59*	4	50.00	1.070
Acessory8	5	60.00	0.950	*Acessory60*	3	66.67	1.000
Acessory9	3	100.00	0.990	*Acessory61*	24	70.83	1.156
Acessory10	8	75.00	1.000	*Acessory62*	2	50.00	0.991
Acessory11	38	86.84	0.404	*Acessory63*	8	75.00	1.000
Acessory12	9	77.78	1.000	*Acessory64*	5	80.00	1.000
Acessory13	2	50.00	0.991	*Acessory65*	14	64.29	1.084
Acessory14	26	92.31	0.231	*Acessory66*	6	66.67	0.967
Acessory15	23	56.52	0.464	*Acessory67*	3	66.67	1.000
Acessory16	19	73.68	1.000	*Acessory68*	14	64.29	1.084
Acessory17	5	100.00	1.068	*Acessory69*	10	80.00	1.000
Acessory18	3	100.00	0.990	*Acessory70*	5	80.00	1.000
Acessory19	4	25.00	0.394	*Acessory71*	4	100.00	0.948
Acessory20	3	100.00	0.990	*Acessory72*	7	57.14	1.055
Acessory21	2	100.00	1.000	*Acessory73*	3	100.00	0.990

Acessory22	37	78.38	0.987	*Acessory74*	18	50.00	0.398
Acessory23	4	50.00	1.070	*Acessory75*	2	50.00	0.991
Acessory24	4	100.00	0.979	*Acessory76*	11	90.91	1.053
Acessory25	5	60.00	0.950	*Acessory77*	3	66.67	1.000
Acessory26	3	0.00	0.234	*Acessory78*	80	83.75	0.293
Acessory27	5	80.00	1.000	*Acessory79*	16	87.50	1.036
Acessory28	5	80.00	1.000	*Acessory80*	6	83.33	1.000
Acessory29	4	100.00	0.948	*Acessory81*	19	89.47	0.550
Acessory30	10	30.00	0.212	*Acessory82*	2	0.00	0.385
Acessory31	6	83.33	1.000	*Acessory83*	15	100.00	0.324
Acessory32	82	73.17	1.000	*Acessory84*	15	93.33	0.412
Acessory33	2	50.00	0.991	*Acessory85*	4	75.00	1.000
Acessory34	2	50.00	0.991	*Acessory86*	77	72.73	1.000
Acessory35	14	78.57	1.101	*Acessory87*	3	100.00	0.990
Acessory36	3	33.33	0.786	*Acessory88*	7	57.14	1.055
Acessory37	3	0.00	0.234	*Acessory89*	3	66.67	1.000
Acessory38	11	63.64	1.039	*Acessory90*	9	88.89	1.124
Acessory39	28	82.14	1.115	*Acessory91*	2	50.00	0.991
Acessory40	3	66.67	1.000	*Acessory92*	5	60.00	0.950
Acessory41	3	0.00	0.234	*Acessory93*	56	69.64	0.952
Acessory42	3	66.67	1.000	*Acessory94*	2	0.00	0.385
Acessory43	5	60.00	0.950	*Acessory95*	19	63.16	1.123
Acessory44	9	88.89	1.124	*Acessory96*	13	61.54	1.089
Acessory45	3	66.67	1.000	*Acessory97*	54	64.81	0.886
Acessory46	13	61.54	1.089	*Acessory98*	5	80.00	1.000
Acessory47	36	97.22	**0.038**	*Acessory99*	5	80.00	1.000
Acessory48	9	77.78	1.000	*Acessory100*	2	100.00	1.000
Acessory49	19	47.37	0.337	*Acessory101*	3	66.67	1.000
Acessory50	16	62.50	1.110	*Acessory102*	187	65.78	0.349
Acessory51	3	100.00	0.990	*Acessory103*	30	63.33	1.146
Acessory52	24	95.83	0.232				

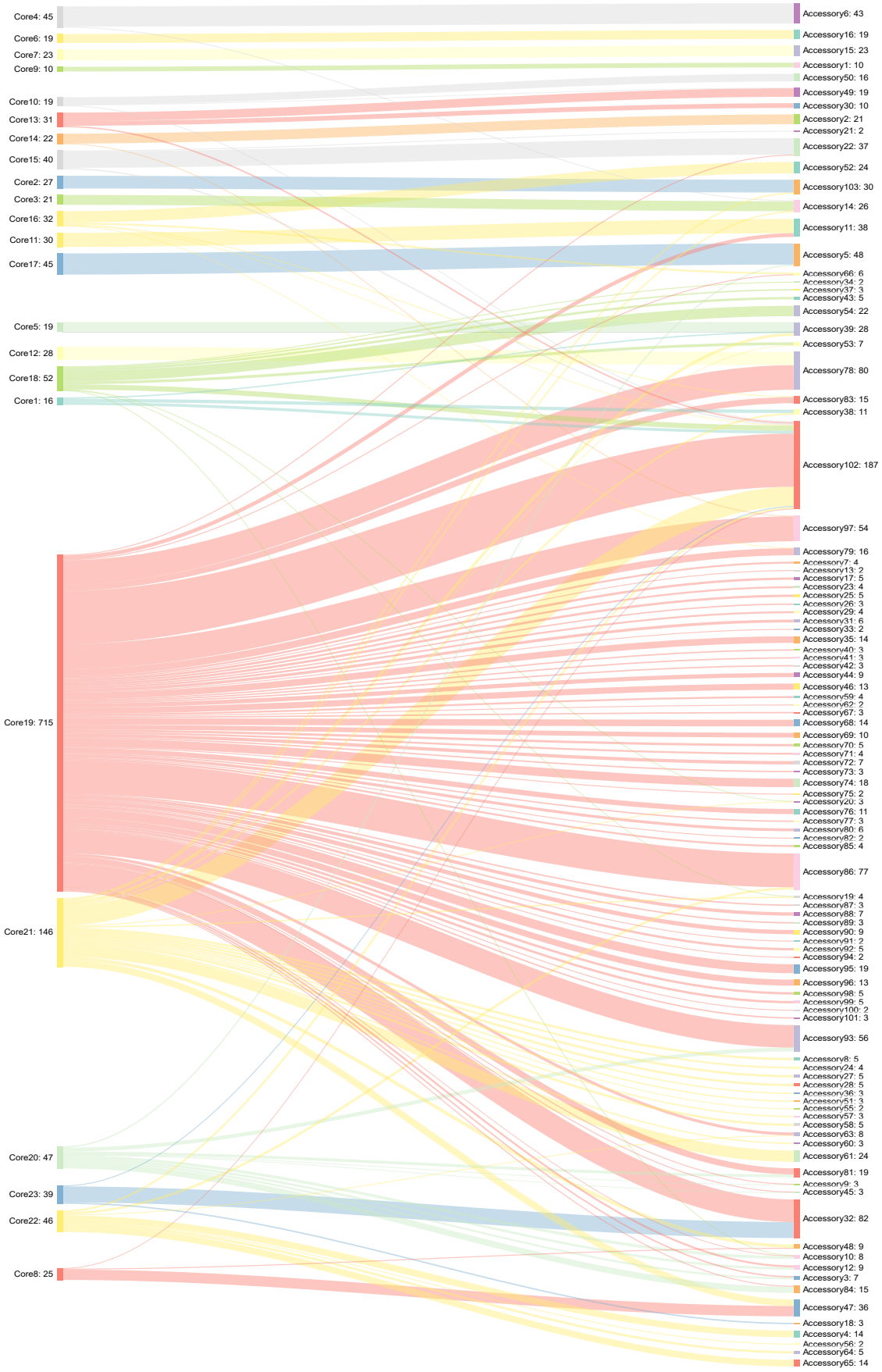

Figure 4-21: Sankey diagram showing dispersal of strain between core and accessory groups. Core groups were identified using level 1 of the Fastbaps hierarchical clustering of the core SNP alignment. Accessory groups were determined using clustering of the accessory genome with mandrake.

Visualisation of the clustering generated by mandrake is displayed in Figure 4-22 and Figure 4-23 with the core and accessory groups used to annotate the strains. Strains which are more closely related to each other would be expected to cluster together in tighter groups. Figure 4-22a illustrates the accessory clustering with the core groupings used to annotate the strains. In this image, the strains belonging to the same core groups appear close to one another, however the individual core group are not fully separated by their accessory groups. This is particularly true of the larger core groups (Core19 and Core21) which envelop other smaller groups in the core phylogeny (Figure 4-8). In terms of the accessory groups, in general strains which belonged to the accessory groups were found clustered together except for those belonging to Acessory102. This accessory group was the largest and consisted of 187 strains which were spread out across the plot in Figure 4-22b. In contrast, the 82 strains belonging to the second largest group, Acessory32, were found closer together in a tighter group (Figure 4-22b). The clinically associated Accessory47 group was also found to be present in a tight cluster, which could be expected to due to its inclusion of similar MLST types (Figure 4-22b).

Figure 4-23 shows the accessory clustering annotated with information on whether the strain belongs to a clinical or environmental niche. When considering the distribution of clinical and environmental strains across the accessory clustering, both clinical and environmental strains were dispersed across the clusters and were not focussed in specific areas (Figure 4-23a). However, when looking at the distribution of niche in terms of the core (Figure 4-23b) or accessory groupings (Figure 4-23c) the clustering shows the presence of more clinical and environmental leaning groups. This is more prevalent in the accessory clustering in Figure 4-23c due to the larger number of accessory groups that are prone to bias because of their smaller size.

Overall, clustering based on the accessory genome was able to identify more smaller groups, the large number of accessory groups identified prevented those skewed to a clinical or

environmental niche from being revealed. Additionally, the spatial clustering of groups with more clinical or environmental strains within were surrounded by other groups and not fully isolated.

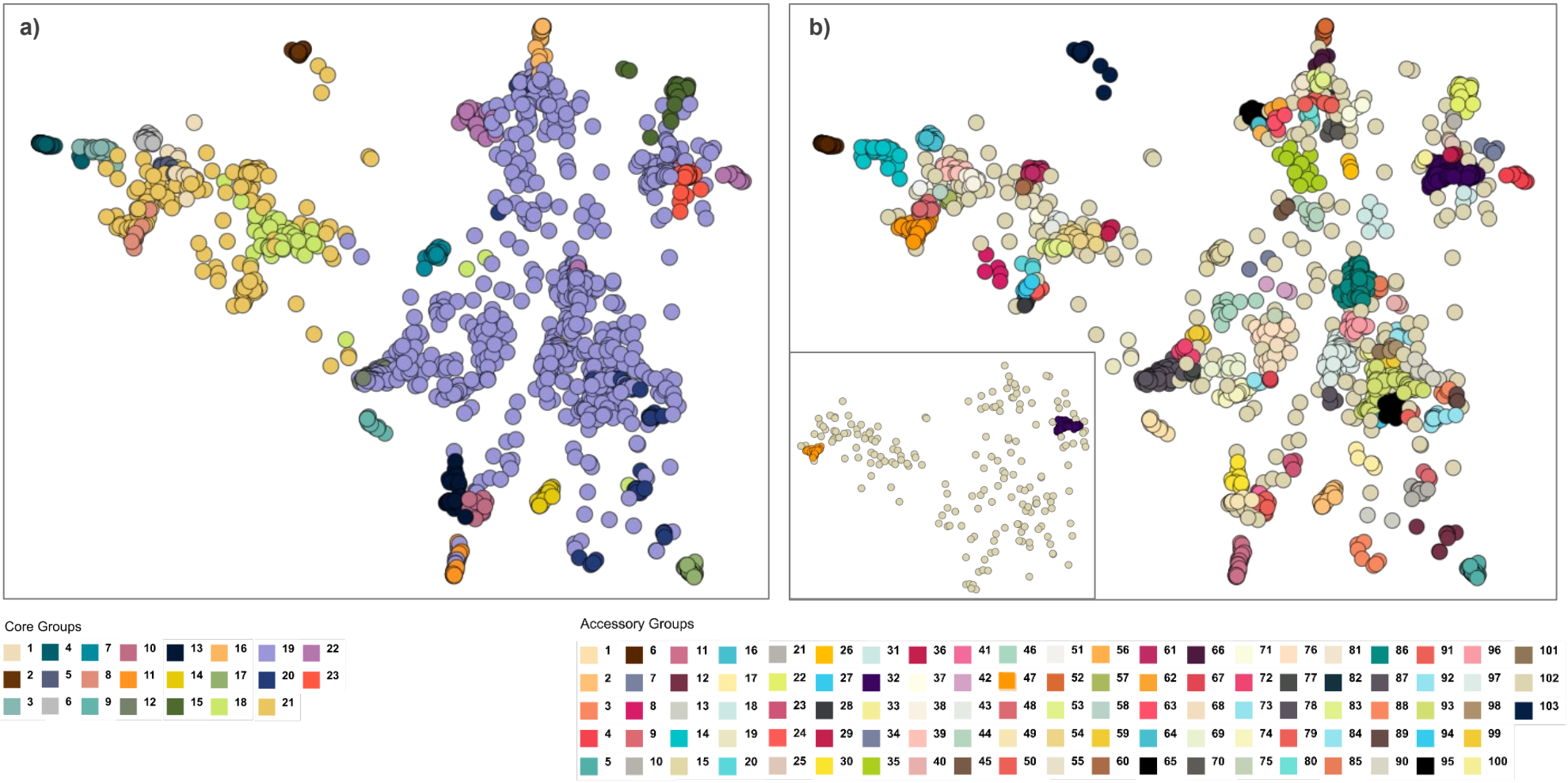

Figure 4-22: Spatial clustering of Pseudomonas aeruginosa *strains based on the accessory genome. Clustering was generated using Mandrake (217) with a) showing the strains annotated according to their core group and b) showing the strains annotated according to their accessory group which also depicts a subset of the clustering showing only Accessory 32, Acessory47, and Accessory102 in the inset box.*

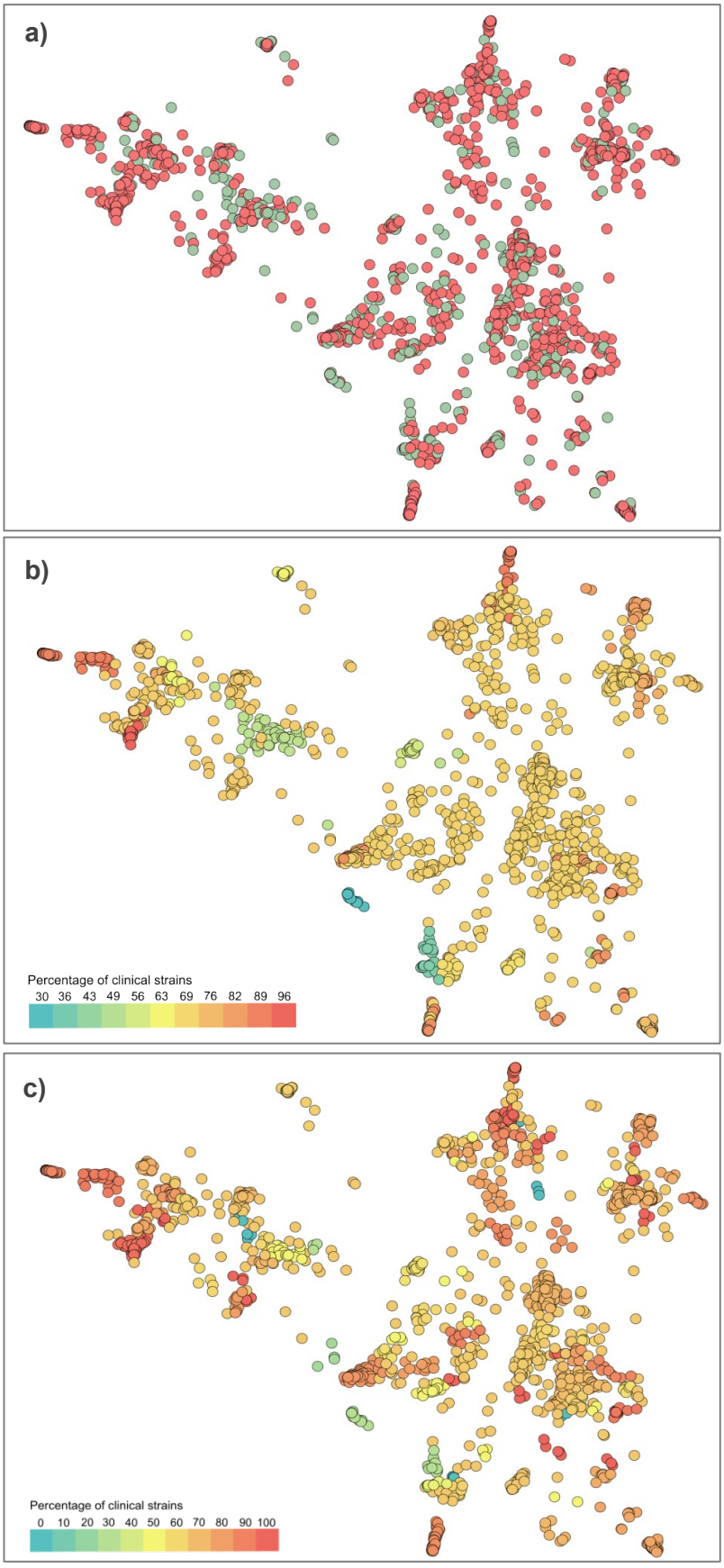

Figure 4-23: Distribution of clinical strains against spatial clustering based on the accessory genome. Clustering was determined by Mandrake (217) and strains have been annotated according to a) whether they are clinical or environmental, b) the percentage of clinical strains within its core group and c) the percentage of clinical strains within its accessory group.

4.3 Discussion

P. aeruginosa is often described as an organism with the ability to survive in both environmental and clinical niches. As the composition of these two difference niches is varied strains are required to adapt to be successful. The goal of this chapter was to examine the difference between *P. aeruginosa* strains from these two niches to determine ways to identify their origins.

4.3.1 Sourcing *Pseudomonas aeruginosa* from the environment

P. aeruginosa has been associated with many different types of clinical infections and as such strains are routinely isolated from clinical settings. As a result, the online repositories are heavily biased towards clinical strains, with low numbers of environmental strains. Furthermore, interest in environmental *P. aeruginosa* tends to favour environments which may potentially act as an infection source, for example hospital sinks. Therefore, the presence of true environmental *P. aeruginosa* in online repositories is low. In this study, only one environmental sample out of the 177 collected was found to be positive for *P. aeruginosa*. As each sampling location was selected based on their low human activity, it supports the finding by Crone *et al.* which indicated that the occurrence of *P. aeruginosa* in environments with non-intense human activity is low (86). This was further supported by the isolation of *P. aeruginosa* from thirteen water samples taken from public bathing sites which are regularly exposed to human interaction.

Environmental isolates are less likely to be in contact with antibiotics that are used in clinical settings. As a result, it could be expected that strains from environmental settings are susceptible to clinical antibiotics. Isolation of *P. aeruginosa* from UK public bathing sites is not routinely reported and therefore the resistance levels of *P. aeruginosa* in these environments has not been previously described. Despite this, *E. coli* isolated from public waters in the UK

have been shown to harbour bla_{CTX-M} providing the strains with antibiotic resistance phenotypes (294). Additionally, *P. aeruginosa* isolated from swimming pools, hot tubs, rivers, cave water, and water treatment plants have also shown resistance phenotypes (295-299). In this study, the environmental isolates obtained from water and swimming pools mostly showed susceptible phenotypes with a few strains showing resistance to one antibiotics class by being one doubling dilution over the resistance breakpoint (Table 4-8). This includes the isolates obtained from the Environment Agency (Strains PA2617 to PA2633) which were obtained from natural bathing sites. Currently, studies on natural bathing sites in the UK have not reported resistance levels of *P. aeruginosa* strains and so it is unclear whether antibiotic resistant phenotypes should be expected in *P. aeruginosa* isolated from these environments.

4.3.2 Lineages in the pangenome

Previously, the pangenome of *P. aeruginosa* was found to consist of 54,272 genes with 665 being defined as core genes due to their presence in all genomes (143). The approach in this study was slightly more lenient by taking the core genes as those present in at least 99% of the strains. This resulted in the detection of a larger core genome consisting of 4,482 genes but a smaller pangenome made of 38,840 genes. As the *P. aeruginosa* species is defined as an open genome, the addition of more strains should increase the size of the pangenome (248). However, the larger dataset set included in this study (2,611) compared to that used by Freschi *et al.* (1,311) did not conform to this. This is possibly due to variation in the annotation programmes used to label genes in the pangenomes as well as the inclusion of PA7-like strains by Freschi *et al.* despite their genetic variation.

Phylogenies based on MLST genes and core genome SNPs have shown the presence of clades that biased towards either clinical or environmental niches (Section 4.1.2). In comparison to the studies by Dean *et al.* and Gómez-Martínez *et al.* this study utilised a larger dataset allowing for the identification of 23 core groups. Of these, three showed a greater association towards

clinical niches (Core4, Core8, and Core16) and three showed a greater association towards an environmental niche (Core9, Core13, and Core18). This was similar to the studies by Dean *et al.* and Gómez-Martínez *et al.* which showed that smaller clades within the major clades described by *Freschi et al.* could be more biased to a specific niche (Dean and Wain, unpublished) (270). Additionally, this study also showed the core groups to have an association beyond a generic clinical niche by also displaying an association towards specific isolation sources. Some of these association could be linked to specific MLST types (Core4 with ST235 and Core8 with ST357). The MLST type ST235 has previously been linked with both MDR and extensively drug-resistant (XDR) profiles and has a wide distribution across five continents (300). The association of ST235 with Core4 appeared to be coupled with a link to urinary tract infections (Table 4-7and Figure 4-15), however clones of ST235 have been identified as causative agents of bacteraemia and respiratory infections (including from cystic fibrosis patients) in addition to urinary tract infections (301-304). Likewise, ST357, which is also associated with MDR infections, was associated with the Core8 group which was found to be associated with bacteraemia infections (Table 4-7and Figure 4-15). Despite this association, ST357 has been isolated from multiple sources including urinary tract, respiratory, and skin infections as well in bacteraemia infections (305-307). Hence, neither MLST type appears to be completely unique to a particular type of infection and the associations seen in this study require further investigation to confirm if they are genuine. As information on isolation source in this study was reliant on metadata available in public databases it is possible that not all infection sources are recorded or that some are over-represented.

The core phylogeny seen in the study (Figure 4-8) was visually similar to the one described by Freschi *et al.* (Figure 4-1) and therefore the smaller 23 core groups identified could be linked to the five major clades (143). When considering the dendrograms inferred from the gene flow and nucleotide diversity between the core groups they are organised according to the major clades described by Freschi *et al.* (Figure 4-10 and Figure 4-12). Hence, the gene flow and nucleotide diversity are more similar between core groups from the same major clade. In terms

of gene flow within the two largest clades, those belonging to Group 1 appeared to show higher levels of genes flow within the groups than within Group 2 or between Groups 1 and 2 (Figure 4-11). This is akin to the observation by Ozer *et al.* where phylogroup A, which corresponds to Group 1, showed higher recombination rates and therefore higher levels of gene flow then phylogroup B, which corresponds to Group 2 (248). In contrast to Group 1, Group 2 showed lower levels of gene flow than seen between Group 1 and 2, this was also observed by *Ozer et al.* which showed Group 2 isolates to have lower recombination rates relative to the rest of the *P. aeruginosa* population (248). The results in this study also show that the level of variation in gene flow within and between Groups 1 and 2 becomes smaller when Core18, Core19, Core20, Core21, and Core22 are excluded. Additionally, the exclusion of these groups alters the difference in gene flow seen both within and between Group 1 and Group 2. This indicates that the Core18, Core19, Core20, Core21, and Core22 alone are responsible for approximately half the gene flow observed within and between Group 1 and Group 2. The reasoning behind why Group 1 and Group 2 display differing levels of gene flow is not fully understood though Ozer *et al.* suggested the variation in gene flow between Group 1 and Group 2 may be due to the habitation of distinct ecological niches or through genetic barriers between the strains (248). As, the core groups identified in this study were also characterised to determine their association towards specific niches and sources the extent at which ecological niche is influencing gene flow could be investigated. Out of the five overlapping core groups with high levels of gene flow, Core18 was the only core group found to show an association towards niche by being more skewed towards environmental origins (Table 4-6) and more specifically towards water sources by both a Wald's and Fisher's test (Table 4-7). Both Core19 and Core21 showed associations with specific sources through the Wald's test, however as this did not translate to the Fisher's test this association was determined to be weak as evident in the Wald's test p-values closeness to significance ($p \leq 0.05$) (Table 4-7). Thus, it did not appear that higher levels of gene flow were associated to a specific niche or isolation source. Therefore, this study does not show evidence for the lack of gene flow or recombination being due to ecological

barriers between Group 1 and Group 2, however further investigation into the effects of the other core groups on geneflow is required to support this.

4.3.3 Biomarkers as representative of niche adaption

Genes aid in the adaption of bacteria to various niches and previous studies have shown the presence of specific genes in *P. aeruginosa* with different origins. (Section 4.1.3.1). In this study, genome-wide associations were used to identify genes and mutations within that are associated with specific niches. The results showed that four genes and four SNPs were associated with either a clinical or environmental lineage. Five genes and 1,294 SNPs were found to be associated with specific clinically or environmentally biased core groups. These genes and SNPs were implicated as biomarkers of niche adaption and the following sections describes those thought to assist in niche adaption in *P. aeruginosa.*

4.3.3.1 Genes identified as biomarkers based on gene presence and absence

The *group_16294* gene, which encodes glutamine synthetase, showed a greater association with the environmental niche. Previously, studies analysing glutamate synthetase concentration in *E. coli* have shown growth in nitrogen-deficient media results in greater levels of glutamate synthetase production when compared to medium with higher concentrations of glutamine and glucose (292, 308). As a result, it can be deduced that bacterium grown in nitrogen-deficient environments with low levels of glutamine would increase production of glutamate synthetase to produce glutamine. Thus, a variant containing functional glutamate synthetase would be advantageous in such conditions.

The *group_14964* gene encodes an OprD-like porin which enables basic amino acids to enter the cell (115). The OprD porin can be appropriated by carbapenem antibiotics and thus non-functional OprD can lead to increases in AMR due to a decrease in membrane permeability

(116). The gene was found to be skewed towards the direction of an environmental niche. As depicted in Figure 4-16, the *group_14964* gene only partially matches the *oprD* gene in PAO1 and is unlikely to encode a fully functional OprD porin. Considering environmental niches are less likely to contain carbapenem antibiotics than a clinical niche, it is unexpected for the *group_14964* gene cluster to be skewed towards an environmental niche.

The *int1* gene identified encodes a class I integron which is involved in enabling recombination and is associated with mobile genetic elements. In terms of environmental niches, *intI1* has been detected in sewage and manure-treated soil environments where mobile genetic elements are involved in the diversification of the bacterial populations present (309-311). It should be noted that *intI1* is also key in clinical niches where it is able to assist in the dissemination of antimicrobial resistance and virulence genes. Previous studies have shown *intI1* genes identified in clinically isolated strains to be distant from those with environmental origins and are situated within a single clade (Figure 4-24) (312). The *int1* gene cluster identified in this study were skewed in the direction of the clinical niche. Therefore, it could be expected for the *int1* gene identified in this study to also be part of a clade with clinical origins, however the diversity of *int1* in strains in this dataset needs to be investigated to confirm if this is also true in this study.

Figure 4-24: Phylogenetic tree depicting the relationship of class 1 integrons from clinical and environmental origins. Phylogeny is based in the, intI1 *sequence with strain originating from clinical settings indicated in* ***bold*** *(Tn21, Tn1696, R388 and R46). The tree is constructed with MEGA v3.1 using a neighbour-joining approach and the Kimuar 2-parameter model. Bootstrap scores are calculated from 1000 replicates with the scale bar represents substitutions per nucleotide position. Image is sourced from Figure 3 from Gillings* et al. *(312).*

Within the analysis focussing on only the significantly associated clinical and environmental groups the *group_8976* gene was identified as being associated with the clinical niche. The gene encodes a cysteine hydrolase however the exact function is unknown. Within *P. aeruginosa*, the YcaC cysteine hydrolase has been shown to be expressed during stress and related cysteine hydrolases from other species of bacteria have shown activity against antibiotics (313). If the product of *group_8976* also shows activity towards antibiotics under conditions of stress, its presence in clinical strains would be an interesting correlation. Therefore, further work on the *group_8976* gene is required to confirm if it provides resistance to antibiotics.

The *group_16540* and *group_12508* genes represent an MFS transporter and a GntR family transcriptional regulator. Both genes showed an association with a clinical niche and so it could be expected that these genes are beneficial in clinical environments. MFS transporters are efflux proteins which can export antibiotics out of the cell contributing to antimicrobial resistance and so could be present in clinical strains where it will be beneficial (314). The GntR family transcriptional regulator is involved in the regulation of gene expression. The exact genes effected by the product of *group_12508* is currently unknown and it is therefore unknown what impact their expression could have on survival in the clinical environment.

4.3.3.2 Single nucleotide polymorphisms identified as biomarkers

SNPs were identified in the intergenic region between *birA* and the 5S rRNA gene and were skewed in the direction of an environmental niche. Mutations in this specific region are not well studied and therefore the effects of the two SNPs identified in this region are unclear. The intergenic region between genes can acts as regulatory sites which can enhance or discourage gene expression. The 5S rRNA forms part of the ribosome and changes in gene expression could influence protein synthesis in the strains. Bacterial genomes can undergo structural genome rearrangement around sites containing ribosomal operons with the PAO1 strain showing four genome fragments that can be rearranged around the ribosomal operons (315). The genome structure can influence growth and gene expression in strains. Presently it is unclear what the influence of mutations in the intergenic regions preceding the 5S rRNA have on the ability of a bacterial genome to rearrange itself. Therefore, further investigation into the genome structure present in the strains containing the SNPs is required. This would require long read sequencing to cover the regions containing the ribosomal operon to ascertain the locations of the ribosomal operons and the number of copies present in the genome.

Another SNP was identified in the intergenic regions between the *thrB* and *nrdJb* genes which showed association towards a clinical niche. The two genes encode a homoserine kinase which

is involved in the production of L-threonine and the class II ribonucleotide reductase subunit NrdJb which is involved in the production of deoxyribonucleotides required for DNA synthesis and repair. Previous studies on L-threonine production have indicated that *thrB* mutants do not lead to threonine autotrophy and instead also requires a mutation in *thrH* (316, 317). It is unclear if *thrB* expression is affected by mutations in the intergenic regions following the gene and what the status of the *thrH* gene is. Hence, the effects of the SNP on the levels of L-threonine production is not known. In *P. aeruginosa,* the class II ribonucleotide reductase has been suggested to react to DNA damage and to be important for the pathogenicity of the strain (318, 319). Presently, it is unclear if the SNP in *nrdJb* gene alters the level of gene expression however its location downstream of the gene makes this unlikely.

The SNPs identified from the significant core groups which caused nonsynonymous changes where within the *rmd* and *fdhD* genes which were both associated with clinical niches. The *rmd* gene codes for GDP-4-keto-6-deoxy-D-mannose reductase which is involved in the synthesis of GDP-D-rhamnose (320). D-rhamnose itself involved in the production of the A-band O-polysaccharide structure of lipopolysaccharide, also known as the common polysaccharide antigen, which is implicated in chronic lung infections (321, 322). Whilst the impact of a mutation at position 277 of the *rmd* amino acid sequence has not previously been described, knockout mutations of *rmd* have prevented the production of the common polysaccharide antigen (323). Therefore, it is unclear if the production of the common polysaccharide antigen structure is compromised within the strains containing the Thr277Ala mutation. The *fdhD* gene encodes FdhD which is required to facilitate the transfer of sulphur required for formate dehydrogenase activity (324). Mutations at the 180th position of the amino acid sequence of *fdhD* have not previously been described in *P. aeruginosa.* However, Cys121Ala, His171Ala, and dual Cys121Ala/Cys124Ala mutations in the *fdhD* gene in *E. coli* have been shown to either reduce or prevent its activity respectively (324, 325). It should be noted that in the same study a Cys124Ala mutation in *fdhD* of *E. coli* did not show any difference in activity to the wildtype *fdhD* (324). Therefore, it appears mutations in specific locations in *fdhD* are required to alter

the activity of FdhD, whether these locations translate to the 180th position in *fdhD* from *P. aeruginosa* is currently unknown.

4.3.4 Influence of the accessory genome in niche adaption

Previously it has been indicated that the presence of specific accessory genome elements correlates with virulence in *Caenorhabditis elegans* and thus it could be expected that these genetic elements could act as biomarkers (326). To investigate this possibility in the context of *P. aeruginosa*, this study used clustering of the accessory genome which identified a larger number of accessory groups than core groups. These accessory groups were able to isolate smaller groups of strains leaning towards clinical or environmental origins, however statistical analysis was unable to confirm these associations due to the large number of accessory groups containing small numbers of isolates. Regardless of the lack of statistical significance in this study, the clustering was able to show that the accessory genome also plays an important role in niche adaptation.

Currently it is unclear if accessory genome elements are found across different core groups. Nevertheless, the strains belonging to specific accessory groups were not spread amongst multiple core groups indicating that the accessory genome was not shared between multiple core groups. This was also evident in the gene flow of the groups where little gene flow was observed between most of the core groups apart from a few larger overlapping groups. Due to this, it is unlikely there is a specific accessory genome element that can act as a general biomarker of niche adaption for all strains within the *P. aeruginosa* species. Thus, it appears the core genome was able to provide an initial adaption towards niche with the accessory genome providing the basis for the strain to become more specialised to the niche. This can be through increased or decreased virulence or changes in antibiotic tolerance (326-328).

Chapter 5 - The switch from environmental to clinical niche

5.1 Introduction

P. aeruginosa has been shown to colonise both clinical and environmental niches. Successful colonisation of the clinical niche requires genes involved in virulence and antimicrobial resistance. Previous laboratory experiments have shown that exposure to chloramphenicol can "switch-on" efflux pumps that are naturally present in the *P. aeruginosa* genome and lead to antibiotic resistant phenotypes (Correia *et al*., unpublished). Further mutations can then arise to "switch-off" the efflux pumps restoring the organism to an antibiotic susceptible phenotype. Thus, the inherent characteristics present in *P. aeruginosa* provide the guidelines for allowing the organism to adapt to various niches.

5.1.1 Regulation of the *mexEF-oprN* operon

The MexEF-OprN efflux pump plays a key role in AMR and has been associated with resistance to carbapenems and fluroquinolones (120, 127, 329-331). As with the other RND multidrug efflux pumps produced by *P. aeruginosa*, overexpression of the MexEF-OprN efflux pump and the subsequent efflux of antibiotics is the cause of the resistance phenotype (332). However, MexEF-OprN does not contribute to intrinsic antibiotic resistance in *P. aeruginosa* and is quiescent in wild type strains; instead, its role in resistance is part of an adaptive response (329, 332, 333). This adaptive response is due to mutations within the genes responsible for controlling the expression of the *mexEF-OprN* operon (334-337).

In wild type *P. aeruginosa* strains, the *mexS* gene encodes MexS, an oxidoreductase whose electrophilic substrate transforms MexT into its active format. Therefore, functional MexS acts as a suppressor to MexT by reducing the substrate (Figure 5-1) (338, 339). MexT is the

transcription activator for the *mexEF-oprN* operon and positively regulates the production of MexEF-OprN that will remove the electrophilic substrate from the cell (338, 340).

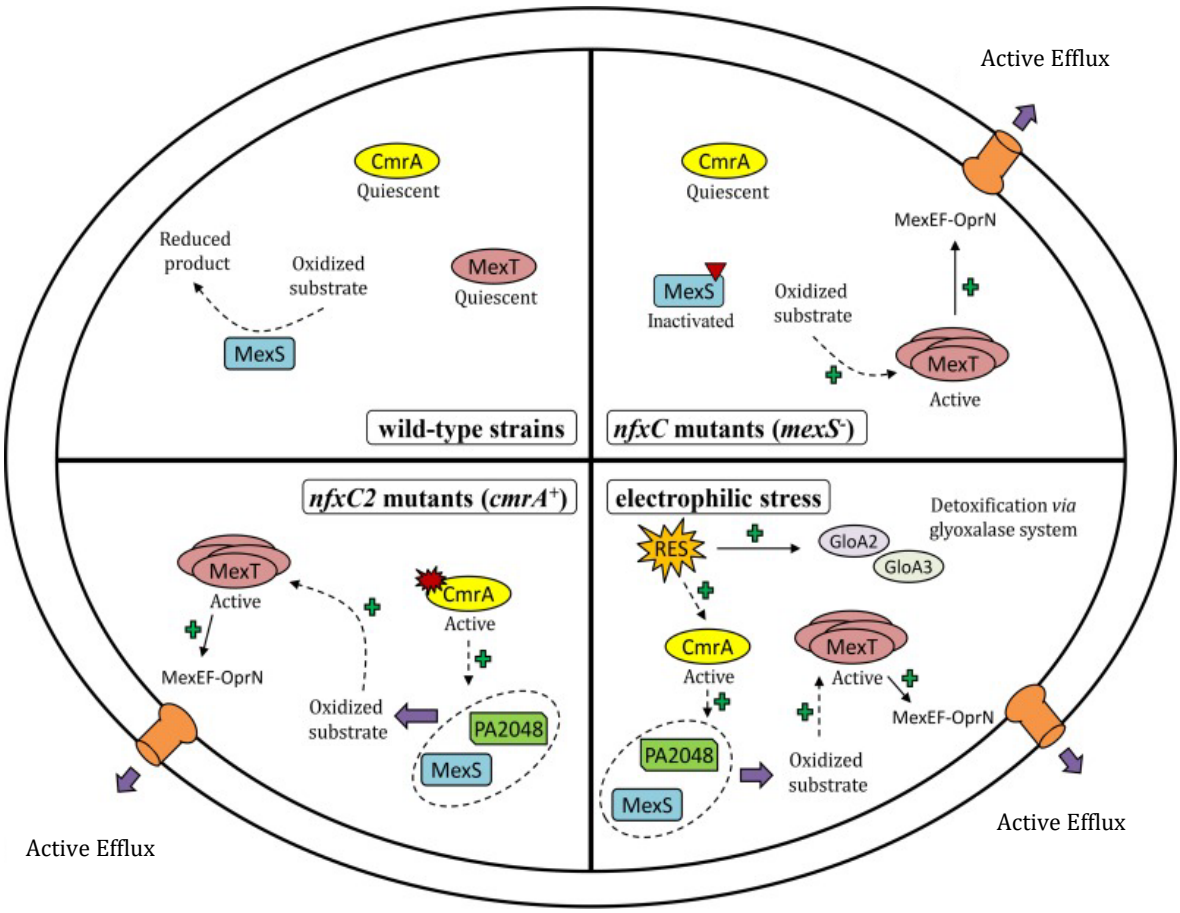

Figure 5-1: Regulation of the MexEF-OprN efflux pump. In wild-type strains MexS reduces its substrate preventing expression of mexEF-oprN. *In nfxC mutants, CmrA remains quiescent but with MexS inactive oxidised substrates build-up thus activating MexT and efflux. During electrophilic stress from the presence of reactive electrophilic species, CmrA becomes active leading PA2048 and MexS to interact which results in a build-up of oxidised substrates. In* nfxC2 *mutants CmrA is active and therefore it upregulates PA2048 resulting in MexT activation and thus active efflux through MexEF-OprN. Image is adapted from Juarez et al. (334)*

The interactions between MexS and MexT are vital to maintaining the balance of MexEF-OprN expression. Mutations in the *mexS* gene that impair its function result in the build-up of oxidised substrates that results in the continuous activation of MexT (336, 337). Alternatively, *P. aeruginosa* strains that originally coded inactive *mexS* and *mexT* genes can switch to an active

version of *mexT* that leads to the continuous expression of *mexT* (334, 335). The ensuing overexpression of MexEF-OprN causes the efflux of antibiotics, such as norfloxacin, chloramphenicol, and trimethoprim (329, 341). Moreover, active *mexT* causes the decreased expression of the OprD outer membrane porin and therefore prevents the entry of imipenem into the cell (340, 342). This highlights the ability of a single mutation to transform *P. aeruginosa* into the MDR *nfxC* phenotype. The *nfxC* mutants were defined by their spontaneous resistance to norfloxacin through mechanisms which had not previously been described (343). These mutant strains are characterised by their resistance to fluoroquinolones, imipenem, and chloramphenicol (343). Hence, *P. aeruginosa* strains that switch to this phenotype are suited to a clinical niche where they are likely to encounter fluroquinolone, imipenem, and chloramphenicol antibiotics.

5.1.1.1 Activation of MexEF-OprN through CmrA

As described by Juarez *et al*., CmrA is a regulator belonging to the AraC family that is quiescent in wild-type strains (344). It has been shown that when in an active state, CmrA is involved in the overexpression of the MexEF-OprN efflux pump. Activation of the regulator can occur through mutations in its gene sequence or the presence of reactive electrophilic species (344). When active, CmrA upregulates a putative quinol monooxygenase, PA2048, which is thought to act alongside MexS to generate oxidised substrates (Figure 5-1). As previously mentioned, the presence of oxidised substrates encourages the formation of active MexT that activates expression of the *mexEF-oprN* operon (338). Thus, the effects of active CmrA allows for the generation of a resistant phenotype like the phenotype caused by inactive MexS, whilst keeping MexS in its wildtype format. Thus, strains with mutations activating CmrA are labelled as *nfxC2* mutants (344).

5.1.2 Regulation of the *mexCD-oprJ* operon

The MexCD-OprJ efflux pump is another one of the RND efflux pumps contained by *P. aeruginosa.* Substrates of the MexCD-OprJ efflux pump includes fluroquinolone antibiotics, and as such activation of the efflux pump results in a fluroquinolone resistant phenotype. In strains expressing the MexCD-OprJ efflux pump, hypersusceptibility to beta-lactams and aminoglycosides is also seen which differentiates these strains from the *nfxC* mutants (345-347). In contrast to the *mexEF-oprN* operon, the *mexCD-oprJ* efflux pump is controlled solely by a transcriptional repressor, NfxB (345). In wildtype strains, the NfxB repressor binds to the inverted repeat upstream of the *mexC* gene which then prevents the transcription of *mexC* (Figure 5-2). Hence, mutations to *nfxB* prevent NfxB from being able to bind to the inverted repeat which allows transcription of the *mexCD-oprJ* operon (348, 349)(Figure 5-2). Once transcribed, the MexCD-OprJ becomes active and can export fluroquinolone antibiotics out of the cell. Additionally, it is hypothesised that the precursors that activate the transcriptional regulator of AmpC are exported from the cell by MexCD-OprJ resulting in hypersusceptibility to beta-lactams (350).

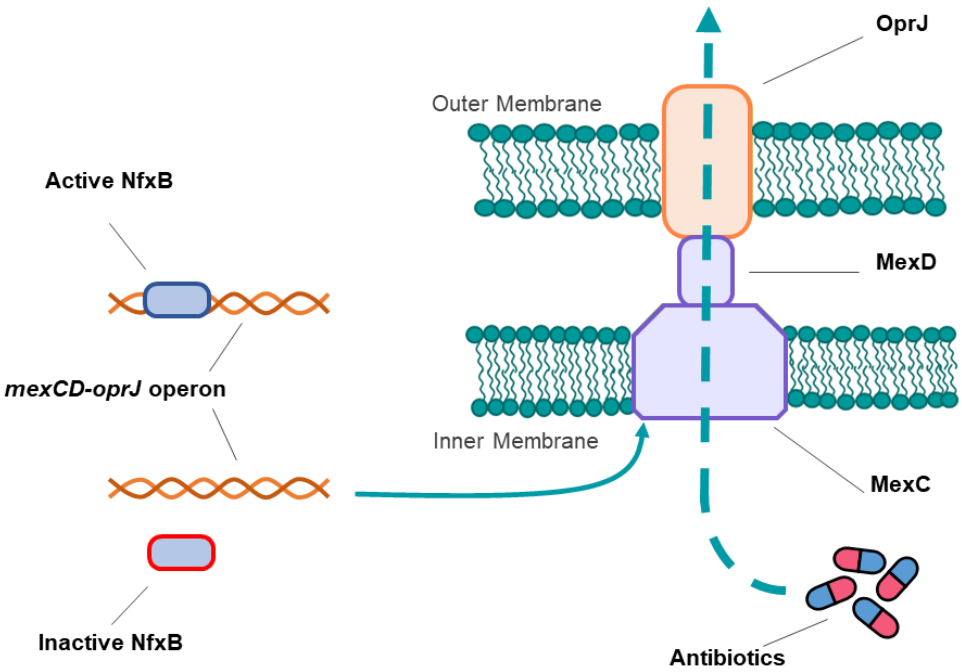

Figure 5-2: Regulation of the MexCD-OprJ efflux pump by NfxB. In its active format NfxB binds to the region upstream of the mexCD-oprJ *operon which prevents its transcription. Mutations that inactivate NfxB prevent this binding from occurring allowing transcription of the operon which in turn results in the efflux of fluoroquinolone antibiotics.*

5.1.3 Resistance through non-efflux mediated mechanisms

5.1.3.1 Chloramphenicol

Chloramphenicol inhibits protein synthesis by binding to the 50S subunit of the bacterial ribosome. In addition to efflux, resistance to chloramphenicol can also be achieved by the production of chloramphenicol acetyltransferase which modifies the antibiotic to prevents its ability to bind to the ribosome (351). The *catB* gene, which encodes chloramphenicol acetyltransferase, confers resistance to chloramphenicol in *P. aeruginosa* when highly expressed with specific mutations adding to resistance levels (352, 353). Additionally, a variant of the gene has also been found to be unique amongst the PA7-like cluster of strains (143, 249).

5.1.3.2 Ciprofloxacin

Resistance mechanisms to fluroquinolones, such as ciprofloxacin, in *P. aeruginosa* include mutations in the DNA replication machinery that is targeted by the antibiotic. This consist of DNA gyrase, encoded for by *gyrA* and *gyrB,* and DNA topoisomerase IV, encoded for by *parC,* and *parE.* Additionally, outer membrane porins that provide ciprofloxacin with a route of entry into the cell may also acquire mutations that prevent its entry into the cell. These specific mechanisms are described in Section 1.2.3.1.

5.1.4 Bacterial growth in human plasma

Plasma is one of the components that make up blood. It contains coagulants, plasma proteins, electrolytes, immunoglobulins, and other substances such as enzymes and nutrients (354). These can play key roles in the immune response to a bacterial infection through opsonisation and phagocytosis of bacteria, activation of complement which results in the formation of a major attack complex which leads to bacterial lysis, and the presence of proteins that can counteract attacks by bacteria and inhibit bacterial processes (355-359). Studies assessing the effect of human plasma on *S. aureus* have shown changes in cellular morphology, gene expression, and in some cases antimicrobial activity (360, 361). With regards to *P. aeruginosa,* studies have shown survival rates vary when the organism is grown in human blood or plasma (362). This can be influenced by the presence of specific genes and mutations that can enable *P. aeruginosa* persistence and evasion from plasma-mediated killing (363).

5.1.5 The cost of advantageous traits

As previously mentioned, epistasis plays a role in bacteria fitness (Section 1.1.9). Traits such as antimicrobial resistance mechanisms and virulence factors give bacterial species an advantage in specific niches such as during the course of infection. Nevertheless, the

production of these traits can be costly to the bacterial strain and result in decreased fitness in the absence of antimicrobial or host selection, as another trait is compromised (364).

Outer membrane porins can act as a point of entry for nutrients into the cell. However, porins also act as a point of entry for some antibiotics (365). When growing in the presence of an antibiotic, bacterial strains will reduce the permeability of their membrane to prevent antibiotic entry by reducing the levels of porin expression (366, 367). This reduced permeability decreases the amount of nutrients entering the cell and if there are no compensatory mutations, it will reduce the fitness of the bacteria in situations where the selective antibiotic pressure is removed (367). Additionally, the overexpression of efflux pumps which export toxins from the bacterial cell have been shown to reduce the production of various virulence factors (368). Hence, traits which provide the bacteria with an advantage in one specific niche experience a trade-off which negatively impacts their fitness within another niche.

5.1.6 Chapter aims

Considering the ability of *P. aeruginosa* to increase and decrease resistance to antibiotics, the aims of this chapter were to characterise the fitness of existing chloramphenicol exposed mutant strains along with their parent and revertant strains. Following this, evolution experiments will be used to reveal if similar mutations occur when strains are exposed to chloramphenicol or ciprofloxacin in media containing human plasma. The specific objectives covered by the section include:

1. Evolve environmental *P. aeruginosa* isolates under simulated clinical conditions to characterise the switch from the environment to a clinical setting.
2. Uncover the impact of mutations which alter tolerance to antibiotics on bacterial fitness.

5.2 Results

5.2.1 Growth of strains reverting to reduced chloramphenicol tolerance

Mutations to the suppressor of the MexEF-OprN efflux pump, *mexS*, prevent the suppression of the transcriptional activator, MexT, resulting in the continuous "switching-on" of the MexEF-OprN efflux pump which results in a phenotype with increased tolerance to chloramphenicol. Reversion to a more sensitive phenotype occurs through secondary mutations in *mexT*, preventing its activation and hence "switches-off" the efflux pump. To access the impact of mutations in *mexS* and *mexT*, we used strains containing variations of these mutations (Table 5-1) previously evolved under chloramphenicol selection (Section 2.1.4), alongside their ancestral parental strain to measure the bacterial growth rate to measure bacterial fitness. In this study, revertants are defined as strains which showed a reduction in their MIC when compared against the mutant. As revertants derived from strain A were created in BHI and revertants from strain B were derived from SSM9PR, the growth assays in the following section were performed in the media in which the reversion occurred.

Table 5-1: Minimum inhibitors concentration (MIC) of chloramphenicol for strains with mutations to the regulators of the mexEF-oprN *operon. Brain Heart Infusion (BHI) is a nutrient rich media and SSM9PR is a defined minimal media. MICs are reported as μg/ml.*

Strain		mexS mutation	mexT mutation	Growth media	
				BHI	SSM9PR
A	Parent	wildtype	wildtype	64	128
A1	Mutant	Phe273Leu	wildtype	>128	>128
A1.1	Revertant	absent	absent	32	32
A1.2	Revertant	absent	absent	32	32
A2	Mutant	Leu303fs	wildtype	>128	>128
A2.1	Revertant	Leu303fs	Ser155Asn	32	32
A2.2	Revertant	Leu303fs	Arg51fs	32	32
B	Parent	wildtype	wildtype	32	64
B3	Mutant	Ala27fs	wildtype	>128	>128
B3.1	Revertant	Ala27fs	Tyr191fs	32	32

Due to the absence of *mexS* and *mexT,* in the A1.1 and A1.2 revertant strains their raw sequences were aligned to the PAO1 genomes (NC_002516.2) along with the sequences of their respective parent and mutant. These alignments were visualised in IGB (Figure 5-3) which showed the presence of a large deletion in revertant A1.1 covering 68,646 bp and a smaller deletion in revertant A1.2 covering 16,806bp. In a few places, some short reads were found to align to the reference within these deleted regions, however this was suspected to be due to homology with areas elsewhere in the genome and so were not investigated further. Whilst the A1.1 deletion covered the entire *mexEF-oprN* operon the A1.2 only covered the operon up to the *mexE* gene. (Figure 5-3). Together the deletions between the two strains overlapped a region covering 7,000 bp which included hypothetical proteins, the Pseudomonas type III repressor gene C PtrC, probable transcriptional regulators, and the *mexEF-opr*N operon up to *mexE* (Table 5-2). This region is highlighted in red in Figure 5-3. An illustration of how this compares to the mutations seen in the *mexEF-oprN* operon of the other mutants and revertant strains is depicted in Figure 5-4.

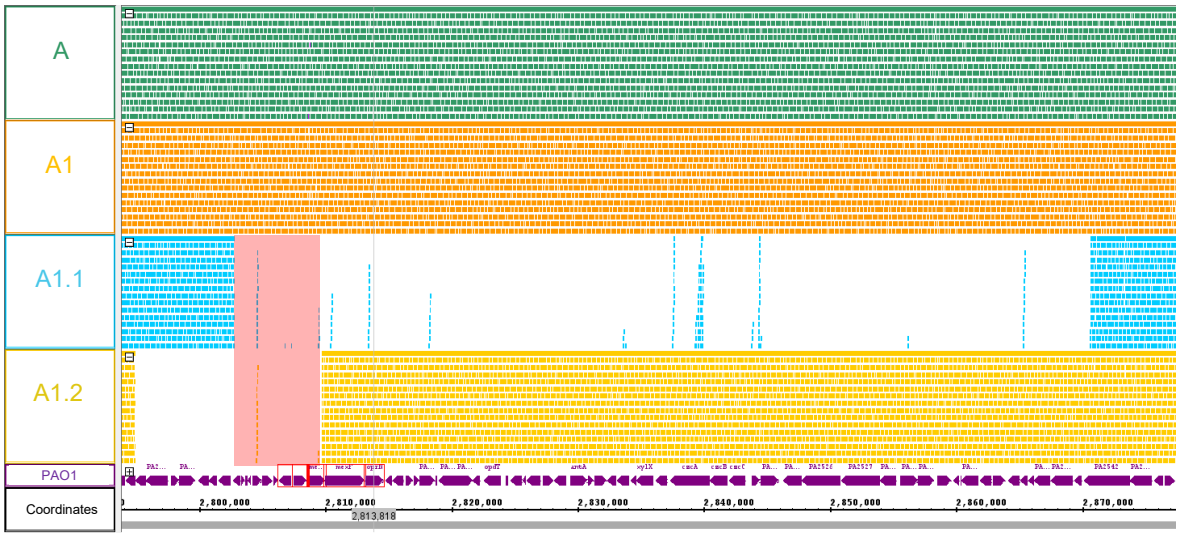

Figure 5-3: Alignment of the A1.1 and A1.2 revertants strains to the PAO1 type strain. Alignments are visualised in the integrated genome browser (IGB) with reads mapped to the PAO1 type strain (NC_002516.2) (221). For the purpose of visualisation, the stacking height is set to 15 with the reads of the parent in green, mutant in orange, revertant A1.1 in blue, and revertant A1.2 in yellow. Annotation of the PAO1 strain is depicted in purple with the mexEF-oprN *operon outlined by the red boxes. Highlighted in red is the deleted regions that overlaps between both A1.1 and A1.2 revertant strains.*

Table 5-2: Genes deleted by both the A1.1 and A1.2 revertant strains.

Gene	Product
PA2484	Hypothetical protein
PA2485	Hypothetical protein
ptrC	Pseudomonas type III repressor gene C, PtrC
PA2487	Probable transcriptional regulator
PA2488	Probable transcriptional regulator
PA2489	Probable transcriptional regulator
PA2490	Hypothetical protein
mexS	Oxidoreductase MexS
mexT	Transcriptional regulator MexT
mexE	RND multidrug efflux membrane fusion protein MexE precursor

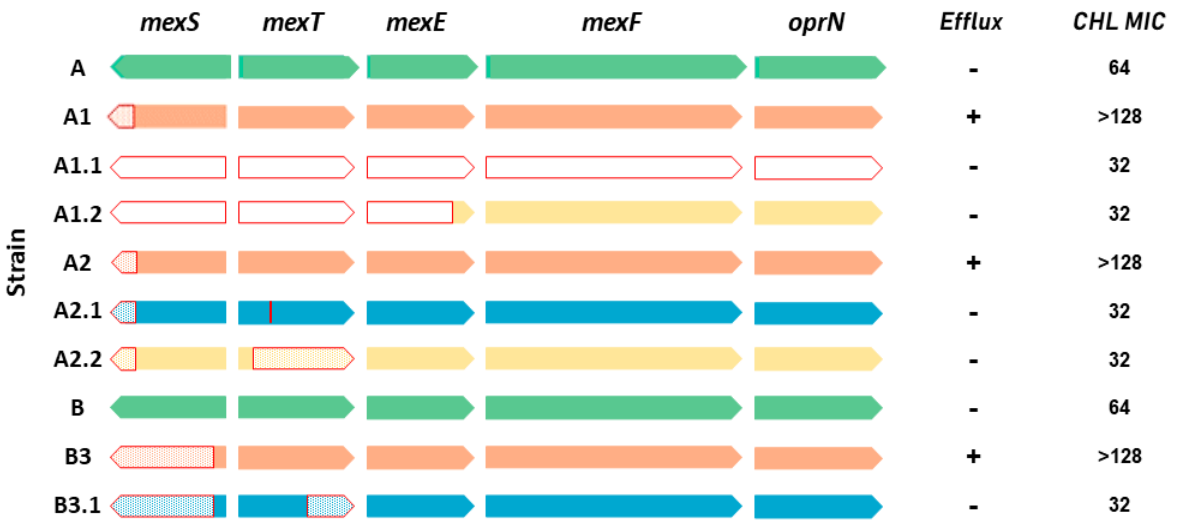

Figure 5-4: Illustration of mutations within the mexEF-oprN *operon (not to scale) of strains evolved in chloramphenicol. Parent strains are indicated in green, (A and B) resistant mutants in orange (A1, A2, and B3) and revertants in blue or yellow (A1.1, A1.2, A2.1, A2.2, and B3.1). SNPs are indicated by red lines, frameshifts are filled with a dotted pattern outlined in red, and larger deletions are blank also outlined in red. CHL MICs are taken as the MIC found in the broth the reversion occurred, this was BHI for strain A and SSM9PR for strain B.*

Bacterial growth was measured over 16 hours by OD_{600} in the presence and absence of a sub-inhibitory concentration of chloramphenicol (8μg/ml), determined as the concentrations two MIC doubling dilutions below the most sensitive strain (Table 5-1). Growth curves using the media in which reversion to the sensitive phenotype occurred (BHI for revertants A1.1, A1.2, A2.1, and A2.2, and SSM9PR for B3.1) are displayed in Figure 5-5.

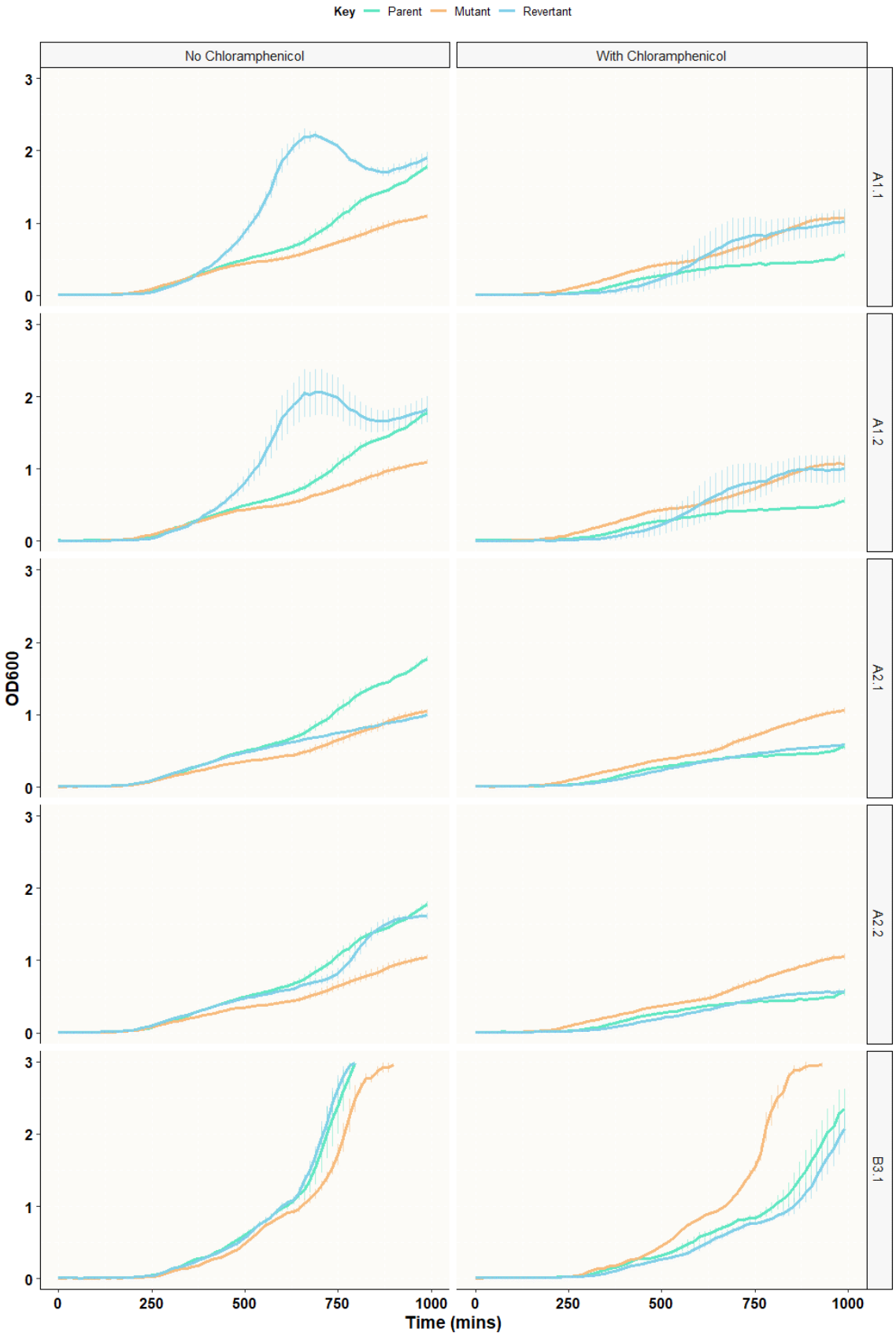

Figure 5-5: Bacterial growth curves of strains with varying mutations in mexS *and* mexT. *Growth is plotted as the mean absorbance at* OD_{600} *based on ten replicates, from two independent experiments with five replicates each, in the presence and absence of a sub-inhibitory concentration of chloramphenicol (8µg/ml). Curves are coloured according to strain; with green representing the wild-type parent, orange for mutants with mexS mutations and blue for the revertant strains with double* mexS/mexT *mutations. Error bars represent the 95% confidence intervals.*

Bacterial growth curves were analysed with Growthcurver (206) to produce metrics for the growth rate and the area under the curve in order to assess bacterial fitness (Appendix - Table 18). Growth rate was used as a proxy for estimating relative fitness, calculated as described in Section 2.5.7.2, with Figure 5-6 displaying data for relative fitness and the area under the bacterial growth curves generated from ten replicates from two independent experiments with five replicates each.

The largest increase in relative fitness over the parental strain (*Mdn* = 1.01, *IQR* = 0.16) was seen in revertants A1.1 (*Mdn* = 3.92, *IQR* = 0.26; Mann-Whitney test *U* = 100, *p* = 0.000274) and A1.2 (*Mdn* = 3.72, *IQR* = 0.32; *U* = 100, *p* = 0.000274) when grown in the absence of chloramphenicol. Both A1.1 and A1.2 contained deletions of both *mexS* and *mexT* in addition to a partial or complete deletion of *mexE* (Figure 5-4) This indicated that reversion through deletion of *mexS, mexT,* and a complete or partial deletion of *mexE* provided the greatest fitness advantage in the absence of antibiotic pressure. Likewise, the area under the curve for both A1.1(*Mdn* = 23.12, *IQR* = 2.37; Mann-Whitney test *U* = 100, *p* = 0.000274) and A1.2 (*Mdn* = 23.03, *IQR* = 2.44; Mann-Whitney test *U* = 100, *p* = 0.000274) revertants showed the greatest increase over its respective parent (*Mdn* = 17.18, *IQR* = 0.54). When cultured in the presence of sub-inhibitory concentrations of chloramphenicol, the advantage in relative fitness and increase in the area under the curve of the revertants A1.1 (Relative fitness: *Mdn* = 1.61, *IQR* = 0.29; Mann-Whitney test *U* = 100, *p* = 0.000274. Area under the curve: *Mdn* = 8.92, *IQR* = 0.98; Mann-Whitney test *U* = 100, *p* = 0.000274) and A1.2 (Relative fitness: *Mdn* = 1.67, *SD* = 0.40; Mann-Whitney test *U* = 100, *p* = 0.000274. Area under the curve: *Mdn* = 8.80, *IQR* = 2.34; Mann-Whitney test *U* = 100, *p* = 0.000274) over its ancestral parent (Relative fitness: *Mdn* = 0.98, *IQR* = 0.19. Area under the curve: *Mdn* = 6.06, *IQR* = 0.30) was retained. For the related mutant strain A1, relative fitness in both the absence and presence of chloramphenicol were similar to the ancestral parent strain A (No CHL: *Mdn* = 1.08, *IQR*= 0.37; Mann-Whitney test *U* = 59, *p* = 0.521. With CHL: *Mdn* = 1.04, *IQR* = 0.20; Mann-Whitney test *U* = 55, *p* = 0.734). However, when

considering the area under the growth curve, the A1 mutant strain had a greater area under the curve in the presence of chloramphenicol (*Mdn*= 10.99, *IQR* = 0.87; Mann-Whitney test *U* = 100, *p* = 0.000274) and reduced in the absence (*Mdn* = 11.22, *IQR* = 0.26; Mann-Whitney test *U* = 0, *p* = 0.00022) when compared against its parent strain.

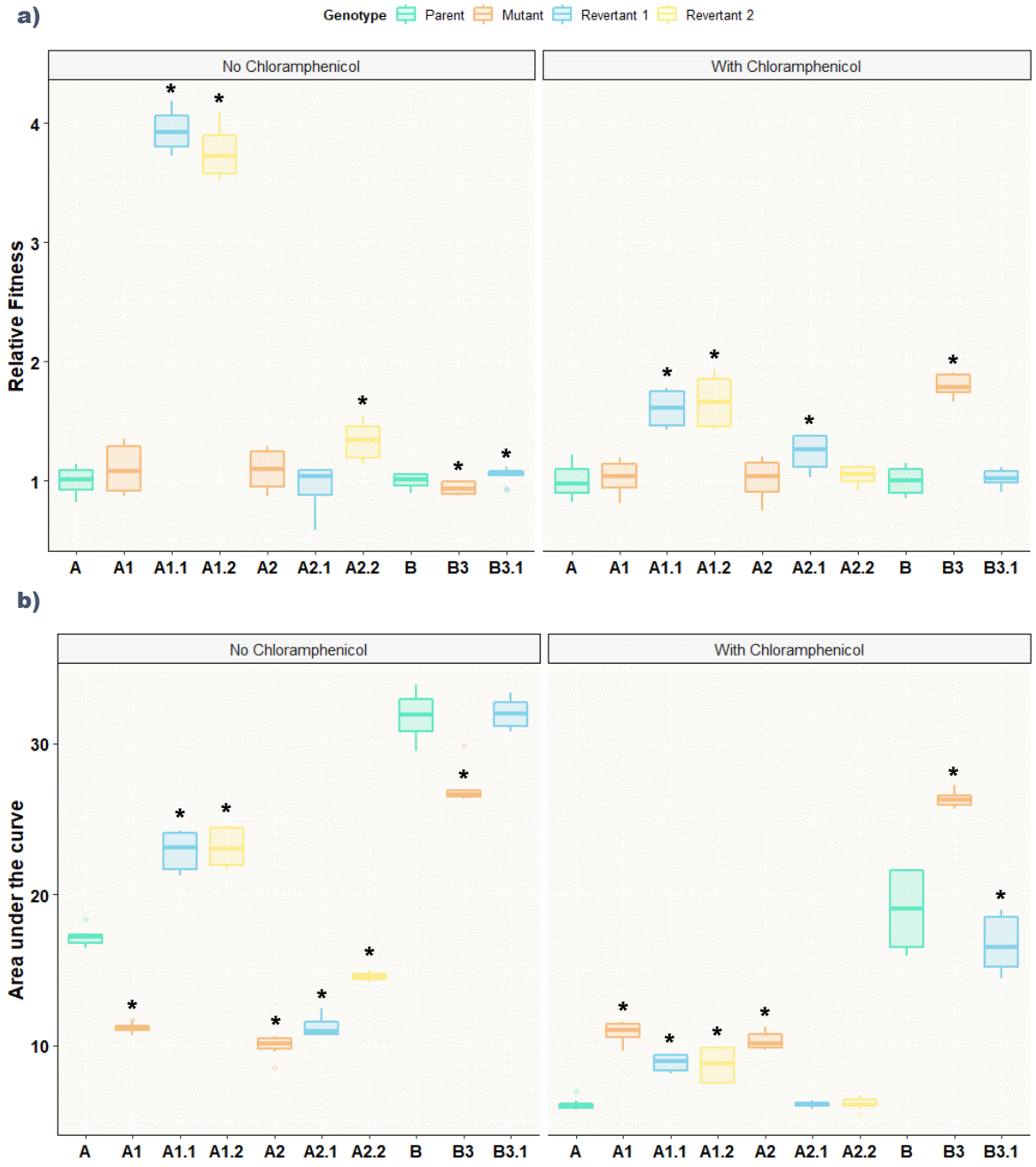

Figure 5-6: a) Relative fitness and b) Area under the curve determined from growth curves of strains with mutations in mexS *and* mexT. *Strains were grown in the presence and absence of a sub-inhibitory concentration of chloramphenicol (8µg/ml) in the broth in which the reversions occurred. Error bars depict the 95% confidence intervals of ten replicates and strains with a significant difference (p ≤ 0.05), as determined by a Mann-Whitney U test, from its ancestral parent strain are marked with (*).*

Of the remaining revertant strains generated from parent strain A, A2.2 (*Mdn* = 1.34, *SD* = 0.26; Mann-Whitney test *U* = 99, *p* = 0.000738 respectively) was the only revertant to obtain a significant advantage when considering the relative fitness when grown in the absence of sub-inhibitory concentration of chloramphenicol. However, the additional pressure of chloramphenicol resulted in no difference in relative fitness between revertant A2.2 (*Mdn* = 1.06, IQR = 0.12; Mann-Whitney test *U* = 62, *p* = 0.578 respectively) and its ancestral parent. The second revertant produced by the A2 resistant mutant strain, A2.1 (*Mdn* = 1.04, IQR = 0.21; Mann-Whitney test *U* = 44 *p* = 0.678) was determined to have no difference in relative fitness over its parent strain when in antibiotic free conditions however relative fitness (*Mdn* = 1.06, *IQR* = 0.12; Mann-Whitney test *U* = 88, *p* = 0.014) improved when grown in the presence sub-inhibitory levels of chloramphenicol. In terms of the area under the curve both revertants showed a reduced area to the parent (A2.1: *Mdn* = 10.97, *IQR* = 0.82; Mann-Whitney test *U* = 0, *p* = 0.00022. A2.2: *Mdn* = 14.57, *IQR* = 0.30; Mann-Whitney test *U* = 0, *p* = 0.00022) when no chloramphenicol was present, but similar areas when the antibiotic was present at sub-inhibitory levels (A2.1: *Mdn* = 6.11, *IQR* = 0.20; Mann-Whitney test *U* = 61, *p* = 0.512. A2.2: *Mdn* = 6.08, *IQR* = 0.37; Mann-Whitney test *U* = 62, *p* = 0.512). For the mutant strain A2, relative fitness was like the ancestral parent regardless of chloramphenicol presence (No CHL: *Mdn* = 1.10, *IQR* = 0.30; Mann-Whitney test *U* = 67, *p* = 0.254. With CHL: *Mdn* = 1.04, *IQR* = 0.24; Mann-Whitney test *U* = 57, *p* = 0.748) however, the area under the growth curve was reduced (*Mdn* = 10.11, *IQR* = 0.67; Mann-Whitney test *U* = 0, *p* = 0.00022*)* in the absence of chloramphenicol and increased (*Mdn* = 10.15, *IQR* = 0.88; Mann-Whitney test *U* = 100, *p* = 0.000366) in the presence with respect to the parent strain A.

The second parental strain, B, produced one mutant strain, B3, with a Ala27fs *mexS* mutation which subsequently reverted to a sensitive phenotype in SSM9PR media through a Tyr191fs *mexT* mutation to produce strain B3.1. Though the relative fitness of the revertant strain B3.1 was greater than the parent (*Mdn* = 1.01, *IQR* = 0.10) in the absence of chloramphenicol (*Mdn*

= 1.07, *IQR* = 0.04; Mann-Whitney test *U* = 22, *p* = 0.038) it was the same as the parent (*Mdn* = 1.00, *IQR* = 0.20) in the presence (*Mdn* = 1.02, *IQR* = 0.10; Mann-Whitney test *U* = 44, *p* = 0.0678). Conversely, when considering the area under the growth curves the areas was the same between the parent (*Mdn* = 31.92, IQR = 2.16) and revertant strains (*Mdn* = 31.98, *IQR* = 1.57, Mann-Whitney test *U* = 46, *p* = 0.791) in the absence of chloramphenicol, but reduced (*Mdn* = 16.49, IQR = 3.27; Mann-Whitney test *U* = 100, *p* = 0.000274) when both strains were grown in the present of chloramphenicol (*Mdn* = 19.06, *IQR* = 5.1). For the B3 mutant relative fitness (*Mdn* = 0.94, *IQR* = 0.10; Mann-Whitney test *U* = 80, *p* = 0.038) and the area under the curve (*Mdn* = 26.64, *IQR* = 0.39; Mann-Whitney test *U* = 99, *p* = 0.000369) was both less than the parent strain when no chloramphenicol was present. However, with the addition of chloramphenicol the mutant strain showed an increase in fitness (*Mdn* = 1.78, *IQR* = 0.15; Mann-Whitney test *U* = 0, *p* = 0.000274) and area under the curve (*Mdn* = 26.26, *IQR* = 0.65; Mann-Whitney test *U* = 0, *p* = 0.000274) over the parent strain.

Discrepancies were seen between the relative fitness and area under the curve with the two metrics disagreeing over which strain had the advantage in the varying conditions. The Growthcurver programme used to determine the growth rate and area under the curve metrics fits the growth curve data provided to a logistic equation (206). Based on the equation bacterial growth rate is calculated and used as a proxy to reveal the relative fitness. On the other hand, the area under the curve was taken as the area under the experimental curve. Therefore, it is possible for the two metrics to show varying significance due to approach in which they are derived. While both metrics provide valuable interpretations of the growth curves, in cases where the two metrics were inconsistent, the area under the curve was favoured due to its derivation from the experimental data.

Taking this into account, differences in fitness varied according to the mutations present in the strain with the largest increases seen in the A1.1 and A1.2 revertants with a deletion of *mexS*

and mexT in addition to a partial or complete deletion of *mexE* regardless of the presence of a sub-inhibitory concentration of chloramphenicol. In addition to outperforming their parent strain, both the A1.1 and A1.2 revertants showed greater relative fitness and area under the curve than their A1 mutant strain, however this advantage over the mutant was understandably not retained in the presence of chloramphenicol with respect to area under the curve.

5.2.2 Evolution of environmental *Pseudomonas aeruginosa* to clinical conditions

5.2.2.1 Selection of plasma concentration

To investigate the evolution of environmental strains to a clinical niche we selected three *P. aeruginosa* strains isolated from environmental sources and exposed them to MHB supplemented with human plasma as described in Section 2.5.2. To determine a suitable concentration of plasma to evolve environmental strains in, growth curves were generated for three environmental strains PA232 (strain C), PA63 (strain D), and PA2629 (strain E) in media supplemented with varying levels of human plasma (Figure 5-7).

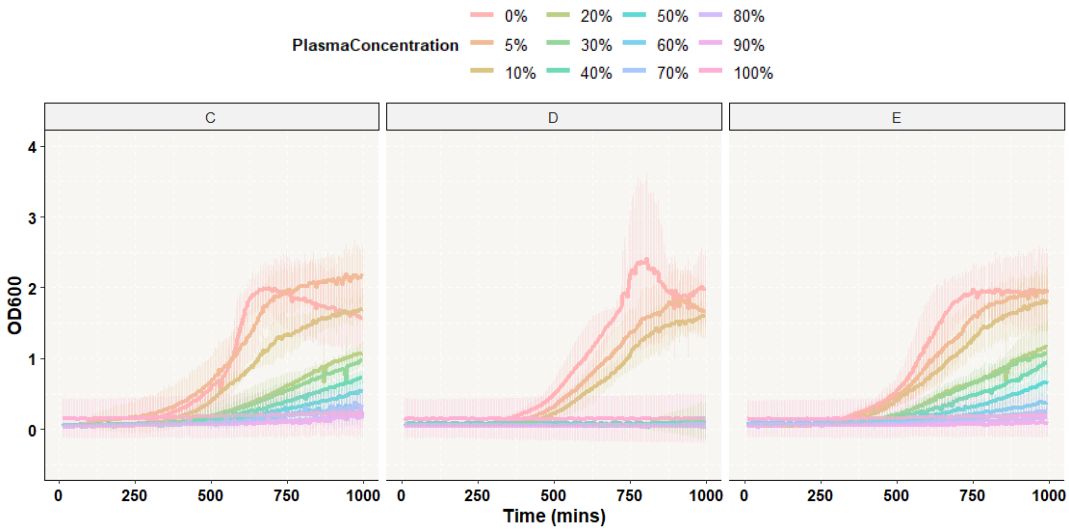

Figure 5-7: Growth of three Pseudomonas aeruginosa *strains isolated from environmental sources grown in MHB with varying concentrations of human plasma. Growth is plotted as the mean optical density at 600nm with error bars depicting 95% confidence intervals based on 4 replicates generated from 2 independent experiments.*

A two-way repeated measures ANOVA, confirmed for each of the strains that there was a significant interaction between plasma concentration and time on the OD_{600} (C: $F(11,7200) = 5154.62$, $p \leq 0.05$; D: $F(11, 7200) = 4377.71$, $p \leq 0.05$; and E: $F(11, 7200) = 4775.53$, $p \leq 0.05$). Follow up post-hoc tests were used to determine if plasma concentration influenced the OD_{600} at the last time point. For all three strains the one-way ANOVA confirmed that at the last time point, 995 mins, there was a difference in OD_{600} across the plasma concentrations (C, $p \leq 0.05$; D, $p \leq 0.05$; and E, $p \leq 0.05$). To determine the specific plasma concentrations at which there were differences pairwise students *t*-tests were performed comparing the OD_{600} between each plasma concentration at 995 mins (Appendix - Table 17). The *t*-test showed a plasma concentration of 10% (C: $M = 10.22$, $SD = 0.60$. E: $M = 10.13$, $SD = 0.75$) to be the highest concentration where no difference was seen when compared to growth in 0% plasma for strains C ($M = 13.97$, $SD = 2.65$; $p = 0.282$) and E ($M = 13.97$, $SD = 2.83$; $p = 0.536$). Though a significant difference was seen between 0% plasma ($M = 13.76$, $SD = 3.05$) and 10% plasma for strain D ($M = 8.17$, $SD = 1.28$; $p = 0.00382$), the p-value was much smaller than that for the difference seen between 0% and 20% ($p = 4.88 \times 10^{-17}$) at which point no growth was detectable for strain D. Thus, a concentration of 10% human plasma in MHB was used to evolve all three environmental strains to more clinically relevant conditions.

5.2.2.2 Characterisation of antimicrobial resistance in evolved strains

Previous experiments showed the reversion of *P. aeruginosa* strains through double *mexS/mexT* mutation (Correia *et al*., unpublished). To investigate whether environmental strains would develop similar mutations in *mexS* and *mexT* we evolved isolates obtained from the environment to simulated clinical conditions. The environmental strains were conditioned over 48 hours, and then passaged in MHB + 10% plasma with either chloramphenicol or ciprofloxacin with five replicates per strain. Evolved strains were passaged in antibiotic free MHB to produce strains reverting to a more sensitive phenotype. MIC testing confirmed five of the replicates to have developed increased tolerance to chloramphenicol after five (final

concentration of 256 μg/ml) or seven (final concentration of 1024 μg/ml) passages which then reduced when grown for ten passages in media without the antibiotic pressure (Table 5-3). For strains evolved in ciprofloxacin, four replicates had increased ciprofloxacin tolerance after 15 passages (final concentration of 256 μg/ml) when compared to its parent strain, though strain D2 showed a marginal increase, which reduced after being passaged in antibiotic free media (Table 5-3).

As shown in Table 5-3, mutants generated from strain C in chloramphenicol and ciprofloxacin resulted in increased MIC values for the drugs in the mutants for the antibiotic in which they were evolved, with no obvious changes seen in the other antibiotics. The revertant strains generated from the strain C mutants then reduced the MIC values with no changes in the other antibiotics. In terms of strain D, the chloramphenicol evolved mutant showed an MIC increase for chloramphenicol only. However, from the two ciprofloxacin evolved mutants one showed an increase to both chloramphenicol and ciprofloxacin MIC with the ciprofloxacin MIC reaching the breakpoint for resistance. The revertant generated from this mutant showed a reduce level of resistance to ciprofloxacin only which was still above the breakpoint for resistance. The other mutant showed a small increase in its ciprofloxacin MIC which reduced in the revertant, and while small changes were seen in the chloramphenicol concentrations this was only by one doubling dilution. Finally, for strain E evolution in both chloramphenicol and ciprofloxacin resulted in increases to all the tested antibiotics. However, the ciprofloxacin evolved mutant only showed an increase in imipenem by one doubling dilution. The chloramphenicol evolved revertant from strain E was restored to its formed MIC values, with chloramphenicol slightly lower by one doubling dilution. The revertant of the ciprofloxacin evolved strain showed a small decrease in chloramphenicol MIC by one doubling dilution and a decrease in ciprofloxacin MIC that remained above the resistance breakpoint. In terms of its imipenem MIC, another increase was detected in the revertant that was one doubling dilution above its mutant.

Table 5-3: Minimum inhibitory concentration for antibiotics against environmental strains evolved in human plasma and antibiotics. MICs were performed in MHB + 10% plasma and are reported in µg/ml with concentrations classed as resistant by EUCAST guidelines for ciprofloxacin and imipenem (291) highlighted in red. CHL, chloramphenicol; CIP, ciprofloxacin; IMP, imipenem.

Strain		Evolution conditions	Passages*	*mexS* genotype	*mexT* genotype	CHL**	CIP	IMP
C	Parent			wildtype	wildtype	32	≤ 0.25	1
C1	Mutant	CHL	5	Ser60Phe	wildtype	256	≤ 0.25	1
C1.1	Revertant	CHL	10	Ser60Phe	Trp277*	16	≤ 0.25	1
C2	Mutant	CHL	7	Arg332Cys	wildtype	256	≤ 0.25	2
C2.1	Revertant	CHL	10	missing	missing	8	≤ 0.25	1
C3	Mutant	CHL	7	Leu281Arg	wildtype	256	≤ 0.25	2
C3.1	Revertant	CHL	10	Leu281Arg	Gly113Asp	8	≤ 0.25	1
C4	Mutant	CIP	15	wildtype	wildtype	16	128	0.25
C4.1	Revertant	CIP	10	wildtype	wildtype	16	≤ 0.25	1
D	Parent			wildtype	wildtype	16	≤ 0.25	0.5
D1	Mutant	CHL	5	Leu186Phe	wildtype	128	≤ 0.25	1
D1.1	Revertant	CHL	10	Leu186Phe	Thr19Pro	8	≤ 0.25	0.5
D2	Mutant	CIP	15	wildtype	wildtype	32	0.5	1
D2.1	Revertant	CIP	10	wildtype	wildtype	16	≤ 0.25	1
D3	Mutant	CIP	5	wildtype	wildtype	128	128	1
D3.1	Revertant	CIP	10	wildtype	wildtype	64	8	1
E	Parent			wildtype	wildtype	16	≤ 0.25	1
E1	Mutant	CHL	5	Partial deletion	wildtype	128	1	4
E1.1	Revertant	CHL	10	Partial deletion	Arg48Cys	8	≤ 0.25	1
E2	Mutant	CIP	15	wildtype	wildtype	128	16	2
E2.1	Revertant	CIP	10	wildtype	wildtype	64	1	4

* *Represents the number of passages the strain went through before no growth was detected.*

** *As there are no defined MIC breakpoints for chloramphenicol in P. aeruginosa, the parental strains were considered sensitive for the purposes of the experiment.*

Table 5-4 and Table 5-5 show the SNPs identified in genes in the chloramphenicol and ciprofloxacin evolved strains that were not present in the control strains. Full tables of SNPs identified are displayed in Appendix - Table 19, Appendix - Table 20, and Appendix - Table 21 for chloramphenicol, ciprofloxacin, and the control strains respectively. The SNPs present in Table 5-4 and Table 5-5 were identified using breseq and were filtered according to their frequency with only SNPs >90% included. In some cases, SNPs present in the mutant strain were not present in the revertant. This was an unexpected occurrence as the revertant strains

evolved from the mutants and should therefore contain the same SNPs. The disappearance of SNPs in the revertant could be explained by a deletion event such as that seen in revertant C2.1 (Table 5-4) which included the genes containing the SNP, however, this was not the case in all instances. Therefore, alignment files were input into the Integrated Genome Browser (IGB) (221) to confirm the presence of SNPs which were not detected in the revertants. This confirmed that the SNPs missing in revertants were not due to gene deletions that may have missed detection. Instead, the variant callers used to identify the SNPs were unable to fully resolve which mutations were present as both high sequence quality and reasonable coverage depth is necessary (215, 222). Additionally, cases were seen where the SNPs detected in the mutants were shown to contain sequencing reads both for and against the SNP in both the mutant and its respective revertant (Figure 5-8). In these cases, variant callers will struggle to determine the nucleotide at that position and thus its output will vary. Furthermore, the variant callers used, breseq and snippy, will not be able to reliably call SNPs in regions containing gene duplications due to limitations that arise from aligning short sequencing reads to a reference. Presently, short-read sequencing alone is unable to fully resolve repetitive regions in the genomes. Hybrid genomes assemblies which combine both long-read and short-read sequences can resolve these regions and therefore will need to be performed to confirm the presence of SNPs.

As previous experiments have shown mutations in the *mexEF-oprN* operon to develop in chloramphenicol evolved strains, whole genome alignments were visualised in IGB to confirm the completeness of the operon (221). Figure 5-9 depicts an illustration of the operon in evolved strains. Whilst the chloramphenicol evolved mutants developed mutations within *mexS* to confer increased chloramphenicol tolerance, the ciprofloxacin evolved strains did not, instead they developed mutations in other genes involved in ciprofloxacin resistance (Table 5-5). Despite the ciprofloxacin evolved D2 strain showing only a marginal increase in ciprofloxacin tolerance that was below the EUCAST resistance breakpoints for *P. aeruginosa*

(291), the strain developed mutations in genes associated with ciprofloxacin resistance (*gyrA* and *nfxB*), and thus was named as a mutant for the purposes of the study. Additionally, the D3.1 and E2.1 revertant strains still retained resistance according to the EUCAST breakpoint for ciprofloxacin (> 0.5 μg/ml), however they both showed a reduction in MIC by four doubling dilutions and thus were named as revertants for the purposes of this study (291).

Table 5-4: Mutations identified in chloramphenicol evolved strains. The mutations shown are those found only in the mutant strain does not include those also found in the control strain, full lists of the mutations identified are available in Appendix - Table 19.

Strain		Gene	Mutation	Ancestor	Strain	Type	Effect	Product
C1	Mutant	*wspA* ←	Asp419Gly	T	C	sub	Missense	Methyl-accepting chemotaxis protein
		mexS ←	Ser60phe	G	A	sub	Missense	Oxidoreductase MexS
		C_02551 ←	Pro146Pro	G	C	sub	Synonymous	Hypothetical protein
C1.1	Revertant	*wspA* ←	Asp419Gly	T	C	sub	Missense	Methyl-accepting chemotaxis protein
		mexS ←	Ser60phe	G	A	sub	Missense	Oxidoreductase MexS
		mexT →	Trp277*	G	A	sub	Stop gain	Multidrug efflux system transcriptional regulator MexT
C2	Mutant	*cmrA* ←	Gly142Ser	C	T	sub	Missense	AraC family transcriptional regulator CmrA
		mnmG →	Ala99Thr	G	A	sub	Missense	tRNA uridine-5-carboxymethylaminomethyl(34) synthesis enzyme MnmG
		mexS ←	Arg332Cys	G	A	sub	Missense	Oxidoreductase MexS
		hisF ←	Gly256Arg	C	G	sub	Missense	Imidazole glycerol phosphate synthase subunit HisF
C2.1	Revertant	*hmpA* ←	Gln48His	C	G	sub	Missense	NO-inducible flavohemoprotein
		cmrA ←	Gly142Ser	C	T	sub	Missense	AraC family transcriptional regulator CmrA
		mnmG →	Ala99Thr	G	A	sub	Missense	tRNA uridine-5-carboxymethylaminomethyl(34) synthesis enzyme MnmG
		pilR	Leu42_Glu46 del	GCTCGCGGG CCAGCAA	G	del	Deletion	Two-component system response regulator PilR
		C_04529–C_04569	Δ43,475 bp	wildtype		del	Deletion	40 genes
		C_4927–C_4959	Δ40,131 bp	wildtype		del	Deletion	32 genes
		C_05093–C_05152	Δ70,601 bp	wildtype		del	Deletion	60 genes
C3	Mutant	*mexS* ←	Leu281Arg	A	C	sub	Missense	Oxidoreductase MexS
		hisF ←	Gly256Arg	C	G	sub	Missense	Imidazole glycerol phosphate synthase subunit HisF
C3.1	Revertant	*fleQ* ←	Val383Gly	A	C	sub	Missense	Transcriptional regulator FleQ
		mexS ←	Leu281Arg	A	C	sub	Missense	Oxidoreductase MexS
		mexT →	Gly113Asp	G	A	sub	Missense	Multidrug efflux system transcriptional regulator MexT
D1	Mu	*mexS* ←	Leu186Phe	G	A	sub	Missense	Oxidoreductase MexS

		phzC	Δ343 bp	wildtype		sub	Deletion	phenazine biosynthesis protein PhzC
		mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC
D1.1	Revertant	*mexS* ←	Leu186Phe	G	A	sub	Missense	Oxidoreductase MexS
		mexT →	Thr19Pro	A	C	sub	Missense	Multidrug efflux system transcriptional regulator MexT
		D_04695 ←	Gly165Gly	C	G	sub	Synonymous	threonylcarbamoyl-AMP synthase
E1	Mutant	*dipA* →	Asp825Asn	G	A	sub	Missense	Phosphodiesterase DipA
		mexS ←	Δ91 bp	wildtype		del	Deletion	Oxidoreductase MexS
		E_02751 ←	ArgAsp65LeuAsp	GCGCTG	GAGCTA	sub	Missense	Hypothetical protein
E1.1	Revertant	*dipA* →	Asp825Asn	G	A	sub	Missense	Phosphodiesterase DipA
		mexS ←	Δ91 bp	wildtype		del	Deletion	Oxidoreductase MexS
		mexT →	Arg48Cys	C	T	sub	Missense	Multidrug efflux system transcriptional regulator MexT
		E_04710 ←	Gln291Glu	G	C	sub	Missense	NAD(P)(+) transhydrogenase (Re/Si-specific) subunit beta
		rpoA →	Val286Leu	G	C	sub	Missense	DNA-directed RNA polymerase subunit alpha

Table 5-5: Mutations identified in ciprofloxacin evolved strains. The mutations shown are those found only in the mutant strain does not include those also found in the control strain, full lists of the mutations identified are available in Appendix - Table 20.

Strain		Gene	Mutation	Ancestor	Strain	Type	Effect	Product
C4	Mutant	*parC* ←	Arg518Cys	G	A	sub	Missense	DNA topoisomerase 4 subunit A
		chpA ←	Gln1137*	G	A	sub	Stop gain	Chemotaxis signal transduction system protein ChpA
		C_01688 ←	Thr287fs	G	GTC	ins	Frameshift	LTA synthase family protein
		fliG ←	Leu160fs	ACGATATCC AGG	A	del	Frameshift	Flagellar motor switch protein FliG
		gyrB ←	Ser466Tyr	G	T	sub	Missense	DNA gyrase subunit B
		hexR →	Ser275_Arg2 77del	AGCGCAGC CT	A	del	Deletion	Transcriptional regulator HexR
		gyrA →	Thr83Ala	A	G	sub	Missense	DNA gyrase subunit A
		rplC ←	His68Tyr	G	A	sub	Missense	50S ribosomal protein L3
		C_00129 →	Pro22Gln	C	A	sub	Missense	Quinone oxidoreductase
		nfxB ←	Δ741 bp	wildtype	Δ741 bp	sub	Deletion	Efflux pump transcriptional repressor NfxB
		phzF	Δ464 bp	wildtype	Δ464 bp	sub	Deletion	Phenazine biosynthesis protein PhzF
		C_05880 →	Ala402Ala	C	G	sub	Synonymous	MFS transporter
C4.1	Revertant	*parC* ←	Arg518Cys	G	A	sub	Missense	DNA topoisomerase 4 subunit A
		chpA ←	Gln1137*	G	A	sub	Stop gain	Chemotaxis signal transduction system protein ChpA
		C_01688 ←	Thr287fs	G	GTC	ins	Frameshift	LTA synthase family protein
		fliG ←	Leu160fs	ACGATATCC AGG	A	del	Frameshift	Flagellar motor switch protein FliG
		gyrB ←	Ser466Tyr	G	T	sub	Missense	DNA gyrase subunit B
		hexR →	Ser275_Arg2 77del	AGCGCAGC CT	A	sub	Deletion	Transcriptional regulator HexR
		mexC →	Tyr217*	C	A	sub	Stop gain	Multidrug efflux RND transporter periplasmic adaptor subunit MexC
		gyrA →	Thr83Ala	A	G	sub	Missense	DNA gyrase subunit A
		rplC ←	His68Tyr	G	A	sub	Missense	50S ribosomal protein L3

	nfxB ←	Δ741 bp	wildtype	Δ741 bp	sub	Deletion	Efflux pump transcriptional repressor NfxB
	C_06081–C_06089	Δ8,095 bp	wildtype		sub	Deletion	*C_06081*, *C_06082*, *C_06083*, *C_06084*, *C_06085*, *C_06086*, *C_06087*, *C_06088*, *C_06089*
	C_06121–C_06123	Δ3,225 bp	wildtype		sub	Deletion	*C_06121, C_06122, C_06123*
	C_02734-C_02777	Δ48,799 bp	wildtype		del	Deletion	43 genes
D2 Mutant	*D_00441* →	Glu225fs	A	AGC	ins	Frameshift	ABC transporter substrate-binding protein
	relA →	His442Tyr	C	T	sub	Missense	GTP diphosphokinase
	spoT ←	His472fs	TTGAGCGCATG	T	del	Frameshift	bifunctional GTP diphosphokinase/guanosine-3'%2C5'-bis pyrophosphate 3'-pyrophosphohydrolase
	nfxB ←	Arg23fs	GTCGCTCGC	G	del	Frameshift	Efflux pump transcriptional repressor NfxB
	mexC →	Arg36fs	TGC	T	del	Frameshift	Multidrug efflux RND transporter periplasmic adaptor subunit MexC
	arnC →	Ala263_Asn267del	CCGCCTGGGCCGGCAA	C	sub	Deletion	Undecaprenyl-phosphate 4-deoxy-4-formamido-L-arabinose transferase
	D_04260 ←	Met460fs	C	CA	ins	Frameshift	bifunctional prephenate dehydrogenase/3-phosphoshikimate 1-carboxyvinyltransferase
	D_04260 ←	Arg457fs	C	CGG	ins	Frameshift	bifunctional prephenate dehydrogenase/3-phosphoshikimate 1-carboxyvinyltransferase
	gyrA ←	Asp87Asn	C	T	sub	Missense	DNA gyrase subunit A
	D_04443 →	Thr59_Ala61dup	A	ATCGCCACCG	sub	Insertion	Acyl-CoA thioesterase
D2.1 Revertant	*D_00441* →	Glu225fs	A	AGC	ins	Frameshift	ABC transporter substrate-binding protein
	relA →	His442Tyr	C	T	sub	Missense	GTP diphosphokinase
	spoT ←	His472fs	TTGAGCGCATG	T	del	Frameshift	Bifunctional GTP diphosphokinase/guanosine-3'%2C5'-bis pyrophosphate 3'-pyrophosphohydrolase
	nfxB ←	Arg23fs	GTCGCTCGC	G	del	Frameshift	Efflux pump transcriptional repressor NfxB
	mexC →	Arg36fs	TGC	T	del	Frameshift	Multidrug efflux RND transporter periplasmic adaptor subunit MexC
	arnC →	Ala263_Asn267del	CCGCCTGGGCCGGCAA	C	del	Deletion	Undecaprenyl-phosphate 4-deoxy-4-formamido-L-arabinose transferase
	D_04260 ←	Met460fs	C	CA	ins	Frameshift	Bifunctional prephenate dehydrogenase/3-phosphoshikimate 1-carboxyvinyltransferase
	D_04260 ←	Arg457fs	C	CGG	ins	Frameshift	Bifunctional prephenate dehydrogenase/3-phosphoshikimate 1-carboxyvinyltransferase

		gyrA ←	Asp87Asn	C	T	sub	Missense	DNA gyrase subunit A
		D_04443 →	Thr59_Ala61 dup	A	ATCGC CACCG	sub	Insertion	Acyl-CoA thioesterase
D3	Mutant	*D_00441* →	Ala227fs	C	CGAGC T	ins	Frameshift	ABC transporter substrate-binding protein
		D_02366 →	Ala176_Arg1 77insArgAla	G	GGCCC GC	sub	Insertion	Histidine-tRNA ligase
		nfxB ←	Arg163Gln	C	T	sub	Missense	Efflux pump transcriptional repressor NfxB
		gyrB ←	Ser466Phe	G	A	sub	Missense	DNA gyrase subunit B
		edd →	Ile530fs	CCATCGCC GGCG	C	del	Frameshift	Phosphogluconate dehydratase
D3.1	Revertant	*parS* →	Arg385His	G	A	sub	Missense	Histidine kinase
		nfxB ←	Arg163Gln	C	T	sub	Missense	Efflux pump transcriptional repressor NfxB
		gyrB ←	Ser466Phe	G	A	sub	Missense	DNA gyrase subunit B
E2	Mutant	*nfxB* ←	His109fs	C	CGGGT	ins	Frameshift	Efflux pump transcriptional repressor NfxB
		pilV ←	Cys164fs	GGCGTTGA CGCA	G	del	Frameshift	Type 4a pilus minor pilin PilV
		gyrB ←	Ser466Tyr	G	T	sub	Missense	DNA gyrase subunit B
		E_04760 ←	Ala30Glu	C	A	sub	Missense	BMP family ABC transporter substrate-binding protein
		E_05464 ←	Pro25Ala	C	A	sub	Missense	Hypothetical protein
E2.1	Revertant	*nfxB* ←	His109fs	C	CGGGT	ins	Frameshift	Efflux pump transcriptional repressor NfxB
		mexC →	Arg36fs	TGC	T	del	Frameshift	Multidrug efflux RND transporter periplasmic adaptor subunit MexC
		pilV ←	Cys164fs	GGCGTTGA CGCA	G	del	Frameshift	Type 4a pilus minor pilin PilV
		gyrB ←	Ser466Tyr	G	T	sub	Missense	DNA gyrase subunit B
		E_03887 →	Ala163Glu	C	A	sub	Missense	TetR family transcriptional regulator
		E_04760 ←	Ala30Glu	C	A	sub	Missense	BMP family ABC transporter substrate-binding protein

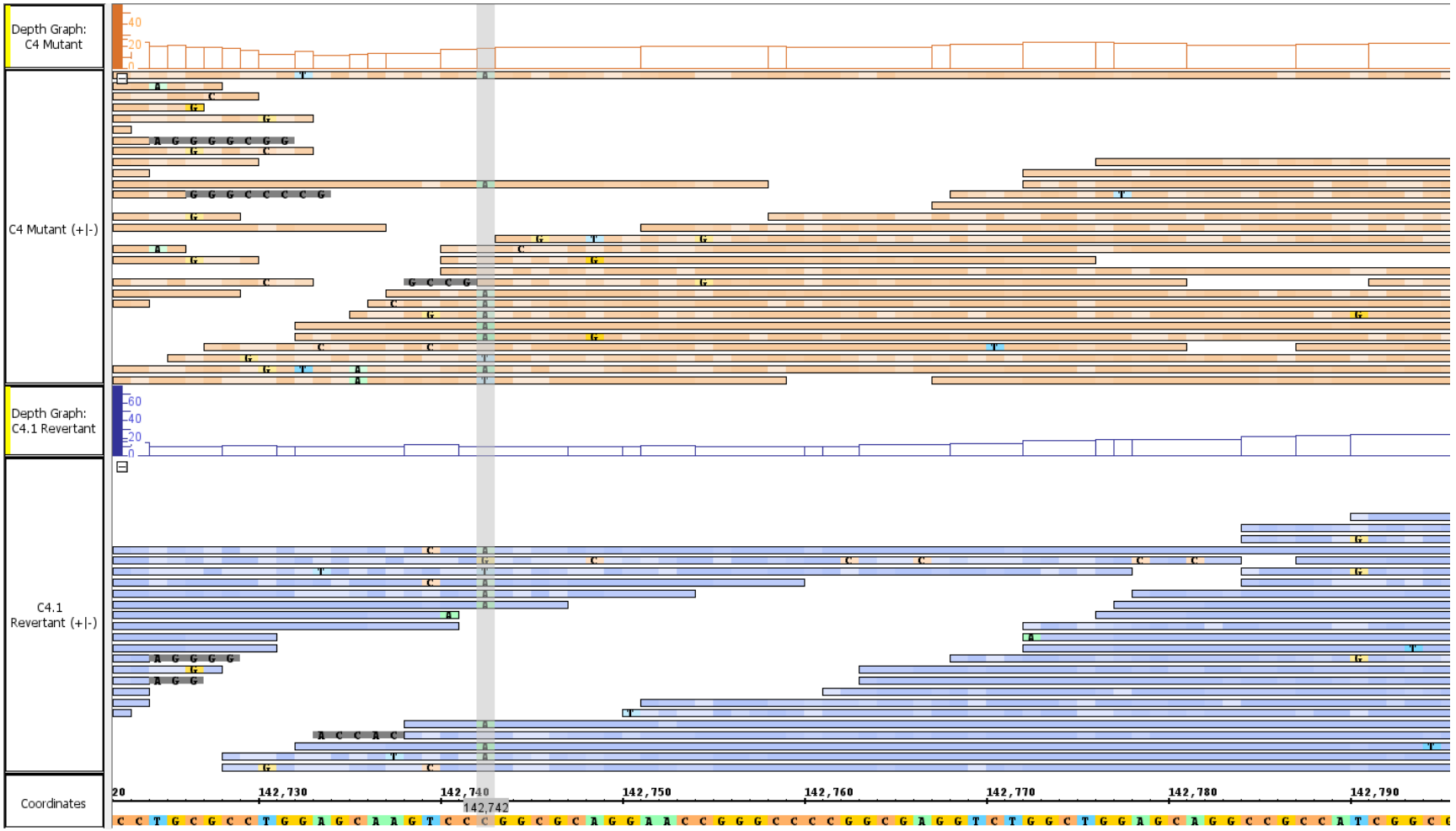

Figure 5-8: Alignment of the C4 mutant and C4.1 revertant sequencing reads to the ancestral parent strain C. Alignment is visualised in the integrated genome browser (221) and depicts the reads mapping to the first contig at position 142,742 in the strain C de novo *assembly. Mismatched bases are coloured according to the nucleotide base present, with colours shaded according to the quality of the base in the sequence read, lighter colours indicate lower quality scores with deeper shades indicating higher quality.*

Figure 5-9: Illustration of mutations within the mexEF-oprN *operon (not to scale) of strains evolved in clinical conditions with chloramphenicol. Parent strains are indicated in green, (C, D and E) resistant mutants in orange (C1, C2, C3, D1, and E1) and revertants in blue (C1.1, C2.1, C3.1, D1.1, and E1.1). SNPs are indicated by red lines, frameshifts are filled with a dotted pattern outlined in red, and larger deletions are blank also outlined in red. The chloramphenicol (CHL) MICs are reported in µg/ml as the MIC determined in MHB + 10%. The 'Efflux' column indicates whether the genotype suggests efflux is active (+) or inactive (-).*

5.2.2.2.1 Genetic changes established in chloramphenicol evolved strains

Of the chloramphenicol evolved strains, mutations within *mexS* were consistently found across all evolved mutants. For four of the mutants (C1, C2, C3, D1), SNPs resulting in missense mutations were identified in *mexS* with the final mutant (E1) showing no SNPs for *mexS.* Instead, visualisation of an alignment of the mutants using its parent strain as the reference showed a 99 base pair deletion in the gene (Figure 5-9). Due to the role of *mexS* as the transcriptional repressor of the *mexEF-oprN* operon, these mutations may result in continuous expression and efflux of chloramphenicol to generate a resistant phenotype. In addition to a *mexS* mutation, the C2 mutant also contained a mutation in the chloramphenicol resistance activator gene, cmrA (Table 5-4).

As seen in previous experiments (Correia *et al*., unpublished), reversion to a more sensitive phenotype, can occur in *mexS* mutants through mutations in *mexT.* In four of the revertant strains SNPs in *mexT* were detected, however in the case of the C2.1 revertant the *mexT* gene was not found. Therefore, the sequencing reads of the revertant were mapped to the parent strain and were visualised in IGB to confirm the presence of mutations in the region of the *mexEF-oprN* operon. No reads were found to map to the contig containing the operon. Coverage depth of alignments were then analysed to assess the mapping of sequencing reads in the alignment where a single large deletion in the genomic sequence was detected resulting in the removal of 132 genes. This is shown as three deletions of 40, 32, and 60 genes in Table 5-4 and Figure 5-10. The deletion included the *mexEF-oprN* operon and its regulators *mexS* and *mexT* in addition to *oprD,* which is downregulated by MexT, hence MexEF-oprN mediated efflux was not possible in C2.1. Other genes involved in the deletion include other efflux pumps, transcriptional regulators, and metabolic proteins (Table 5-6).

The *hisF* gene which encodes the imidazole glycerol phosphate synthase subunit HisF, was seen to develop the same mutation (Gly256Arg) in both the chloramphenicol evolved C2 and C3 mutants and was absent in both respective revertant strains. The C2 and C3 mutants were evolved in the same conditions independently of one another and thus the development of the same SNP in both strains appears would appear to show parallel evolution to the simulated clinical conditions it was subjected to. However, the specific mutation to the *hisF* gene also appeared in one of the control strains (Strain C – Replicate 3 , Appendix - Table 21), thus it is unlikely for the SNP to have developed in response to exposure to chloramphenicol though it is possible the SNP developed in response to long term exposure to MHB + 10% plasma.

When compared to their parental strain, mutant and revertant strains were found to also have additional SNPs in genes other than *mexS* and *mexT* (Table 5-4). However, the genes containing these SNPs were not universally altered across all mutant and revertant strains and the gene

involved had no known links to chloramphenicol. Therefore, only *mexS* was considered responsible for chloramphenicol resistance with *cmrA* potentially being involved in combination with *mexS* in mutant C2. Reversion to a more sensitive phenotype was associated with alterations in *mexT* either through SNPs or large deletions covering the regions encoding *mexT*.

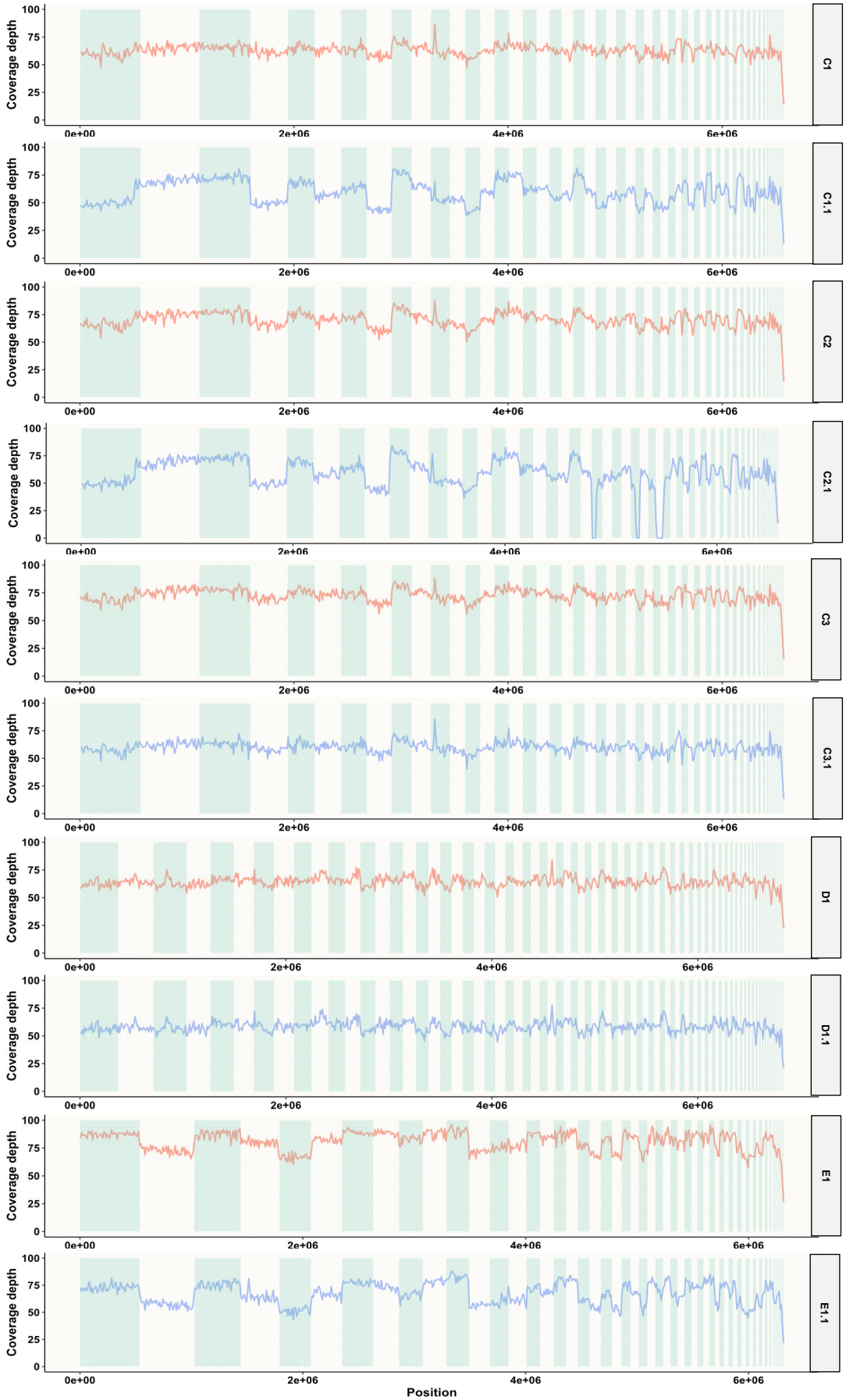

Figure 5-10: Coverage depth of sequencing reads generated from strains evolved in chloramphenicol. Reads are mapped to the genome assembly of the respective parental strain and plotted as the average coverage over 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.

Table 5-6: List of genes deleted in revertant C2.1. The genes involved in the mexEF-oprN *operon are contained in the genes labelled C_5109 to C_5113.*

Gene	Product	Gene	Product
C_4529	sodium:alanine symporter	C_4953	phenol degradation protein
C_4530	LysR family transcriptional regulator	C_4954	cytochrome P450
C_4531	aldo/keto reductase	C_4955	thiol:disulfide interchange protein DsbG
C_4532	phosphatidate cytidylyltransferase	C_4956	redoxin domain-containing protein
C_4533	1-acyl-sn-glycerol-3-phosphate acyltransferase	C_4957	Thiol:disulfide interchange protein DsbD 2
C_4534	hypothetical protein	C_4958	response regulator
C_4535	serine/threonine protein phosphatase	C_4959	two-component sensor histidine kinase
C_4536	alpha/beta fold hydrolase	C_5093	c-type cytochrome
C_4537	CDP-alcohol phosphatidyltransferase family protein	C_5094	cytochrome c4
C_4538	translocation/assembly module TamB	C_5095	LLM class flavin-dependent oxidoreductase
C_4539	outer membrane protein assembly factor	C_5096	TetR/AcrR family transcriptional regulator
C_4540	N-acetyltransferase	C_5097	hypothetical protein
C_4541	exodeoxyribonuclease III	C_5098	hypothetical protein
C_4542	hypothetical protein	C_5099	hypothetical protein
C_4543	lactoylglutathione lyase	C_5100	AraC family transcriptional regulator
C_4544	transcriptional regulator	C_5101	AraC family transcriptional regulator
C_4545	membrane protein	C_5102	cupin domain-containing protein
C_4546	TerC family protein	C_5103	hypothetical protein
C_4547	membrane protein	C_5104	fimbrial protein
C_4548	acyl-CoA dehydrogenase	C_5105	molecular chaperone
C_4549	LysR family transcriptional regulator	C_5106	autotransporter domain-containing protein
C_4550	acyl-CoA dehydrogenase	C_5107	chemotaxis protein CheY
C_4551	acetyl-CoA C-acyltransferase	C_5108	putative N-octanoylanthranilate hydrolase AqdA1
C_4552	3-hydroxyacyl-CoA dehydrogenase	C_5109	oxidoreductase MexS
C_4553	AMP-binding protein	C_5110	multidrug efflux system transcriptional regulator MexT
C_4554	AraC family transcriptional regulator	C_5111	multidrug efflux RND transporter periplasmic adaptor subunit MexE
C_4555	AMP-binding protein	C_5112	multidrug efflux RND transporter permease subunit MexF
C_4556	MgtC/SapB family protein	C_5113	TolC family protein
C_4557	hypothetical protein	C_5114	putative minor fimbrial subunit LpfD
C_4558	hypothetical protein	C_5115	damage-inducible protein DinB
C_4559	hypothetical protein	C_5116	LysR family transcriptional regulator
C_4560	hypothetical protein	C_5117	ankyrin repeat domain-containing protein
C_4561	methyl-accepting chemotaxis protein I	C_5118	nucleoside deaminase
C_4562	integral membrane protein	C_5119	MFS transporter

C_4563	hypothetical protein	C_5120	hypothetical protein
C_4564	SulP family inorganic anion transporter	C_5121	kinase
C_4565	Trans-aconitate 2-methyltransferase	C_5122	SMI1/KNR4 family protein
C_4566	hypothetical protein	C_5123	hypothetical protein
C_4567	NAD(P)/FAD-dependent oxidoreductase	C_5124	OprD family porin
C_4568	hypothetical protein	C_5125	hypothetical protein
C_4569	sensor domain-containing phosphodiesterase	C_5126	catechol 1,2-dioxygenase
C_4927	protease modulator HflK	C_5127	muconolactone Delta-isomerase
C_4928	polysaccharide deacetylase family protein	C_5128	muconate cycloisomerase
C_4929	hypothetical protein	C_5129	LysR family transcriptional regulator
C_4930	glycine cleavage system protein T	C_5130	AraC family transcriptional regulator
C_4931	L-serine dehydratase	C_5131	anthranilate 1,2-dioxygenase large subunit
C_4932	serine hydroxymethyltransferase	C_5132	anthranilate 1,2-dioxygenase small subunit
C_4933	glycine dehydrogenase (aminomethyl-transferring)	C_5133	anthranilate dioxygenase reductase
C_4934	glycine cleavage system protein GcvH	C_5134	1,6-dihydroxycyclohexa-2,4-diene-1-carboxylate dehydrogenase
C_4935	LysR family transcriptional regulator	C_5135	2Fe-2S iron-sulfur cluster binding domain-containing protein
C_4936	amidohydrolase	C_5136	benzoate 1,2-dioxygenase subunit beta
C_4937	sigma-54-dependent transcriptional regulator	C_5137	benzoate 1,2-dioxygenase subunit alpha
C_4938	hypothetical protein	C_5138	AraC family transcriptional regulator
C_4939	esterase family protein	C_5139	CusA/CzcA family heavy metal efflux RND transporter
C_4940	YgdI/YgdR family lipoprotein	C_5140	efflux RND transporter periplasmic adaptor subunit
C_4941	class I SAM-dependent methyltransferase	C_5141	TolC family protein
C_4942	N-acetyltransferase	C_5142	response regulator
C_4943	hypothetical protein	C_5143	sensor histidine kinase
C_4944	PepSY domain-containing protein	C_5144	hypothetical protein
C_4945	ferrioxamine receptor FoxA	C_5145	RND transporter
C_4946	peptide ABC transporter substrate-binding protein	C_5146	multidrug efflux RND transporter permease subunit MuxC
C_4947	sigma-70 family RNA polymerase sigma factor	C_5147	multidrug efflux RND transporter permease subunit MuxB
C_4948	transcriptional regulator	C_5148	multidrug efflux RND transporter periplasmic adaptor subunit MuxA
C_4949	gentisate 1%2C2-dioxygenase	C_5149	TldD/PmbA family protein
C_4950	FAA hydrolase family protein	C_5150	TldD/PmbA family protein
C_4951	MFS transporter	C_5151	pyridoxal phosphate-dependent aminotransferase
C_4952	glutathione S-transferase	C_5152	thiol peroxidase

5.2.2.2.2 Genetic changes established in ciprofloxacin evolved strains

For strains evolved in ciprofloxacin, mutations in multiple genes known to have associations with fluroquinolone resistance were detected in all four of the mutant strains (Table 5-5). These included mechanisms involved in DNA replication as well as efflux pumps.

In the *gyrA* gene which encodes subunit A of DNA gyrase, the SNPs seen in mutants C4 and D2 resulted in the amino acid changes Thr83Ala and Asp87Asn, both of which are within the quinolone resistance determining region (QRDR) found between amino acid position 67 to 106 (Table 5-5) (369). The B subunit of DNA gyrase is encoded by *gyrB* and SNPs in the ciprofloxacin evolved strains were identified in three mutants all at the same position. Both the C4 and E2 mutants contained Ser466Tyr changes in the amino acid sequence with mutant D3 containing a Ser466Phe alteration. These mutations are within the QRDR region spanning amino acid positions 429 to 585 (370). Together the *parC* and *parE* genes encode the subunits which form DNA topoisomerase IV. In the ciprofloxacin mutant strains, no mutations were detected in *parE* with respect to the sensitive parental strains. In terms of *parC,* mutant C4 developed a SNP resulting in an Arg518Cys change in its amino acid sequence. The QRDR of *parC* occurs earlier in the amino acid sequence around positions 82 to 84, therefore the impact of an amino acid change at position 518 is unclear having not previously being reported.

The *nfxB* gene is the transcriptional repressor of the *mexCD-oprJ* operon and was shown to contain SNPs in the ciprofloxacin evolved mutants D2 (Arg23fs), D3 (Arg163Gln), and E2 (His109fs) (Figure 5-11 and Table 5-5). Like MexEF-OprN, the MexCD-OprJ efflux pump is not part of the intrinsic resistance seen in *P. aeruginosa* but overexpression of the pump results in constitutive efflux of a range of antimicrobials (371). The mutation seen in *nfxB* in the D3 mutant has previously been identified in a ciprofloxacin evolved *P. aeruginosa* isolates where it led to a ciprofloxacin resistant phenotype, however mutations to other efflux pumps was also detected in this strain (372). The specific frameshift mutations seen in mutants D2 and E2 have

not previously been described. Nevertheless, a frameshift mutation would result in a mistranslation and thus a non-functional protein. Additionally, alternative frameshift mutations in *nfxB* have resulted in hyperexpression of MexCD-OprJ (371). The remaining mutant, C4 did not appear to contain any SNPs within *nfxB* when assessed with snippy. Instead, visualisation of the alignment and analysis with breseq using the strain C parent as the reference strain showed no reads mapped to *nfxB* indicating deletion of the gene (Figure 5-11). Therefore, repression of the *mexCD-oprJ* operon was not possible resulting in its constitutive expression.

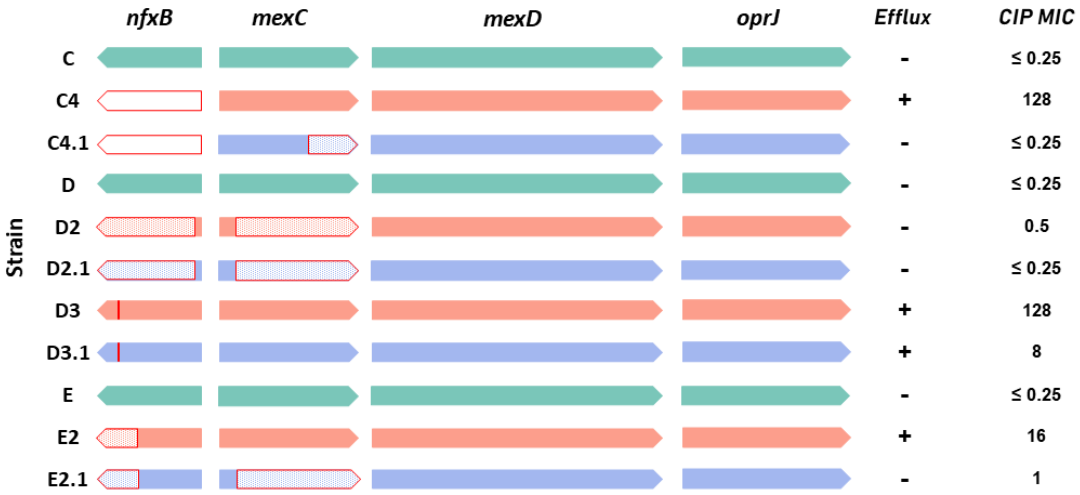

Figure 5-11: Illustration of mutations within the mexCD-oprJ *operon (not to scale) of strains evolved in the clinical conditions with ciprofloxacin. Parent strains are indicated in green, (C, D and E) resistant mutants in orange (C4, D2, D3, and E2) and revertants in blue (C4.1, D2.1, D3.1, and E2.1). SNPs are indicated by red lines, frameshifts are filled with a dotted pattern outlined in red, and larger deletions are blank also outlined in red. CIP MICs are reported in µg/ml as the ciprofloxacin MIC determined in MHB + 10% plasma.*

As previously mentioned, the MexCD-OprJ efflux pumps contribute to the removal of antibiotics from varying classes outside of the cell. The RND transporter periplasmic adaptor subunit MexC was shown to have a mutation (Arg36fs) in its amino acid sequence resulting in a frameshift for the D2 mutant (Figure 5-11 and Table 5-5). As the mutation would prevent the function of the MexCD-OprJ efflux pump, its acquisition by the D2 mutant is unexpected for a strain evolved in ciprofloxacin but would explain the smaller increase seen in the ciprofloxacin

MIC between D2 and its parent. The other ciprofloxacin mutants did not develop *mexC* mutations, and two of the revertants, C4.1 and E2.1, both obtained mutations in the gene resulting in a stop gain (Tyr217*) and frameshift (Arg36fs). Thus, both the D2 mutant and E2.1 revertant contained the same mutation to *mexC* with both strains showing similar MICs to ciprofloxacin (0.5 μg/ml and 1 μg/ml respectively). The *mexC* mutations seen in these strains result in the mistranslation of *mexC* and thus a non-functional protein resulting in MexCD-OprJ mediated efflux being comprised. Hence, the two revertants evolved lower ciprofloxacin MICs than their ancestral mutant strain through *mexC* mutations, with one revertant retaining the previously gained *mexC* to exhibit lower ciprofloxacin tolerance.

Due to the observation of large deletions in the chloramphenicol evolved strains, coverage depth of the ciprofloxacin evolved mutant and revertant strains was assessed by aligning the strains to their respective parents. Figure 5-12 depicts the coverage depth across the genomes and illustrates the majority of mutant and revertant strains lacked large deletions in their sequence. The one strain in with a large deletion in its genome when compared to its parent was seen was revertant C4.1, which resulted in the deletion of 55 genes, shown as a deletion of 9, 3, and 43 genes in Table 5-5 and Figure 5-12. The genes in question varied in function including those involved in biofilm production, transport across the cell membrane, metabolism, and virulence (Table 5-7).

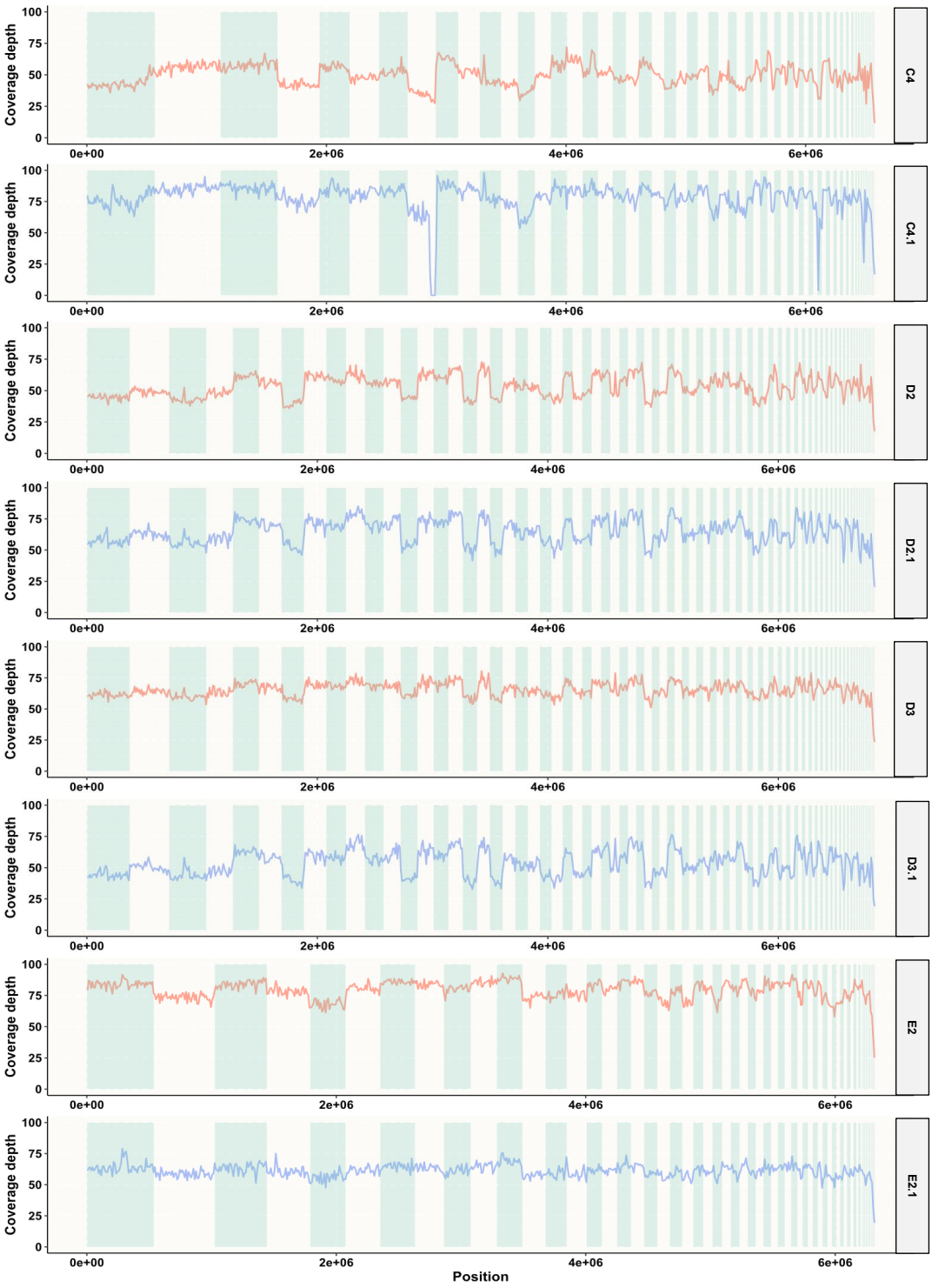

Figure 5-12: Coverage depth of sequencing reads generated from strains evolved in ciprofloxacin. Reads are mapped to the genome assembly of the respective parental strain with and plotted as the average coverage of 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.

Table 5-7: List of genes deleted in revertant C4.1

Gene	Product	Gene	Product
C_2734	LLM class flavin-dependent oxidoreductase	*C_2762*	acyltransferase family protein
C_2735	ABC transporter ATP-binding protein	*C_2763*	FAD-binding protein
C_2736	ABC transporter permease	*C_2764*	DNA topoisomerase IB
C_2737	ABC transporter permease subunit	*C_2765*	inner centromere protein
C_2738	hypothetical protein	*C_2766*	Bkd operon transcriptional regulator
C_2739	hypothetical protein	*C_2767*	hypothetical protein
C_2740	putative aminopeptidase	*C_2768*	3-methyl-2-oxobutanoate dehydrogenase (2-methylpropanoyl-transferring) subunit alpha
C_2741	TonB-dependent receptor	*C_2769*	2-oxoisovalerate dehydrogenase subunit beta
C_2742	LLM class flavin-dependent oxidoreductase	*C_2770*	2-oxo acid dehydrogenase subunit E2
C_2743	5'/3'-nucleotidase SurE	*C_2771*	dihydrolipoamide dehydrogenase
C_2744	F420-dependent glucose-6-phosphate dehydrogenase	*C_2772*	transcriptional regulator
C_2745	F420-dependent glucose-6-phosphate dehydrogenase	*C_2773*	sodium:alanine symporter family protein
C_2746	FMNH2-dependent alkanesulfonate monooxygenase	*C_2774*	7-cyano-7-deazaguanine/7-aminomethyl-7-deazaguani ne transporter
C_2747	FMNH2-dependent alkanesulfonate monooxygenase	*C_2775*	PilZ domain-containing protein
C_2748	sigma-54-dependent Fis family transcriptional regulator	*C_2776*	lysophospholipid acyltransferase
C_2749	MOSC domain-containing protein	*C_2777*	DNA-3-methyladenine glycosylase I
C_2750	hypothetical protein	C_6091	TIGR02099 family protein
C_2751	undecaprenyl-phosphate glucose phosphotransferase	C_6092	ribonuclease G
C_2752	mannose-1-phosphate guanylyltransferase/mannose-6-phosphate isomerase	C_6093	maf-like protein
C_2753	glycosyltransferase family 2 protein	C_6094	rod shape-determining protein MreD
C_2754	biofilm formation protein PslD	C_6095	hypothetical protein
C_2755	biofilm formation protein PslE	C_6096	hypothetical protein
C_2756	glycosyl transferase family 1	C_6097	hypothetical protein
C_2757	biofilm formation protein PslG	C_6098	type VI secretion system tip protein VgrG
C_2758	glycosyltransferase	C_6099	tRNA-Ala(tgc)
C_2759	glycosyltransferase family 1 protein	C_6121	asparaginase
C_2760	biofilm formation protein PslJ	C_6122	pyoverdine biosynthesis protein PvcA
C_2761	membrane protein	C_6123	TauD/TfdA family dioxygenase

Whilst the development *gyrB* and *nfxB* mutations in the D3 mutant can explain the increase in MIC, the causes of a reduction in MIC seen in the D3.1 revertant remain unclear. The D3 mutant from which it evolved also contained mutations to *D_00441* and *D_02366,* an ABC transporter substrate-binding protein and Histidine-tRNA ligase, which appeared to be gained from duplications in the gene sequences, in addition to an 11bp deletion in *edd,* a Phosphogluconate dehydratase. The revertant, which had an MIC above the resistance breakpoint retained the mutations in *gyrB* and *nfxB,* however contained none of the aforementioned mutations from the D3 mutant. Instead, the D3.1 revertant developed a Arg385His mutation in *parS*, a histidine kinase protein that forms part of a two-component regulatory system with *parR*. The ParRS regulator has been associated with the down regulation off efflux pumps (373, 374). Hence, the reduction in ciprofloxacin MIC in the D3.1 may have been due to a reduction in efflux of the antibiotic.

Within the strain D mutants, mutations to *D_00441*, an ABC transporter substrate-binding protein, were identified (Table 5-5). Different mutations were detected in each of the mutant strains with only the D2.1 revertant appearing to retain the mutation. The site of these mutations were two nucleotide positions apart suggesting that the region the mutation is located in may also be important. Whilst it is unclear how these SNPs could influence changes in ciprofloxacin tolerance, none of the strain D control strains developed mutations to these genes. Additionally, both strains were evolved in the same conditions as independent replicates and therefore the fact different mutations developed in the gene for both the D2 and D3 ciprofloxacin evolved strains suggests that they may be involved in allowing the strain to better adapt to ciprofloxacin supplemented MHB + 10% plasma.

Overall, all the ciprofloxacin evolved mutants developed mutations in multiple genes able to confer ciprofloxacin resistant phenotypes with the combinations and effects differing across strains. For example, both the D3 and E2 mutants contained *nfxB* and *gyrB* mutations. Previous

experiments on *P. aeruginosa* with this combination of mutations have shown high levels of ciprofloxacin resistance occur when both are present (370). Despite this, the strain which both contained *nfxB* and *gyrB* mutations had varying levels of resistance with E2 containing a less pronounced increase at an MIC of 16 μg/ml as opposed to the 128 μg/ml seen in D3. Additionally, the highly ciprofloxacin resistant C4 mutant deleted the *nfxB* gene in addition to the combination of *gyrA, gyrB,* and *parC* mutations leading to an MIC of 128 μg/ml. In summary, variations in the genes responsible for ciprofloxacin resistance resulted in varying increases to MICs suggesting the combination of genes mutated is important in determining the level of resistance achieved.

5.2.2.2.3 Mutations identified across ciprofloxacin and chloramphenicol evolved strains

Mutations in genes that contribute to the same processes were also seen across the strains and replicates (Table 5-4 and Table 5-5) indicative of adaption regardless of the antibiotic pressure. For instance, the chloramphenicol evolved mutant D1 developed a mutation to *phzC* and the ciprofloxacin evolve mutant C4 developed mutations in *phzF*. In both cases these mutations were not detected in the respective mutant strains though it is unclear if this is due to the variant callers being unable to successful identify the SNP in the revertants. Mutations in the *pilR* and *pilV* genes were seen in the chloramphenicol evolved C2 mutant and the ciprofloxacin evolved E2 mutant respectively. The genes are both connected to type IV pili: *pilR* forms part of a two-component system that regulates expression of the type IV pilus major subunit PilA and *pilV* encodes a minor pilin which is involved in assembly of the type IV pili (375, 376). The chloramphenicol evolved C3.1, and ciprofloxacin evolved C4 and C4.1, both showed mutations to genes involved in flagella. The *fleQ* gene encodes a transcriptional regulator and the *fliG* genes encodes the C-ring protein which forms part of the membrane complex of flagella (377). Mutations to flagella were not detected in any of the other strains, replicate, or control strain indicating that these were unique to these strains (Table 5-4 and Table 5-5). Both type IV pili

and flagella provide motility to bacteria and so it is possible this ability is compromised in these strains.

5.2.2.3 Fitness of environmental strains exposed to clinical conditions

The revertant strains which developed increased susceptibility to antibiotics after evolution in sub-inhibitory concentrations where subjected to growth curve analysis to assess their fitness against their ancestral antibiotic tolerant mutant and antibiotic sensitive parent strains. Growth curves were performed under sub-inhibitor concentrations on antibiotics determined to be two MIC doubling dilution below the lowest MIC. For ciprofloxacin this was found to be 0.008 μg/ml and in chloramphenicol this was 2 μg/ml.

5.2.2.3.1 Fitness of chloramphenicol evolved strains

From the three revertants generated from strain C, revertant C2.1 showed the greatest increase in area under the curve (*Mdn* = 18.12, *IQR* = 0.79; Mann-Whitney test *U* = 0, *p* = 0.000183) over its ancestral parent in the absence of chloramphenicol (Area under the curve: *Mdn* = 11.81, *IQR* = 0.38) (Figure 5-13 and Figure 5-14). The C2.1 revertant contained a deletion that included the *mexEF-oprN* operon and its regulators *mexS* and *mexT,* like the A1.1 and A1.2 revertants seen in Section 5.2. In contrast, the C2.1 revertant appeared to have a similar area under the curve (*Mdn* = 4.41, *IQR* = 1.13; Mann-Whiteney *U* = 52, *p* = 0.910) to its parent (*Mdn* = 4.14 *IQR* = 1.00) when chloramphenicol was present restoring the increase in area seen by the mutant back to the levels of the parent. As expected of a strain evolved in the presence of antibiotics, the C2 mutant also showed a greater area under the curve (*Mdn* = 14.64, *IQR* = 0.36; Mann-Whitney *U* = 0, *p* = 0.000183) when chloramphenicol was present. Without the antibiotic pressure the C2 mutant, also showed a greater increase in area under the curve (*Mdn* = 16.09, *IQR* = 0.63; Mann-Whitney test *U* = 0, *p* = 0.000183) than its parent, suggesting the mutations gained by the strain were beneficial in both circumstances. Hence the advantage gained by the

C2 mutant would make it seem that reversion to a lower chloramphenicol susceptibility was not needed, however when considering the area under the curve the C2.1 revertant gained an advantage (Mann-Whitney $U = 0$, $p = 0.000183$) when grown in the antibiotic free media in which it reverted.

The other revertants produced from strain C, appeared to also show a reduction in area under the curve (C1.1: *Mdn* = 7.78, *IQR* = 0.56; Mann-Whitney test $U = 100$, $p = 0.000183$. C3.1: *Mdn* = 7.59, *IQR* = 0.53; Mann-Whitney test $U = 100$, $p = 0.000183$) (Figure 5-13 and Figure 5-14) when grown in the absence of antibiotics and thus strains C1.1 and C3.1 showed they were disadvantaged when compared to its parent. Due to the revertant developing lower chloramphenicol susceptibility in antibiotic free media, it would be expected that the revertants would perform better than its ancestral mutant strain in these conditions. However, this was not the case for revertant C3.1, which was outperformed by the C3 mutant (Area under the curve: *Mdn* = 7.59, *IQR* = 0.53; Mann-Whitney $U = 100$, $p = 0.000183$) in the absence of chloramphenicol and thus reversion through a Gly113Asp mutation in *mexT* did not appear to be beneficial to bacterial fitness. Overall, the result from these strains is like the results seen in the previous experiment (Section 5.2), where deletion of the *mexEF-oprN* operon and its regulators showed the greatest increase in fitness. Hence, it appears reversion through the complete deletion of *mexS* and *mexT* produces the strains with fittest phenotypes.

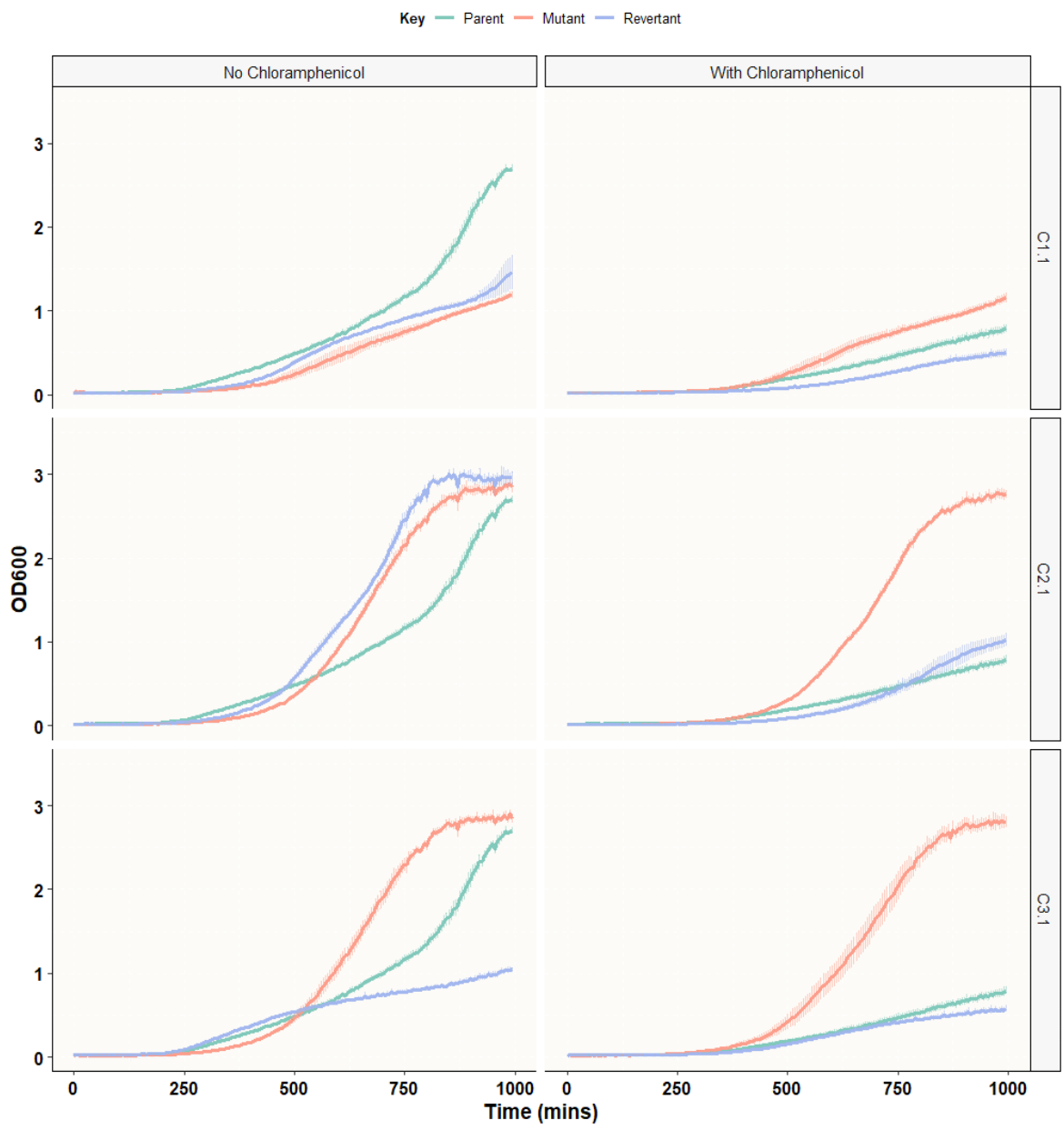

Figure 5-13: Growth curves of revertant strains C1.1, C2.1, and C3.1 in MHB + 10% plasma with their respective chloramphenicol evolved mutant and ancestral parent strains. Growth is plotted as the mean absorbance at OD_{600} based on ten replicates, from two independent experiments with five replicates each, in the presence and absence of a sub-inhibitory concentration of chloramphenicol (2μg/ml). Error bars represent the 95% confidence intervals.

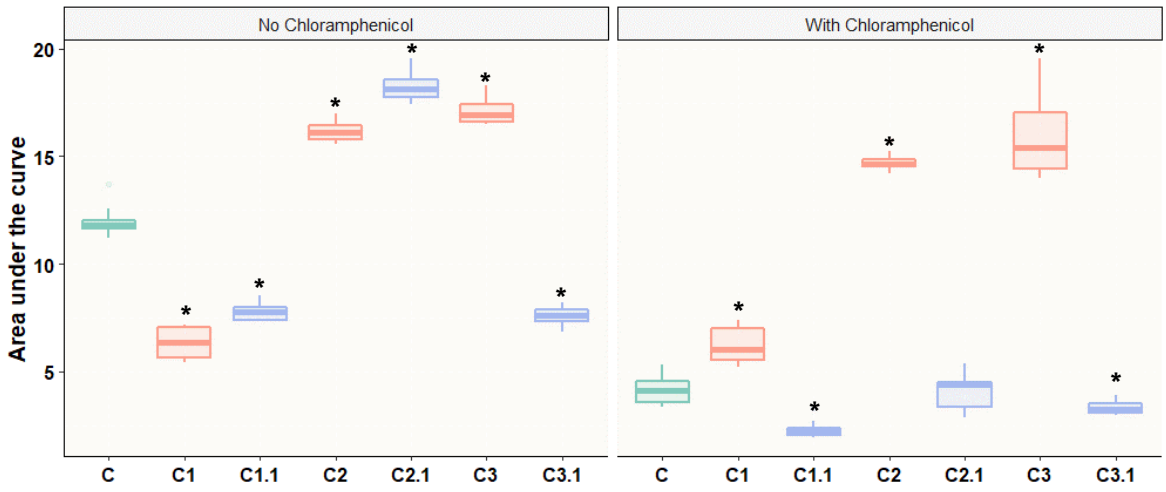

*Figure 5-14: Area under the curve determined from growth curves of Strain C (PA232) with mutations in mexS and mexT. Strains were grown in the presence and absence of a sub-inhibitory concentration of chloramphenicol (2µg/ml) with error bars depict the 95% confidence intervals of ten replicates from 2 independent experiments. Strains with a significant difference (p ≤ 0.05) to its parent strain were determined by a Mann-Whitney U test and are marked with a * symbol.*

From the parent strain D, one mutant evolved in the presence of chloramphenicol through a *mexS* Leu186Phe mutation which then developed a *mexT* Thr18Pro mutation when grown in antibiotic free media to "switch-off" MexEF-OprN mediated efflux. When considering the area under the curve, the D1.1 mutation appeared to have a slight increase in area (*Mdn* = 4.25, *IQR* = 2.25) over both the parent (*Mdn* = 3.00, = *IQR* = 1.00; Mann-Whitney *U* = 29, *p* = 0.279) and mutant (*Mdn* = 3.14, *IQR* = 1.62; Mann-Whitney *U* = 45, *p* = 0.734) when looking at the bacteria growth curves in the absence of chloramphenicol (Figure 5-15), however this was not determined to be significant (Figure 5-16). With the added pressure of a sub-inhibitory concentration if chloramphenicol, the D1 mutant (*Mdn* = 2.19, *IQR* = 2.48) gained an advantage in terms of area under the curve over the parental strain (*Mdn* = 1.00, *IQR* = 0.54; Mann-Whitney *U* = 13, *p* = 0.006) and the revertant (*Mdn* = 0.41, *IQR* = 0.45; Mann-Whitney *U* = 100, *p* =0.000549). In contrast, the D1.1 revertant had a smaller area when compared to the parent (Mann-Whitney *U* = 87, *p* = 0.006). Therefore, reversion through the mutations seen in strain D1.1 did not appear to provide a fitness advantage over either the parent or the mutant in the conditions tested.

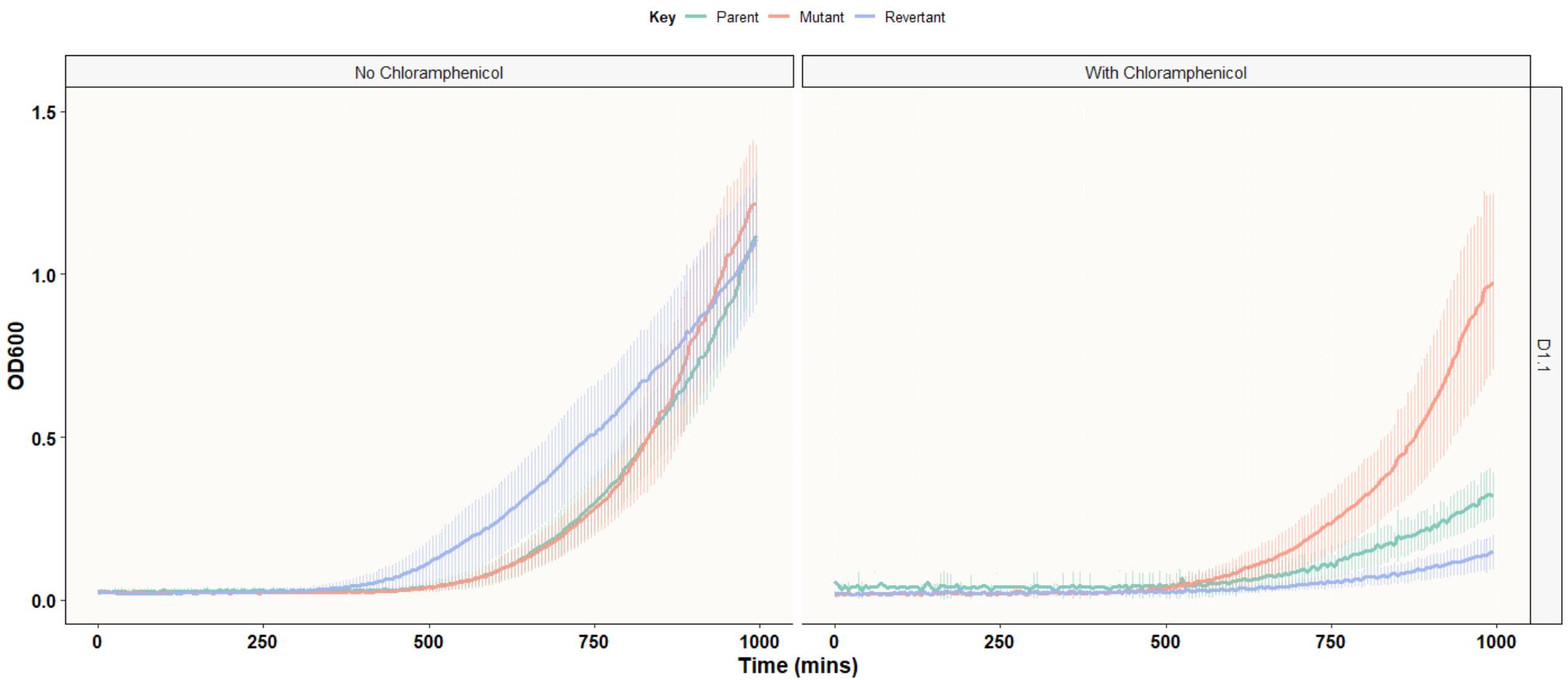

Figure 5-15: Growth curves of revertant strain D1.1 in MHB + 10% plasma with its respective chloramphenicol evolved mutant and ancestral parent strain. Growth is plotted as the mean absorbance at OD_{600} based on ten replicates, from two independent experiments with five replicates each, in the presence and absence of a sub-inhibitory concentration of chloramphenicol (2µg/ml). Error bars represent the 95% confidence intervals.

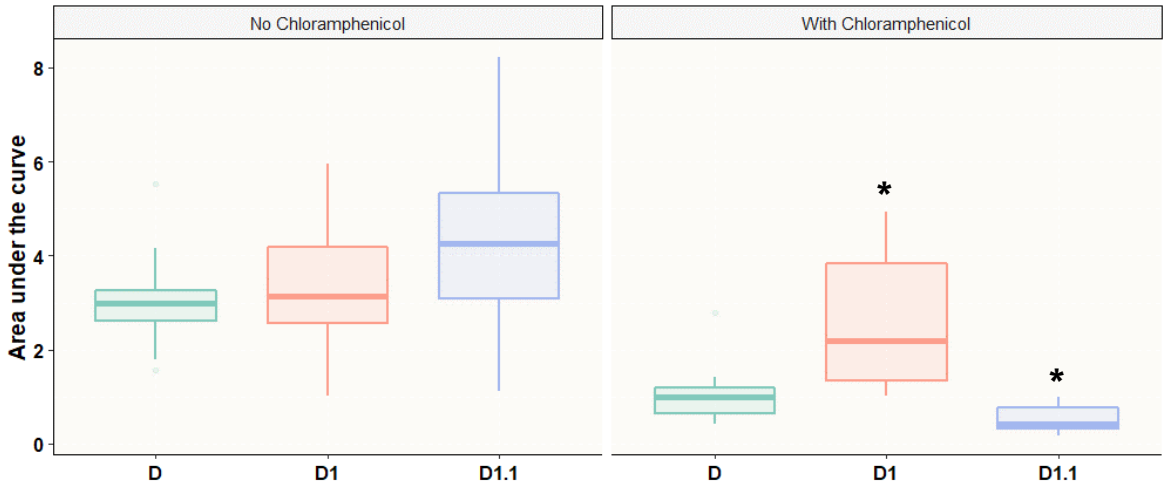

*Figure 5-16: Area under the curve determined from growth curves of Strain D (PA63) evolved in chloramphenicol. Strains were grown in the presence and absence of a sub-inhibitory concentration of chloramphenicol (2µg/ml) with error bars depict the 95% confidence intervals of ten replicates from 2 independent experiments. Strains with a significant difference (p ≤ 0.05) to its parent strain were determined by a Mann-Whitney U test and are marked with a * symbol.*

The final environmental strain evolved in chloramphenicol was parent strain E, which developed a partial deletion in its *mexS* gene to "switch-on" efflux in the E1 mutants, followed by a *mexT* Arg48Cys to "switch-off" efflux in revertant E1.1. As expected, the E1 mutant gained an advantage in area under the curve (*Mdn* = 6.78, *IQR* = 3.45) over the parent (*Mdn* = 3.10, *IQR* = 0.25; Mann-Whitney *U* = 0, *p* = 0.00274) and the E1.1 revertant (*Mdn* = 2.48, *IQR* = 2.31; Mann-Whitney *U* = 100, *p* = 0.000274) when grown in the presence of chloramphenicol. The E1.1 revertant was shown to have restored its area to similar levels as the parent (Mann-Whitney *U* = 53, *p* = 0.850) when grown with chloramphenicol, however without the antibiotic the E1.1 revertant developed an increased area (*Mdn* = 13.69, *IQR* = 3.13) over the parent (*Mdn* = 9.61, *IQR* = 2.65; Mann-Whitney *U* = 0, *p* = 0.000274) and the mutant (*Mdn* = 8.52, *IQR* = 3.45; Mann-Whitney *U* = 0, *p* = 0.000274). Therefore, is the case strain E, reversion through a double *mexS* and *mexT* mutant provided a fitness advantage over the parent when no antibiotic pressure was present and restored fitness levels to that of the parent when antibiotic pressure was present.

Overall, all the environmental strains evolved with chloramphenicol in MHB + 10% plasma developed mutations in *mexS* resulting in constitutive efflux. Once grown in the absence of antibiotic pressure, all mutant strains reverted to a more sensitive phenotype through mutations to *mexT*. Of all the revertant strains identified, the greatest increase in bacterial fitness was seen in revertant C2.1 where the mutations seen in *mexS* and *mexT* were caused by a deletion of the *mexEF-oprN* operon.

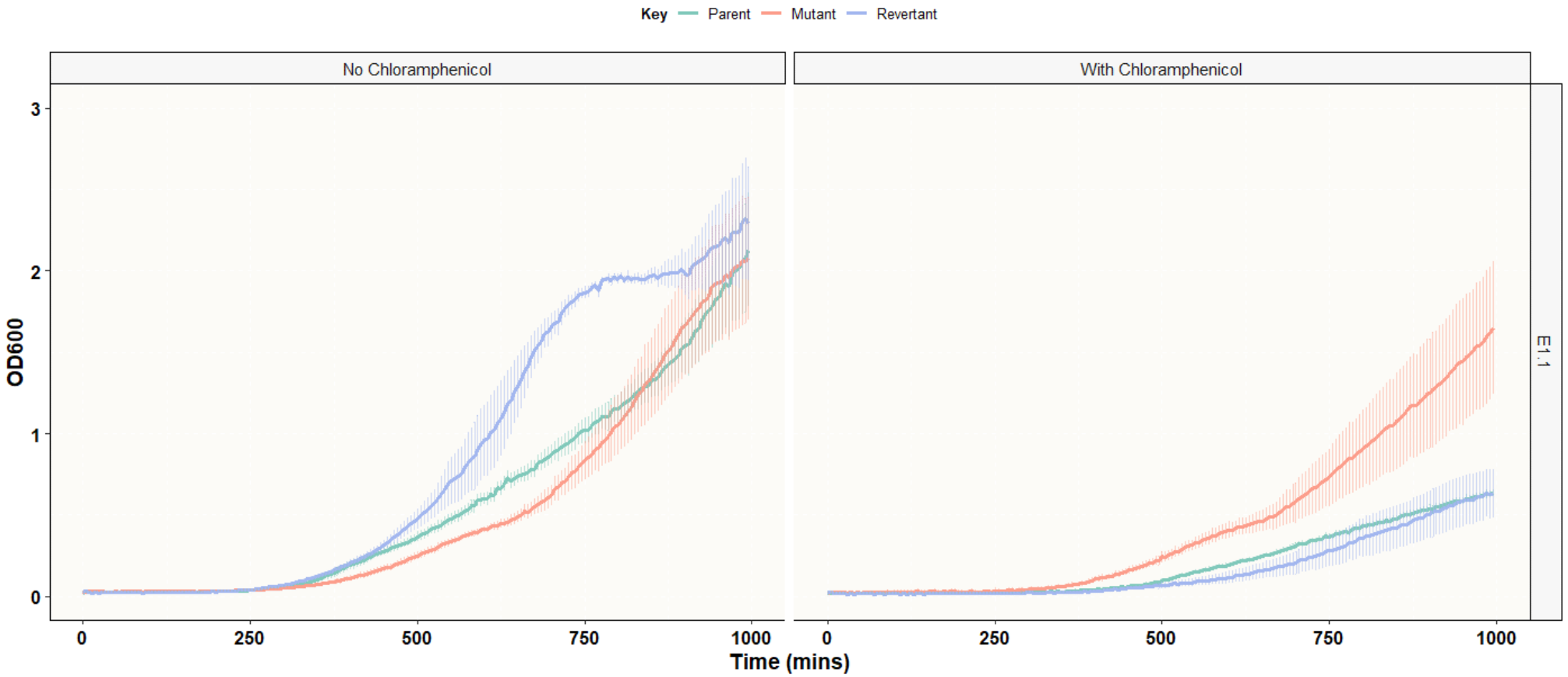

Figure 5-17: Growth curves of revertant strain E1.1 in MHB + 10% plasma with its respective chloramphenicol evolved mutant and ancestral parent strain. Growth is plotted as the mean absorbance at OD_{600} based on ten replicates, from two independent experiments with five replicates each in the presence and absence of a sub-inhibitory concentration of chloramphenicol (2µg/ml). Error bars represent the 95% confidence intervals.

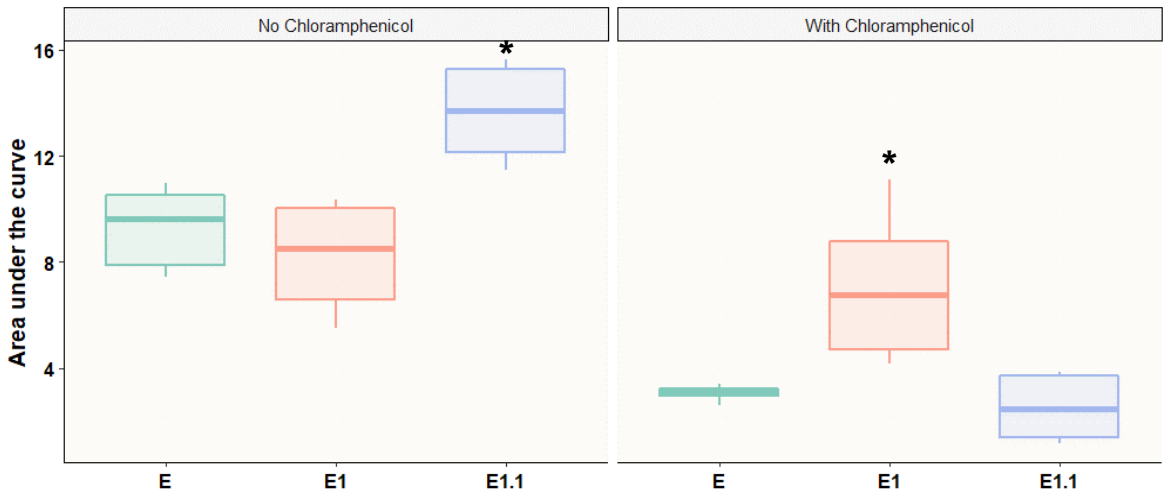

*Figure 5-18: Area under the curve determined from growth curves of Strain E (PA2629) evolved in chloramphenicol. Strains were grown in the presence and absence of a sub-inhibitory concentration of chloramphenicol (2µg/ml) with error bars depict the 95% confidence intervals of ten replicates from two independent experiments. Strains with a significant difference (p ≤ 0.05) to its parent strain were determined by a Mann-Whitney U test and are marked with a * symbol.*

5.2.2.3.2 Fitness of ciprofloxacin evolved strains

When exposed to increasing concentrations of ciprofloxacin, strain C developed mutations in *nfxB,* the transcriptional repressor of the *mexCD-oprJ* operon, as well as *gyrA, gyrB,* and *parC.* Once the antibiotic pressure was removed, the evolved mutant strain reduced its tolerance to ciprofloxacin through a mutation in *mexC* to "switch-off" MexCD-OprJ mediated efflux. Whilst it would be expected for mutants evolved in ciprofloxacin to show greater fitness when grown in the presence of the antibiotics, this was not the case for the C4 mutant. When looking at the area under the curve for the strains grown in sub-inhibitory concentration of ciprofloxacin the C4 mutant (*Mdn* = 2.40, *IQR* = 0.45) and C4.1 revertant strain (*Mdn* = 3.05, *IQR* = 0.31) both showed smaller areas when compared to their ancestral parent strain C (*Mdn* = 13.34, *IQR* = 1.23; C4: Mann-Whitney $U = 100$, $p \leq 0.05$; C4.1: Mann-Whitney $U = 100$, $p = 0.000274$). Furthermore, the C4.1 revertant showed a slightly larger area under the curve (Mann-Whitney $U = 90$, $p = 0.003$) than its ciprofloxacin evolved ancestral mutant C4, implying that functional *mexC* provides a cost. In the absence of ciprofloxacin, similar results are seen in regards to the parental strain (*Mdn* = 14.71, *IQR* = 2.26) which shows a larger area under the curve that both

its C4 mutant (*Mdn* = 2.63, *IQR* = 0.48; Mann-Whitney *U* = 100, *p* = 0.000274) and its C4.1 revertant *Mdn* = 2.44, *IQR* = 0.59; Mann-Whitney *U* = 100, *p* = 0.000274). In terms of the C4 mutant and C4.1 revertant when grown in the absence of ciprofloxacin, the mutant strain appeared to have a slight advantage in area under the curve however this was not determined to be significant (Mann-Whitney *U* = 64, *p* = 0.307). In summary, the C4 mutant which contained four mutations (*gyrA, gyrB, nfxB,* and *parC*) involved in ciprofloxacin resistance did not provide an advantage to the strain when grown with and without sub-inhibitory concentrations of ciprofloxacin. Furthermore, this lack of advantage in either condition was also seen in the revertant strain which evolved from the mutant suggesting the mutation it gained did not provide any advantages to the strain.

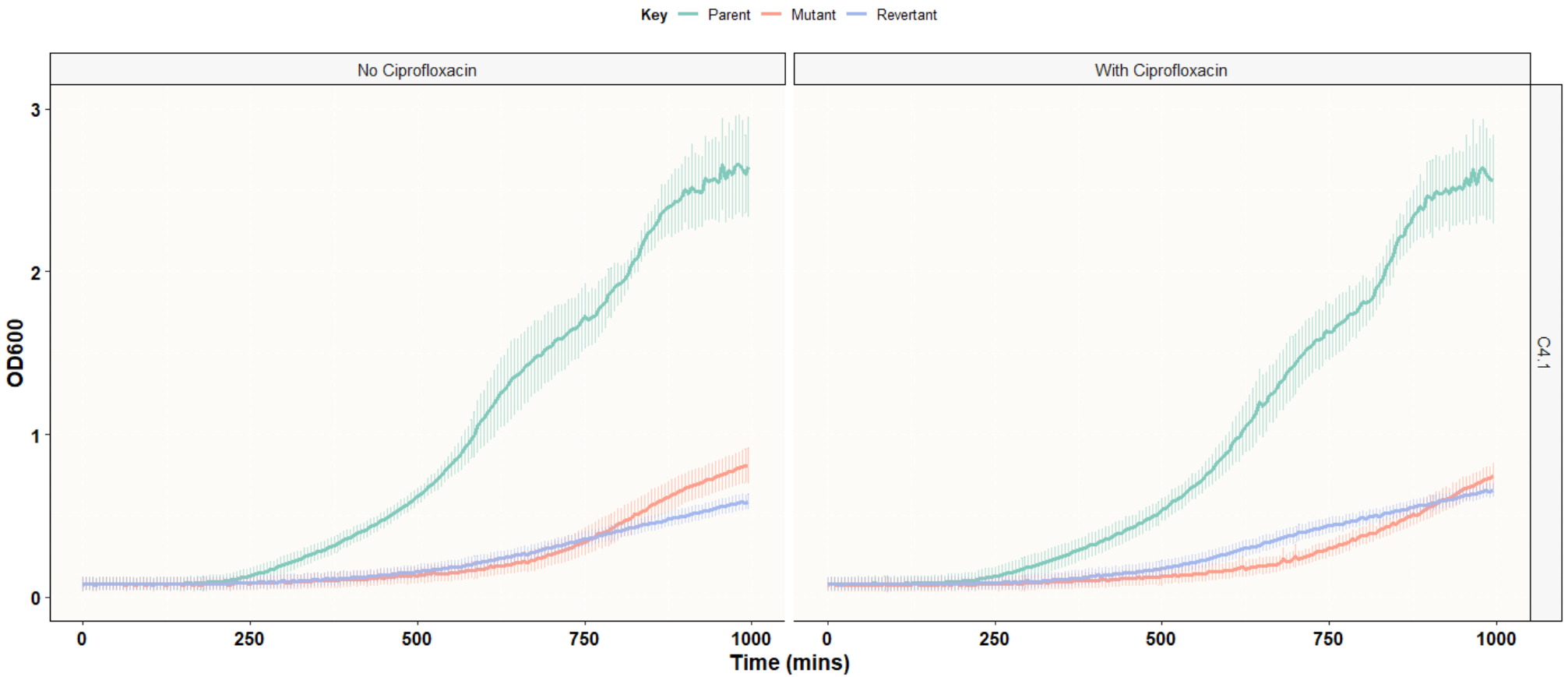

Figure 5-19: Growth curves of revertant strain C4.1 in MHB + 10% plasma with its respective ciprofloxacin evolved mutant and ancestral parent strain. Growth is plotted as the mean absorbance at OD_{600} based on ten replicates, from two independent experiments with five replicates each, in the presence and absence of a sub-inhibitory concentration of ciprofloxacin (0.008 µg/ml). Error bars represent the 95% confidence intervals.

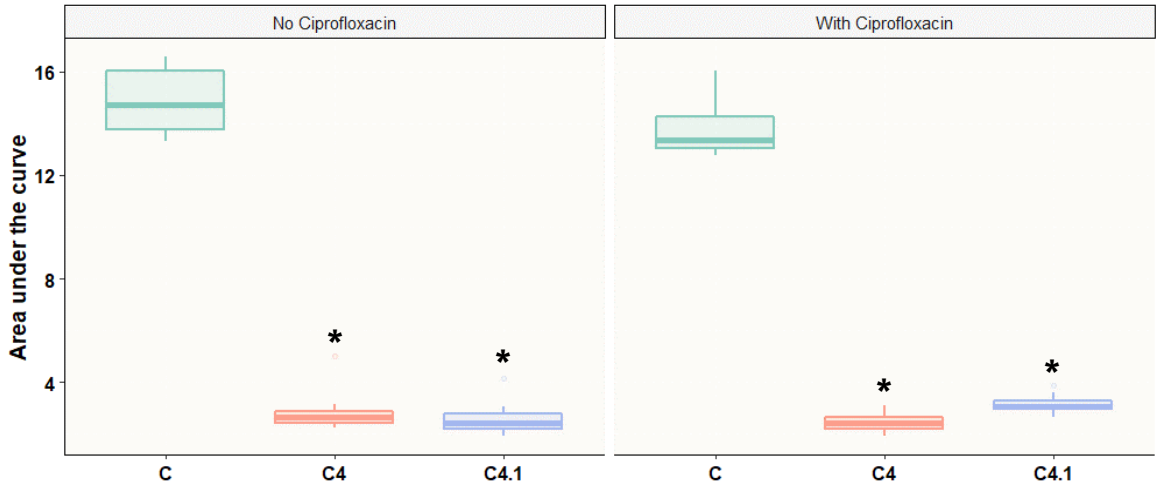

*Figure 5-20: Area under the curve determined from growth curves of Strain C (PA232) evolved in ciprofloxacin. Strains were grown in the presence and absence of a sub-inhibitory concentration of ciprofloxacin (0.008 µg/ml) with error bars depict the 95% confidence intervals of ten replicates from 2 independent experiments. Strains with a significant difference (p ≤ 0.05) to its parent strain were determined by a Mann-Whitney U test and are marked with a * symbol.*

The second environmental strain evolved in ciprofloxacin, strain D, produced two mutant strains with higher ciprofloxacin MICs that the parent which then reverted to lower MIC after growth in antibiotic free media. One of the mutants, D2, evolved mutations in the *nfxB* and *gyrA* genes which have been associated with increased ciprofloxacin tolerance, in addition to a *mexC* which is associated with reduced tolerance to ciprofloxacin. The revertant strain which evolved from the D2 mutant, D2.1, contained the same mutations and did not appear to have any additional mutations to result in a further reduction to ciprofloxacin tolerance, despite showing a lower ciprofloxacin MIC. The other mutant evolved from strain D was the D3 mutant which developed mutations in *gyrB* and *nfxB* to increase its ciprofloxacin MIC. The revertant linked to it, D3.1, reverted to a lower but still resistant MIC for ciprofloxacin, however no additional mutations that could be involved in reversion were identified in the strain. When compared to the parental strain (No CIP: *Mdn* = 1.31, *IQR* = 1.64. CIP: *Mdn* = 1.97, *IQR* = 1.28), both the D2 (No CIP: *Mdn* = 2.04, *IQR* = 1.77; Mann-Whitney *U* = 31, p = 0.18. CIP: *Mdn* = 2.34, *IQR* = 1.75; Mann-Whitney *U* = 41, p = 0.579) and D2.1 (No CIP: *Mdn* = 2.20, *IQR* = 1.74; Mann-Whitney *U* = 28, p = 0.13. CIP: *Mdn* = 3.21, *IQR* = 3.10; Mann-Whitney *U* = 34, p = 0.301) strains

did not show any significant differences in their area under the curve. Despite this, both the mutant and revertant strains showed a small increase in the area over the parent in both conditions. In the case of the D3.1 revertant, area under the curve (No CIP: *Mdn* =4.12, *IQR* = 1.02. CIP: *Mdn* = 4.44, *IQR* = 0.50) was greater than the parental strain both in the absence (*Mdn* = 1.31, *IQR* = 1.64; Mann-Whitney $U = 9$, $p = 0.0004$) and presence (*Mdn* = 1.97, *IQR* = 1.28; Mann-Whitney $U = 8$, $p = 0.003$). Unexpectedly, the D3 mutant strain, which was evolved in ciprofloxacin, showed a small area under the curve (*Mdn* = 0.27, *IQR* = 0.11) than both the parent strain (Mann-Whitney $U = 95$, $p = 0.002$) and revertant strain (Mann-Whitney $U = 100$, $p = 0.000915$) in presence of ciprofloxacin. Similarly, this was also seen when the mutant was grown in the absence of the antibiotic (*Mdn* = 0.30, *IQR* = 0.38), where both the more sensitive parent (Mann-Whitney $U = 100$, $p = 0.000459$) and revertant strains (Mann-Whitney $U = 0$, $p = 0.000458$). In conclusion the mutations seen in the D2 mutant and 2.1 revertant did not appear to change the fitness of the strains despite altering the tolerance to ciprofloxacin. In addition, the development of both *gyrB* and *nfxB* mutations was seen in both the D3 and D3.1 mutants, however only the D3.1 showed an advantage over the parental strain suggesting that other mutation developed in the revertant strains may have provided the strain with improved fitness of both its ancestors.

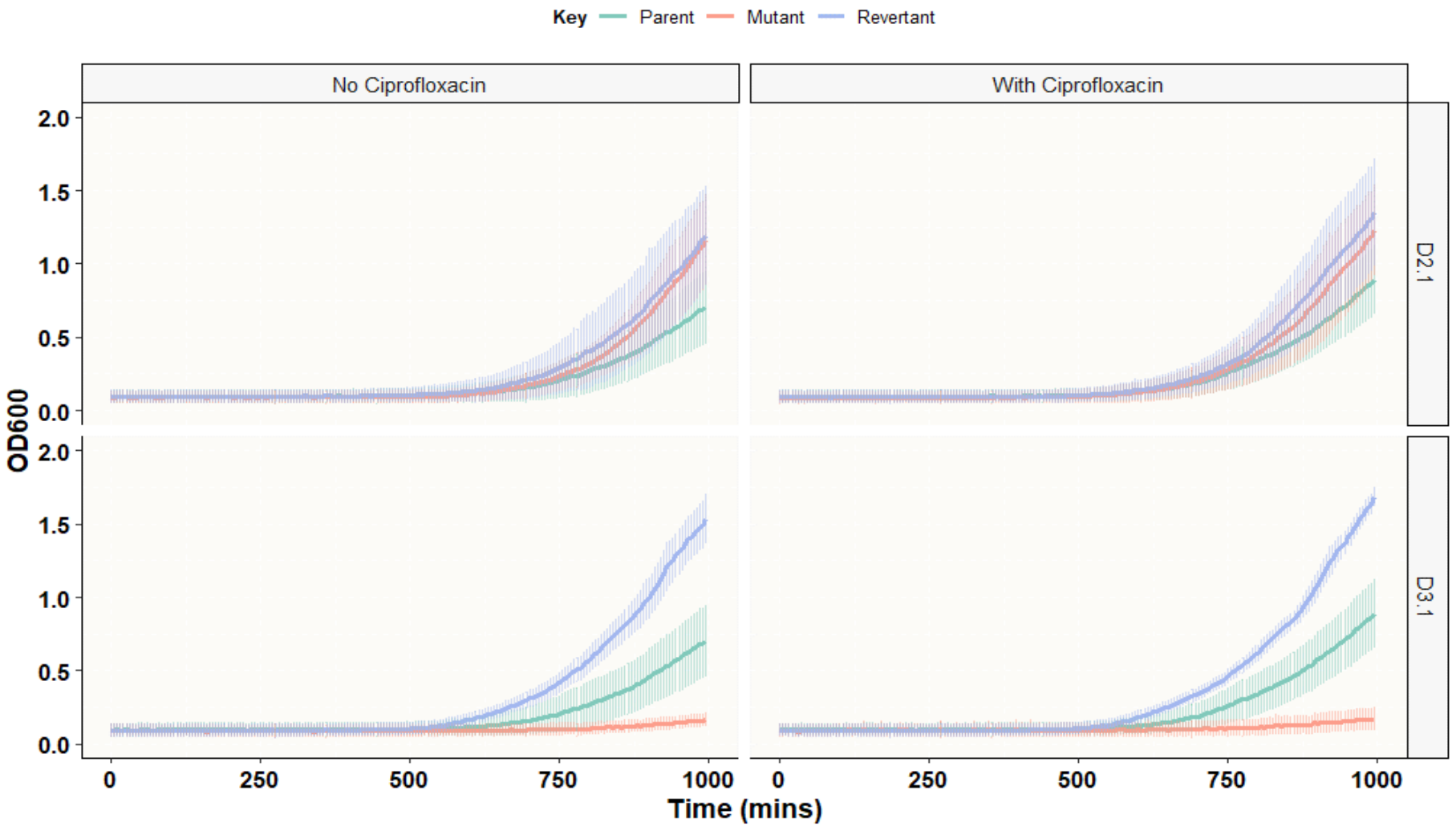

Figure 5-21: Growth curves of revertant strains D2.1 and D3.1 in MHB + 10% plasma with their respective ciprofloxacin evolved mutant and ancestral parent strains. Growth is plotted as the mean absorbance at OD_{600} based on ten replicates, from two independent experiments with five replicates each, in the presence and absence of a sub-inhibitory concentration of ciprofloxacin (0.008 µg/ml). Error bars represent the 95% confidence intervals.

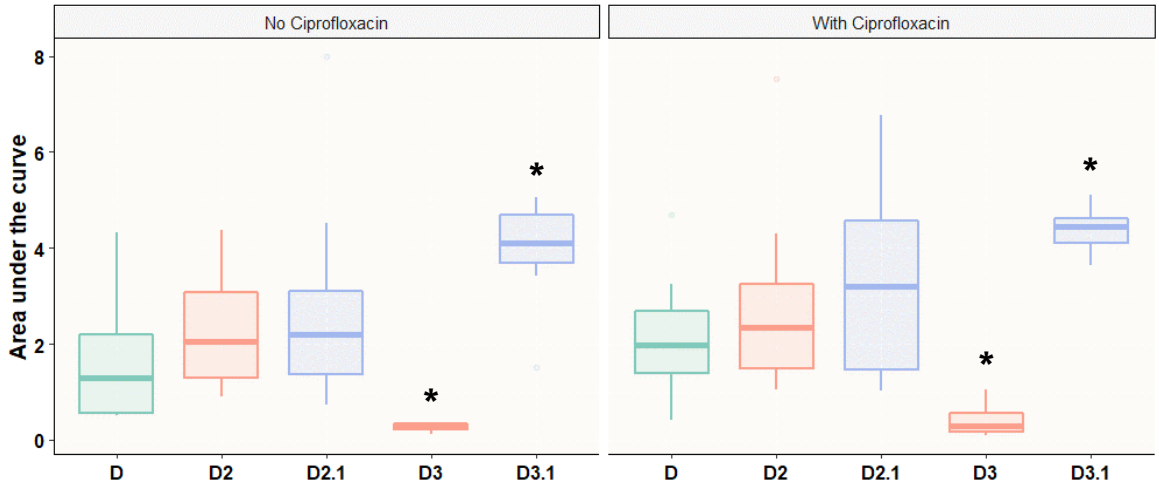

*Figure 5-22: Area under the curve determined from growth curves of Strain D (PA63) evolved in ciprofloxacin. Strains were grown in the presence and absence of a sub-inhibitory concentration of ciprofloxacin (0.008 µg/ml) with error bars depict the 95% confidence intervals of ten replicates from two independent experiments. Strains with a significant difference (p ≤ 0.05) to its parent strain were determined by a Mann-Whitney U test and are marked with a * symbol.*

The last environmental strain evolved in clinical conditions using ciprofloxacin was strain E. Whilst under the pressure of ciprofloxacin, the strain developed mutations in the ciprofloxacin resistance genes *gyrB* and *nfxB* in order to grow in the presence of the antibiotic and was named E2. After removal of the antibiotic, the strain reduced its MIC in ciprofloxacin through a mutation in *mexC* creating the revertant E2.1. When looking at the area under the curves generated by the E1 mutant (No CIP: *Mdn* = 11.62, *IQR* = 4.63. CIP: *Mdn* = 11.49, *IQR* = 3.63), slight increases over the parental strain (No CIP: *Mdn* = 11.30, *IQR* = 3.69. CIP: *Mdn* = 10.05, *IQR* = 2.55) were seen however this increase was not determined significant (No CIP: Mann-Whitney *U* = 44, *p* = 0.678. CIP : Mann-Whitney *U* = 31, *p* = 0.162). Unlike the mutant, the E2.1 revertant strain which evolved from it showed a much larger increase in its area under the curve when grown in the absence (*Mdn* = 15.31, *IQR* = 2.92; Mann-Whitney *U* = 8, *p* = 0.005) and presence (*Mdn* = 15.67, *IQR* = 3.13; Mann-Whitney *U* = 3, *p* = 0.001) which was determined to be significant. Therefore, the development of mutation a *mexC* that "switches-off" MexCD-OprJ efflux in the revertant provides an advantage for the strain in both conditions.

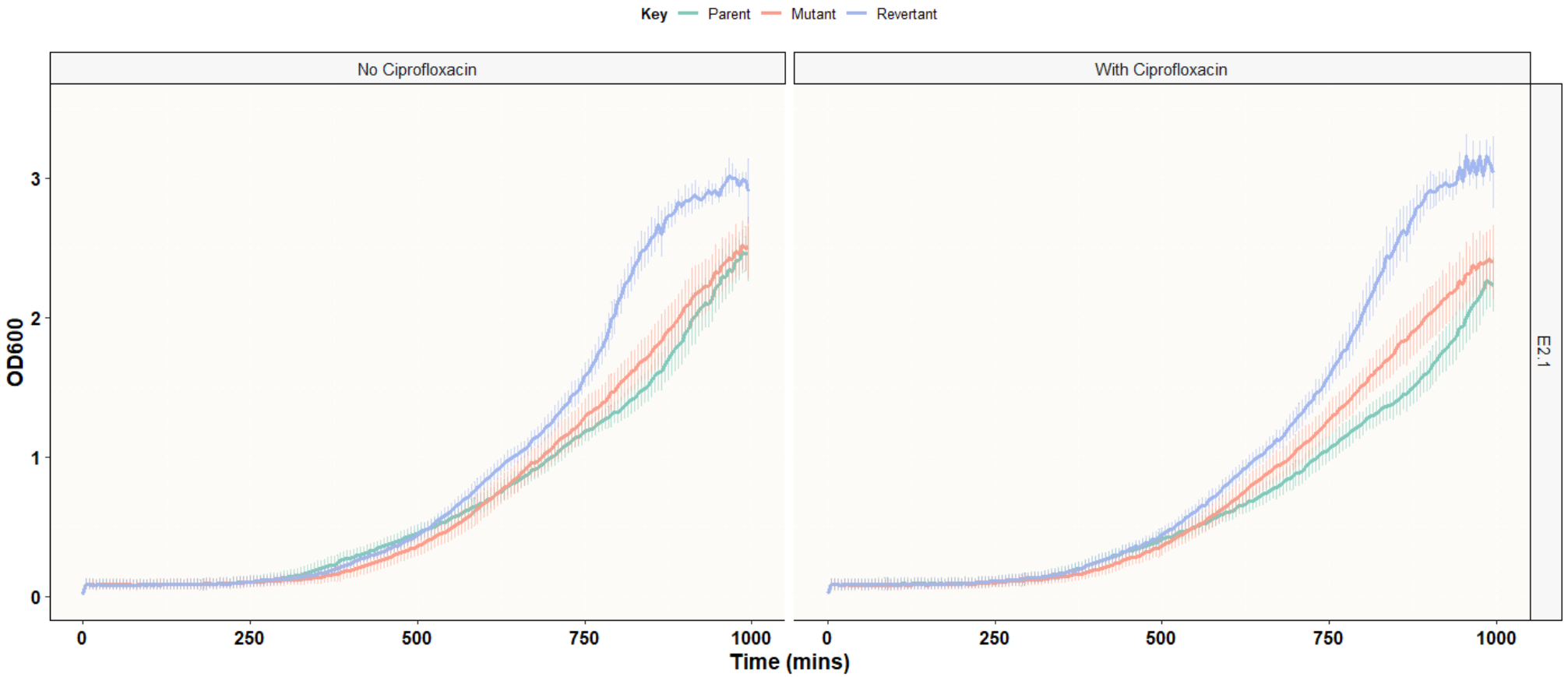

Figure 5-23: Growth curves of revertant strain E2.1 in MHB + 10% plasma with its respective ciprofloxacin evolved mutant and ancestral parent strain. Growth is plotted as the mean absorbance at OD_{600} based on ten replicates, from two independent experiments with five replicates each, in the presence and absence of a sub-inhibitory concentration of ciprofloxacin (0.008 µg/ml). Error bars represent the 95% confidence intervals.

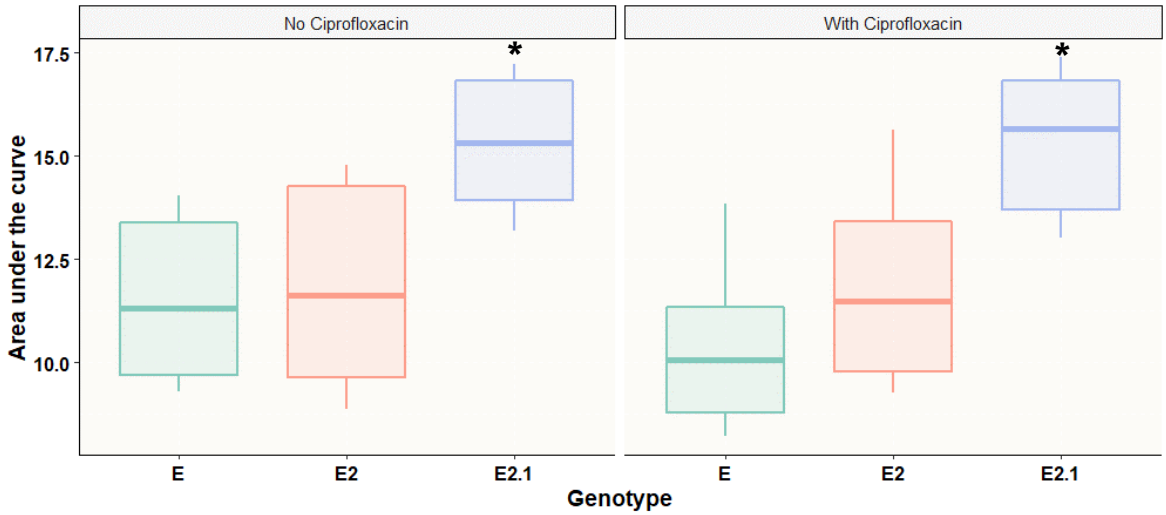

*Figure 5-24: Area under the curve determined from growth curves of Strain E (PA2629) evolved in ciprofloxacin. Strains were grown in the presence and absence of a sub-inhibitory concentration of ciprofloxacin (0.008 µg/ml) with error bars depict the 95% confidence intervals of ten replicates from two independent experiments. Strains with a significant difference ($p \leq 0.05$) to its parent strain were determined by a Mann-Whitney U test and are marked with a * symbol.*

Overall, all three environmental strains evolved in ciprofloxacin developed mutants and revertants which had varying fitness levels, in terms of area under their growth curve, with respect to their ancestral parent strain. Mutations resulting in increased MIC than the parent appeared to show similar or reduced fitness levels to the parent, suggesting the evolution of ciprofloxacin resistance was not advantageous. Despite this, two of the mutant strains evolved into revertant strains, D3.1 and E2.1, with increases in fitness over both the mutant itself and their ancestral parent. While the mutations developed in these revertants both involved *gyrB* and *nfxB*, they could not solely be identified as the reasons for the fitness increase due to the presence of these mutations in the C4.1 revertant strain which had a reduced fitness to its parental strain.

5.3 Discussion

5.3.1 Evolution in chloramphenicol results in mutations to antibiotic resistance-causing genes

All strains evolved in MHB + 10% plasma and chloramphenicol developed mutation in *mexS* followed by a mutation in *mexT* after removal of the antibiotics. Hence, the addition and removal of chloramphenicol from *P. aeruginosa* cultures can "switch-on" and "switch-off" efflux mediated by MexEF-OprN as seen in previous studies (Correia *et al.*, unpublished). A summary of the mutations acquired and their effect on the fitness of the mutant and revertant strains is summarised in Table 5-8.

Table 5-8: Summary of mutations effecting chloramphenicol tolerance in chloramphenicol evolved mutant and revertants. Table includes genes which are known to alter chloramphenicol tolerance with fitness calculated with respect to the area under the curve in media with and without a sub-inhibitory concentration of chloramphenicol (2 μg/ml).

Strain		Fitness relative to the parent		Fitness relative to the mutant		CHL MIC	Genes**	
		No CHL	CHL	No CHL	CHL		mexS	mexT
A1	Mutant	less	greater			>128*	sub	
A1.1	Revertant	greater	greater	greater	less	32*	del	del
A1.2	Revertant	greater	greater	greater	less	32*	del	del
A2	Mutant	less	greater			>128*	fs	
A2.1	Revertant	less	greater	greater	less	32*	fs	sub
A2.2	Revertant	less	greater	greater	less	32*	fs	fs
B3	Mutant	less	greater			>128*	fs	
B3.1	Revertant	same	less	greater	less	32*	fs	fs
C1	Mutant	less	greater			256	sub	
C1.1	Revertant	less	less	greater	less	16	sub	stop
C2	Mutant	greater	greater			256	sub	
C2.1	Revertant	greater	same	greater	less	8	del	del
C3	Mutant	greater	greater			256	sub	
C3.1	Revertant	less	less	less	less	8	sub	sub
D1	Mutant	same	greater			128	sub	
D1.1	Revertant	same	less	same	less	8	sub	sub
E1	Mutant	same	greater			128	del	
E1.1	Revertant	greater	same	greater	less	8	del	sub

** The chloramphenicol MIC is reported as the MIC found in the media in which the reversion occurred.*

*** The type of mutation indicated by the gene "sub" represent substitution mutations, "del" represents a deletion of the gene, and "fs" represents a gene with a frameshift.*

5.3.1.1 The type of mutation present in mexS *influences fitness levels*

As expected of strains which have been evolved in chloramphenicol, all mutant strains showed greater areas under the curve, when grown in the presence of chloramphenicol. The increase in fitness appeared to be linked to mutations in *mexS* gene as no other genes were found to be commonly affected by mutations across the other mutants. In the absence of chloramphenicol, the area under the curve for these mutants varied according to the *mexS* mutation seen in the strains.

The mutations seen in *mexS* of mutants A1, A2 and B3 resulted in frameshifts which lead to a smaller area under the curve when compared to their respective parent (Table 5-8). As frameshift mutations alter the amino acid sequence following the mutation, the resulting product is unlike its original wildtype format. Therefore, the larger areas seen in these two strains is likely due to the disruption of *mexS.* Fragmentation of the *mexS* gene was seen in the E1 mutant due to a small deletion of 91 bps within the middle of the gene. As with frameshifts, mutations leading to fragmentation of a gene alter the product formed by the gene. Hence, it could be expected for the area under the curve of strains with a fragmented *mexS* gene to show a difference in area to its parent. This was not seen in the E1 mutant strain however, the area under the growth curve did appear to show a slight but not significant reduction (Figure 5-18: Area under the curve determined from growth curves of Strain E (PA2629) evolved in chloramphenicol. Strains were grown in the presence and absence of a sub-inhibitory concentration of chloramphenicol (2µg/ml) with error bars depict the 95% confidence intervals of ten replicates from two independent experiments. Strains with a significant difference ($p \leq 0.05$) to its parent strain were determined by a Mann-Whitney U test and are marked with a * symbol.). The SNPs seen in *mexS* of C1, C2, C3, and D1 were located in various position throughout the gene sequence with each SNP showing different fitness levels to its respective parent in terms of the area under the curve. The SNPs in C2 and C3 were found towards the end of the *mexS* sequence and caused changes at positions 332 and 281 in the

amino acid sequence. Both of these changes resulted in a greater area under the curve with respect to their parent strains (Table 5-8). Conversely, the mutation seen in *mexS* from the C1 mutant occurred earlier affecting the amino acid expressed at position 60 resulting in a smaller area compared to its parent (Table 5-8).

As the location and specific mutation obtained by a gene can influence the structure of its product, particularly if located in key regions of the product such as a binding domain, the structure of MexS was obtained through UniProt (223). At present, the features of the MexS protein have not fully been described and so it is difficult to ascertain whether the *mexS* mutations described in this study are impacting specific domains or features of the protein. Despite this, the results of this study show that frameshifts and SNPs which occur early in the gene sequence result in worse fitness when no chloramphenicol is present. In contrast, better fitness was seen in *mexS* mutants grown in the absence of chloramphenicol where SNPs occurred late in the gene sequence. A previous study by Richardot *et al.* has shown different *mexS* mutations can alter *mexE* expression to varying degrees (336). Thus, it appears that the level of disruption caused by a mutation appears to influence the fitness levels through changes in MexEF-OprN expression. To confirm this further investigation into how mutations alter MexS structure and expression of the *mexEF-oprN* operon is required.

Few studies have examined the fitness of *mexS* mutation on bacterial fitness, and so it is unclear how comparable the specific mutations observed in this study are to previously tested mutations. However, mutations in *mexS* have previously been shown to be responsible for increases in chloramphenicol tolerance (336). This included a strain with a chloramphenicol MIC of 2,048 μg/ml that contained a Ser60Phe mutation like the C1 mutant found in this study (336). Additionally, short-term exposure to ciprofloxacin has previously produced a ciprofloxacin resistant mutant through a mutation at Leu186Phe in MexS as seen in the C3 mutant evolved in this study (378). The mutations in *mexS* observed in the other

chloramphenicol mutants created in this study do not appear to have been previously reported. Additionally, mutants overexpressing MexEF-OprN have previously been shown to consume more oxygen than strains expressing wildtype levels and thus experience a reduction in fitness when under anaerobic conditions (379).

5.3.1.2 The influence of **mexT** *mutations in altering fitness levels*

Revertants with a deletion of the *mexS* and disruption of *mexT* genes from the genome appeared to provide the fittest phenotype, in terms of area under the curve, in the absence of pressure from sub-inhibitory levels of chloramphenicol. This was despite the variation in the length of deletion covering the *mexS* and *mexT* region. In the presence of sub-inhibitory concentrations of chloramphenicol, both A1.1 and A1.2 revertants retained a fitter phenotype. Conversely, the remaining revertants with a *mexS* deletion and *mexT* disruption, C2.1 and E1.1, showed a similar fitness to their parents (Table 5-8 and Figure 5-13).

The A1.1 revertant contained a deletion that also covered the *mexEF-oprN* operon and the A1.2 revertant contained an even smaller deletion that only partially covered the *mexEF-oprN* operon (Table 5-8). Between the two of these revertant strains, a small overlap in the regions deleted was observed covering approximately 7,000 bp long, which affected ten genes starting from PA2484, a hypothetical protein, and ending at midway through the *mexE* gene (Figure 5-3 and Table 5-2). As these strains both evolved from the same mutant, the increase in area under the curve seen in these strains is most likely linked to these ten genes (Table 5-2). The C2.1 revertant also contained a SNP within the *cmrA* gene known to influence chloramphenicol resistance in addition to a large deletion including the entire *mexEF-oprN* operon (Table 5-4) (344). As CmrA acts on MexS, the increased area under the curve seen in revertant C2.1 is unlikely due CmrA as the *mexS* gene is deleted in this revertant. Each of the deletions seen in these strains covered different regions of the genomes but all included *mexS* and *mexT.*

Deletion of *mexT* has previously been identified in a *P. aeruginosa* strain isolated from a cystic fibrosis patient (380). As with the strain in this study, the strain found by Warren *et al.* contained a deletion of *mexT* occurred from a deletion of ~105,000 bp which included gene involved in virulence, however whether this led to changes in fitness was not determined. Additionally, MexT can influence expression of other genes in the cell (381). Correia *et al.* indicated that mutations in the MexT regulator can alter virulence networks resulting in a more virulent strain that is more susceptible to antibiotics (Correia *et al*., unpublished). As the study by Correia *et al.* involved strains which contained *mexT* in a mutant form it is unclear whether the higher virulence levels would also translate to the fitter strains with deletions of *mexT,* particularly as virulence genes are included in some of the strains with deletions.

The revertants without deleterious mutations of *mexS* and *mexT* contained SNP mutations instead which resulted in non-synonymous changes and frameshift in the *mexS* and *mexT* gene. Unlike strains with a deletion of *mexT*, these revertants either had reduced or similar areas under the curve to the parent (Table 5-8). Currently, it is unclear whether the mutant *mexT* genes contained by these strains are expressed and whether its product is functional within the *P. aeruginosa* cell. This can be resolved by transcriptomic sequencing and/or quantitative reverse transcriptomic PCR of RNA transcripts. This will also help to confirm that the increased area under the curve seen in the A1.1, A1.2, and C2.1 revertants was solely due to loss of *mexT* or a general loss of a large number of genes that are costly to the strain.

As the deletion of large regions including *mexS* and *mexT* have been observed in clinical isolates, it is important to ascertain if deletions in *mexT* perform in the same way as mutants with non-synonymous changes and frameshifts as described by Correria *et al.* (Correia *et al*., unpublished) (380). Based on the growth curve data, deletion of *mexS* and *mexT* produces the most competitive strain in chloramphenicol-free environments. This could be expected as strains in these conditions have no demand for an efflux pump which can export

chloramphenicol from the cell. Therefore, it would be expected for strains with this genotype to proliferate in populations of *P. aeruginosa* in chloramphenicol free environments. If this genotype shows itself to be highly virulent, it indicates that chronically infected patients may possible develop highly virulent but antibiotic sensitive strains such as those evolved in this study. Therefore, it is important to conduct further analysis involving virulence assays and direct competition between various *P. aeruginosa* genotypes to determine which *mexT* deletions lead to both a more virulent and competitive strain. Additionally, the deletion of genes surrounding the *mexEF-oprN* operon, particularly the region seen in both A1.1 and A1.2, require investigation to confirm if their deletion provides fitter phenotypes in strains with functional *mexEF-oprN.*

5.3.1.3 CmrA in revertants

In the strain C2 mutant, an additional mutation was observed in the *cmrA* gene, the product of which has been described to interact with MexS (344). Specifically mutations at the sites Ala68Val, Leu89Gln, His204Leu and Asn214Lys have been shown to alter the structure of CmrA resulting in an active form that influences wildtype MexS to increase the presence of oxidised substrates activating MexT and thus production of the MexEF-oprN efflux pump (Figure 5-25) (344). The Gly142Ser mutation seen in the *cmrA* gene of mutant strain C2 has not previously been identified to our knowledge. Additionally, *mexS* contained a missense mutation and thus it is unclear whether CmrA is in an active form and if it is able to influence the MexS variant present in the C2 mutant.

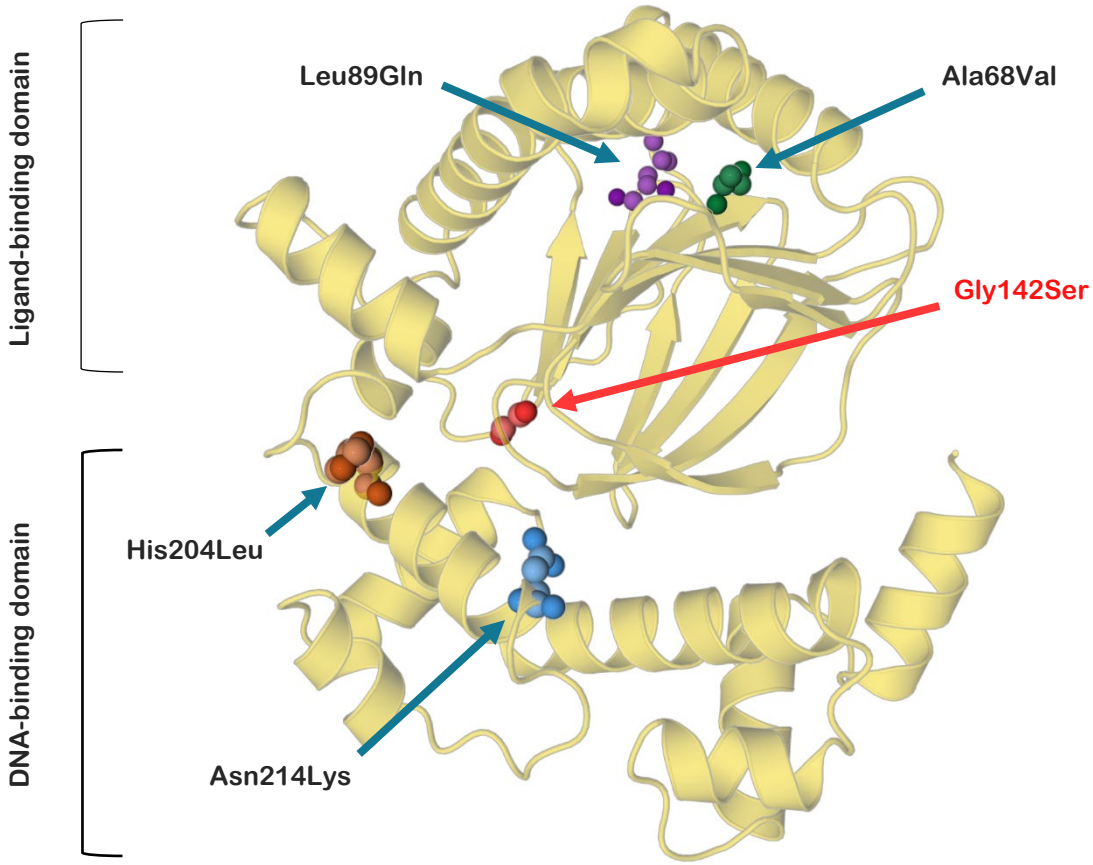

Figure 5-25: Protein structure of CmrA. Structure is predicted from the cmrA *gene sequence from* P. aeruginosa *PA14 (Uniprot ID: A0A0H2ZA95) with annotations representing the mutation identified in this study in addition to those previously identified. Visualisation is achieved using protein imager (225) and is based on Figure 1 from Juarez* et al. *(334). The Gly142Ser mutant detected in this study is highlighted in red.*

5.3.2 Evolution in ciprofloxacin leads to mutations in antibiotic resistance determining genes

Within the mutants evolved in ciprofloxacin numerous mutations developed in multiple genes that have previously been described to increase resistance towards ciprofloxacin. As with the mutants evolved in chloramphenicol, this included efflux pumps, however this was not the MexEF-OprN pump which can also provide resistance to ciprofloxacin through its overexpression (382). Instead, the ciprofloxacin evolved mutants and revertants developed mutations affecting the expression (*nfxB* and *parS*) and function of the MexCD-OprJ efflux pump (*mexC*) (348, 373). A summary of these mutations and the effect they have on fitness and ciprofloxacin tolerance is displayed in Table 5-9. In addition to efflux pumps, this study also

found mutations within genes encoding products targeted by ciprofloxacin such as *gyrA, gyrB,* and *parC* which are involved in DNA replication (Table 5-5) (383).

Table 5-9: Summary of mutations effecting ciprofloxacin tolerance in the ciprofloxacin evolved mutant and revertants. Table includes genes which are known to cause ciprofloxacin resistance mutations or influence the function of efflux. Fitness is calculated using the area under the curve in media with and without ciprofloxacin (0.008 µg/ml).

Strain		Fitness relative to the parent		Fitness relative to the mutant		CIP MIC	Genes*					
		No CIP	CIP	No CIP	CIP		parC	gyrA	gyrB	nfxB	mexC	parS
C4	Mutant	less	less			128	sub	sub	sub	del		
C4.1**	Revertant	less	less	similar	greater	≤0.25	sub	sub	sub	del	stop	
D2	Mutant	similar	similar			0.5		sub		fs	fs	
D2.1	Revertant	similar	similar	similar	similar	≤0.25		sub		fs	fs	
D3	Mutant	less	less			128			sub	sub		
D3.1	Revertant	greater	greater	greater	greater	8			sub	sub		sub
E2	Mutant	similar	similar			16			sub	fs		
E2.1	Revertant	greater	greater	greater	greater	1			sub	fs	fs	

** The type of mutation indicated by the gene "sub" represent substitution mutations, "del" represents a deletion of the gene, and "fs" represents a gene with a frameshift.*

***The C4.1 revertant strain also contained a large deletion covering several genes, however their ability to alter ciprofloxacin tolerance is unclear.*

5.3.2.1 Mutations in DNA replication machinery and efflux increase ciprofloxacin resistance

Mutations to the transcriptional regulator of the MexCD-OprJ efflux pump, NfxB, were observed in all the ciprofloxacin evolved mutants regardless of the size of the increase in ciprofloxacin tolerance (Table 5-9). These mutations were present in conjunction with mutations to genes coding for products involved in DNA replication that are the target of ciprofloxacin. The combination of mutations present in a strain appears to influence the levels of ciprofloxacin resistance gained by the strain (149, 370). Specifically, combinations that involved both

mutations affecting efflux pumps in addition to *gyrA* and *parC* appears to result in the highest levels of resistance (370). In this study the two mutants with the highest levels of ciprofloxacin resistance, C4 and D3, both contained *nfxB* and *gyrB* mutations with C4 containing an additional mutation in *parC*. The specific missense mutation seen in the *nfxB* gene of strain D3, Arg163Gln, has previously been identified in a ciprofloxacin evolved *P. aeruginosa* isolate also containing mutations in the following genes involved in efflux: *mexY* (Arg251His), *mexX* (Ala38Thr), *mexZ* (Gly68Asp), *mexS* (Val104Ala); and β-lactamase expression: *ampR* (Ala16Val), *ampD* (Thr47Ile), and *ampDh3* (Pro55Ser) resulting in a resistant ciprofloxacin MIC of 2 μg/mL (372). The D3 mutant did not contain any of the mutations in the aforementioned genes, and so it is likely the additional Ser466Phe mutation in *gyrB* contributed to the high-level resistance observed by the strain. As the E2 mutant also contained mutations to both *nfxB* and *gyrB* it is unlikely that the combination of mutations in *nfxB* and *gyrB* alone are responsible for high-level resistance. Instead, it appears the specific mutation obtained by the strain is also important in influencing the degree of resistance that can be acquired by a strain. This may offer an explanation for why the C4 mutant contained *gyrA, gyrB,* and *parC* mutations in addition to *nfxB* as a second mutation in *gyrB* alone may not have been sufficient in allowing the strain to survive high ciprofloxacin levels. Therefore, it appears that the specific combinations of genes mutated alone cannot predicted the level of resistance acquired.

In terms of fitness relative to the parent strain all ciprofloxacin mutants either showed less or similar levels of fitness regardless of the presence of ciprofloxacin (Table 5-9). This was despite the mutants being evolved to withstand higher concentrations of ciprofloxacin. Hence, it could be expected for the mutants to show greater fitness in the presence of the antibiotic in which they were evolved like seen in the chloramphenicol evolved mutants. However, this was not the case for the ciprofloxacin mutants in this study. Nevertheless, it is possible the use of subinhibitory concentrations of ciprofloxacin for the growth curve experiments provided a low

level of stress to the parent strain that may have been overcome by inherent resistance mechanisms that remained intact in the parent but not the mutant. Additionally, previous studies have indicated that mutations which lead to high-level ciprofloxacin resistance, through mutations involving *gyrA, gyrB, parC. parE,* and *nfxb,* result in greater fitness costs compared to mutants with low-level resistance mutants (149). Specifically, mutations at the 83rd and 87th position of the *gyrA* amino acid sequence led to reduced supercoiling which in turn slows down the rate of DNA replication, however this is not true of all mutations detected in *gyrA* (149, 383). To address the reduction in supercoiling, compensatory mutations are required (149), however mutations which could improve supercoiling were not detected in any of the mutants in this study (Table 5-5). Therefore, the reduction in fitness in these strains is likely the result of inefficient DNA replication machinery. Overall, the results of this study support the notion that high-level resistance results in greater fitness costs in the absence of compensatory mutations when grown in antibiotic free conditions.

5.3.2.2 Reduction in ciprofloxacin tolerance occurs through mutations reducing efflux

The acquisition of ciprofloxacin mutations by strains appears to coincide with fitness costs. To compensate for this loss of fitness, the strains in this study appeared to develop mutations that would reduce efflux activity after evolution in ciprofloxacin free media. The C4.1, D2.1, and E2.1 mutants overcame this fitness loss through a mutation in *mexC* which encodes part of the MexCD-OprJ efflux pump. Mutations within this gene have not previously been described and so it is unclear whether the mutation prevents the efflux pump from functioning. However, if the mutation prevents the functioning of the MexCD-OprJ efflux pump it could be expected that the efflux of ciprofloxacin is prevented in these strains. This would result in the reduction in ciprofloxacin MIC observed by these strains.

The D3.1 revertant was the only strain to not develop a mutation in *mexC* to "switch-off" efflux. Instead, the revertant retained its ciprofloxacin resistance-causing mutations in addition to a mutation in *parS*, which forms part of a two-component regulatory system ParRS. The ParRS regulator has been associated with genes involved in antimicrobial resistance including: the *arnBCADTEF-ugd* operon, involved with lipopolysaccharide modification; the *mexEF-oprN* and *mexXY-oprM* operons, involved in efflux of antimicrobials; and *oprD*, a gene encoding an outer membrane porin (373, 374, 384). Mutant strains containing combinations of *parR* and *parS* knockouts have shown downregulation of both the *mexEF-oprN* and *mexXY-oprM* operons. This would suggest that MexEF-OprN and MexXY-OprM mediated efflux is compromised in these mutants (373, 374). As such, the *parS* mutation seen in D3.1 is likely "switching-off" efflux mediated through these pumps. As the substrates include ciprofloxacin their downregulation is possibly contributing to the increased susceptibility seen in the D3.1 revertant.

Fitness of the D2.1, D3.1, and E2.1 revertants, as indicated by the area under the curve, was similar or greater than their respective parent and mutant strains. The remaining revertant, C4.1 showed lower fitness than its parent in both conditions. However, when compared against the C4 mutant its fitness was greater in the presence of ciprofloxacin and the same in its absence. The reduction in fitness by the C4.1 revertant over its parent strain appeared to be due to the retention of the mutations causing a loss of fitness acquired by its ancestral mutant, C4. Presently, the fitness of mutants reverting to a reduced ciprofloxacin tolerance has not been described for strains with *parS* and *mexC* mutation. However, these mutations which reduce efflux appear to improve or have no effect on fitness of strains which have evolved higher ciprofloxacin resistance.

5.3.2.3 Mutation to mexC *prevents the development of high-level ciprofloxacin resistance*

Despite developing mutations to the *nfxB* and *gyrA* genes, the D2 mutant did not appear to increase the ciprofloxacin MIC to a level that could be considered resistant. This was likely due to a mutation in *mexC*, which would have prevented the expression of a functional efflux system thereby nullifying the initial *nfxB* mutation. As such the only mutation contributing to ciprofloxacin resistance appeared to be in *gyrA.* As previously mentioned, mutation at the 87th position of *gyrA* has been described to reduce fitness, however, the *gyrA* mutations described by Kugelberg *et al.* were not the same as that seen in D2 (149). Therefore, the similar fitness levels seen between the D2 strain and its parent strain appear to show that the Asp87Asn mutation does not alter fitness, however further investigation is required to determine its effect on supercoiling of DNA. After removal of the antibiotic pressure, new mutations in the revertant, which had a small reduction in MIC of at least one doubling dilution, could not be identified and as such the fitness levels remained the same between the strains. Presently, it is unclear what the exact ciprofloxacin MIC of the revertant is. Hence, antimicrobial susceptibility testing covering a lower ciprofloxacin range is required to confirm the extent of the increase ciprofloxacin susceptibility.

5.3.3 Mutations identified in both ciprofloxacin and chloramphenicol evolved strains

Within the strains evolved in MHB + 10% plasma, mutations affecting phenazine biosynthesis, type IV pili, and flagella were identified across the strains regardless of whether ciprofloxacin or chloramphenicol was used to evolve the strains. Both the *phzC* and *phzF* genes are involved in phenazine biosynthesis, a secondary metabolite that can activate specific transcription factors and are involved in intracellular signalling in *P. aeruginosa* (385, 386). As type IV pili are involved in adhesion and motility it is likely that the mutation in these gene have affected the organism's capabilities in these fields. As with the type IV pili, flagella also contribute to motility of the organisms. As such it appears that the pressures cause by the presence of antibiotics and 10% plasma leads to mutation in components involved in motility. However, as

these mutations evolved regardless of which antibiotic was present, it's likely that they developed as a response to a combination of antibiotic pressure and the culture conditions which involved a liquid medium. In general, these mutations appear to affect the signalling and motility of the strains. However, it is unclear if fitness is altered by these mutations and whether they evolved as part of an evolutionary trajectory or as a response to the culture conditions.

5.3.4 The evolutionary pathways taken to "switch-on" and "switch-off" resistance

Both exposure to chloramphenicol and ciprofloxacin resulted in mutations which "switch-on" efflux. This is then followed by a subsequent mutation to "switch-off" or downregulate efflux after the antibiotics is removed from the media. Therefore, it appeared that efflux appears to be a favoured route for resistance as it allows strains to revert to a less tolerant phenotype and undo the fitness cost incurred from increased efflux. Moreover, the ciprofloxacin evolved mutants had additional mutation in DNA replication machinery helping to increase the strains tolerance to ciprofloxacin. Mutations to DNA replication machinery were retained by the revertant strains which allowed some of the revertant strains to retain some resistance to ciprofloxacin. A similar occurrence has been seen in vancomycin-susceptible strains *S. aureus* which had previously been adapted display intermediate levels of resistance to vancomycin (387). The genetic traces of prior vancomycin adaption in these now susceptible strains allowed strains to re-evolve to become vancomycin-intermediate strains with the additional benefits of increased fitness (387). Thus, it is possible that the retention of mutations in DNA replication allows *P. aeruginosa* revertants to re-evolve to their previous high-level resistance towards ciprofloxacin in a more efficient and effective manner. In the case of the *mexC* revertants, it is unclear if this could be through the overexpression of the MexCD-OprJ efflux pump as this would require a reversal of the initial mutation to re-functionalise MexC. Furthermore, it is unknown if such a mutation is possible in *mexC* as mutations in this gene have not previously been described in *in vitro* or clinical settings. Additionally, multiple efflux

systems are present in *P. aeruginosa,* so it is possible one of these efflux systems will be utilised as part of a pathways towards resistance that was previously inaccessible to the original parent strain. It should be noted that this study did not consider how these mutations arise in a population of *P. aeruginosa* strains. Therefore, it is possible that some of the mutations seen in the revertants may not survive when in a competition against strains with other mutations. This could include strains which initially had weaker fitness but managed to survive and proliferate in the population once the conditions changed to favour the previously weaker strain. Additionally, the order in which mutations established in ciprofloxacin mutants is unclear and whether these mutations develop as part of a move towards a fitter phenotype requires investigation. Hence, a full fitness landscape could not be determined for these strain sets, as a result it could not be determined if any of the genotypes observed in these experiments allowed the strain to reach peak fitness levels for the conditions in which they were tested.

Chapter 6 - Conclusion

The ability of bacteria such as *P. aeruginosa* to adapt to their surroundings allows them to successfully colonise different niches. The aim of this study was to identify the mechanisms that allow this to happen and uncover the routes *P. aeruginosa* takes to become antibiotic resistant superbugs.

Historically, the 16S rRNA sequence has been an efficient and cost-effective way to speciate bacteria. However, the method is accompanied with caveats that can prevent the full delineation of species that are closely related, which will result in errors when defining the pangenome of a species. This is evident in the *P. aeruginosa* species where the PA7-like group of strains are well described to be an outlier. In this study, PA7-like strains were shown not to fit the characteristics of *P. aeruginosa* and therefore provide support for the reclassification of ATCC 9027, which is part of the PA7-like group, as the type strain for the novel species *P. paraeruginosa* (262, 263). Currently, not all PA7-like strains have been reclassified as *P. paraeruginosa* in the NCBI taxonomy databases (accessed: 2nd August 2023). The reasoning for this is likely due to the time it takes to update databases. However, if this is caused by a lack of evidence, this study shows that all PA7-like strains show greater resemblance to the *P. paraeruginosa* type strain (ATCC 9027) than the *P. aeruginosa* type strain (PAO1). Consequently, all strains belonging to the PA7-like group within this study should be re-classified as *P. paraeruginosa*.

The difference between *P. paraeruginosa* and the *P. aeruginosa* species can be identified through comparisons of their genome sequences and by genetic markers defined by *Rudra et al.* (262). This study has investigated these differences in further detail and has showed that PA7-like strains can be isolated by the alignments of 16 ribosomal proteins. Investigation into

whether these genetic differences also translate to phenotypic differences showed that there were observable differences in carbon utilisation when concerning D-alanine, glycerol, L-serine, mono methyl succinate, and pyruvic acid as the carbon source. However, the mechanisms responsible for these differences need to be elucidated to confirm if this is due to differences in the metabolic pathways. Unlike the difference in carbon utilisation, the antibiotic resistance profiles between the two groups appeared to be similar to one another. In contrast, the mechanisms responsible for the antibiotic resistance profiles appeared to differ. This was seemingly due to variations in genes involved in antimicrobial resistance including efflux pumps and outer membrane porins which when expressed change the permeability of the membrane. Mechanisms, such as efflux pumps, are key mechanisms in the inherent resistance of *P. aeruginosa*. This was evident in the evolution experiments conducted in this study which has shown mutations in the regulation or components forming of these pumps can be used to "switch-on" and "switch-off" efflux and thus alter tolerance towards antibiotics. As such, it is possible that mechanisms responsible for causing the resistance profiles seen in PA7-like strains are different to *P. aeruginosa* despite the shared similarity in their phenotypic profiles. Whilst it still needs to be investigated, differences in membrane permeability may affect how resistance develops in the PA7-like strains. The consequence of this would require different management plans when it comes to treating infections caused by this group of strains.

The *P. aeruginosa* core genome has been described as consisting of five major clades (143), though removal of the divergent PA7-like strains adjusts this to four. Hierarchical clustering of the core genome alignment further breaks down these clades to show 23 core groups. Six of these groups showed an association towards a clinical or environmental niche which allowed for the identification of genes and SNPs that were associated with a niche. The roles of the genes identified as biomarkers varied from being involved in the transport of substrates across the cell membrane, being part of metabolic processes in the cell, or even recombination. The presence or absence of these genes have the potential to determine survival in a given niche;

however, further investigation into how the genes identified enable niche survival is required. Likewise, SNPs were identified in intergenic regions and within the *rmd* and *fdhD*, genes. The effect of the SNPs detected in the intergenic regions is currently unclear and further analysis is required to reveal whether they are able to influence the expression of the genes encasing the region. Additionally, the SNPs found within in genes have not previously been described and so it is currently unclear how these SNPs assist in niche adaption.

Research into the accessory clustering revealed the presence of 103 groups. Each accessory group was predominantly made-up strains belonging to the same core group; however, the converse was not applicable to the core groups. Hence, the accessory genome does not appear to be shared between core groups of *P. aeruginosa,* which was supported by the lack of observable gene flow between the smaller core groups. Of the 103 accessory groups identified, only one accessory group was found to be associated with bacteraemia isolates and specifically the MLST ST 357. This was due to the large number of groups containing a small number of strains and so some niche-adapted accessory groups were statistically undetectable. Despite this, many of the smaller groups predominantly contained isolates from either clinical or environmental origins. Hence, both the core and accessory genome play a role in niche adaption with the core genome providing some of the characteristics for niche adaption with the accessory genome providing the rest.

In this study, all the chloramphenicol mutant strains developed *mexS* deletions followed by a *mexT* mutation in their respective revertants. The development of these genotypes could simply be explained by the overexpression of the MexEF-OprN pump which “switches-on” efflux of chloramphenicol in resistant mutants followed by a reversion that “switches-off” of efflux in sensitive revertants. In all cases the chloramphenicol mutants showed greater fitness than their respective parent in the presence of chloramphenicol indicating that the increased efflux through a *mexS* mutation provided a fitness advantage in this condition. Therefore, it

could be expected for a strain with these mutations to survive in these conditions. However, increased efflux brings forth consequences as chloramphenicol is not the only substrate of the pump. As such, increased efflux is not a sustainable phenotype which is evident in the *mexT* mutations obtained by the revertants which generally showed greater fitness than the mutant in the absence of chloramphenicol and lower fitness in the presence. The exception to this being the C3.1 revertant which showed lower levels of fitness against both its parent and mutant ancestors. MexT is also involved in the regulation of multiple networks in the bacterial cell including virulence with mutations to *mexT* resulting in a strain with increase virulence (Correia *et al.*, unpublished). The revertants in this study contained a variety of *mexT* mutations which had varying degrees in fitness with respect to their parent and mutant ancestors. In some cases, this fitness change was an increase over both the parent and revertant. This suggests the possibility that revertant *P. aeruginosa* strains can adapt into fitter and more virulent strains after the exposure and removal of chloramphenicol. These revertants show less tolerance towards antibiotics and so appear to be vulnerable in this aspect. Presently, it is unclear if re-exposure of revertant strains could result in a resistant phenotype. However, the lack of fitness of revertant strains in the presence sub-inhibitory concentrations indicates that revertant strains are unlikely to survive within the population without regaining a resistant phenotype. If such an adaption were to occur without impacting the strain's current fitness and virulence, it could lead to the development of an antibiotic resistant strain with greater fitness and virulence than the original mutant.

As with the chloramphenicol evolved strains, some of the ciprofloxacin evolved strains in this study developed a similar strategy of targeting efflux pumps to "switch-on" and "switch-off" resistance. This was achieved through mutations to the *nfxB* regulator leading to the overexpression of the MexCD-OprJ pump and a resistant phenotype in the mutant strains. Mutations to *nfxB* were coupled with secondary mutation in DNA replication machinery which appeared to support the high-level resistance seen in the mutant strains. Currently, it is not

clear if mutations in efflux or DNA replication machinery developed first. Understanding the order in which these mutations develop may help in preventing high-level resistance from developing and so should be further studied. In the revertants, mutations occurred in *mexC,* which likely obstructs the functioning of the MexCD-OprJ pump, and *parS,* which has been linked to decreased expression of efflux pumps. The "switching-off" or downregulation efflux pumps appeared to be coupled with the secondary mutations in DNA replication machinery that developed in the mutants. The routes utilising *mexC* and *parS* taken by revertants showed similar or greater fitness levels than their respective mutants suggesting active efflux compromised fitness in the mutants. Thus, the "switching-off" and downregulation of efflux mechanisms appears to be a better trajectory for *P. aeruginosa* as it allows the strains to decrease tolerance to ciprofloxacin whilst maintaining a resistant and fitter phenotype. This study describes the first report of *mexC* mutation as a means for reversion in *P. aeruginosa.* The lack of their detection in clinical setting suggests that these mutations are rare and unlikely to proliferate in a *P. aeruginosa* population. However, the *mexC* mutation in E2.1 appeared to show that this genotype was fitter than both its parent and mutant ancestors. This indicates that it is possible for this phenotype to proliferate in a clinical setting where treatment with ciprofloxacin is administered and then stopped.

To summarise, this thesis presents work that displays the trajectories taken by *P. aeruginosa* to evolve from an environmental to a clinical niche. This study has shown that the *P. aeruginosa* core genome can reveal groups of strain adapted to specific niches and that strains with similar accessory genomes tend to originate from the same core groups. Additionally, antibiotic resistance can be "switched-on" and "switched-off" in strains and the process of doing so alters the strain's fitness to varying degrees according to the mutations established. By considering how *P. aeruginosa* evolves towards more clinical niches, procedures for treating *P. aeruginosa* can be adapted to prevent its evolution towards highly drug resistant and virulent strains.

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Appendix

Appendix I - Supplementary tables and figures

Appendix - Table 1: List of PA7-like strains.

Project ID	Strain name*	RefSeq accession number	Provider	Reference
PA259	***PA32***		In-house collection	
PA508	***Pseudomonas aeruginosa ATCC 9027****	GCF_001294675.1	Thermo Scientific	(388, 389)
PA580	***Pseudomonas aeruginosa AUS217***	GCF_003839875.1		(143)
PA628	***Pseudomonas aeruginosa AUS483***	GCF_003839025.1		(143)
PA828	***Pseudomonas aeruginosa AZPAE14901***	GCF_000791105.1		(390)
PA868	***Pseudomonas aeruginosa AZPAE14941****	GCF_000789725.1		(390)
PA964	***Pseudomonas aeruginosa AZPAE15042****	GCF_000790465.1		(390)
PA1129	***Pseudomonas aeruginosa CLJ1***	GCF_003032395.1	Ina Attrée	(391)
PA1130	***Pseudomonas aeruginosa CLJ3****	GCF_003057595.1		(391)
PA1145	***Pseudomonas aeruginosa CR1****	GCF_003025345.2		(392)
PA1646	***Pseudomonas aeruginosa LMG 5031***	GCF_003837245.1	BCCM/LMG Bacteria Collection	(143)
PA1780	***Pseudomonas aeruginosa MRSN 3705****	GCF_003968965.1	BEI Resources	(393)
PA1794	***Pseudomonas aeruginosa MRSN 6241***	GCF_003968155.1	BEI Resources	(394)
PA1802	***Pseudomonas aeruginosa MRSN 8141****	GCF_003968475.1	BEI Resources	(395)
PA2045	***Pseudomonas aeruginosa PA7***	GCF_000017205.1	Leibniz Institute DSMZ Collection	(249)
PA2078	***Pseudomonas aeruginosa PABL 043****	GCF_003411505.1	Alan R. Hauser	(396, 397)
PA2506	***Pseudomonas aeruginosa VRFPA01***	GCF_000335395.2		(398)
PA2541	***Pseudomonas aeruginosa WH-SGI-V-07261***	GCF_001452985.1	bioMérieux Global Strain Collection	(399)
PA2548	***Pseudomonas aeruginosa WH-SGI-V-07287***	GCF_001454675.1		(399)
PA2634	***Pseudomonas aeruginosa IHMA87****	In-house collection	Ina Attrée	(390, 400)

** Indicates strains which have been re-classified as* Pseudomonas paraeruginosa *(262). Taxonomy is based on the NCBI Taxonomy browser accessed 2nd August 2023 (401).*

*** The "*Pseudomonas aeruginosa *IHMA87" strain is a duplicate of the "*Pseudomonas aeruginosa *AZPAE15042" strain kindly provided by Ina Attrée and was used in place of AZPAE15042 for phenotypic tests (390, 400).*

Appendix - Table 2: List of Pseudomonas *strains used in comparison against the PA7-like strains . The nomenclature status of each strain is labelled according to the LPSN database (accessed: 5th December 2022).*

Strain name*	***Nomenclature status***	***RefSeq accession number***	***Reference***
Azomonas agilis DSM 375	Correct name	GCF_007830255.1	(402)
Pseudomonas aeruginosa DSM50071.1	Correct name	GCF_900167195.1	(85)
Pseudomonas aeruginosa DSM50071.2	Correct name	GCF_001042925.1	(85)
Pseudomonas aeruginosa LESB58	Correct name	GCF_000026645.1	(403)
***PA2204:** Pseudomonas aeruginosa PAO1*	Correct name	GCF_000006765.1	(171)
***PA2448:** Pseudomonas aeruginosa PA14*	Correct name	GCF_000014625.1	(404)
***PA1305:** Pseudomonas aeruginosa PAK**	Correct name	GCF_902172305.2	(405)
Pseudomonas alcaligenes NBRC 14159	Correct name	GCF_000467105.1	(406)
Pseudomonas campi S1-A32-2	Correct name	GCF_013200955.2	(407)
Pseudomonas chlororaphis LMG 5004	Correct name	GCF_001269625.1	(408)
Pseudomonas citronellolis LMG 18378	Correct name	GCF_900112375.1	(409)
Pseudomonas composti CCUG 59231	Correct name	GCF_900115475.1	(410)
Pseudomonas delhiensis CCM 7361	Correct name	GCF_900099945.1	(411)
Pseudomonas fluorescens DSM 50090	Correct name	GCF_001269845.1	(408)
Pseudomonas furukawaii KF707	Correct name	GCF_000262065.2	(412)
Pseudomonas humi CCA1	Synonym of *P. citronellolis*	GCF_001748265.1	(413)
Pseudomonas indoloxydans JCM 14246	Not validly published	GCF_003052605.1	(414)
Pseudomonas jinjuensis JCM 21621	Correct name	GCF_900103845.1	(415)
Pseudomonas knackmussii B13	Correct name	GCF_000689415.1	(416)
Pseudomonas lactis DSM 29167	Correct name	GCF_001439845.1	(417)
Pseudomonas lalkuanensis PE08	Correct name	GCF_008807375.1	(418)
Pseudomonas mucoides P154a	Correct name	GCF_015461845.1	(419)
Pseudomonas nicosulfuronedens LAM1902	Correct name	GCF_005877905.1	(420)
Pseudomonas nitritireducens WZBFD3-5A2	Synonym of *P. nitroreducens*	GCF_010994165.1	(421)
Pseudomonas nitroreducens NBRC 12694	Correct name	GCF_002091755.1	(422)
Pseudomonas nosocomialis A31/70	Synonym of *Stutzerimonas nosocomialis*	GCF_005876855.1	(423)
Pseudomonas otitidis DSM 17224	Correct name	GCF_900111835.1	(424)
Pseudomonas panipatensis CCM 7469	Correct name	GCF_900099785.1	(425)
Pseudomonas peli DSM 17833	Correct name	GCF_900099645.1	(426)
Pseudomonas pseudoalcaligenes NBRC 14167	Synonym of *Pseudomonas oleovorans*	GCF_002091775.1	(427)

Pseudomonas putida NBRC 14164	Correct name	GCF_000412675.1	(428)
Pseudomonas sediminis PI11	Not validly published	GCF_002741105.1	(429)
Pseudomonas stutzeri	Correct name	GCF_000219605.1	(430)
Pseudomonas synxantha DSM 18928	Correct name	GCF_001439725.1	(417)
Pseudomonas syringae KCTC 12500	Correct name	GCF_000507185.2	(431)
Pseudomonas tohonis TUM18999	Correct name	GCF_012767755.2	(432)
Pseudomonas toyotomiensis JCM 15604	Correct name	GCF_900115695.1	(433)

** The* Pseudomonas aeruginosa *PAK strain was kindly provided by Cynthia Whitchurch (405).*

Appendix - Table 3: List of strains included in the project.

Project ID	Strain name	RefSeq accession number	Clonally linked	Source	Source Type	PA7-like strain included			PA7-like strains removed		MLST ST
						Core Group	Accessory Group	RC Group	Core Group	RC Group	
PA1	51279	In-house collection	No	Clinical	Unknown	12	2	1	14	1	395
PA2	15TB0702	In-house collection	No	Environment	Home environment	2	39	10	5	10	298
PA3	15TB0703	In-house collection	No	Environment	Home environment	19	54	8	18	9	1990
PA4	15TB0713	In-house collection	No	Clinical	Unknown	16	5	11	17	14	155
PA5	15TB0714	In-house collection	No	Clinical	Unknown	15	32	12	23	12	244
PA6	15TB0715	In-house collection	No	Clinical	Unknown	18	9	12	19	12	260
PA7	15TB0716	In-house collection	Yes	Clinical	Unknown	16		11	17	14	179
PA9	15TB0718	In-house collection	No	Clinical	Unknown	15	32	12	23	12	244
PA10	15TB0719	In-house collection	No	Clinical	Unknown	19	43	8	18	9	279
PA11	15TB0720	In-house collection	Yes	Clinical	Unknown	18		12	19	12	260
PA12	15TB0721	In-house collection	No	Clinical	Unknown	16	5	11	17	14	179
PA13	15TB0722	In-house collection	No	Clinical	Unknown	2	39	10	5	10	446
PA14	15TB0740	In-house collection	Yes	Clinical	Unknown	18		13	19	11	591
PA15	15TB0741	In-house collection	No	Clinical	Unknown	18	96	13	19	12	Undefined
PA16	15TB0742	In-house collection	Yes	Clinical	Urinary Tract	2		10	5	10	446
PA17	15TB0743	In-house collection	Yes	Clinical	Unknown	18		10	19	10	988
PA18	15TB0744	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA19	15TB0745	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA20	15TB0746	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA21	15TB0747	In-house collection	Yes	Clinical	Unknown	18		13	19	12	Undefined
PA22	15TB0748	In-house collection	No	Clinical	Unknown	15	32	12	23	12	244
PA23	15TB0749	In-house collection	Yes	Clinical	Unknown	18		13	19	12	Undefined
PA24	15TB0750	In-house collection	No	Clinical	Respiratory Tract	19	61	10	21	10	207

PA25	***15TB0751***	In-house collection	Yes	Clinical	Respiratory Tract	19		10	21	10	207
PA26	***15TB0752***	In-house collection	No	Clinical	Unknown	19	102	12	21	4	671
PA27	***15TB0753***	In-house collection	No	Clinical	Unknown	19	51	10	21	10	620
PA28	***15TB0754***	In-house collection	Yes	Clinical	Unknown	12		1	14	1	395
PA29	***15TB0755***	In-house collection	Yes	Clinical	Unknown	1		12	2	4	253
PA30	***15TB0756***	In-house collection	Yes	Clinical	Unknown	11		11	13	14	252
PA31	***15TB0757***	In-house collection	No	Clinical	Unknown	18	31	13	19	11	591
PA32	***15TB0758***	In-house collection	Yes	Clinical	Respiratory Tract	19		10	21	10	207
PA33	***15TB0760***	In-house collection	Yes	Clinical	Cystic Fibrosis	18		9	19	5	254
PA34	***15TB0761***	In-house collection	Yes	Clinical	Unknown	18		9	19	5	254
PA35	***15TB0762***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA36	***15TB0763***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA37	***15TB0764***	In-house collection	Yes	Clinical	Urinary Tract	2		10	5	10	446
PA38	***15TB0765***	In-house collection	No	Clinical	Urinary Tract	19	61	13	21	13	313
PA39	***15TB0766***	In-house collection	No	Clinical	Urinary Tract	12	2	1	14	1	395
PA40	***15TB0767***	In-house collection	Yes	Clinical	Urinary Tract	19		10	21	10	2326
PA41	***15TB0768***	In-house collection	Yes	Clinical	Unknown	18		6	22	7	175
PA42	***15TB0769***	In-house collection	Yes	Clinical	Unknown	18		6	22	7	175
PA43	***15TB0770***	In-house collection	No	Clinical	Unknown	18	65	6	22	7	175
PA44	***15TB0772***	In-house collection	No	Clinical	Urinary Tract	11	49	11	13	14	252
PA45	***15TB0773***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA46	***15TB0774***	In-house collection	Yes	Clinical	Cystic Fibrosis	9		9	11	5	17
PA47	***15TB0775***	In-house collection	No	Clinical	Respiratory Tract	9	11	9	11	5	17
PA48	***15TB0776***	In-house collection	No	Clinical	Respiratory Tract	1	103	12	2	4	253
PA49	***15TB0777***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA50	***15TB0778***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA51	***15TB0779***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA52	***15TB0780***	In-house collection	No	Clinical	Respiratory Tract	14	66	2	16	2	111
PA53	***15TB0781***	In-house collection	Yes	Clinical	Respiratory Tract	14		2	16	2	111
PA54	***15TB0782***	In-house collection	No	Clinical	Unknown	7	15	7	7	8	Undefined

PA55	***15TB0783***	In-house collection	Yes	Clinical	Unknown	18		10	19	10	988
PA56	***15TB0784***	In-house collection	No	Clinical	Unknown	18	79	10	19	10	988
PA57	***15TB0785***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA58	***15TB0786***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA59	***15TB0787***	In-house collection	Yes	Clinical	Cystic Fibrosis	18		9	19	5	254
PA60	***15TB0792***	In-house collection	No	Environment	Other environmental source	19	37	8	18	9	3514
PA61	***15TB0793***	In-house collection	No	Environment	Other environmental source	11	49	11	13	14	252
PA62	***15TB0794***	In-house collection	No	Clinical	Unknown	18	79	10	19	10	988
PA63	***15TB0795***	In-house collection	No	Environment	Other environmental source	1	103	12	2	4	253
PA64	***15TB0796***	In-house collection	No	Environment	Other environmental source	19	48	10	8	10	357
PA65	***15TB0800***	In-house collection	Yes	Clinical	Unknown	1		12	2	4	253
PA66	***15TB0801***	In-house collection	Yes	Clinical	Unknown	1		12	2	4	253
PA67	***15TB0802***	In-house collection	Yes	Clinical	Unknown	8		10	6	10	309
PA68	***15TB0803***	In-house collection	Yes	Clinical	Unknown	19		13	21	13	313
PA69	***15TB0804***	In-house collection	Yes	Clinical	Unknown	18		12	19	12	1091
PA70	***15TB0805***	In-house collection	No	Clinical	Unknown	18	86	12	19	12	1091
PA71	***15TB0806***	In-house collection	Yes	Clinical	Unknown	15		12	23	12	244
PA72	***15TB0807***	In-house collection	No	Clinical	Unknown	18	32	12	19	12	643
PA73	***15TB0839***	In-house collection	Yes	Clinical	Unknown	12		1	14	1	395
PA74	***15TB0840***	In-house collection	Yes	Clinical	Unknown	12		1	14	1	395
PA75	***15TB0841***	In-house collection	Yes	Clinical	Unknown	12		1	14	1	395
PA76	***15TB0842***	In-house collection	Yes	Clinical	Unknown	7		7	7	8	Undefined
PA77	***15TB0843***	In-house collection	Yes	Clinical	Unknown	1		12	2	4	253
PA78	***15TB0844***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA79	***15TB0845***	In-house collection	Yes	Clinical	Unknown	12		1	14	1	395
PA80	***15TB0846***	In-house collection	Yes	Clinical	Unknown	7		7	7	8	Undefined
PA81	***15TB0847***	In-house collection	Yes	Clinical	Unknown	1		12	2	4	253
PA82	***15TB0848***	In-house collection	Yes	Clinical	Unknown	1		12	2	4	253
PA83	***15TB0849***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253
PA84	***15TB0850***	In-house collection	Yes	Clinical	Respiratory Tract	1		12	2	4	253

PA85	***15TB0851***	In-house collection	Yes	Clinical	Unknown	15		12	23	12	244
PA86	***15TB0852***	In-house collection	Yes	Clinical	Unknown	18		12	19	12	643
PA87	***15TB0853***	In-house collection	Yes	Clinical	Unknown	18		12	19	12	643
PA88	***15TB0854***	In-house collection	Yes	Clinical	Urinary Tract	19		10	21	10	620
PA89	***15TB0855***	In-house collection	No	Clinical	Cystic Fibrosis	18	73	9	19	5	254
PA90	***15TB0856***	In-house collection	Yes	Clinical	Unknown	1		12	2	4	253
PA91	***15TB0915***	In-house collection	No	Environment	Clinical environment: Dental, Hospital	13	50	9	10	12	27
PA92	***15TB0921***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA93	***15TB0922***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA94	***15TB0924***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA95	***15TB0925***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA96	***15TB0926***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA97	***15TB0927***	In-house collection	No	Environment	Clinical environment: Dental, Hospital	12	2	1	14	1	395
PA98	***15TB0928***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA99	***15TB0929***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA100	***15TB0930***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA101	***15TB0931***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA102	***15TB0932***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA103	***15TB0933***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA104	***15TB0934***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA105	***15TB0935***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA106	***15TB0936***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA107	***15TB0937***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395

PA108	***15TB0938***	In-house collection	Yes	Environment	Clinical environment: Dental, Hospital	12		1	14	1	395
PA109	***16TB0654***	In-house collection	Yes	Clinical	Unknown	19		8	18	9	136
PA110	***16TB0655***	In-house collection	No	Clinical	Unknown	15	32	12	23	12	244
PA111	***16TB0656***	In-house collection	Yes	Clinical	Unknown	18		13	20	12	1591
PA112	***16TB0657***	In-house collection	No	Clinical	Unknown	18	9	11	20	14	390
PA113	***16TB0658***	In-house collection	No	Clinical	Unknown	18	79	11	19	14	878
PA114	***16TB0659***	In-house collection	Yes	Clinical	Unknown	8		10	6	10	309
PA115	***16TB0660***	In-house collection	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA116	***16TB0661***	In-house collection	Yes	Clinical	Bone and Joint	8		10	6	10	309
PA117	***16TB0662***	In-house collection	Yes	Clinical	Unknown	19		10	21	10	1027
PA118	***16TB0663***	In-house collection	Yes	Clinical	Unknown	15		12	23	12	244
PA119	***16TB0664***	In-house collection	No	Clinical	Bacteraemia	2	39	10	5	10	446
PA120	***16TB0665***	In-house collection	Yes	Clinical	Unknown	18		11	19	14	878
PA121	***16TB0666***	In-house collection	Yes	Clinical	Unknown	8		10	6	10	309
PA122	***16TB0667***	In-house collection	Yes	Clinical	Unknown	19		10	21	10	1027
PA123	***16TB0668***	In-house collection	Yes	Clinical	Unknown	2		10	5	10	446
PA124	***16TB0669***	In-house collection	Yes	Clinical	Unknown	19		3	21	3	532
PA125	***16TB0670***	In-house collection	Yes	Clinical	Bone and Joint	19		10	21	10	1027
PA126	***16TB0671***	In-house collection	No	Clinical	Unknown	19	102	3	21	3	532
PA127	***16TB0672***	In-house collection	No	Clinical	Bacteraemia	19	54	8	18	9	Undefined
PA128	***16TB0673***	In-house collection	Yes	Clinical	Unknown	15		12	23	12	244
PA129	***16TB0674***	In-house collection	Yes	Clinical	Bacteraemia	8		10	6	10	309
PA130	***16TB0675***	In-house collection	No	Clinical	Unknown	18	93	13	20	12	1591
PA131	***16TB0676***	In-house collection	No	Clinical	Unknown	19	102	10	21	10	1027
PA132	***16TB0677***	In-house collection	No	Clinical	Bacteraemia	8	16	10	6	10	309
PA133	***16TB0678***	In-house collection	Yes	Clinical	Unknown	18		11	20	14	390
PA134	***16TB0679***	In-house collection	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	86	9	19	5	132
PA135	***16TB0680***	In-house collection	No	Clinical	Unknown	19	54	8	18	9	136
PA136	***16TB0681***	In-house collection	Yes	Clinical	Unknown	2		10	5	10	446

PA137	***16TB0682***	In-house collection	No	Clinical	Bone and Joint	19	48	3	21	3	1284
PA138	***16TB0683***	In-house collection	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA139	***16TB0685***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA140	***16TB0686***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA141	***16TB0687***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA142	***16TB0688***	In-house collection	No	Environment	Other environmental source	11	49	11	13	14	252
PA143	***16TB0689***	In-house collection	No	Environment	Other environmental source	19	37	8	18	9	3514
PA144	***16TB0690***	In-house collection	No	Environment	Other environmental source	11	49	11	13	14	252
PA145	***16TB0691***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA146	***16TB0692***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA147	***16TB0693***	In-house collection	No	Environment	Other environmental source	18	102	13	19	11	2465
PA148	***16TB0694***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA149	***16TB0695***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA150	***16TB0696***	In-house collection	No	Environment	Other environmental source	11	49	11	13	14	252
PA151	***16TB0697***	In-house collection	No	Environment	Lab	11	49	11	13	14	252
PA152	***16TB0698***	In-house collection	No	Environment	Lab	11	49	11	13	14	252
PA153	***16TB0699***	In-house collection	No	Environment	Lab	19	37	8	18	9	3514
PA154	***16TB0700***	In-house collection	Yes	Environment	Home environment	11		11	13	14	252
PA155	***16TB0701***	In-house collection	No	Environment	Home environment	11	49	11	13	14	252
PA156	***16TB0723***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA157	***16TB0724***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA158	***16TB0725***	In-house collection	No	Environment	Other environmental source	11	49	11	13	14	252
PA159	***16TB0726***	In-house collection	Yes	Environment	Other environmental source	11		11	13	14	252
PA160	***16TB1027***	In-house collection	No	Environment	Water: Swimming Pool	8	16	10	6	10	309
PA161	***16TB1028***	In-house collection	Yes	Environment	Water: Swimming Pool	12		1	14	1	395
PA162	***16TB1029***	In-house collection	No	Environment	Water: Swimming Pool	19	102	8	18	9	667
PA163	***16TB1030***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA164	***16TB1031***	In-house collection	Yes	Environment	Water: Swimming Pool	19		8	18	9	667
PA165	***16TB1032***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA166	***16TB1033***	In-house collection	Yes	Environment	Water: Swimming Pool	19		12	21	12	1248

PA167	***16TB1034***	In-house collection	No	Environment	Water: Swimming Pool	11	102	11	13	14	252
PA168	***16TB1035***	In-house collection	Yes	Environment	Water: Swimming Pool	19		12	21	12	1248
PA169	***16TB1036***	In-house collection	Yes	Environment	Water: Swimming Pool	12		1	14	1	395
PA170	***16TB1037***	In-house collection	Yes	Environment	Water: Swimming Pool	16		11	17	14	179
PA171	***16TB1038***	In-house collection	Yes	Environment	Water: Swimming Pool	12		1	14	1	395
PA172	***16TB1039***	In-house collection	No	Environment	Water: Swimming Pool	16	5	11	17	14	179
PA173	***16TB1040***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA174	***16TB1041***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA175	***16TB1042***	In-house collection	No	Environment	Water: Swimming Pool	19	61	13	21	13	313
PA176	***16TB1043***	In-house collection	Yes	Environment	Water: Swimming Pool	12		1	14	1	395
PA177	***16TB1044***	In-house collection	No	Environment	Water: Swimming Pool	15	32	12	23	12	244
PA178	***16TB1045***	In-house collection	Yes	Environment	Water: Swimming Pool	15		12	23	12	244
PA179	***16TB1046***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA180	***16TB1047***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA181	***16TB1048***	In-house collection	No	Environment	Water: Swimming Pool	15	32	12	23	12	244
PA182	***16TB1049***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA183	***16TB1050***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA184	***16TB1051***	In-house collection	Yes	Environment	Water: Swimming Pool	11		11	13	14	252
PA185	***16TB1052***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA186	***16TB1054***	In-house collection	Yes	Environment	Water: Swimming Pool	19		12	21	12	1248
PA187	***16TB1055***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA188	***16TB1056***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA189	***16TB1057***	In-house collection	No	Environment	Water: Swimming Pool	19	27	12	21	4	560
PA190	***16TB1058***	In-house collection	Yes	Environment	Water: Swimming Pool	19		12	21	12	1248
PA191	***16TB1059***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA192	***16TB1060***	In-house collection	No	Environment	Water: Swimming Pool	1	103	12	2	4	253
PA193	***16TB1061***	In-house collection	Yes	Environment	Water: Swimming Pool	19		12	21	12	1248
PA194	***16TB1062***	In-house collection	No	Environment	Water: Swimming Pool	19	102	12	21	12	1248
PA195	***16TB1063***	In-house collection	Yes	Environment	Water: Swimming Pool	12		1	14	1	395
PA196	***16TB1064***	In-house collection	Yes	Environment	Water: Swimming Pool	19		12	21	12	1248

PA197	***16TB1065***	In-house collection	No	Environment	Water: Swimming Pool	12	2	1	14	1	395
PA198	***16TB1066***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA199	***16TB1068***	In-house collection	Yes	Environment	Water: Swimming Pool	1		12	2	4	253
PA200	***16TB1069***	In-house collection	Yes	Environment	Water: Swimming Pool	19		12	21	12	1248
PA201	***16TB1070***	In-house collection	No	Environment	Water: Swimming Pool	2	39	10	5	10	298
PA202	***Pseudomonas_aeruginosa_5034388498_20_10898***	GCF_004371275.1	No	Clinical	Cystic fibrosis	18	93	9	19	12	1455
PA203	***Pseudomonas_aeruginosa_578_A_6765***	GCF_002312355.1	Yes	Clinical	Respiratory tract	9		9	11	5	17
PA204	***Pseudomonas_aeruginosa_ATCC_BAA_2114_5907***	GCF_002237055.1	No	Clinical	Respiratory tract	18	69	6	19	7	969
PA205	***DB050***	In-house collection	No	Environment	Food	18	65	6	22	7	389
PA206	***DB057***	In-house collection	No	Environment	Food	18	41	5	19	6	1228
PA207	***DB078***	In-house collection	No	Environment	Food	18	86	8	19	12	Undefined
PA208	***DC053***	In-house collection	Yes	Environment	Food	18		5	19	6	1228
PA209	***DC063***	In-house collection	No	Environment	Food	18	41	5	19	6	1228
PA210	***DP067***	In-house collection	No	Environment	Food	18	86	8	19	12	Undefined
PA211	***Pseudomonas_aeruginosa_DUN_007_2_10076***	GCF_003835765.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	845
PA212	***Pseudomonas_aeruginosa_DZ_B1_6106***	GCF_002094805.1	No	Environment	Animal	18	86	13	19	12	385
PA213	***Pseudomonas_aeruginosa_EGD_AQ8_7184***	GCF_002896925.1	No	Environment	Sewage/Wastewater	19	61	10	21	10	207
PA214	***GCA_002025755.1_ASM202575v1_genomic***	GCA_002025755.1	No	Environment	Plants	12	2		14		395
PA215	***GCA_013260445.1_ASM1326044v1_genomic***	GCA_013260445.1	No	Environment	Plants	18	102	12	19	12	1395
PA216	***GCA_013395035.1_ASM1339503v1_genomic***	GCA_013395035.1	Yes	Environment	Plants	18		13	19	12	Undefined
PA217	***GCA_013467585.1_ASM1346758v1_genomic***	GCA_013467585.1	No	Environment	Plants	18	35	13	19	12	Undefined
PA218	***GCA_013467605.1_ASM1346760v1_genomic***	GCA_013467605.1	Yes	Environment	Plants	18		13	19	12	Undefined
PA219	***GCA_014892595.1_ASM1489259v1_genomic***	GCA_014892595.1	No	Environment	Plants	10	78	5	12	6	274
PA220	***GCA_900478745.1_32018_A01_genomic***	GCA_900478745.1	No	Environment	Plants	19	54	8	18	9	1920
PA221	***GCF_012102115.1_ASM1210211v1_genomic***	GCA_012102115.1	Yes	Environment	Animal	18		12	19	12	549
PA222	***GCF_012102215.1_ASM1210221v1_genomic***	GCA_012102215.1	No	Environment	Animal	18	32	12	19	12	549
PA223	***GCF_012102225.1_ASM1210222v1_genomic***	GCA_012102225.1	Yes	Environment	Animal	18		12	19	12	549
PA224	***GCF_013619435.1_ASM1361943v1_genomic***	GCA_013619435.1	No	Environment	Animal	17	86	11	22	14	146
PA225	***GCF_015626655.1_ASM1562665v1_genomic***	GCA_015626655.1	No	Environment	Animal	18	102	9	19	5	885
PA226	***GCF_015626695.1_ASM1562669v1_genomic***	GCA_015626695.1	Yes	Environment	Animal	10		5	12	6	274

PA227	***GCF_015704805.1_ASM1570480v1_genomic***	GCA_015704805.1	No	Environment	Animal	18	78	8	19	12	1600
PA228	***GCF_902807105.1_PBIO724_genomic***	GCA_902807105.1	No	Environment	Animal	16	5	11	17	14	179
PA229	***GCF_902807215.1_PBIO712_genomic***	GCA_902807215.1	Yes	Environment	Animal	16		11	17	14	179
PA230	***Pseudomonas_aeruginosa_LCT_PA220_459***	GCF_000439855.1	No	Environment	Other environmental source	16	5	11	17	14	155
PA231	***Pseudomonas_aeruginosa_LCT_PA41_460***	GCF_000439875.1	No	Environment	Other environmental source	16	5	11	17	14	155
PA232	***LWR011-2***	In-house collection	No	Environment	Plants	7	15	7	7	8	195
PA233	***MR 96136***	In-house collection	No	Clinical	Unknown	19	47	10	8	10	3396
PA234	***Pseudomonas_aeruginosa_nmrcch_6_2018_5871***	GCF_003340635.1	No	Clinical	Bacteraemia	19	61	13	21	13	313
PA235	***Pseudomonas_aeruginosa_Ocean_100_5904***	GCF_002263645.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	11	21	14	2329
PA236	***Pseudomonas_aeruginosa_Ocean_1187_6137***	GCF_002263585.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA237	***Pseudomonas_aeruginosa_Ocean_1206_6130***	GCF_002263615.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA238	***Pseudomonas_aeruginosa_Ocean_222_6755***	GCF_002263575.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	61	13	21	13	313
PA239	***Pseudomonas_aeruginosa_PA_CL508_10956***	GCF_004372445.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA240	***Pseudomonas_aeruginosa_PA_CL513_10974***	GCF_004372815.1	Yes	Environment	Clinical environment: Dental, Hospital	1		12	2	4	Undefined
PA241	***Pseudomonas_aeruginosa_PA_CL520_10950***	GCF_004372325.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	179
PA242	***Pseudomonas_aeruginosa_PA_CL522b_10947***	GCF_004372275.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	155
PA243	***Pseudomonas_aeruginosa_PA_W22_10320***	GCF_003841625.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	97	9	19	5	3600
PA244	***Pseudomonas_aeruginosa_PA_W9_10328***	GCF_003841805.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		13	19	12	2123
PA245	***PA11***	In-house collection	No	Clinical	Respiratory Tract	19	102	10	21	10	1632
PA246	***PA12***	In-house collection	Yes	Clinical	Respiratory Tract	19		10	21	10	207
PA247	***PA14***	In-house collection	No	Clinical	Respiratory Tract	2	39	10	5	10	446
PA248	***PA15***	In-house collection	No	Clinical	Respiratory Tract	18	86	11	19	14	443
PA249	***PA16***	In-house collection	Yes	Clinical	Unknown	19		10	8	10	357
PA250	***PA17***	In-house collection	No	Clinical	Respiratory Tract	19	47	3	21	3	773
PA251	***PA18***	In-house collection	Yes	Clinical	Unknown	19		10	8	10	357
PA252	***PA19***	In-house collection	No	Clinical	Respiratory Tract	19	61	10	21	10	207

PA253	***PA20***	In-house collection	Yes	Clinical	Respiratory Tract	18		11	19	14	443
PA254	***PA21***	In-house collection	No	Clinical	Respiratory Tract	16	5	11	17	14	155
PA255	***PA23***	In-house collection	Yes	Clinical	Respiratory Tract	3		10	4	10	235
PA256	***PA24***	In-house collection	Yes	Clinical	Respiratory Tract	2		10	5	10	446
PA257	***PA30***	In-house collection	Yes	Clinical	Unknown	19		10	8	10	357
PA258	***PA31***	In-house collection	No	Clinical	Respiratory Tract	19	39	10	21	10	319
PA259	***PA32***	In-house collection	No	Clinical	Respiratory Tract	5		4			Undefined
PA260	***PA33***	In-house collection	Yes	Clinical	Unknown	19		3	21	3	773
PA261	***PA34***	In-house collection	No	Clinical	Respiratory Tract	19	102	10	8	10	357
PA262	***PA35***	In-house collection	No	Clinical	Respiratory Tract	4	14	10	3	10	308
PA263	***PA36***	In-house collection	Yes	Clinical	Respiratory Tract	2		10	5	10	446
PA264	***PA38***	In-house collection	No	Clinical	Respiratory Tract	3	6	10	4	10	235
PA265	***PF03***	In-house collection	No	Environment	Animal	18	86	8	19	12	Undefined
PA266	***PF06***	In-house collection	Yes	Environment	Animal	18		8	19	12	Undefined
PA267	***PF08***	In-house collection	Yes	Environment	Animal	18		8	19	12	Undefined
PA268	***PF09***	In-house collection	Yes	Environment	Animal	18		8	19	12	Undefined
PA269	***PF10***	In-house collection	Yes	Environment	Animal	18		8	19	12	Undefined
PA270	***PF23***	In-house collection	No	Environment	Animal	18	41	5	19	6	1228
PA271	***PF40***	In-house collection	Yes	Environment	Animal	18		8	19	12	Undefined
PA272	***PF47***	In-house collection	Yes	Environment	Animal	18		8	19	12	Undefined
PA273	***Pseudomonas_aeruginosa_PPF_21_6614***	GCF_002312245.1	No	Environment	Clinical environment: Dental, Hospital	19	39	10	1	10	Undefined
PA274	***Pseudomonas_aeruginosa_001_5A_10078***	GCF_003835785.1	Yes	Clinical	Cystic fibrosis	15		12	23	12	244
PA275	***Pseudomonas_aeruginosa_001_6_10053***	GCF_003835295.1	Yes	Clinical	Cystic fibrosis	15		12	23	12	244
PA276	***Pseudomonas_aeruginosa_020MIC_10043***	GCF_003835095.1	Yes	Clinical	Cystic fibrosis	12		1	14	1	395
PA277	***Pseudomonas_aeruginosa_0C4A_isolate_679_9919***	GCF_003698425.1	No	Clinical	Urinary tract	18	77	9	19	12	198
PA278	***Pseudomonas_aeruginosa_0C4A_isolate_RP45_3624***	GCF_001500245.1	No	Clinical	Cystic fibrosis	18	102	9	19	12	Undefined
PA279	***Pseudomonas_aeruginosa_10_10842***	GCF_004370105.1	No	Clinical	Cystic fibrosis	10	78	5	12	6	2834
PA280	***Pseudomonas_aeruginosa_1042828174_20_10861***	GCF_004370505.1	Yes	Clinical	Cystic fibrosis	18		9	19	12	663
PA281	***Pseudomonas_aeruginosa_1042828174_21_10860***	GCF_004370455.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	845

PA282	***Pseudomonas_aeruginosa_105738_3985***	GCF_001601595.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	81	13	20	12	621
PA283	***Pseudomonas_aeruginosa_105777_3982***	GCF_001560865.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	102	5	19	6	1419
PA284	***Pseudomonas_aeruginosa_105819_3987***	GCF_001601745.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	35	9	19	12	3045
PA285	***Pseudomonas_aeruginosa_105857_3986***	GCF_001601665.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	15	18	12	23	12	244
PA286	***Pseudomonas_aeruginosa_105880_3984***	GCF_001601585.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	48	3	21	3	1284
PA287	***Pseudomonas_aeruginosa_1090_10259***	GCF_003840155.1	No	Environment	Animal	18	32	11	19	11	Undefined
PA288	***Pseudomonas_aeruginosa_1098_10263***	GCF_003840225.1	Yes	Environment	Animal	19		13	21	13	313
PA289	***Pseudomonas_aeruginosa_110238627_10857***	GCF_004370405.1	Yes	Clinical	Cystic fibrosis	16			17		155
PA290	***Pseudomonas_aeruginosa_11987_2_5_6282***	GCF_003185875.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	8	18	9	667
PA291	***Pseudomonas_aeruginosa_12_4_4_59_3618***	GCF_001482325.1	No	Clinical	Burn	18	46	13	19	11	152
PA292	***Pseudomonas_aeruginosa_130_7339***	GCF_002411845.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		9	19	12	234
PA293	***Pseudomonas_aeruginosa_1334_14_10731***	GCF_004193735.1	No	Clinical	Eye	18	83	9	19	12	234
PA294	***Pseudomonas_aeruginosa_136S260811BSL_PA1_11083***	GCF_004375385.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	514
PA295	***Pseudomonas_aeruginosa_136S260811BSL_PA3_11092***	GCF_004375585.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	514
PA296	***Pseudomonas_aeruginosa_138244_7581***	GCF_000215775.3	No	Clinical	Respiratory tract	18	102	6	22	7	175
PA297	***Pseudomonas_aeruginosa_140_7096***	GCF_002411815.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		9	19	12	234
PA298	***Pseudomonas_aeruginosa_142_10879***	GCF_004370875.1	No	Clinical	Cystic fibrosis	18	86	6	19	7	2746
PA299	***Pseudomonas_aeruginosa_144S190811BSL_PA2_11079***	GCF_004375295.1	No	Clinical	Cystic fibrosis	18	73	9	19	12	Undefined
PA300	***Pseudomonas_aeruginosa_145S200511BSL_PA2_11078***	GCF_004375285.1	No	Clinical	Cystic fibrosis	18	79	9	19	12	Undefined
PA301	***Pseudomonas_aeruginosa_146_Assistante_6000***	GCF_002312175.1	Yes	Environment	Clinical environment: Dental, Hospital	19		10	1	10	Undefined
PA302	***Pseudomonas_aeruginosa_14649_3306***	GCF_001414105.1	No	Clinical	Respiratory tract	18	93	9	19	12	192
PA303	***Pseudomonas_aeruginosa_14650_3305***	GCF_001414085.1	No	Clinical	Respiratory tract	18	93	9	19	12	192
PA304	***Pseudomonas_aeruginosa_14651_3307***	GCF_001414155.1	No	Clinical	Respiratory tract	16	5	11	17	14	179
PA305	***Pseudomonas_aeruginosa_14672_3308***	GCF_001414165.1	Yes	Clinical	Respiratory tract	18		9	19	12	192
PA306	***Pseudomonas_aeruginosa_14673_3309***	GCF_001414175.1	Yes	Clinical	Respiratory tract	18		9	19	12	192
PA307	***Pseudomonas_aeruginosa_148_6330***	GCF_000647595.2	No	Environment	Animal	8	16	10	6	10	Undefined

PA308	***Pseudomonas_aeruginosa_15_10837***	GCF_004370015.1	No	Clinical	Cystic fibrosis	18	102	6	19	7	709
PA309	***Pseudomonas_aeruginosa_151_Assistante_6118***	GCF_002312145.1	Yes	Environment	Clinical environment: Dental, Hospital	19		10	21	10	Undefined
PA310	***Pseudomonas_aeruginosa_1510_10353***	GCF_003863825.1	No	Clinical	Cystic fibrosis	18	97	13	19	11	584
PA311	***Pseudomonas_aeruginosa_152504sp2_10256***	GCF_003840095.1	No	Clinical	Respiratory tract	19	27	12	21	4	560
PA312	***Pseudomonas_aeruginosa_1622_10340***	GCF_003863575.1	No	Clinical	Cystic fibrosis	18	100	11	19	14	Undefined
PA313	***Pseudomonas_aeruginosa_1631_10350***	GCF_003863775.1	No	Clinical	Cystic fibrosis	18	95	12	19	12	Undefined
PA314	***Pseudomonas_aeruginosa_163940_9946***	GCF_003721395.1	No	Clinical	Gastrointestinal	18	32	12	19	12	549
PA315	***Pseudomonas_aeruginosa_164130_11975***	GCF_008244545.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA316	***Pseudomonas_aeruginosa_17_10836***	GCF_004369995.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	179
PA317	***Pseudomonas_aeruginosa_1714_10346***	GCF_003863685.1	No	Clinical	Cystic fibrosis	18	102	13	19	11	242
PA318	***Pseudomonas_aeruginosa_173_6579***	GCF_002312055.1	No	Clinical	Respiratory tract	18	102	8	19	9	633
PA319	***Pseudomonas_aeruginosa_174313_11923***	GCF_006861745.1	Yes	Clinical	Burn	18		9	19	5	664
PA320	***Pseudomonas_aeruginosa_174319_11922***	GCF_006861735.1	No	Clinical	Burn	18	25	9	19	5	664
PA321	***Pseudomonas_aeruginosa_175S070312EX2DAY21_PA1_11080***	GCF_004375325.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	514
PA322	***Pseudomonas_aeruginosa_175S070312EX2DAY21_PA2_11100***	GCF_004378755.1	No	Clinical	Cystic fibrosis	18	78	13	19	11	514
PA323	***Pseudomonas_aeruginosa_1811_13R031_12048***	GCF_009676765.1	No	Clinical	Respiratory tract	12	2	1	14	1	395
PA324	***Pseudomonas_aeruginosa_1811_18R001_12049***	GCF_009676785.1	Yes	Clinical	Respiratory tract	12		1	14	1	395
PA325	***Pseudomonas_aeruginosa_18G_11014***	GCF_004373595.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined
PA326	***Pseudomonas_aeruginosa_19_10878***	GCF_004370865.1	No	Clinical	Cystic fibrosis	17	86	11	19	14	683
PA327	***Pseudomonas_aeruginosa_192S190811BSL_PA2_11077***	GCF_004375275.1	Yes	Clinical	Cystic fibrosis	18		13	19	12	Undefined
PA328	***Pseudomonas_aeruginosa_192S190811BSL_PA3_11076***	GCF_004375265.1	No	Clinical	Cystic fibrosis	18	93	13	19	12	Undefined
PA329	***Pseudomonas_aeruginosa_19660_593***	GCF_000481765.1	No	Environment	Animal	19	54	8	18	9	Undefined
PA330	***Pseudomonas_aeruginosa_197S020911BSL_PA1_11075***	GCF_004375205.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	514
PA331	***Pseudomonas_aeruginosa_197S020911BSL_PA2_11074***	GCF_004375195.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	514
PA332	***Pseudomonas_aeruginosa_197S020911BSL_PA4_11073***	GCF_004375185.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	514
PA333	***Pseudomonas_aeruginosa_19R_10978***	GCF_004372905.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined
PA334	***Pseudomonas_aeruginosa_19SJO_11095***	GCF_004378685.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined
PA335	***Pseudomonas_aeruginosa_19SJV_11013***	GCF_004373585.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined
PA336	***Pseudomonas_aeruginosa_19SV_10966***	GCF_004372645.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined
PA337	***Pseudomonas_aeruginosa_1BAE_isolate_KK1_9927***	GCF_003698585.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	155

PA338	***Pseudomonas_aeruginosa_20_10834***	GCF_004369945.1	No	Clinical	Cystic fibrosis	18	86	9	19	5	480
PA339	***Pseudomonas_aeruginosa_201s070911bsl_PA1_11088***	GCF_004375495.1	No	Clinical	Cystic fibrosis	18	102	13	19	12	Undefined
PA340	***Pseudomonas_aeruginosa_201s070911bsl_PA2_11071***	GCF_004375165.1	Yes	Clinical	Cystic fibrosis	18		13	19	12	282
PA341	***Pseudomonas_aeruginosa_2042723558_10892***	GCF_004371145.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	845
PA342	***Pseudomonas_aeruginosa_21_10833***	GCF_004369935.1	No	Clinical	Cystic fibrosis	18	93	12	19	11	Undefined
PA343	***Pseudomonas_aeruginosa_21_10846***	GCF_004370195.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	Undefined
PA344	***Pseudomonas_aeruginosa_21107_12107***	GCF_009830185.1	Yes	Clinical	Cystic fibrosis	18		9	19	12	2744
PA345	***Pseudomonas_aeruginosa_21114_12106***	GCF_009830175.1	No	Clinical	Cystic fibrosis	18	67	9	19	12	2744
PA346	***Pseudomonas_aeruginosa_21167_12108***	GCF_009830195.1	Yes	Clinical	Cystic fibrosis	18		9	19	12	2744
PA347	***Pseudomonas_aeruginosa_21168_12110***	GCF_009830215.1	Yes	Clinical	Cystic fibrosis	18		9	19	12	2744
PA348	***Pseudomonas_aeruginosa_2253_6046***	GCF_002193735.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	65	6	22	7	389
PA349	***Pseudomonas_aeruginosa_2320_7153***	GCF_002193655.1	No	Clinical	Respiratory tract	1	103	12	2	4	253
PA350	***Pseudomonas_aeruginosa_2321_6508***	GCF_002193745.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	102	13	19	12	Undefined
PA351	***Pseudomonas_aeruginosa_2325_6593***	GCF_002193685.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	17	22	6	15	7	245
PA352	***Pseudomonas_aeruginosa_2328_7259***	GCF_002193665.1	No	Clinical	Body fluid	18	25	9	19	12	447
PA353	***Pseudomonas_aeruginosa_2330_6007***	GCF_002193675.1	No	Clinical	Eye	16	5	11	17	14	179
PA354	***Pseudomonas_aeruginosa_2353_6286***	GCF_002194075.1	No	Clinical	Bacteraemia	18	4	9	22	12	348
PA355	***Pseudomonas_aeruginosa_2357_6857***	GCF_002193975.1	No	Clinical	Respiratory tract	3	6	10	4	10	235
PA356	***Pseudomonas_aeruginosa_239A_isolate_13121_1_9926***	GCF_003698565.1	No	Clinical	Respiratory tract	18	4	9	22	12	Undefined
PA357	***Pseudomonas_aeruginosa_243931_11950***	GCF_007559125.1	No	Clinical	Urinary tract	3	14	10	4	10	235
PA358	***Pseudomonas_aeruginosa_24Pae112_9634***	GCF_003433235.1	No	Clinical	Bacteraemia	3	6	10	4	10	235
PA359	***Pseudomonas_aeruginosa_2570_6256***	GCF_002193755.1	Yes	Clinical	Bacteraemia	18		6	22	7	389
PA360	***Pseudomonas_aeruginosa_259S240811BSL_PA1_11060***	GCF_004374515.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA361	***Pseudomonas_aeruginosa_259S240811BSL_PA2_11070***	GCF_004375115.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA362	***Pseudomonas_aeruginosa_2600_12045***	GCF_009650545.1	No	Clinical	Cystic fibrosis	18	102	5	19	6	859
PA363	***Pseudomonas_aeruginosa_2623_6965***	GCF_002193765.1	Yes	Clinical	Bacteraemia	16		11	17	14	179
PA364	***Pseudomonas_aeruginosa_265_5866***	GCF_002312545.1	Yes	Clinical	Respiratory tract	16		11	17	14	179
PA365	***Pseudomonas_aeruginosa_2671_5848***	GCF_002193925.1	Yes	Clinical	Bacteraemia	18		9	22	12	348
PA366	***Pseudomonas_aeruginosa_278S180511BSL_PA1_11069***	GCF_004375075.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17

PA367	***Pseudomonas_aeruginosa_279_6928***	GCF_002312385.1	Yes	Clinical	Respiratory tract	9		9	11	5	17
PA368	***Pseudomonas_aeruginosa_282_7227***	GCF_002312115.1	Yes	Clinical	Respiratory tract	18		13	19	11	Undefined
PA369	***Pseudomonas_aeruginosa_293S080611BSL_PA1_11067***	GCF_004374685.1	No	Clinical	Cystic fibrosis	19	53	8	21	9	Undefined
PA370	***Pseudomonas_aeruginosa_293S080611BSL_PA2_11054***	GCF_004374405.1	No	Clinical	Cystic fibrosis	19	102	8	21	9	Undefined
PA371	***Pseudomonas_aeruginosa_295s071211BSL_PA2_11051***	GCF_004374365.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA372	***Pseudomonas_aeruginosa_297_6956***	GCF_002312755.1	No	Clinical	Respiratory tract	18	81	10	19	10	853
PA373	***Pseudomonas_aeruginosa_29S030611BSL_PA1_11087***	GCF_004375475.1	No	Clinical	Cystic fibrosis	18	78	6	19	7	170
PA374	***Pseudomonas_aeruginosa_2C22_isolate_57P31PA_9912***	GCF_003698025.1	Yes	Clinical	Respiratory tract	10		5	12	6	274
PA375	***Pseudomonas_aeruginosa_2D9A_isolate_AUS23_6462***	GCF_002276485.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	775
PA376	***Pseudomonas_aeruginosa_313s141011BSL_PA1_11066***	GCF_004374625.1	No	Clinical	Cystic fibrosis	18	97	9	19	5	Undefined
PA377	***Pseudomonas_aeruginosa_3141_10640***	GCF_003976075.1	No	Clinical	Respiratory tract	15	32	12	23	12	244
PA378	***Pseudomonas_aeruginosa_318S170811BSL_PA1_11048***	GCF_004374295.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA379	***Pseudomonas_aeruginosa_318S170811BSL_PA2_11049***	GCF_004374305.1	No	Clinical	Cystic fibrosis	10	78	5	12	6	274
PA380	***Pseudomonas_aeruginosa_326S290611BSL_PA1_11046***	GCF_004374265.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	564
PA381	***Pseudomonas_aeruginosa_326S290611BSL_PA3_11063***	GCF_004374595.1	No	Clinical	Cystic fibrosis	18	46	12	19	12	Undefined
PA382	***Pseudomonas_aeruginosa_32SB_10977***	GCF_004372875.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined
PA383	***Pseudomonas_aeruginosa_32SP_10979***	GCF_004372915.1	No	Environment	Hydrocarbon contamination	18	88	11	19	14	Undefined
PA384	***Pseudomonas_aeruginosa_333S200112BSL_PA1_11043***	GCF_004374185.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	564
PA385	***Pseudomonas_aeruginosa_34JS_10965***	GCF_004372635.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined
PA386	***Pseudomonas_aeruginosa_354_6648***	GCF_002312535.1	No	Clinical	Respiratory tract	10	78	5	12	6	274
PA387	***Pseudomonas_aeruginosa_358_5856***	GCF_002312375.1	Yes	Clinical	Respiratory tract	9		9	11	5	17
PA388	***Pseudomonas_aeruginosa_359_6313***	GCF_002312455.1	No	Clinical	Respiratory tract	17	86	11	19	14	683
PA389	***Pseudomonas_aeruginosa_37s051011BSL_PA1_11086***	GCF_004375455.1	No	Clinical	Cystic fibrosis	18	102	9	19	12	2633
PA390	***Pseudomonas_aeruginosa_39016_9914***	GCF_003698065.1	No	Clinical	Eye	3	6	10	4	10	235
PA391	***Pseudomonas_aeruginosa_39145_10248***	GCF_003839945.1	No	Clinical	Eye	13	102	9	10	12	27
PA392	***Pseudomonas_aeruginosa_392_6207***	GCF_002312405.1	No	Clinical	Respiratory tract	16	5	11	17	14	179
PA393	***Pseudomonas_aeruginosa_3C1A_isolate_Jpn1563_9934***	GCF_003698715.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	101	11	19	14	876
PA394	***Pseudomonas_aeruginosa_3C52_K_isolate_968333S_9933***	GCF_003698705.1	No	Clinical	Respiratory tract	18	83	9	19	12	234
PA395	***Pseudomonas_aeruginosa_4_10885***	GCF_004370985.1	No	Clinical	Cystic fibrosis	18	78	13	19	11	2498
PA396	***Pseudomonas_aeruginosa_4014_7122***	GCF_002157485.1	No	Environment	Farm environment	18	63	9	19	12	1858

PA397	***Pseudomonas_aeruginosa_403_6033***	GCF_002312695.1	No	Clinical	Respiratory tract	18	78	13	19	11	217
PA398	***Pseudomonas_aeruginosa_4064320487_10869***	GCF_004370635.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	155
PA399	***Pseudomonas_aeruginosa_4084334344_10886***	GCF_004370995.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	299
PA400	***Pseudomonas_aeruginosa_4084336477_10884***	GCF_004370975.1	No	Clinical	Cystic fibrosis	18	12	11	20	14	Undefined
PA401	***Pseudomonas_aeruginosa_4094345258_10870***	GCF_004370665.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	179
PA402	***Pseudomonas_aeruginosa_4114358565_10891***	GCF_004371095.1	No	Clinical	Cystic fibrosis	18	86	9	19	12	663
PA403	***Pseudomonas_aeruginosa_4124363474_15_10864***	GCF_004370535.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA404	***Pseudomonas_aeruginosa_4124363505_10873***	GCF_004370735.1	Yes	Clinical	Cystic fibrosis	18		9	19	12	663
PA405	***Pseudomonas_aeruginosa_462_7255***	GCF_002312065.1	No	Clinical	Respiratory tract	9	11	9	11	5	17
PA406	***Pseudomonas_aeruginosa_5_10844***	GCF_004370145.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA407	***Pseudomonas_aeruginosa_5014375233_10849***	GCF_004370235.1	No	Clinical	Cystic fibrosis	16	5	11	17	14	Undefined
PA408	***Pseudomonas_aeruginosa_5024379144_14_10899***	GCF_004371305.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	179
PA409	***Pseudomonas_aeruginosa_5024382738_26_10855***	GCF_004370385.1	Yes	Clinical	Cystic fibrosis	17		11	19	14	683
PA410	***Pseudomonas_aeruginosa_5054408350_18_10868***	GCF_004370625.1	No	Clinical	Cystic fibrosis	18	78	12	19	12	Undefined
PA411	***Pseudomonas_aeruginosa_5054408350_20_10895***	GCF_004371225.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	569
PA412	***Pseudomonas_aeruginosa_5054408350_22_10896***	GCF_004371235.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	Undefined
PA413	***Pseudomonas_aeruginosa_506_6117***	GCF_002312615.1	No	Clinical	Respiratory tract	18	44	13	19	11	884
PA414	***Pseudomonas_aeruginosa_519119_11949***	GCF_007559105.1	No	Clinical	Gastrointestinal	17	21	13	15	13	360
PA415	***Pseudomonas_aeruginosa_578_B_6724***	GCF_002312235.1	No	Clinical	Respiratory tract	18	78	13	19	11	514
PA416	***Pseudomonas_aeruginosa_57RV_10964***	GCF_004372615.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined
PA417	***Pseudomonas_aeruginosa_57SJ_10976***	GCF_004372845.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined
PA418	***Pseudomonas_aeruginosa_585_5890***	GCF_002312465.1	Yes	Clinical	Respiratory tract	18		13	19	11	514
PA419	***Pseudomonas_aeruginosa_5920_10134***	GCF_003836925.1	No	Environment	Plants	18	86	9	19	12	Undefined
PA420	***Pseudomonas_aeruginosa_5985_10930***	GCF_004371915.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA421	***Pseudomonas_aeruginosa_5987_10929***	GCF_004371905.1	No	Clinical	Cystic fibrosis	18	102	13	19	11	Undefined
PA422	***Pseudomonas_aeruginosa_59882_10926***	GCF_004371845.1	Yes	Clinical	Cystic fibrosis	17		6	15	7	1684
PA423	***Pseudomonas_aeruginosa_59883_10940***	GCF_004372125.1	No	Clinical	Cystic fibrosis	17	21	6	15	7	1684
PA424	***Pseudomonas_aeruginosa_59903_10924***	GCF_004371805.1	No	Clinical	Cystic fibrosis	18	102	9	19	11	1157
PA425	***Pseudomonas_aeruginosa_5991_10925***	GCF_004371825.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA426	***Pseudomonas_aeruginosa_5994_10922***	GCF_004371755.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17

PA427	***Pseudomonas_aeruginosa_5995_10920***	GCF_004371715.1	No	Clinical	Cystic fibrosis	18	102	8	19	9	Undefined
PA428	***Pseudomonas_aeruginosa_5996_10939***	GCF_004372085.1	No	Clinical	Cystic fibrosis	18	87	9	19	5	Undefined
PA429	***Pseudomonas_aeruginosa_5997_10919***	GCF_004371705.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA430	***Pseudomonas_aeruginosa_59992_10917***	GCF_004371645.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	Undefined
PA431	***Pseudomonas_aeruginosa_5BR2_10129***	GCF_003836815.1	No	Clinical	Cystic fibrosis	18	102	13	19	11	Undefined
PA432	***Pseudomonas_aeruginosa_60002_10914***	GCF_004371575.1	No	Clinical	Cystic fibrosis	16	5	11	17	14	Undefined
PA433	***Pseudomonas_aeruginosa_6003_7301***	GCF_002193895.1	Yes	Clinical	Bacteraemia	18		9	22	12	348
PA434	***Pseudomonas_aeruginosa_6005_6833***	GCF_002193825.1	No	Clinical	Bacteraemia	19	102	3	21	3	532
PA435	***Pseudomonas_aeruginosa_6007_7004***	GCF_002193845.1	No	Clinical	Bacteraemia	18	65	6	22	7	175
PA436	***Pseudomonas_aeruginosa_6010_7063***	GCF_002194085.1	No	Clinical	Bacteraemia	18	68	13	19	11	Undefined
PA437	***Pseudomonas_aeruginosa_6014_6074***	GCF_002194095.1	No	Clinical	Bacteraemia	15	32	12	23	12	244
PA438	***Pseudomonas_aeruginosa_60503_11947***	GCF_007559065.1	Yes	Clinical	Respiratory tract	19		3	21	3	773
PA439	***Pseudomonas_aeruginosa_6077_592***	GCF_000481745.1	No	Clinical	Eye	3	6	10	4	10	235
PA440	***Pseudomonas_aeruginosa_60862_10909***	GCF_004371505.1	No	Clinical	Cystic fibrosis	18	102	13	19	11	Undefined
PA441	***Pseudomonas_aeruginosa_6087_10908***	GCF_004371485.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	Undefined
PA442	***Pseudomonas_aeruginosa_6089_10905***	GCF_004371415.1	Yes	Clinical	Cystic fibrosis	18		6	19	7	170
PA443	***Pseudomonas_aeruginosa_6090_10907***	GCF_004371445.1	No	Clinical	Cystic fibrosis	18	29	12	19	12	Undefined
PA444	***Pseudomonas_aeruginosa_60922_10904***	GCF_004371405.1	No	Clinical	Cystic fibrosis	18	93	11	19	11	488
PA445	***Pseudomonas_aeruginosa_6093_10901***	GCF_004371325.1	No	Clinical	Cystic fibrosis	18	102	8	19	9	2617
PA446	***Pseudomonas_aeruginosa_6095_10902***	GCF_004371335.1	Yes	Clinical	Cystic fibrosis	18		9	19	12	Undefined
PA447	***Pseudomonas_aeruginosa_60973_10876***	GCF_004370815.1	No	Clinical	Cystic fibrosis	18	102	12	19	12	1395
PA448	***Pseudomonas_aeruginosa_6102_10874***	GCF_004370775.1	No	Clinical	Cystic fibrosis	18	102	13	19	11	299
PA449	***Pseudomonas_aeruginosa_62_10631***	GCF_003975905.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	97	13	19	12	Undefined
PA450	***Pseudomonas_aeruginosa_62_606***	GCF_000482025.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	97	13	19	12	2569
PA451	***Pseudomonas_aeruginosa_6D92_H_isolate_AMT0023_34_9922***	GCF_003698485.1	No	Clinical	Cystic fibrosis	18	11	8	19	12	1394
PA452	***Pseudomonas_aeruginosa_6D92_H_isolate_AMT0060_2_9929***	GCF_003698625.1	No	Clinical	Cystic fibrosis	14	52	2	16	2	111
PA453	***Pseudomonas_aeruginosa_7_10883***	GCF_004370965.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA454	***Pseudomonas_aeruginosa_707A_6541***	GCF_002312575.1	Yes	Clinical	Respiratory tract	9		9	11	5	17
PA455	***Pseudomonas_aeruginosa_712_7178***	GCF_002312095.1	Yes	Clinical	Respiratory tract	9		9	11	5	17
PA456	***Pseudomonas_aeruginosa_78RV_10963***	GCF_004372595.1	Yes	Environment	Hydrocarbon contamination	18		11	19	14	Undefined

PA457	***Pseudomonas_aeruginosa_8488_6602***	GCF_002964295.1	No	Clinical	Bacteraemia	18	90	13	19	11	1639
PA458	***Pseudomonas_aeruginosa_8489_6027***	GCF_002964255.1	No	Clinical	Bacteraemia	15	32	12	23	12	244
PA459	***Pseudomonas_aeruginosa_8490_5987***	GCF_002964275.1	No	Clinical	Bacteraemia	19	24	12	21	4	671
PA460	***Pseudomonas_aeruginosa_8491_6171***	GCF_002942025.1	No	Clinical	Bacteraemia	18	102	13	19	11	12
PA461	***Pseudomonas_aeruginosa_85_6935***	GCF_002411915.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	47	3	21	3	773
PA462	***Pseudomonas_aeruginosa_8508_6836***	GCF_002942045.1	No	Clinical	Bacteraemia	18	32	13	19	11	931
PA463	***Pseudomonas_aeruginosa_856_10261***	GCF_003840205.1	No	Environment	Animal	6	1	8	9	9	3244
PA464	***Pseudomonas_aeruginosa_886_1_10257***	GCF_003840105.1	No	Environment	Animal	18	102	9	19	12	641
PA465	***Pseudomonas_aeruginosa_9_10881***	GCF_004370895.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	155
PA466	***Pseudomonas_aeruginosa_903_10262***	GCF_003840215.1	No	Environment	Animal	19	102	10	21	10	2644
PA467	***Pseudomonas_aeruginosa_9092533235_10863***	GCF_004370525.1	No	Clinical	Cystic fibrosis	15	32	12	23	12	244
PA468	***Pseudomonas_aeruginosa_934436V_10253***	GCF_003840045.1	Yes	Clinical	Respiratory tract	13		9	10	12	27
PA469	***Pseudomonas_aeruginosa_97_9520***	GCF_002411865.3	No	Clinical	Urinary tract	18	83	9	19	12	234
PA470	***Pseudomonas_aeruginosa_982_10260***	GCF_003840165.1	No	Environment	Animal	18	95	10	19	12	Undefined
PA471	***Pseudomonas_aeruginosa_994_10258***	GCF_003840145.1	No	Environment	Animal	17	86	11	19	14	Undefined
PA472	***Pseudomonas_aeruginosa_A1_A2448_10060***	GCF_003835445.1	No	Clinical	Urinary tract	18	80	8	19	9	Undefined
PA473	***Pseudomonas_aeruginosa_A10_10136***	GCF_003836965.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	11	30	13	13	13	409
PA474	***Pseudomonas_aeruginosa_A11_10135***	GCF_003836945.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		13	19	11	149
PA475	***Pseudomonas_aeruginosa_A13_10140***	GCF_003837045.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	69	13	19	11	149
PA476	***Pseudomonas_aeruginosa_A15_10139***	GCF_003837025.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	7	15	7	7	8	Undefined
PA477	***Pseudomonas_aeruginosa_A17_10132***	GCF_003836875.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	12	97	1	14	1	395
PA478	***Pseudomonas_aeruginosa_A19_10174***	GCF_003837725.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	10	78	5	12	6	274
PA479	***Pseudomonas_aeruginosa_A22_10131***	GCF_003836865.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	93	12	19	11	Undefined
PA480	***Pseudomonas_aeruginosa_A237_10137***	GCF_003836985.1	No	Environment	Animal	18	93	13	19	13	1207
PA481	***Pseudomonas_aeruginosa_A3_10073***	GCF_003835695.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	27
PA482	***Pseudomonas_aeruginosa_A3_H638_10059***	GCF_003835405.1	No	Clinical	Bacteraemia	19	48	10	21	12	Undefined
PA483	***Pseudomonas_aeruginosa_A681_11948***	GCF_007559085.1	No	Clinical	Respiratory tract	10	78	5	12	6	274

PA484	***Pseudomonas_aeruginosa_Aa249_10103***	GCF_003836305.1	Yes	Clinical	Burn	12		1	14	1	Undefined
PA485	***Pseudomonas_aeruginosa_AA43_9975***	GCF_003833745.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	708
PA486	***Pseudomonas_aeruginosa_AES1M_10829***	GCF_004355125.1	No	Clinical	Cystic fibrosis	18	86	6	19	7	649
PA487	***Pseudomonas_aeruginosa_AES1R_10830***	GCF_004355145.1	No	Clinical	Cystic fibrosis	18	86	6	19	7	649
PA488	***Pseudomonas_aeruginosa_AG1_12046***	GCF_009662315.1	No	Clinical	Respiratory tract	14	52	2	16	2	111
PA489	***Pseudomonas_aeruginosa_AH16_480***	GCF_000287875.1	No	Clinical	Respiratory tract	16	5	11	17	14	155
PA490	***Pseudomonas_aeruginosa_AL191_9960***	GCF_003833445.1	No	Clinical	Cystic fibrosis	19	48	3	21	3	1284
PA491	***Pseudomonas_aeruginosa_AMT0005_135_10613***	GCF_003975535.1	No	Clinical	Cystic fibrosis	18	102	6	22	7	389
PA492	***Pseudomonas_aeruginosa_AMT0005_138_10187***	GCF_003838585.1	Yes	Clinical	Cystic fibrosis	18		6	22	7	Undefined
PA493	***Pseudomonas_aeruginosa_AMT0006_65_10609***	GCF_003975435.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	845
PA494	***Pseudomonas_aeruginosa_AMT0020_84_10185***	GCF_003838535.1	No	Clinical	Cystic fibrosis	19	102	10	21	10	2665
PA495	***Pseudomonas_aeruginosa_AMT0026_2_10608***	GCF_003975425.1	Yes	Clinical	Cystic fibrosis	1		12	2	4	253
PA496	***Pseudomonas_aeruginosa_AMT0026_67_10180***	GCF_003838445.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	179
PA497	***Pseudomonas_aeruginosa_AMT0046_109_10179***	GCF_003838405.1	No	Clinical	Cystic fibrosis	18	90	13	19	12	1527
PA498	***Pseudomonas_aeruginosa_AMT0071_76_10266***	GCF_003840305.1	Yes	Clinical	Cystic fibrosis	1		12	2	4	253
PA499	***Pseudomonas_aeruginosa_assembly_GCF_0007517151_2507***	GCF_000751715.1	No	Environment	Clinical environment: Dental, Hospital	12	2	1	14	1	395
PA500	***Pseudomonas_aeruginosa_AT19_10301***	GCF_003841005.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	Undefined
PA501	***Pseudomonas_aeruginosa_AT31_10255***	GCF_003840085.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	27
PA502	***Pseudomonas_aeruginosa_AT7_10307***	GCF_003841125.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	Undefined
PA503	***Pseudomonas_aeruginosa_ATCC_14886_678***	GCF_000297275.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	95	12	19	12	260
PA504	***Pseudomonas_aeruginosa_ATCC_15692_4007***	GCF_001729505.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	32	12	19	12	549
PA505	***Pseudomonas_aeruginosa_ATCC_27853_3989***	GCF_001618925.1	No	Clinical	Nosocomial infections	16	5	11	17	14	155
PA506	***Pseudomonas_aeruginosa_ATCC_27853_9518***	GCF_001687285.1	No	Clinical	Respiratory tract	16	5	11	17	14	155
PA507	***Pseudomonas_aeruginosa_ATCC_33988_2508***	GCF_000756575.1	No	Environment	Hydrocarbon contamination	18	102	12	19	12	1232
PA508	***Pseudomonas_aeruginosa_ATCC_9027_3202***	GCF_001294675.1	No	Clinical	Ear	5		4		n/a	2230
PA510	***Pseudomonas_aeruginosa_ATCC_BAA_2108_6531***	GCF_002237025.1	No	Clinical	Respiratory tract	18	63	11	19	14	Undefined
PA511	***Pseudomonas_aeruginosa_ATCC_BAA_2109_6682***	GCF_002236985.1	No	Clinical	Respiratory tract	18	97	9	19	5	Undefined
PA512	***Pseudomonas_aeruginosa_ATCC_BAA_2110_5942***	GCF_002237075.1	No	Clinical	Respiratory tract	18	74	13	19	11	Undefined
PA513	***Pseudomonas_aeruginosa_ATCC_BAA_2111_5918***	GCF_002238215.1	No	Clinical	Respiratory tract	10	78	5	12	6	274

PA514	***Pseudomonas_aeruginosa_ATCC_BAA_2112_6992***	GCF_002237085.1	No	Clinical	Respiratory tract	18	76	9	19	12	3024
PA515	***Pseudomonas_aeruginosa_ATCC_BAA_2113_6125***	GCF_002237015.1	No	Clinical	Respiratory tract	18	90	13	19	12	2743
PA516	***Pseudomonas_aeruginosa_AU10272_3944***	GCF_001554705.1	Yes	Clinical	Cystic fibrosis	18		9	22	12	348
PA517	***Pseudomonas_aeruginosa_AU10410_3945***	GCF_001554735.1	No	Clinical	Cystic fibrosis	18	4	9	22	12	348
PA518	***Pseudomonas_aeruginosa_AU11990_3972***	GCF_001555255.1	No	Clinical	Cystic fibrosis	18	93	13	19	11	553
PA519	***Pseudomonas_aeruginosa_AU12424_3952***	GCF_001554875.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	553
PA520	***Pseudomonas_aeruginosa_AU12528_3948***	GCF_001554785.1	No	Clinical	Cystic fibrosis	19	24	12	21	4	671
PA521	***Pseudomonas_aeruginosa_AU13212_3936***	GCF_001554545.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	Undefined
PA522	***Pseudomonas_aeruginosa_AU13213_3939***	GCF_001554615.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	Undefined
PA523	***Pseudomonas_aeruginosa_AU15431_3938***	GCF_001554585.1	No	Clinical	Cystic fibrosis	13	102	9	10	12	Undefined
PA524	***Pseudomonas_aeruginosa_AU17550_3959***	GCF_001555015.1	Yes	Clinical	Cystic fibrosis	18		13	19	12	Undefined
PA525	***Pseudomonas_aeruginosa_AU18068_3967***	GCF_001555155.1	No	Clinical	Cystic fibrosis	18	85	11	19	14	443
PA526	***Pseudomonas_aeruginosa_AU18274_3954***	GCF_001554915.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	553
PA527	***Pseudomonas_aeruginosa_AU19319_3964***	GCF_001555115.1	No	Clinical	Cystic fibrosis	18	99	13	19	12	Undefined
PA528	***Pseudomonas_aeruginosa_AU23529_3980***	GCF_001555425.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	17
PA529	***Pseudomonas_aeruginosa_AU25210_3961***	GCF_001555055.1	No	Clinical	Cystic fibrosis	18	86	9	19	12	792
PA530	***Pseudomonas_aeruginosa_AU6923_3966***	GCF_001555145.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	Undefined
PA531	***Pseudomonas_aeruginosa_AU7511_3920***	GCF_001545255.1	No	Clinical	Cystic fibrosis	11	49	11	13	14	Undefined
PA532	***Pseudomonas_aeruginosa_AU8251_3947***	GCF_001554775.1	Yes	Clinical	Cystic fibrosis	19		12	21	4	671
PA533	***Pseudomonas_aeruginosa_AU9017_3950***	GCF_001554825.1	No	Clinical	Cystic fibrosis	18	93	13	19	11	553
PA534	***Pseudomonas_aeruginosa_AU9899_3975***	GCF_001555325.1	No	Clinical	Cystic fibrosis	10	78	5	12	6	Undefined
PA535	***Pseudomonas_aeruginosa_AUS021_10270***	GCF_003840385.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	266
PA536	***Pseudomonas_aeruginosa_AUS026_10230***	GCF_003839465.1	No	Clinical	Cystic fibrosis	18	76	13	19	11	777
PA537	***Pseudomonas_aeruginosa_AUS050_10201***	GCF_003838875.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	155
PA538	***Pseudomonas_aeruginosa_AUS054_10281***	GCF_003840605.1	No	Clinical	Cystic fibrosis	18	93	13	20	12	788
PA539	***Pseudomonas_aeruginosa_AUS058_10229***	GCF_003839445.1	No	Clinical	Cystic fibrosis	18	78	6	19	7	Undefined
PA540	***Pseudomonas_aeruginosa_AUS077_10221***	GCF_003839285.1	No	Clinical	Cystic fibrosis	18	86	10	19	12	801
PA541	***Pseudomonas_aeruginosa_AUS083_10239***	GCF_003839685.1	No	Clinical	Cystic fibrosis	18	78	13	19	12	259
PA542	***Pseudomonas_aeruginosa_AUS088_10238***	GCF_003839665.1	No	Clinical	Cystic fibrosis	18	93	12	19	11	262
PA543	***Pseudomonas_aeruginosa_AUS105_10216***	GCF_003839175.1	No	Clinical	Cystic fibrosis	18	102	13	19	12	821

PA544	***Pseudomonas_aeruginosa_AUS110_10680***	GCF_003976865.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		9	19	12	826
PA545	***Pseudomonas_aeruginosa_AUS111_10283***	GCF_003840635.1	No	Clinical	Urinary tract	18	29	12	19	12	827
PA546	***Pseudomonas_aeruginosa_AUS119_10220***	GCF_003839255.1	No	Environment	Animal	18	98	9	19	5	835
PA547	***Pseudomonas_aeruginosa_AUS122_10663***	GCF_003976545.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	81	13	19	11	838
PA548	***Pseudomonas_aeruginosa_AUS124_10218***	GCF_003839215.1	No	Environment	Animal	18	59	13	19	11	840
PA549	***Pseudomonas_aeruginosa_AUS125_10681***	GCF_003976875.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	59	11	19	14	841
PA550	***Pseudomonas_aeruginosa_AUS128_10664***	GCF_003976555.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	12	21	4	843
PA551	***Pseudomonas_aeruginosa_AUS136_10679***	GCF_003976855.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	46	13	19	11	850
PA552	***Pseudomonas_aeruginosa_AUS138_10215***	GCF_003839165.1	No	Environment	Animal	18	32	9	19	12	Undefined
PA553	***Pseudomonas_aeruginosa_AUS139_10660***	GCF_003976465.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	10	19	10	853
PA554	***Pseudomonas_aeruginosa_AUS141_10677***	GCF_003976805.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	64	6	22	7	485
PA555	***Pseudomonas_aeruginosa_AUS148_10214***	GCF_003839145.1	Yes	Clinical	Cystic fibrosis	17		13	15	13	862
PA556	***Pseudomonas_aeruginosa_AUS149_10191***	GCF_003838665.1	Yes	Environment	Animal	18		13	19	12	863
PA557	***Pseudomonas_aeruginosa_AUS150_10210***	GCF_003839065.1	No	Clinical	Bacteraemia	17	22	13	15	13	Undefined
PA558	***Pseudomonas_aeruginosa_AUS151_10213***	GCF_003839125.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	93	13	20	12	865
PA559	***Pseudomonas_aeruginosa_AUS153_10662***	GCF_003976505.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	97	13	19	11	867
PA560	***Pseudomonas_aeruginosa_AUS154_10212***	GCF_003839105.1	No	Environment	Animal	18	92	13	19	12	Undefined
PA561	***Pseudomonas_aeruginosa_AUS155_10657***	GCF_003976425.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	97	13	19	11	869
PA562	***Pseudomonas_aeruginosa_AUS156_10661***	GCF_003976495.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	96	8	19	13	870
PA563	***Pseudomonas_aeruginosa_AUS158_10623***	GCF_003975735.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	90	13	19	11	872
PA564	***Pseudomonas_aeruginosa_AUS165_10211***	GCF_003839085.1	No	Environment	Animal	18	78	13	19	12	879
PA565	***Pseudomonas_aeruginosa_AUS174_10676***	GCF_003976775.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	74	13	19	11	888
PA566	***Pseudomonas_aeruginosa_AUS175_10675***	GCF_003976765.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	86	9	19	12	826
PA567	***Pseudomonas_aeruginosa_AUS176_10658***	GCF_003976445.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	12	19	4	890

PA568	***Pseudomonas_aeruginosa_AUS177_10624***	GCF_003975755.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	13	19	12	891
PA569	***Pseudomonas_aeruginosa_AUS178_10622***	GCF_003975725.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	96	13	19	11	892
PA570	***Pseudomonas_aeruginosa_AUS183_10252***	GCF_003840005.1	No	Environment	Animal	18	102	8	19	12	6
PA571	***Pseudomonas_aeruginosa_AUS185_10251***	GCF_003839995.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	86	9	19	5	8
PA572	***Pseudomonas_aeruginosa_AUS186_10304***	GCF_003841055.1	No	Environment	Animal	19	54	8	18	9	Undefined
PA573	***Pseudomonas_aeruginosa_AUS195_10302***	GCF_003841015.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	96	11	19	11	115
PA574	***Pseudomonas_aeruginosa_AUS205_10250***	GCF_003839985.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	70	9	19	12	143
PA575	***Pseudomonas_aeruginosa_AUS207_10244***	GCF_003839865.1	No	Environment	Animal	18	86	11	19	14	145
PA576	***Pseudomonas_aeruginosa_AUS209_10673***	GCF_003976745.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	13	19	12	161
PA577	***Pseudomonas_aeruginosa_AUS210_10247***	GCF_003839915.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	93	12	19	12	166
PA578	***Pseudomonas_aeruginosa_AUS213_10296***	GCF_003840895.1	No	Environment	Animal	18	102	10	19	12	169
PA579	***Pseudomonas_aeruginosa_AUS214_10684***	GCF_003976965.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	93	8	19	12	172
PA580	***Pseudomonas_aeruginosa_AUS217_10245***	GCF_003839875.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	5		4			2230
PA581	***Pseudomonas_aeruginosa_AUS221_10674***	GCF_003976755.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	8	18	9	205
PA582	***Pseudomonas_aeruginosa_AUS222_10672***	GCF_003976685.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	10	78	5	12	6	209
PA583	***Pseudomonas_aeruginosa_AUS225_10241***	GCF_003839785.1	No	Environment	Animal	18	102	13	19	10	214
PA584	***Pseudomonas_aeruginosa_AUS226_10670***	GCF_003976665.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	6	1	8	9	9	215
PA585	***Pseudomonas_aeruginosa_AUS227_10669***	GCF_003976655.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	54	8	18	9	Undefined
PA586	***Pseudomonas_aeruginosa_AUS229_10299***	GCF_003840965.1	No	Environment	Animal	18	102	13	19	13	221
PA587	***Pseudomonas_aeruginosa_AUS232_10240***	GCF_003839755.1	No	Environment	Animal	7	15	7	7	8	224
PA588	***Pseudomonas_aeruginosa_AUS258_10671***	GCF_003976675.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	97	13	19	12	Undefined
PA589	***Pseudomonas_aeruginosa_AUS263_10274***	GCF_003840455.1	No	Clinical	Urinary tract	18	35	12	19	12	932
PA590	***Pseudomonas_aeruginosa_AUS265_10678***	GCF_003976845.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	13	19	13	645
PA591	***Pseudomonas_aeruginosa_AUS275_10242***	GCF_003839825.1	No	Clinical	Bacteraemia	18	97	9	19	5	231

PA592	***Pseudomonas_aeruginosa_AUS277_10665***	GCF_003976565.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	75	12	19	12	564
PA593	***Pseudomonas_aeruginosa_AUS283_10226***	GCF_003839375.1	Yes	Environment	Animal	19		10	21	10	620
PA594	***Pseudomonas_aeruginosa_AUS301_10290***	GCF_003840785.1	No	Clinical	Bacteraemia	18	44	13	19	12	275
PA595	***Pseudomonas_aeruginosa_AUS305_10265***	GCF_003840285.1	Yes	Clinical	Cystic fibrosis	18		13	19	12	381
PA596	***Pseudomonas_aeruginosa_AUS306_10288***	GCF_003840715.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	32	13	19	12	381
PA597	***Pseudomonas_aeruginosa_AUS307_10190***	GCF_003838645.1	No	Clinical	Bacteraemia	18	32	13	19	12	381
PA598	***Pseudomonas_aeruginosa_AUS309_10193***	GCF_003838685.1	Yes	Environment	Animal	18		13	19	12	381
PA599	***Pseudomonas_aeruginosa_AUS311_10659***	GCF_003976455.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	35	10	19	12	854
PA600	***Pseudomonas_aeruginosa_AUS321_10291***	GCF_003840805.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA601	***Pseudomonas_aeruginosa_AUS336_10236***	GCF_003839585.1	No	Environment	Animal	18	78	13	19	12	508
PA602	***Pseudomonas_aeruginosa_AUS339_10233***	GCF_003839525.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	17	22	13	15	13	360
PA603	***Pseudomonas_aeruginosa_AUS343_10295***	GCF_003840885.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	95	12	19	12	Undefined
PA604	***Pseudomonas_aeruginosa_AUS344_10194***	GCF_003838695.1	Yes	Clinical	Urinary tract	18		12	19	12	266
PA605	***Pseudomonas_aeruginosa_AUS345_10195***	GCF_003838705.1	Yes	Environment	Animal	18		12	19	12	266
PA606	***Pseudomonas_aeruginosa_AUS353_10276***	GCF_003840475.1	No	Environment	Animal	18	32	13	19	11	931
PA607	***Pseudomonas_aeruginosa_AUS355_10228***	GCF_003839425.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	95	13	19	11	553
PA608	***Pseudomonas_aeruginosa_AUS389_10285***	GCF_003840685.1	No	Environment	Animal	18	32	12	19	12	611
PA609	***Pseudomonas_aeruginosa_AUS392_10209***	GCF_003839035.1	No	Environment	Animal	18	78	13	19	11	903
PA610	***Pseudomonas_aeruginosa_AUS407_10235***	GCF_003839565.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	102	9	19	12	270
PA611	***Pseudomonas_aeruginosa_AUS422_10196***	GCF_003838765.1	No	Clinical	Respiratory tract	18	69	13	19	11	242
PA612	***Pseudomonas_aeruginosa_AUS423_10300***	GCF_003840975.1	No	Environment	Animal	18	74	13	19	11	242
PA613	***Pseudomonas_aeruginosa_AUS430_10278***	GCF_003840545.1	No	Clinical	Urinary tract	18	32	12	19	12	907
PA614	***Pseudomonas_aeruginosa_AUS434_10205***	GCF_003838965.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	155
PA615	***Pseudomonas_aeruginosa_AUS438_10249***	GCF_003839965.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	16		11	17	14	155
PA616	***Pseudomonas_aeruginosa_AUS439_10200***	GCF_003838865.1	Yes	Clinical	Ear	16		11	17	14	155
PA617	***Pseudomonas_aeruginosa_AUS440_10267***	GCF_003840315.1	Yes	Clinical	Ear	16		11	17	14	155

PA618	***Pseudomonas_aeruginosa_AUS441_10197***	GCF_003838785.1	Yes	Environment	Animal	16		11	17	14	Undefined
PA619	***Pseudomonas_aeruginosa_AUS442_10199***	GCF_003838825.1	Yes	Environment	Animal	16		11	17	14	155
PA620	***Pseudomonas_aeruginosa_AUS449_10614***	GCF_003975555.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	54	8	18	9	930
PA621	***Pseudomonas_aeruginosa_AUS452_10668***	GCF_003976645.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	86	11	19	11	257
PA622	***Pseudomonas_aeruginosa_AUS455_10654***	GCF_003976365.1	Yes	Clinical	Urinary tract	16		11	17	14	179
PA623	***Pseudomonas_aeruginosa_AUS456_10653***	GCF_003976335.1	Yes	Environment	Animal	16		11	17	14	179
PA624	***Pseudomonas_aeruginosa_AUS460_10293***	GCF_003840835.1	Yes	Environment	Animal	17		13	15	13	Undefined
PA625	***Pseudomonas_aeruginosa_AUS462_10298***	GCF_003840945.1	No	Clinical	Bacteraemia	17	22	6	15	7	245
PA626	***Pseudomonas_aeruginosa_AUS465_10243***	GCF_003839845.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	12	19	12	147
PA627	***Pseudomonas_aeruginosa_AUS471_10234***	GCF_003839545.1	No	Clinical	Ear	19	102	10	21	10	296
PA628	***Pseudomonas_aeruginosa_AUS483_10208***	GCF_003839025.1	No	Environment	Animal	5		4			1978
PA629	***Pseudomonas_aeruginosa_AUS485_10284***	GCF_003840655.1	No	Environment	Animal	19	34	8	18	9	913
PA630	***Pseudomonas_aeruginosa_AUS489_10204***	GCF_003838935.1	No	Clinical	Respiratory tract	18	86	13	19	12	1635
PA631	***Pseudomonas_aeruginosa_AUS491_10277***	GCF_003840495.1	No	Clinical	Respiratory tract	18	86	13	19	12	918
PA632	***Pseudomonas_aeruginosa_AUS496_10203***	GCF_003838925.1	No	Clinical	Respiratory tract	18	97	13	19	11	919
PA633	***Pseudomonas_aeruginosa_AUS499_10207***	GCF_003839005.1	No	Clinical	Respiratory tract	18	86	13	19	12	385
PA634	***Pseudomonas_aeruginosa_AUS500_10656***	GCF_003976405.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	8	21	9	Undefined
PA635	***Pseudomonas_aeruginosa_AUS501_10619***	GCF_003975655.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	19	10	21	10	365
PA636	***Pseudomonas_aeruginosa_AUS502_10246***	GCF_003839885.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	16		11	17	14	179
PA637	***Pseudomonas_aeruginosa_AUS503_10225***	GCF_003839365.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		12	19	11	810
PA638	***Pseudomonas_aeruginosa_AUS504_10231***	GCF_003839475.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	63	6	22	7	389
PA639	***Pseudomonas_aeruginosa_AUS505_10620***	GCF_003975665.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	8	18	9	Undefined
PA640	***Pseudomonas_aeruginosa_AUS506_10282***	GCF_003840625.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	78	13	19	12	863
PA641	***Pseudomonas_aeruginosa_AUS507_10206***	GCF_003838975.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	11	49	11	13	14	252
PA642	***Pseudomonas_aeruginosa_AUS510_10618***	GCF_003975645.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	68	13	19	13	2952

PA643	***Pseudomonas_aeruginosa_AUS511_10617***	GCF_003975615.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	53	8	18	9	926
PA644	***Pseudomonas_aeruginosa_AUS512_10616***	GCF_003975605.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	54	10	18	10	927
PA645	***Pseudomonas_aeruginosa_AUS516_10667***	GCF_003976595.1	No	Environment	Home environment	8	16	10	6	10	309
PA646	***Pseudomonas_aeruginosa_AUS517_10292***	GCF_003840825.1	No	Environment	Home environment	19	61	13	21	13	313
PA647	***Pseudomonas_aeruginosa_AUS518_10297***	GCF_003840925.1	No	Environment	Home environment	13	50	9	10	12	27
PA648	***Pseudomonas_aeruginosa_AUS523_10666***	GCF_003976585.1	No	Environment	Home environment	18	22	6	19	7	709
PA649	***Pseudomonas_aeruginosa_AUS525_10683***	GCF_003976945.1	No	Environment	Home environment	19	60	10	21	10	207
PA650	***Pseudomonas_aeruginosa_AUS526_10615***	GCF_003975575.1	No	Environment	Home environment	18	99	13	19	11	1475
PA651	***Pseudomonas_aeruginosa_AUS527_10682***	GCF_003976905.1	No	Environment	Home environment	18	89	8	19	9	633
PA652	***Pseudomonas_aeruginosa_AUS537_10275***	GCF_003840465.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	27
PA653	***Pseudomonas_aeruginosa_AUS595_10198***	GCF_003838815.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	155
PA654	***Pseudomonas_aeruginosa_AUS674_10272***	GCF_003840425.1	No	Clinical	Cystic fibrosis	18	102	6	19	7	1102
PA655	***Pseudomonas_aeruginosa_AUS717_10652***	GCF_003976325.1	No	Clinical	Cystic fibrosis	18	72	9	19	5	775
PA656	***Pseudomonas_aeruginosa_AZPAE12136_2383***	GCF_000796555.1	No	Clinical	Cystic fibrosis	18	63	6	22	7	389
PA657	***Pseudomonas_aeruginosa_AZPAE12140_2385***	GCF_000796615.1	No	Clinical	Cystic fibrosis	18	90	13	19	12	782
PA658	***Pseudomonas_aeruginosa_AZPAE12147_2394***	GCF_000796795.1	No	Clinical	Cystic fibrosis	13	50	9	10	12	Undefined
PA659	***Pseudomonas_aeruginosa_AZPAE12148_2395***	GCF_000796825.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA660	***Pseudomonas_aeruginosa_AZPAE12153_2399***	GCF_000796925.1	No	Clinical	Cystic fibrosis	18	78	13	19	11	116
PA661	***Pseudomonas_aeruginosa_AZPAE12410_2404***	GCF_000797045.1	No	Clinical	Cystic fibrosis	18	93	12	19	11	1239
PA662	***Pseudomonas_aeruginosa_AZPAE12411_2405***	GCF_000797055.1	No	Clinical	Cystic fibrosis	18	102	13	19	11	1011
PA663	***Pseudomonas_aeruginosa_AZPAE12413_2407***	GCF_000797125.1	No	Clinical	Cystic fibrosis	18	84	13	19	12	782
PA664	***Pseudomonas_aeruginosa_AZPAE12419_2414***	GCF_000797265.1	No	Clinical	Cystic fibrosis	18	102	5	19	6	Undefined
PA665	***Pseudomonas_aeruginosa_AZPAE13756_2573***	GCF_000797395.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA666	***Pseudomonas_aeruginosa_AZPAE13757_2337***	GCF_000795405.1	No	Clinical	Respiratory tract	17	86	11	22	14	146
PA667	***Pseudomonas_aeruginosa_AZPAE14352_2349***	GCF_000795735.1	No	Clinical	Intra-abdominal tract	18	59	12	19	11	3119
PA668	***Pseudomonas_aeruginosa_AZPAE14353_2350***	GCF_000795765.1	No	Clinical	Intra-abdominal tract	3	6	10	4	10	235
PA669	***Pseudomonas_aeruginosa_AZPAE14359_2351***	GCF_000795785.1	Yes	Clinical	Intra-abdominal tract	19		13	21	13	313
PA670	***Pseudomonas_aeruginosa_AZPAE14372_2561***	GCF_000795845.1	Yes	Clinical	Intra-abdominal tract	19		10	21	10	319
PA671	***Pseudomonas_aeruginosa_AZPAE14373_2355***	GCF_000795875.1	No	Clinical	Intra-abdominal tract	19	54	8	18	9	3470

PA672	***Pseudomonas_aeruginosa_AZPAE14379_2563***	GCF_000795925.1	No	Clinical	Intra-abdominal tract	18	102	13	19	11	242
PA673	***Pseudomonas_aeruginosa_AZPAE14381_2356***	GCF_000795945.1	No	Clinical	Intra-abdominal tract	14	52	2	16	2	111
PA674	***Pseudomonas_aeruginosa_AZPAE14390_2358***	GCF_000795985.1	Yes	Clinical	Intra-abdominal tract	18		13	19	12	381
PA675	***Pseudomonas_aeruginosa_AZPAE14393_2359***	GCF_000796005.1	Yes	Clinical	Intra-abdominal tract	19		13	21	13	313
PA676	***Pseudomonas_aeruginosa_AZPAE14394_2360***	GCF_000796045.1	Yes	Clinical	Intra-abdominal tract	18		6	22	7	175
PA677	***Pseudomonas_aeruginosa_AZPAE14395_2361***	GCF_000796065.1	No	Clinical	Intra-abdominal tract	19	102	10	21	10	365
PA678	***Pseudomonas_aeruginosa_AZPAE14398_2565***	GCF_000796095.1	Yes	Clinical	Intra-abdominal tract	19		3	21	3	773
PA679	***Pseudomonas_aeruginosa_AZPAE14402_2362***	GCF_000796085.1	No	Clinical	Intra-abdominal tract	18	29	13	19	12	2711
PA680	***Pseudomonas_aeruginosa_AZPAE14403_2363***	GCF_000796125.1	No	Clinical	Intra-abdominal tract	18	65	6	22	7	175
PA681	***Pseudomonas_aeruginosa_AZPAE14404_2364***	GCF_000796145.1	No	Clinical	Intra-abdominal tract	19	61	12	21	12	1248
PA682	***Pseudomonas_aeruginosa_AZPAE14410_2365***	GCF_000796175.1	No	Clinical	Intra-abdominal tract	18	32	12	19	12	1053
PA683	***Pseudomonas_aeruginosa_AZPAE14415_2366***	GCF_000796205.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA684	***Pseudomonas_aeruginosa_AZPAE14422_2367***	GCF_000796225.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA685	***Pseudomonas_aeruginosa_AZPAE14437_2369***	GCF_000796255.1	No	Clinical	Urinary tract	2	39	10	5	10	298
PA686	***Pseudomonas_aeruginosa_AZPAE14441_2370***	GCF_000796285.1	No	Clinical	Urinary tract	18	71	13	19	12	292
PA687	***Pseudomonas_aeruginosa_AZPAE14442_2371***	GCF_000796295.1	No	Clinical	Urinary tract	19	14	8	21	9	2712
PA688	***Pseudomonas_aeruginosa_AZPAE14453_2373***	GCF_000796345.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA689	***Pseudomonas_aeruginosa_AZPAE14463_2374***	GCF_000796365.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA690	***Pseudomonas_aeruginosa_AZPAE14499_2375***	GCF_000796385.1	Yes	Clinical	Urinary tract	18		9	22	12	348
PA691	***Pseudomonas_aeruginosa_AZPAE14505_2376***	GCF_000796405.1	No	Clinical	Respiratory tract	18	79	9	19	12	654
PA692	***Pseudomonas_aeruginosa_AZPAE14509_2377***	GCF_000796425.1	No	Clinical	Urinary tract	19	61	13	21	13	1400
PA693	***Pseudomonas_aeruginosa_AZPAE14526_2378***	GCF_000796445.1	No	Clinical	Respiratory tract	18	93	13	19	12	2615
PA694	***Pseudomonas_aeruginosa_AZPAE14533_2567***	GCF_000796465.1	No	Clinical	Respiratory tract	18	102	13	19	13	3170
PA695	***Pseudomonas_aeruginosa_AZPAE14535_2379***	GCF_000796475.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA696	***Pseudomonas_aeruginosa_AZPAE14538_2380***	GCF_000796505.1	No	Clinical	Respiratory tract	18	101	8	19	13	871
PA697	***Pseudomonas_aeruginosa_AZPAE14550_2296***	GCF_000794425.1	No	Clinical	Respiratory tract	18	86	11	19	11	257
PA698	***Pseudomonas_aeruginosa_AZPAE14554_2295***	GCF_000794405.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA699	***Pseudomonas_aeruginosa_AZPAE14557_2297***	GCF_000794445.1	No	Clinical	Respiratory tract	11	49	11	13	14	498
PA700	***Pseudomonas_aeruginosa_AZPAE14566_2299***	GCF_000794485.1	Yes	Clinical	Urinary tract	16		11	17	14	179
PA701	***Pseudomonas_aeruginosa_AZPAE14570_2298***	GCF_000794455.1	Yes	Clinical	Urinary tract	18		9	22	12	348

PA702	***Pseudomonas_aeruginosa_AZPAE14687_2548***	GCF_000794515.1	No	Clinical	Respiratory tract	18	97	9	19	5	167
PA703	***Pseudomonas_aeruginosa_AZPAE14689_2549***	GCF_000794545.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA704	***Pseudomonas_aeruginosa_AZPAE14690_2301***	GCF_000794555.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA705	***Pseudomonas_aeruginosa_AZPAE14691_2303***	GCF_000794605.1	No	Clinical	Respiratory tract	18	93	13	19	12	847
PA706	***Pseudomonas_aeruginosa_AZPAE14692_2302***	GCF_000794585.1	Yes	Clinical	Intra-abdominal tract	8		10	6	10	309
PA707	***Pseudomonas_aeruginosa_AZPAE14693_2304***	GCF_000794625.1	Yes	Clinical	Intra-abdominal tract	18		9	19	5	1090
PA708	***Pseudomonas_aeruginosa_AZPAE14695_2306***	GCF_000794665.1	Yes	Clinical	Respiratory tract	1		12	2	4	253
PA709	***Pseudomonas_aeruginosa_AZPAE14697_2307***	GCF_000794675.1	No	Clinical	Respiratory tract	18	102	9	19	12	640
PA710	***Pseudomonas_aeruginosa_AZPAE14700_2310***	GCF_000794735.1	Yes	Clinical	Respiratory tract	8		10	6	10	309
PA711	***Pseudomonas_aeruginosa_AZPAE14701_2550***	GCF_000794745.1	Yes	Clinical	Intra-abdominal tract	18		9	22	12	348
PA712	***Pseudomonas_aeruginosa_AZPAE14702_2311***	GCF_000794785.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA713	***Pseudomonas_aeruginosa_AZPAE14703_2312***	GCF_000794805.1	Yes	Clinical	Intra-abdominal tract	3		10	4	10	235
PA714	***Pseudomonas_aeruginosa_AZPAE14704_2313***	GCF_000794825.1	Yes	Clinical	Intra-abdominal tract	18		13	19	11	116
PA715	***Pseudomonas_aeruginosa_AZPAE14705_2352***	GCF_000795805.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA716	***Pseudomonas_aeruginosa_AZPAE14706_2566***	GCF_000796165.1	Yes	Clinical	Intra-abdominal tract	3		10	4	10	235
PA717	***Pseudomonas_aeruginosa_AZPAE14707_2564***	GCF_000796025.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA718	***Pseudomonas_aeruginosa_AZPAE14708_2353***	GCF_000795815.1	Yes	Clinical	Intra-abdominal tract	3		10	4	10	235
PA719	***Pseudomonas_aeruginosa_AZPAE14710_2344***	GCF_000795605.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA720	***Pseudomonas_aeruginosa_AZPAE14711_2417***	GCF_000797345.1	Yes	Clinical	Intra-abdominal tract	16		11	17	14	179
PA721	***Pseudomonas_aeruginosa_AZPAE14712_2411***	GCF_000797205.1	Yes	Clinical	Intra-abdominal tract	4		10	3	10	308
PA722	***Pseudomonas_aeruginosa_AZPAE14713_2571***	GCF_000797085.1	Yes	Clinical	Intra-abdominal tract	14		2	16	2	111
PA723	***Pseudomonas_aeruginosa_AZPAE14714_2569***	GCF_000796845.1	Yes	Clinical	Intra-abdominal tract	14		2	16	2	111
PA724	***Pseudomonas_aeruginosa_AZPAE14715_2390***	GCF_000796725.1	No	Clinical	Intra-abdominal tract	16	5	11	17	14	179
PA725	***Pseudomonas_aeruginosa_AZPAE14716_2342***	GCF_000795535.1	Yes	Clinical	Intra-abdominal tract	4		10	3	10	308
PA726	***Pseudomonas_aeruginosa_AZPAE14717_2568***	GCF_000796605.1	No	Clinical	Intra-abdominal tract	11	102	11	13	14	Undefined
PA727	***Pseudomonas_aeruginosa_AZPAE14718_2562***	GCF_000795905.1	Yes	Clinical	Respiratory tract	18		12	20	11	233
PA728	***Pseudomonas_aeruginosa_AZPAE14719_2403***	GCF_000797025.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA729	***Pseudomonas_aeruginosa_AZPAE14720_2357***	GCF_000795955.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA730	***Pseudomonas_aeruginosa_AZPAE14721_2368***	GCF_000796245.1	Yes	Clinical	Intra-abdominal tract	3		10	4	10	235
PA731	***Pseudomonas_aeruginosa_AZPAE14722_2386***	GCF_000796645.1	Yes	Clinical	Intra-abdominal tract	18		6	22	7	175

PA732	***Pseudomonas_aeruginosa_AZPAE14723_2348***	GCF_000795705.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA733	***Pseudomonas_aeruginosa_AZPAE14724_2354***	GCF_000795865.1	Yes	Clinical	Intra-abdominal tract	14		2	16	2	111
PA734	***Pseudomonas_aeruginosa_AZPAE14725_2314***	GCF_000794845.1	Yes	Clinical	Respiratory tract	9		9	11	5	17
PA735	***Pseudomonas_aeruginosa_AZPAE14726_2315***	GCF_000794865.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA736	***Pseudomonas_aeruginosa_AZPAE14727_2551***	GCF_000794885.1	Yes	Clinical	Intra-abdominal tract	14		2	16	2	111
PA737	***Pseudomonas_aeruginosa_AZPAE14728_2552***	GCF_000794905.1	No	Clinical	Intra-abdominal tract	14	52	2	16	2	111
PA738	***Pseudomonas_aeruginosa_AZPAE14729_2316***	GCF_000794925.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA739	***Pseudomonas_aeruginosa_AZPAE14730_2317***	GCF_000794945.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA740	***Pseudomonas_aeruginosa_AZPAE14731_2553***	GCF_000794965.1	No	Clinical	Respiratory tract	18	78	13	19	11	Undefined
PA741	***Pseudomonas_aeruginosa_AZPAE14732_2318***	GCF_000794985.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA742	***Pseudomonas_aeruginosa_AZPAE14810_2320***	GCF_000795025.1	Yes	Clinical	Urinary tract	18		9	19	5	132
PA743	***Pseudomonas_aeruginosa_AZPAE14811_2321***	GCF_000795045.1	Yes	Clinical	Respiratory tract	18		12	20	11	233
PA744	***Pseudomonas_aeruginosa_AZPAE14812_2322***	GCF_000795065.1	Yes	Clinical	Intra-abdominal tract	4		10	3	10	308
PA745	***Pseudomonas_aeruginosa_AZPAE14813_2323***	GCF_000795085.1	Yes	Clinical	Urinary tract	17		6	15	7	1684
PA746	***Pseudomonas_aeruginosa_AZPAE14814_2324***	GCF_000795105.1	Yes	Clinical	Intra-abdominal tract	12		1	14	1	395
PA747	***Pseudomonas_aeruginosa_AZPAE14815_2325***	GCF_000795115.1	Yes	Clinical	Respiratory tract	12		1	14	1	395
PA748	***Pseudomonas_aeruginosa_AZPAE14816_2554***	GCF_000795145.1	No	Clinical	Respiratory tract	19	28	12	21	4	671
PA749	***Pseudomonas_aeruginosa_AZPAE14817_2326***	GCF_000795165.1	No	Clinical	Urinary tract	18	102	13	19	11	386
PA750	***Pseudomonas_aeruginosa_AZPAE14818_2327***	GCF_000795185.1	No	Clinical	Intra-abdominal tract	18	97	9	19	5	2714
PA751	***Pseudomonas_aeruginosa_AZPAE14819_2328***	GCF_000795205.1	Yes	Clinical	Urinary tract	17		13	15	13	277
PA752	***Pseudomonas_aeruginosa_AZPAE14820_2329***	GCF_000795225.1	No	Clinical	Intra-abdominal tract	18	35	11	19	14	1122
PA753	***Pseudomonas_aeruginosa_AZPAE14821_2330***	GCF_000795235.1	No	Clinical	Urinary tract	17	22	13	15	13	277
PA754	***Pseudomonas_aeruginosa_AZPAE14822_2331***	GCF_000795265.1	Yes	Clinical	Intra-abdominal tract	17		13	15	13	277
PA755	***Pseudomonas_aeruginosa_AZPAE14823_2332***	GCF_000795285.1	Yes	Clinical	Respiratory tract	16		11	17	14	155
PA756	***Pseudomonas_aeruginosa_AZPAE14824_2333***	GCF_000795305.1	Yes	Clinical	Respiratory tract	12		1	14	1	395
PA757	***Pseudomonas_aeruginosa_AZPAE14825_2334***	GCF_000795325.1	No	Clinical	Respiratory tract	18	90	13	19	11	Undefined
PA758	***Pseudomonas_aeruginosa_AZPAE14826_2335***	GCF_000795345.1	No	Clinical	Respiratory tract	4	14	10	3	10	308
PA759	***Pseudomonas_aeruginosa_AZPAE14827_2555***	GCF_000795365.1	Yes	Clinical	Intra-abdominal tract	16		11	17	14	179
PA760	***Pseudomonas_aeruginosa_AZPAE14828_2336***	GCF_000795385.1	No	Clinical	Intra-abdominal tract	18	63	9	19	12	1858
PA761	***Pseudomonas_aeruginosa_AZPAE14829_2288***	GCF_000794195.1	No	Clinical	Respiratory tract	4	14	10	3	10	308

PA762	***Pseudomonas_aeruginosa_AZPAE14830_2287***	GCF_000794185.1	Yes	Clinical	Intra-abdominal tract	3		10	4	10	235
PA763	***Pseudomonas_aeruginosa_AZPAE14831_2546***	GCF_000794175.1	Yes	Clinical	Respiratory tract	18		9	22	12	348
PA764	***Pseudomonas_aeruginosa_AZPAE14832_2545***	GCF_000794165.1	No	Clinical	Respiratory tract	14	66	2	16	2	111
PA765	***Pseudomonas_aeruginosa_AZPAE14833_2290***	GCF_000794265.1	Yes	Clinical	Urinary tract	15		12	23	12	244
PA766	***Pseudomonas_aeruginosa_AZPAE14834_2289***	GCF_000794245.1	Yes	Clinical	Urinary tract	15		12	23	12	244
PA767	***Pseudomonas_aeruginosa_AZPAE14835_2291***	GCF_000794285.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA768	***Pseudomonas_aeruginosa_AZPAE14836_2292***	GCF_000794305.1	No	Clinical	Respiratory tract	18	35	12	19	12	162
PA769	***Pseudomonas_aeruginosa_AZPAE14837_2293***	GCF_000794325.1	No	Clinical	Respiratory tract	14	83	2	16	2	111
PA770	***Pseudomonas_aeruginosa_AZPAE14838_2547***	GCF_000794335.1	No	Clinical	Respiratory tract	18	32	12	19	12	767
PA771	***Pseudomonas_aeruginosa_AZPAE14839_2294***	GCF_000794365.1	Yes	Clinical	Intra-abdominal tract	18		12	19	12	260
PA772	***Pseudomonas_aeruginosa_AZPAE14840_2515***	GCF_000789555.1	No	Clinical	Urinary tract	18	31	9	19	12	1960
PA773	***Pseudomonas_aeruginosa_AZPAE14841_2094***	GCF_000789605.1	No	Clinical	Intra-abdominal tract	15	32	12	23	12	244
PA774	***Pseudomonas_aeruginosa_AZPAE14842_2095***	GCF_000789625.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA775	***Pseudomonas_aeruginosa_AZPAE14843_2096***	GCF_000789635.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA776	***Pseudomonas_aeruginosa_AZPAE14844_2098***	GCF_000789685.1	Yes	Clinical	Intra-abdominal tract	13		9	10	12	27
PA777	***Pseudomonas_aeruginosa_AZPAE14845_2099***	GCF_000789705.1	No	Clinical	Respiratory tract	1	103	12	2	4	253
PA778	***Pseudomonas_aeruginosa_AZPAE14846_2101***	GCF_000789745.1	No	Clinical	Respiratory tract	14	52	2	16	2	111
PA779	***Pseudomonas_aeruginosa_AZPAE14847_2102***	GCF_000789755.1	No	Clinical	Respiratory tract	18	102	13	19	11	2715
PA780	***Pseudomonas_aeruginosa_AZPAE14848_2104***	GCF_000789805.1	No	Clinical	Intra-abdominal tract	18	102	11	19	14	2625
PA781	***Pseudomonas_aeruginosa_AZPAE14850_2103***	GCF_000789785.1	Yes	Clinical	Urinary tract	1		12	2	4	253
PA782	***Pseudomonas_aeruginosa_AZPAE14851_2105***	GCF_000789835.1	Yes	Clinical	Intra-abdominal tract	12		1	14	1	395
PA783	***Pseudomonas_aeruginosa_AZPAE14852_2106***	GCF_000789845.1	No	Clinical	Respiratory tract	18	83	10	19	10	639
PA784	***Pseudomonas_aeruginosa_AZPAE14853_2108***	GCF_000789905.1	Yes	Clinical	Respiratory tract	17		13	15	13	277
PA785	***Pseudomonas_aeruginosa_AZPAE14855_2109***	GCF_000789925.1	No	Clinical	Respiratory tract	18	71	13	19	11	2021
PA786	***Pseudomonas_aeruginosa_AZPAE14856_2111***	GCF_000789965.1	No	Clinical	Respiratory tract	18	98	13	19	11	108
PA787	***Pseudomonas_aeruginosa_AZPAE14857_2113***	GCF_000789995.1	Yes	Clinical	Intra-abdominal tract	9		9	11	5	17
PA788	***Pseudomonas_aeruginosa_AZPAE14858_2114***	GCF_000790025.1	No	Clinical	Intra-abdominal tract	19	48	3	21	3	1284
PA789	***Pseudomonas_aeruginosa_AZPAE14859_2115***	GCF_000790035.1	No	Clinical	Urinary tract	18	102	11	19	14	640
PA790	***Pseudomonas_aeruginosa_AZPAE14860_2116***	GCF_000790065.1	Yes	Clinical	Intra-abdominal tract	4		10	3	10	308
PA791	***Pseudomonas_aeruginosa_AZPAE14861_2117***	GCF_000790085.1	No	Clinical	Intra-abdominal tract	18	86	9	19	5	132

PA792	***Pseudomonas_aeruginosa_AZPAE14862_2517***	GCF_000790105.1	No	Clinical	Urinary tract	18	81	13	20	12	621
PA793	***Pseudomonas_aeruginosa_AZPAE14863_2518***	GCF_000790145.1	No	Clinical	Respiratory tract	19	47	10	8	10	357
PA794	***Pseudomonas_aeruginosa_AZPAE14864_2119***	GCF_000790155.1	No	Clinical	Respiratory tract	18	69	11	19	14	16
PA795	***Pseudomonas_aeruginosa_AZPAE14865_2120***	GCF_000790185.1	Yes	Clinical	Respiratory tract	19		10	8	10	357
PA796	***Pseudomonas_aeruginosa_AZPAE14866_2121***	GCF_000790205.1	No	Clinical	Respiratory tract	18	86	6	19	7	1101
PA797	***Pseudomonas_aeruginosa_AZPAE14867_2122***	GCF_000790215.1	No	Clinical	Respiratory tract	15	32	12	23	12	244
PA798	***Pseudomonas_aeruginosa_AZPAE14868_2123***	GCF_000790245.1	No	Clinical	Intra-abdominal tract	18	69	13	19	11	2572
PA799	***Pseudomonas_aeruginosa_AZPAE14869_2519***	GCF_000790265.1	No	Clinical	Urinary tract	19	39	10	21	10	319
PA800	***Pseudomonas_aeruginosa_AZPAE14870_2125***	GCF_000790305.1	Yes	Clinical	Intra-abdominal tract	2		10	5	10	298
PA801	***Pseudomonas_aeruginosa_AZPAE14871_2520***	GCF_000790325.1	No	Clinical	Urinary tract	18	102	9	19	5	885
PA802	***Pseudomonas_aeruginosa_AZPAE14872_2521***	GCF_000790355.1	Yes	Clinical	Respiratory tract	15		12	23	12	244
PA803	***Pseudomonas_aeruginosa_AZPAE14873_2127***	GCF_000790385.1	No	Clinical	Respiratory tract	18	97	9	19	12	883
PA804	***Pseudomonas_aeruginosa_AZPAE14875_2129***	GCF_000790425.1	No	Clinical	Respiratory tract	18	32	13	19	12	381
PA805	***Pseudomonas_aeruginosa_AZPAE14876_2130***	GCF_000790445.1	No	Clinical	Intra-abdominal tract	18	102	9	19	12	2717
PA806	***Pseudomonas_aeruginosa_AZPAE14877_2132***	GCF_000790485.1	No	Clinical	Respiratory tract	18	78	5	19	6	Undefined
PA807	***Pseudomonas_aeruginosa_AZPAE14878_2522***	GCF_000790505.1	Yes	Clinical	Intra-abdominal tract	19		12	20	4	606
PA808	***Pseudomonas_aeruginosa_AZPAE14879_2133***	GCF_000790525.1	Yes	Clinical	Respiratory tract	18		13	19	11	116
PA809	***Pseudomonas_aeruginosa_AZPAE14880_2134***	GCF_000790545.1	Yes	Clinical	Respiratory tract	18		6	22	7	175
PA810	***Pseudomonas_aeruginosa_AZPAE14882_2137***	GCF_000790605.1	No	Clinical	Respiratory tract	18	93	13	20	12	865
PA811	***Pseudomonas_aeruginosa_AZPAE14883_2139***	GCF_000790645.1	No	Clinical	Respiratory tract	19	102	8	21	9	701
PA812	***Pseudomonas_aeruginosa_AZPAE14884_2140***	GCF_000790655.1	No	Clinical	Respiratory tract	18	87	13	19	12	1184
PA813	***Pseudomonas_aeruginosa_AZPAE14885_2141***	GCF_000790685.1	No	Clinical	Intra-abdominal tract	18	59	12	19	11	3119
PA814	***Pseudomonas_aeruginosa_AZPAE14886_2142***	GCF_000790705.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA815	***Pseudomonas_aeruginosa_AZPAE14887_2143***	GCF_000790725.1	Yes	Clinical	Intra-abdominal tract	3		10	4	10	235
PA816	***Pseudomonas_aeruginosa_AZPAE14888_2523***	GCF_000790785.1	No	Clinical	Intra-abdominal tract	19	3	12	20	4	606
PA817	***Pseudomonas_aeruginosa_AZPAE14889_2146***	GCF_000790805.1	Yes	Clinical	Intra-abdominal tract	19		3	21	3	773
PA818	***Pseudomonas_aeruginosa_AZPAE14890_2147***	GCF_000790825.1	Yes	Clinical	Urinary tract	18		6	22	7	175
PA819	***Pseudomonas_aeruginosa_AZPAE14891_2148***	GCF_000790865.1	Yes	Clinical	Respiratory tract	18		12	19	11	262
PA820	***Pseudomonas_aeruginosa_AZPAE14892_2149***	GCF_000790885.1	Yes	Clinical	Respiratory tract	19		13	21	13	313
PA821	***Pseudomonas_aeruginosa_AZPAE14893_2150***	GCF_000790905.1	No	Clinical	Urinary tract	12	2	1	14	1	395

PA822	***Pseudomonas_aeruginosa_AZPAE14894_2152***	GCF_000790935.1	Yes	Clinical	Intra-abdominal tract	4		10	3	10	308
PA823	***Pseudomonas_aeruginosa_AZPAE14895_2153***	GCF_000790965.1	No	Clinical	Intra-abdominal tract	18	76	13	19	13	968
PA824	***Pseudomonas_aeruginosa_AZPAE14897_2156***	GCF_000791025.1	No	Clinical	Intra-abdominal tract	17	22	6	15	7	1684
PA825	***Pseudomonas_aeruginosa_AZPAE14898_2157***	GCF_000791035.1	Yes	Clinical	Respiratory tract	1		12	2	4	253
PA826	***Pseudomonas_aeruginosa_AZPAE14899_2158***	GCF_000791065.1	No	Clinical	Urinary tract	18	79	8	19	9	Undefined
PA827	***Pseudomonas_aeruginosa_AZPAE14900_2159***	GCF_000791085.1	Yes	Clinical	Intra-abdominal tract	19		10	8	10	Undefined
PA828	***Pseudomonas_aeruginosa_AZPAE14901_2524***	GCF_000791105.1	No	Clinical	Intra-abdominal tract	5		4			Undefined
PA829	***Pseudomonas_aeruginosa_AZPAE14902_2160***	GCF_000791125.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA830	***Pseudomonas_aeruginosa_AZPAE14903_2525***	GCF_000791145.1	No	Clinical	Intra-abdominal tract	18	44	13	19	11	1721
PA831	***Pseudomonas_aeruginosa_AZPAE14904_2526***	GCF_000791155.1	No	Clinical	Intra-abdominal tract	15	32	12	23	12	244
PA832	***Pseudomonas_aeruginosa_AZPAE14905_2542***	GCF_000793615.1	No	Clinical	Respiratory tract	19	27	12	21	4	560
PA833	***Pseudomonas_aeruginosa_AZPAE14906_2544***	GCF_000793915.1	Yes	Clinical	Respiratory tract	19		12	21	4	560
PA834	***Pseudomonas_aeruginosa_AZPAE14907_2268***	GCF_000793705.1	Yes	Clinical	Intra-abdominal tract	18		13	19	11	2069
PA835	***Pseudomonas_aeruginosa_AZPAE14908_2272***	GCF_000793805.1	No	Clinical	Intra-abdominal tract	18	89	8	19	9	633
PA836	***Pseudomonas_aeruginosa_AZPAE14909_2091***	GCF_000789525.1	Yes	Clinical	Intra-abdominal tract	18		6	22	7	175
PA837	***Pseudomonas_aeruginosa_AZPAE14910_2112***	GCF_000789975.1	No	Clinical	Intra-abdominal tract	18	97	9	19	12	241
PA838	***Pseudomonas_aeruginosa_AZPAE14911_2280***	GCF_000793985.1	No	Clinical	Intra-abdominal tract	19	47	3	21	3	532
PA839	***Pseudomonas_aeruginosa_AZPAE14912_2284***	GCF_000794055.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA840	***Pseudomonas_aeruginosa_AZPAE14913_2274***	GCF_000793845.1	Yes	Clinical	Urinary tract	18		6	19	7	1800
PA841	***Pseudomonas_aeruginosa_AZPAE14914_2276***	GCF_000793885.1	Yes	Clinical	Urinary tract	10		5	12	6	274
PA842	***Pseudomonas_aeruginosa_AZPAE14915_2107***	GCF_000789885.1	Yes	Clinical	Urinary tract	18		11	19	14	267
PA843	***Pseudomonas_aeruginosa_AZPAE14916_2281***	GCF_000794005.1	Yes	Clinical	Respiratory tract	18		13	19	11	1605
PA844	***Pseudomonas_aeruginosa_AZPAE14917_2266***	GCF_000793665.1	No	Clinical	Intra-abdominal tract	18	72	13	19	12	1750
PA845	***Pseudomonas_aeruginosa_AZPAE14918_2093***	GCF_000789545.1	No	Clinical	Intra-abdominal tract	18	96	13	19	12	2718
PA846	***Pseudomonas_aeruginosa_AZPAE14919_2516***	GCF_000789815.1	No	Clinical	Respiratory tract	18	92	13	19	12	369
PA847	***Pseudomonas_aeruginosa_AZPAE14920_2270***	GCF_000793745.1	No	Clinical	Urinary tract	19	8	12	21	4	377
PA848	***Pseudomonas_aeruginosa_AZPAE14921_2273***	GCF_000793825.1	Yes	Clinical	Respiratory tract	18		8	19	9	633
PA849	***Pseudomonas_aeruginosa_AZPAE14922_2161***	GCF_000791185.1	No	Clinical	Respiratory tract	18	84	12	20	11	233
PA850	***Pseudomonas_aeruginosa_AZPAE14923_2162***	GCF_000791205.1	Yes	Clinical	Respiratory tract	17		13	15	13	277
PA851	***Pseudomonas_aeruginosa_AZPAE14924_2163***	GCF_000791225.1	Yes	Clinical	Respiratory tract	16		11	17	14	155

PA852	***Pseudomonas_aeruginosa_AZPAE14925_2165***	GCF_000791265.1	No	Clinical	Intra-abdominal tract	18	102	6	19	7	1800
PA853	***Pseudomonas_aeruginosa_AZPAE14926_2166***	GCF_000791275.1	Yes	Clinical	Urinary tract	10		5	12	6	274
PA854	***Pseudomonas_aeruginosa_AZPAE14927_2167***	GCF_000791305.1	No	Clinical	Intra-abdominal tract	18	32	11	19	14	267
PA855	***Pseudomonas_aeruginosa_AZPAE14928_2168***	GCF_000791325.1	No	Clinical	Urinary tract	18	102	13	19	11	1605
PA856	***Pseudomonas_aeruginosa_AZPAE14929_2092***	GCF_000789535.1	Yes	Clinical	Urinary tract	18		12	20	11	233
PA857	***Pseudomonas_aeruginosa_AZPAE14930_2275***	GCF_000793865.1	No	Clinical	Urinary tract	18	86	8	19	9	3346
PA858	***Pseudomonas_aeruginosa_AZPAE14931_2271***	GCF_000793765.1	No	Clinical	Respiratory tract	18	93	12	19	12	266
PA859	***Pseudomonas_aeruginosa_AZPAE14932_2267***	GCF_000793685.1	Yes	Clinical	Respiratory tract	19		13	21	13	313
PA860	***Pseudomonas_aeruginosa_AZPAE14933_2285***	GCF_000794085.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA861	***Pseudomonas_aeruginosa_AZPAE14934_2277***	GCF_000793905.1	No	Clinical	Intra-abdominal tract	18	86	9	19	5	Undefined
PA862	***Pseudomonas_aeruginosa_AZPAE14935_2286***	GCF_000794095.1	Yes	Clinical	Respiratory tract	9		9	11	5	17
PA863	***Pseudomonas_aeruginosa_AZPAE14936_2264***	GCF_000793585.1	No	Clinical	Intra-abdominal tract	18	86	11	19	14	Undefined
PA864	***Pseudomonas_aeruginosa_AZPAE14937_2543***	GCF_000793785.1	Yes	Clinical	Intra-abdominal tract	18		13	20	12	621
PA865	***Pseudomonas_aeruginosa_AZPAE14938_2265***	GCF_000793645.1	No	Clinical	Respiratory tract	4	14	10	3	10	308
PA866	***Pseudomonas_aeruginosa_AZPAE14939_2541***	GCF_000793595.1	No	Clinical	Respiratory tract	18	98	10	19	10	2719
PA867	***Pseudomonas_aeruginosa_AZPAE14940_2278***	GCF_000793945.1	Yes	Clinical	Urinary tract	18		9	22	12	348
PA868	***Pseudomonas_aeruginosa_AZPAE14941_2100***	GCF_000789725.1	No	Clinical	Intra-abdominal tract	5		4			Undefined
PA869	***Pseudomonas_aeruginosa_AZPAE14942_2282***	GCF_000794025.1	Yes	Clinical	Intra-abdominal tract	18		12	20	11	233
PA870	***Pseudomonas_aeruginosa_AZPAE14943_2169***	GCF_000791345.1	No	Clinical	Respiratory tract	18	97	11	19	14	1743
PA871	***Pseudomonas_aeruginosa_AZPAE14944_2173***	GCF_000791425.1	Yes	Clinical	Intra-abdominal tract	9		9	11	5	17
PA872	***Pseudomonas_aeruginosa_AZPAE14945_2172***	GCF_000791405.1	Yes	Clinical	Urinary tract	16		11	17	14	179
PA873	***Pseudomonas_aeruginosa_AZPAE14946_2174***	GCF_000791445.1	No	Clinical	Urinary tract	13	49	9	10	12	27
PA874	***Pseudomonas_aeruginosa_AZPAE14947_2283***	GCF_000794045.1	No	Clinical	Urinary tract	18	83	11	19	14	527
PA875	***Pseudomonas_aeruginosa_AZPAE14948_2176***	GCF_000791485.1	Yes	Clinical	Intra-abdominal tract	1		12	2	4	253
PA876	***Pseudomonas_aeruginosa_AZPAE14949_2177***	GCF_000791495.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA877	***Pseudomonas_aeruginosa_AZPAE14951_2527***	GCF_000791545.1	No	Clinical	Urinary tract	18	81	13	20	12	621
PA878	***Pseudomonas_aeruginosa_AZPAE14952_2180***	GCF_000791585.1	No	Clinical	Intra-abdominal tract	18	86	13	19	11	2069
PA879	***Pseudomonas_aeruginosa_AZPAE14953_2181***	GCF_000791605.1	No	Clinical	Intra-abdominal tract	16	5	11	17	14	179
PA880	***Pseudomonas_aeruginosa_AZPAE14954_2182***	GCF_000791625.1	No	Clinical	Intra-abdominal tract	18	68	13	19	11	285
PA881	***Pseudomonas_aeruginosa_AZPAE14955_2183***	GCF_000791635.1	No	Clinical	Intra-abdominal tract	18	93	12	19	12	260

PA882	***Pseudomonas_aeruginosa_AZPAE14957_2529***	GCF_000791705.1	No	Clinical	Intra-abdominal tract	7	15	7	7	8	2410
PA883	***Pseudomonas_aeruginosa_AZPAE14958_2185***	GCF_000791725.1	Yes	Clinical	Intra-abdominal tract	15		12	23	12	244
PA884	***Pseudomonas_aeruginosa_AZPAE14959_2186***	GCF_000791735.1	No	Clinical	Intra-abdominal tract	19	47	3	21	3	773
PA885	***Pseudomonas_aeruginosa_AZPAE14960_2530***	GCF_000791765.1	No	Clinical	Respiratory tract	19	34	10	18	10	2720
PA886	***Pseudomonas_aeruginosa_AZPAE14961_2187***	GCF_000791785.1	No	Clinical	Respiratory tract	18	93	11	19	14	500
PA887	***Pseudomonas_aeruginosa_AZPAE14962_2188***	GCF_000791805.1	Yes	Clinical	Respiratory tract	19		3	21	3	532
PA888	***Pseudomonas_aeruginosa_AZPAE14963_2189***	GCF_000791825.1	No	Clinical	Respiratory tract	18	95	9	19	5	1090
PA889	***Pseudomonas_aeruginosa_AZPAE14964_2190***	GCF_000791835.1	Yes	Clinical	Respiratory tract	12		1	14	1	Undefined
PA890	***Pseudomonas_aeruginosa_AZPAE14965_2193***	GCF_000791905.1	Yes	Clinical	Respiratory tract	12		1	14	1	Undefined
PA891	***Pseudomonas_aeruginosa_AZPAE14967_2192***	GCF_000791885.1	No	Clinical	Respiratory tract	18	31	8	19	9	2721
PA892	***Pseudomonas_aeruginosa_AZPAE14968_2194***	GCF_000791915.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA893	***Pseudomonas_aeruginosa_AZPAE14969_2195***	GCF_000791945.1	Yes	Clinical	Intra-abdominal tract	4		10	3	10	308
PA894	***Pseudomonas_aeruginosa_AZPAE14970_2196***	GCF_000791965.1	Yes	Clinical	Intra-abdominal tract	4		10	3	10	308
PA895	***Pseudomonas_aeruginosa_AZPAE14972_2199***	GCF_000792025.1	No	Clinical	Intra-abdominal tract	19	102		21		1567
PA896	***Pseudomonas_aeruginosa_AZPAE14973_2201***	GCF_000792065.1	Yes	Clinical	Respiratory tract	12		1	14	1	395
PA897	***Pseudomonas_aeruginosa_AZPAE14974_2531***	GCF_000792085.1	No	Clinical	Respiratory tract	16	5	11	17	14	155
PA898	***Pseudomonas_aeruginosa_AZPAE14975_2202***	GCF_000792095.1	No	Clinical	Respiratory tract	18	78	13	19	12	879
PA899	***Pseudomonas_aeruginosa_AZPAE14976_2203***	GCF_000792115.1	No	Clinical	Respiratory tract	18	81	12	19	11	1295
PA900	***Pseudomonas_aeruginosa_AZPAE14977_2205***	GCF_000792155.1	No	Clinical	Urinary tract	18	76	11	19	14	1437
PA901	***Pseudomonas_aeruginosa_AZPAE14978_2206***	GCF_000792165.1	No	Clinical	Urinary tract	15	102	12	23	12	244
PA902	***Pseudomonas_aeruginosa_AZPAE14979_2207***	GCF_000792205.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA903	***Pseudomonas_aeruginosa_AZPAE14980_2532***	GCF_000792225.1	Yes	Clinical	Intra-abdominal tract	13		9	10	12	27
PA904	***Pseudomonas_aeruginosa_AZPAE14981_2208***	GCF_000792245.1	No	Clinical	Urinary tract	10	78	5	12	6	274
PA905	***Pseudomonas_aeruginosa_AZPAE14982_2210***	GCF_000792285.1	No	Clinical	Respiratory tract	19	53	8	18	9	1420
PA906	***Pseudomonas_aeruginosa_AZPAE14983_2211***	GCF_000792305.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA907	***Pseudomonas_aeruginosa_AZPAE14984_2212***	GCF_000792325.1	Yes	Clinical	Urinary tract	18		12	20	11	233
PA908	***Pseudomonas_aeruginosa_AZPAE14985_2213***	GCF_000792345.1	Yes	Clinical	Respiratory tract	19		10	21	10	1076
PA909	***Pseudomonas_aeruginosa_AZPAE14986_2214***	GCF_000792365.1	No	Clinical	Respiratory tract	18	22	6	15	7	769
PA910	***Pseudomonas_aeruginosa_AZPAE14987_2215***	GCF_000792385.1	No	Clinical	Respiratory tract	2	39	10	5	10	298
PA911	***Pseudomonas_aeruginosa_AZPAE14988_2216***	GCF_000792425.1	No	Clinical	Urinary tract	19	57	10	21	10	1076

PA912	***Pseudomonas_aeruginosa_AZPAE14989_2217***	GCF_000792445.1	No	Clinical	Intra-abdominal tract	19	47	10	8	10	357
PA913	***Pseudomonas_aeruginosa_AZPAE14990_2534***	GCF_000792465.1	Yes	Clinical	Intra-abdominal tract	19		10	21	10	319
PA914	***Pseudomonas_aeruginosa_AZPAE14991_2218***	GCF_000792475.1	No	Clinical	Intra-abdominal tract	19	39	10	1	10	316
PA915	***Pseudomonas_aeruginosa_AZPAE14992_2219***	GCF_000792505.1	No	Clinical	Intra-abdominal tract	18	78	10	19	12	2055
PA916	***Pseudomonas_aeruginosa_AZPAE14993_2220***	GCF_000792515.1	No	Clinical	Urinary tract	9	11	9	11	5	Undefined
PA917	***Pseudomonas_aeruginosa_AZPAE14994_2221***	GCF_000792545.1	Yes	Clinical	Intra-abdominal tract	7		7	7	8	2410
PA918	***Pseudomonas_aeruginosa_AZPAE14995_2222***	GCF_000792565.1	No	Clinical	Intra-abdominal tract	18	97	9	19	5	231
PA919	***Pseudomonas_aeruginosa_AZPAE14996_2223***	GCF_000792575.1	No	Clinical	Intra-abdominal tract	18	46	13	19	11	646
PA920	***Pseudomonas_aeruginosa_AZPAE14997_2224***	GCF_000792605.1	Yes	Clinical	Urinary tract	12		1	14	1	395
PA921	***Pseudomonas_aeruginosa_AZPAE14998_2225***	GCF_000792625.1	Yes	Clinical	Urinary tract	18		9	22	12	348
PA922	***Pseudomonas_aeruginosa_AZPAE14999_2226***	GCF_000792635.1	No	Clinical	Intra-abdominal tract	18	46	12	19	12	557
PA923	***Pseudomonas_aeruginosa_AZPAE15000_2227***	GCF_000792665.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA924	***Pseudomonas_aeruginosa_AZPAE15001_2228***	GCF_000792675.1	No	Clinical	Intra-abdominal tract	18	32	13	19	11	2722
PA925	***Pseudomonas_aeruginosa_AZPAE15002_2229***	GCF_000792705.1	Yes	Clinical	Intra-abdominal tract	14		2	16	2	111
PA926	***Pseudomonas_aeruginosa_AZPAE15003_2230***	GCF_000792725.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA927	***Pseudomonas_aeruginosa_AZPAE15004_2231***	GCF_000792745.1	No	Clinical	Respiratory tract	19	58	10	21	12	Undefined
PA928	***Pseudomonas_aeruginosa_AZPAE15005_2232***	GCF_000792765.1	Yes	Clinical	Respiratory tract	4		10	3	10	308
PA929	***Pseudomonas_aeruginosa_AZPAE15006_2233***	GCF_000792785.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA930	***Pseudomonas_aeruginosa_AZPAE15007_2234***	GCF_000792805.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA931	***Pseudomonas_aeruginosa_AZPAE15008_2235***	GCF_000792825.1	Yes	Clinical	Urinary tract	19		3	21	3	1284
PA932	***Pseudomonas_aeruginosa_AZPAE15009_2236***	GCF_000792845.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA933	***Pseudomonas_aeruginosa_AZPAE15010_2237***	GCF_000792855.1	Yes	Clinical	Respiratory tract	18		6	22	7	175
PA934	***Pseudomonas_aeruginosa_AZPAE15011_2238***	GCF_000792885.1	No	Clinical	Intra-abdominal tract	1	103	12	2	4	253
PA935	***Pseudomonas_aeruginosa_AZPAE15012_2239***	GCF_000792895.1	No	Clinical	Intra-abdominal tract	11	30	11	13	14	252
PA936	***Pseudomonas_aeruginosa_AZPAE15013_2240***	GCF_000792925.1	Yes	Clinical	Intra-abdominal tract	15		12	23	12	244
PA937	***Pseudomonas_aeruginosa_AZPAE15014_2241***	GCF_000792945.1	No	Clinical	Respiratory tract	18	56	6	22	7	1033
PA938	***Pseudomonas_aeruginosa_AZPAE15015_2243***	GCF_000792975.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA939	***Pseudomonas_aeruginosa_AZPAE15016_2242***	GCF_000792965.1	Yes	Clinical	Urinary tract	1		12	2	4	253
PA940	***Pseudomonas_aeruginosa_AZPAE15017_2244***	GCF_000793005.1	No	Clinical	Intra-abdominal tract	7	15	7	7	8	3471
PA941	***Pseudomonas_aeruginosa_AZPAE15018_2245***	GCF_000793025.1	Yes	Clinical	Intra-abdominal tract	9		9	11	5	17

PA942	***Pseudomonas_aeruginosa_AZPAE15019_2246***	GCF_000793045.1	No	Clinical	Respiratory tract	8	16	10	6	10	309
PA943	***Pseudomonas_aeruginosa_AZPAE15020_2535***	GCF_000793055.1	Yes	Clinical	Respiratory tract	12		1	14	1	3063
PA944	***Pseudomonas_aeruginosa_AZPAE15021_2247***	GCF_000793085.1	Yes	Clinical	Intra-abdominal tract	15		12	23	12	244
PA945	***Pseudomonas_aeruginosa_AZPAE15023_2249***	GCF_000793125.1	No	Clinical	Intra-abdominal tract	18	78	13	19	11	2723
PA946	***Pseudomonas_aeruginosa_AZPAE15024_2136***	GCF_000790585.1	No	Clinical	Intra-abdominal tract	1	103	12	2	4	253
PA947	***Pseudomonas_aeruginosa_AZPAE15025_2155***	GCF_000791005.1	Yes	Clinical	Urinary tract	1		12	2	4	253
PA948	***Pseudomonas_aeruginosa_AZPAE15026_2170***	GCF_000791365.1	No	Clinical	Urinary tract	19	60	10	21	10	2724
PA949	***Pseudomonas_aeruginosa_AZPAE15027_2164***	GCF_000791235.1	No	Clinical	Urinary tract	19	20	8	21	9	1086
PA950	***Pseudomonas_aeruginosa_AZPAE15028_2209***	GCF_000792265.1	No	Clinical	Respiratory tract	18	81	13	19	11	463
PA951	***Pseudomonas_aeruginosa_AZPAE15029_2204***	GCF_000792145.1	Yes	Clinical	Respiratory tract	18		12	20	11	233
PA952	***Pseudomonas_aeruginosa_AZPAE15030_2197***	GCF_000791985.1	No	Clinical	Intra-abdominal tract	17	22	6	15	7	245
PA953	***Pseudomonas_aeruginosa_AZPAE15031_2191***	GCF_000791855.1	Yes	Clinical	Intra-abdominal tract	12		1	14	1	395
PA954	***Pseudomonas_aeruginosa_AZPAE15032_2179***	GCF_000791565.1	No	Clinical	Intra-abdominal tract	17	22	13	15	13	360
PA955	***Pseudomonas_aeruginosa_AZPAE15033_2269***	GCF_000793725.1	No	Clinical	Intra-abdominal tract	10	78	5	12	6	274
PA956	***Pseudomonas_aeruginosa_AZPAE15034_2279***	GCF_000793955.1	Yes	Clinical	Respiratory tract	2		10	5	10	298
PA957	***Pseudomonas_aeruginosa_AZPAE15035_2514***	GCF_000789495.1	Yes	Clinical	Respiratory tract	19		12	21	4	560
PA958	***Pseudomonas_aeruginosa_AZPAE15036_2097***	GCF_000789645.1	No	Clinical	Intra-abdominal tract	18	11	9	19	5	406
PA959	***Pseudomonas_aeruginosa_AZPAE15037_2110***	GCF_000789935.1	Yes	Clinical	Intra-abdominal tract	12		1	14	1	395
PA960	***Pseudomonas_aeruginosa_AZPAE15038_2118***	GCF_000790115.1	No	Clinical	Intra-abdominal tract	18	78	13	19	11	116
PA961	***Pseudomonas_aeruginosa_AZPAE15039_2126***	GCF_000790345.1	Yes	Clinical	Urinary tract	8		10	6	10	309
PA962	***Pseudomonas_aeruginosa_AZPAE15040_2151***	GCF_000790915.1	Yes	Clinical	Intra-abdominal tract	10		5	12	6	274
PA963	***Pseudomonas_aeruginosa_AZPAE15041_2144***	GCF_000790735.1	Yes	Clinical	Urinary tract	19		12	20	4	2725
PA964	***Pseudomonas_aeruginosa_AZPAE15042_2131***	GCF_000790465.1	No	Clinical	Urinary tract	5		4			2211
PA965	***Pseudomonas_aeruginosa_AZPAE15043_2145***	GCF_000790765.1	Yes	Clinical	Intra-abdominal tract	2		10	5	10	446
PA966	***Pseudomonas_aeruginosa_AZPAE15044_2200***	GCF_000792045.1	No	Clinical	Intra-abdominal tract	18	4	9	22	12	1320
PA967	***Pseudomonas_aeruginosa_AZPAE15045_2154***	GCF_000790985.1	Yes	Clinical	Urinary tract	1		12	2	4	253
PA968	***Pseudomonas_aeruginosa_AZPAE15046_2124***	GCF_000790285.1	No	Clinical	Urinary tract	18	96	9	19	12	2238
PA969	***Pseudomonas_aeruginosa_AZPAE15047_3102***	GCF_000790835.1	Yes	Clinical	Respiratory tract	2		10	5	10	298
PA970	***Pseudomonas_aeruginosa_AZPAE15048_2536***	GCF_000793135.1	No	Clinical	Urinary tract	18	83	9	19	12	234
PA971	***Pseudomonas_aeruginosa_AZPAE15050_2184***	GCF_000791665.1	Yes	Clinical	Intra-abdominal tract	17		13	15	13	360

PA972	***Pseudomonas_aeruginosa_AZPAE15051_2533***	GCF_000792395.1	Yes	Clinical	Intra-abdominal tract	19		10	21	10	319
PA973	***Pseudomonas_aeruginosa_AZPAE15052_2175***	GCF_000791465.1	No	Clinical	Respiratory tract	18	35	10	19	9	2726
PA974	***Pseudomonas_aeruginosa_AZPAE15053_2138***	GCF_000790625.1	No	Clinical	Urinary tract	18	32	12	19	12	699
PA975	***Pseudomonas_aeruginosa_AZPAE15054_2171***	GCF_000791385.1	Yes	Clinical	Urinary tract	2		10	5	10	298
PA976	***Pseudomonas_aeruginosa_AZPAE15055_2251***	GCF_000793185.1	No	Clinical	Urinary tract	18	63	9	19	5	2727
PA977	***Pseudomonas_aeruginosa_AZPAE15056_2250***	GCF_000793165.1	No	Clinical	Respiratory tract	18	86	9	19	5	635
PA978	***Pseudomonas_aeruginosa_AZPAE15057_2252***	GCF_000793205.1	No	Clinical	Respiratory tract	18	78	13	19	11	2476
PA979	***Pseudomonas_aeruginosa_AZPAE15058_2537***	GCF_000793225.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA980	***Pseudomonas_aeruginosa_AZPAE15059_2253***	GCF_000793245.1	No	Clinical	Respiratory tract	19	61	13	21	13	313
PA981	***Pseudomonas_aeruginosa_AZPAE15060_2254***	GCF_000793255.1	Yes	Clinical	Urinary tract	18		9	22	12	348
PA982	***Pseudomonas_aeruginosa_AZPAE15061_2256***	GCF_000793295.1	No	Clinical	Urinary tract	18	89	8	19	9	633
PA983	***Pseudomonas_aeruginosa_AZPAE15062_2255***	GCF_000793285.1	No	Clinical	Urinary tract	18	102	13	19	11	644
PA984	***Pseudomonas_aeruginosa_AZPAE15063_2257***	GCF_000793315.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA985	***Pseudomonas_aeruginosa_AZPAE15064_2258***	GCF_000793345.1	No	Clinical	Intra-abdominal tract	19	27	13	21	11	1560
PA986	***Pseudomonas_aeruginosa_AZPAE15065_2538***	GCF_000793365.1	No	Clinical	Respiratory tract	18	96	12	19	11	261
PA987	***Pseudomonas_aeruginosa_AZPAE15066_2260***	GCF_000793395.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA988	***Pseudomonas_aeruginosa_AZPAE15067_2539***	GCF_000793415.1	Yes	Clinical	Intra-abdominal tract	19		10	21	10	319
PA989	***Pseudomonas_aeruginosa_AZPAE15068_2261***	GCF_000793445.1	Yes	Clinical	Respiratory tract	9		9	11	5	17
PA990	***Pseudomonas_aeruginosa_AZPAE15069_2262***	GCF_000793455.1	Yes	Clinical	Intra-abdominal tract	16		11	17	14	155
PA991	***Pseudomonas_aeruginosa_AZPAE15070_2263***	GCF_000793485.1	No	Clinical	Urinary tract	12	2	1	14	1	395
PA992	***Pseudomonas_aeruginosa_AZPAE15071_2540***	GCF_000793505.1	Yes	Clinical	Respiratory tract	9		9	11	5	17
PA993	***Pseudomonas_aeruginosa_AZPAE15072_2259***	GCF_000793385.1	Yes	Clinical	Urinary tract	10		5	12	6	274
PA994	***Pseudomonas_aeruginosa_B136_33_191***	GCF_000359505.1	No	Clinical	Gastrointestinal	19	38	12	21	4	1024
PA995	***Pseudomonas_aeruginosa_B14130_10394***	GCF_003952305.1	No	Clinical	Bacteraemia	19	47	10	8	10	357
PA996	***Pseudomonas_aeruginosa_B17932_10395***	GCF_003952325.1	No	Clinical	Bacteraemia	19	47	10	8	10	357
PA997	***Pseudomonas_aeruginosa_B2_10071***	GCF_003835665.1	Yes	Clinical	Cystic fibrosis	1		12	2	4	Undefined
PA998	***Pseudomonas_aeruginosa_B3_T2101_10023***	GCF_003834685.1	No	Clinical	Respiratory tract	18	33	9	19	5	708
PA999	***Pseudomonas_aeruginosa_B41226_10391***	GCF_003950235.1	No	Clinical	Bacteraemia	19	47	10	8	10	357
PA1000	***Pseudomonas_aeruginosa_B9_T2436_10022***	GCF_003834665.1	Yes	Clinical	Respiratory tract	19		10	21	12	Undefined
PA1001	***Pseudomonas_aeruginosa_BA15561_9944***	GCF_003713085.1	No	Clinical	Bacteraemia	19	47	10	8	10	357

PA1002	***Pseudomonas_aeruginosa_BA7823_9659***	GCF_003626935.1	No	Clinical	Bacteraemia	19	47	10	8	10	357
PA1003	***Pseudomonas_aeruginosa_BAMC_07_48_3994***	GCF_001632245.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	61	13	21	13	313
PA1004	***Pseudomonas_aeruginosa_BCW_7427_12127***	GCF_009925095.1	No	Clinical	Respiratory tract	19	102	8	18	9	205
PA1005	***Pseudomonas_aeruginosa_BCW_7428_12126***	GCF_009916345.1	No	Clinical	Gastrointestinal	18	86	11	19	11	Undefined
PA1006	***Pseudomonas_aeruginosa_BJ2_10561***	GCF_003974475.1	No	Clinical	Cystic fibrosis	18	86	8	19	9	2966
PA1007	***Pseudomonas_aeruginosa_BJ4_10535***	GCF_003973915.1	Yes	Clinical	Cystic fibrosis	18		9	19	12	882
PA1008	***Pseudomonas_aeruginosa_BK2_6174***	GCF_002243265.1	No	Clinical	Eye	18	98	10	19	10	2719
PA1009	***Pseudomonas_aeruginosa_BK3_5889***	GCF_002242775.1	No	Clinical	Eye	4	14	10	3	10	308
PA1010	***Pseudomonas_aeruginosa_BK4_6920***	GCF_002242885.1	No	Clinical	Eye	18	83	11	19	14	527
PA1011	***Pseudomonas_aeruginosa_BK5_5983***	GCF_002242915.1	No	Clinical	Eye	18	80	8	19	9	2708
PA1012	***Pseudomonas_aeruginosa_BK6_7000***	GCF_002242855.1	No	Clinical	Eye	19	47	10	8	10	357
PA1013	***Pseudomonas_aeruginosa_BL01_561***	GCF_000481125.1	No	Clinical	Eye	18	35	13	19	12	2629
PA1014	***Pseudomonas_aeruginosa_BL02_560***	GCF_000481105.1	No	Clinical	Eye	9	11	9	11	5	17
PA1015	***Pseudomonas_aeruginosa_BL03_559***	GCF_000481085.1	No	Clinical	Eye	19	3	12	20	4	606
PA1016	***Pseudomonas_aeruginosa_BL04_558***	GCF_000481065.1	No	Clinical	Eye	19	53	8	18	9	667
PA1017	***Pseudomonas_aeruginosa_BL05_557***	GCF_000481045.1	No	Clinical	Eye	18	93	12	19	12	1129
PA1018	***Pseudomonas_aeruginosa_BL06_556***	GCF_000481025.1	No	Clinical	Eye	17	22	6	15	7	245
PA1019	***Pseudomonas_aeruginosa_BL07_555***	GCF_000481005.1	No	Clinical	Eye	18	97	13	19	12	1202
PA1020	***Pseudomonas_aeruginosa_BL08_554***	GCF_000480985.1	No	Clinical	Eye	3	6	10	4	10	235
PA1021	***Pseudomonas_aeruginosa_BL09_553***	GCF_000480965.1	No	Clinical	Eye	8	16	10	6	10	309
PA1022	***Pseudomonas_aeruginosa_BL10_552***	GCF_000480945.1	No	Clinical	Eye	18	78	13	19	12	589
PA1023	***Pseudomonas_aeruginosa_BL11_551***	GCF_000480925.1	No	Clinical	Eye	17	22	6	15	7	245
PA1024	***Pseudomonas_aeruginosa_BL12_550***	GCF_000480905.1	No	Clinical	Eye	18	7	9	19	12	1285
PA1025	***Pseudomonas_aeruginosa_BL13_549***	GCF_000480885.1	No	Clinical	Eye	19	102	10	1	10	316
PA1026	***Pseudomonas_aeruginosa_BL14_548***	GCF_000480865.1	No	Clinical	Eye	3	6	10	4	10	235
PA1027	***Pseudomonas_aeruginosa_BL15_547***	GCF_000480845.1	No	Clinical	Eye	19	102	10	18	10	2623
PA1028	***Pseudomonas_aeruginosa_BL16_546***	GCF_000480825.1	No	Clinical	Eye	1	103	12	2	4	253
PA1029	***Pseudomonas_aeruginosa_BL17_545***	GCF_000480805.1	No	Clinical	Eye	3	6	10	4	10	235
PA1030	***Pseudomonas_aeruginosa_BL18_544***	GCF_000480785.1	No	Clinical	Eye	19	102	13	21	13	1621
PA1031	***Pseudomonas_aeruginosa_BL19_543***	GCF_000480765.1	No	Clinical	Eye	18	102	9	19	12	1631

PA1032	***Pseudomonas_aeruginosa_BL20_542***	GCF_000480745.1	No	Clinical	Eye	8	16	10	6	10	309
PA1033	***Pseudomonas_aeruginosa_BL21_541***	GCF_000480725.1	No	Clinical	Eye	4	14	10	3	10	308
PA1034	***Pseudomonas_aeruginosa_BL22_540***	GCF_000480705.1	No	Clinical	Eye	2	39	10	5	10	298
PA1035	***Pseudomonas_aeruginosa_BL23_539***	GCF_000480685.1	No	Clinical	Eye	18	4	9	22	12	348
PA1036	***Pseudomonas_aeruginosa_BL24_538***	GCF_000480665.1	No	Clinical	Eye	16	5	11	17	14	155
PA1037	***Pseudomonas_aeruginosa_BL25_537***	GCF_000480645.1	No	Clinical	Eye	19	61	13	21	13	313
PA1038	***Pseudomonas_aeruginosa_Bo559_10155***	GCF_003837335.1	No	Clinical	Burn	19	61	13	21	13	Undefined
PA1039	***Pseudomonas_aeruginosa_Br670_10109***	GCF_003836415.1	No	Clinical	Respiratory tract	18	91	12	19	12	260
PA1040	***Pseudomonas_aeruginosa_BWH011_11906***	GCF_006704795.1	Yes	Clinical	Respiratory tract	2		10	5	10	298
PA1041	***Pseudomonas_aeruginosa_BWH029_2052***	GCF_000629145.1	No	Clinical	Respiratory tract	18	93	12	19	12	901
PA1042	***Pseudomonas_aeruginosa_BWH030_2051***	GCF_000629125.1	No	Clinical	Urinary tract	3	14	10	4	10	235
PA1043	***Pseudomonas_aeruginosa_BWH031_11905***	GCF_006704785.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	2		10	5	10	298
PA1044	***Pseudomonas_aeruginosa_BWH031_2050***	GCF_000629105.1	No	Clinical	Respiratory tract	9	11	9	11	5	845
PA1045	***Pseudomonas_aeruginosa_BWH032_2049***	GCF_000629085.1	No	Clinical	Genital tract	18	9	12	19	12	260
PA1046	***Pseudomonas_aeruginosa_BWH033_2048***	GCF_000629065.1	No	Clinical	Urinary tract	15	32	12	23	12	244
PA1047	***Pseudomonas_aeruginosa_BWH035_2047***	GCF_000629045.1	No	Clinical	Ear	18	12	13	19	12	959
PA1048	***Pseudomonas_aeruginosa_BWH036_2046***	GCF_000629025.1	No	Clinical	Genital tract	9	11	9	11	5	845
PA1049	***Pseudomonas_aeruginosa_BWH047_11119***	GCF_005048525.1	No	Clinical	Respiratory tract	3	6	10	4	10	235
PA1050	***Pseudomonas_aeruginosa_BWH049_2075***	GCF_000629605.1	No	Clinical	Urinary tract	19	58	10	21	10	1076
PA1051	***Pseudomonas_aeruginosa_BWH050_2074***	GCF_000629585.1	No	Clinical	Bacteraemia	19	61	13	21	13	313
PA1052	***Pseudomonas_aeruginosa_BWH051_2073***	GCF_000629565.1	No	Clinical	Bacteraemia	9	11	9	11	5	845
PA1053	***Pseudomonas_aeruginosa_BWH052_2072***	GCF_000629545.1	No	Clinical	Urinary tract	18	12	11	20	14	390
PA1054	***Pseudomonas_aeruginosa_BWH053_2071***	GCF_000629525.1	No	Clinical	Bacteraemia	2	39	10	5	10	298
PA1055	***Pseudomonas_aeruginosa_BWH054_2070***	GCF_000629505.1	No	Clinical	Urinary tract	19	54	8	18	9	830
PA1056	***Pseudomonas_aeruginosa_BWH055_2069***	GCF_000629485.1	No	Clinical	Urinary tract	18	83	6	19	7	1800
PA1057	***Pseudomonas_aeruginosa_BWH056_2068***	GCF_000629465.1	No	Clinical	Bacteraemia	18	102	11	19	14	412
PA1058	***Pseudomonas_aeruginosa_BWH057_2067***	GCF_000629445.1	No	Clinical	Bacteraemia	18	102	11	19	14	412
PA1059	***Pseudomonas_aeruginosa_BWH058_2066***	GCF_000629425.1	No	Clinical	Urinary tract	1	103	12	2	4	253
PA1060	***Pseudomonas_aeruginosa_BWH059_2065***	GCF_000629405.1	No	Clinical	Bacteraemia	12	2	1	14	1	395
PA1061	***Pseudomonas_aeruginosa_BWH060_2064***	GCF_000629385.1	No	Clinical	Urinary tract	2	39	10	5	10	298

PA1062	***Pseudomonas_aeruginosa_BWH069_11904***	GCF_006704775.1	Yes	Clinical	Ear	2		10	5	10	446
PA1063	***Pseudomonas_aeruginosa_BWHPSA001_589***	GCF_000481685.1	No	Clinical	Urinary tract	18	97	9	19	12	883
PA1064	***Pseudomonas_aeruginosa_BWHPSA002_588***	GCF_000481665.1	No	Clinical	Bacteraemia	16	5	11	17	14	179
PA1065	***Pseudomonas_aeruginosa_BWHPSA003_587***	GCF_000481645.1	No	Clinical	Respiratory tract	16	5	11	17	14	155
PA1066	***Pseudomonas_aeruginosa_BWHPSA004_586***	GCF_000481625.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	10	78	5	12	6	209
PA1067	***Pseudomonas_aeruginosa_BWHPSA005_585***	GCF_000481605.1	No	Clinical	Urinary tract	9	11	9	11	5	845
PA1068	***Pseudomonas_aeruginosa_BWHPSA006_584***	GCF_000481585.1	No	Clinical	Respiratory tract	3	6	10	4	10	235
PA1069	***Pseudomonas_aeruginosa_BWHPSA007_583***	GCF_000481565.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	17	22	13	15	13	1128
PA1070	***Pseudomonas_aeruginosa_BWHPSA008_582***	GCF_000481545.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	69	13	19	11	299
PA1071	***Pseudomonas_aeruginosa_BWHPSA009_581***	GCF_000481525.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	97	9	19	12	241
PA1072	***Pseudomonas_aeruginosa_BWHPSA010_580***	GCF_000481505.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	78	13	19	11	386
PA1073	***Pseudomonas_aeruginosa_BWHPSA011_579***	GCF_000481485.1	No	Clinical	Respiratory tract	13	50	9	10	12	27
PA1074	***Pseudomonas_aeruginosa_BWHPSA012_578***	GCF_000481465.1	No	Clinical	Respiratory tract	10	78	5	12	6	2632
PA1075	***Pseudomonas_aeruginosa_BWHPSA013_577***	GCF_000481445.1	No	Clinical	Respiratory tract	18	78	6	19	7	170
PA1076	***Pseudomonas_aeruginosa_BWHPSA014_576***	GCF_000481425.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	10	78	5	12	6	209
PA1077	***Pseudomonas_aeruginosa_BWHPSA015_575***	GCF_000481405.1	No	Clinical	Urinary tract	18	95	9	19	12	192
PA1078	***Pseudomonas_aeruginosa_BWHPSA016_574***	GCF_000481385.1	No	Clinical	Ear	18	32	11	19	14	2317
PA1079	***Pseudomonas_aeruginosa_BWHPSA017_573***	GCF_000481365.1	No	Clinical	Urinary tract	16	5	11	17	14	155
PA1080	***Pseudomonas_aeruginosa_BWHPSA018_572***	GCF_000481345.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	102	13	19	12	2636
PA1081	***Pseudomonas_aeruginosa_BWHPSA019_571***	GCF_000481325.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	78	13	19	12	Undefined
PA1082	***Pseudomonas_aeruginosa_BWHPSA020_570***	GCF_000481305.1	No	Clinical	Respiratory tract	18	102	13	19	11	1930
PA1083	***Pseudomonas_aeruginosa_BWHPSA021_569***	GCF_000481285.1	No	Clinical	Respiratory tract	10	78	5	12	6	2632
PA1084	***Pseudomonas_aeruginosa_BWHPSA022_568***	GCF_000481265.1	No	Clinical	Respiratory tract	13	50	9	10	12	27
PA1085	***Pseudomonas_aeruginosa_BWHPSA023_567***	GCF_000481245.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	9	11	9	11	5	17
PA1086	***Pseudomonas_aeruginosa_BWHPSA024_566***	GCF_000481225.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	9	11	9	11	5	845
PA1087	***Pseudomonas_aeruginosa_BWHPSA025_565***	GCF_000481205.1	No	Clinical	Respiratory tract	18	99	11	19	14	2625

PA1088	***Pseudomonas_aeruginosa_BWHPSA027_563***	GCF_000481165.1	No	Clinical	Respiratory tract	1	103	12	2	4	253
PA1089	***Pseudomonas_aeruginosa_BWHPSA028_562***	GCF_000481145.1	No	Clinical	Respiratory tract	11	49	11	13	14	252
PA1090	***Pseudomonas_aeruginosa_BWHPSA037_2500***	GCF_000520455.1	No	Clinical	Respiratory tract	18	102	12	19	11	Undefined
PA1091	***Pseudomonas_aeruginosa_BWHPSA038_2041***	GCF_000520435.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	38	10	21	10	Undefined
PA1092	***Pseudomonas_aeruginosa_BWHPSA039_2040***	GCF_000520415.1	No	Clinical	Urinary tract	16	5	11	17	14	179
PA1093	***Pseudomonas_aeruginosa_BWHPSA040_2039***	GCF_000520395.1	No	Clinical	Respiratory tract	10	78	5	12	6	274
PA1094	***Pseudomonas_aeruginosa_BWHPSA041_2038***	GCF_000520375.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	17	22	13	15	13	277
PA1095	***Pseudomonas_aeruginosa_BWHPSA042_2037***	GCF_000520355.1	No	Clinical	Respiratory tract	18	96	13	19	12	Undefined
PA1096	***Pseudomonas_aeruginosa_BWHPSA043_2036***	GCF_000520335.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	53	8	18	9	926
PA1097	***Pseudomonas_aeruginosa_BWHPSA044_2035***	GCF_000520315.1	No	Clinical	Urinary tract	1	103	12	2	4	253
PA1098	***Pseudomonas_aeruginosa_BWHPSA045_2034***	GCF_000520295.1	No	Clinical	Respiratory tract	12	2	1	14	1	395
PA1099	***Pseudomonas_aeruginosa_BWHPSA046_2033***	GCF_000520275.1	No	Clinical	Respiratory tract	18	12	11	20	14	390
PA1100	***Pseudomonas_aeruginosa_BWHPSA047_2032***	GCF_000520255.1	No	Clinical	Respiratory tract	18	42	11	19	14	2699
PA1101	***Pseudomonas_aeruginosa_BWHPSA048_2031***	GCF_000520235.1	No	Clinical	Urinary tract	9	11	9	11	5	845
PA1102	***Pseudomonas_aeruginosa_C1913C_isolate_C1913C_9509***	GCF_000705155.1	No	Clinical	Cystic fibrosis	18	12	13	19	12	782
PA1103	***Pseudomonas_aeruginosa_C5311_10173***	GCF_003837705.1	No	Clinical	Cystic fibrosis	18	93	9	19	12	192
PA1104	***Pseudomonas_aeruginosa_C8_T3532_10057***	GCF_003835385.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA1105	***Pseudomonas_aeruginosa_C9_P1814_10361***	GCF_003934225.1	Yes	Clinical	Intra-abdominal tract	3		10	4	10	235
PA1107	***Pseudomonas_aeruginosa_CCBH18249_10728***	GCF_004146325.1	Yes	Clinical	Urinary tract	17		13	15	13	277
PA1108	***Pseudomonas_aeruginosa_CCBH276_11107***	GCF_004785835.1	Yes	Clinical	Nosocomial infections	17		13	15	13	277
PA1109	***Pseudomonas_aeruginosa_CCBH3462_11106***	GCF_004785815.1	Yes	Clinical	Nosocomial infections	17		13	15	13	277
PA1110	***Pseudomonas_aeruginosa_CCBH4850_10730***	GCF_004152855.1	No	Clinical	Urinary tract	17	22	13	15	13	277
PA1111	***Pseudomonas_aeruginosa_CCBH5939_10729***	GCF_004152825.1	Yes	Clinical	Urinary tract	17		13	15	13	277
PA1112	***Pseudomonas_aeruginosa_CCUG_51971_11974***	GCF_008195485.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA1113	***Pseudomonas_aeruginosa_CCUG_59347_11972***	GCF_008180895.1	No	Clinical	Respiratory tract	18	84	12	20	11	233
PA1114	***Pseudomonas_aeruginosa_CCUG_70744_6254***	GCF_003194245.1	No	Clinical	Respiratory tract	12	2	1	14	1	395
PA1115	***Pseudomonas_aeruginosa_CCUG_73744_11977***	GCF_008244625.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	3		10	4	10	235
PA1116	***Pseudomonas_aeruginosa_CCUG_73745_11978***	GCF_008244635.1	Yes	Clinical	Bacteraemia	3		10	4	10	235

PA1117	***Pseudomonas_aeruginosa_CF127_10010***	GCF_003834445.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	179
PA1118	***Pseudomonas_aeruginosa_CF16053_11976***	GCF_008244575.1	No	Clinical	Bacteraemia	18	75	13	19	12	3351
PA1119	***Pseudomonas_aeruginosa_CF18_601***	GCF_000481925.1	No	Clinical	Cystic fibrosis	18	11	8	19	12	1394
PA1120	***Pseudomonas_aeruginosa_CF27_600***	GCF_000481905.1	No	Clinical	Cystic fibrosis	18	64	13	22	12	485
PA1121	***Pseudomonas_aeruginosa_CF5_10056***	GCF_003835365.1	Yes	Clinical	Cystic fibrosis	16		11	17	14	179
PA1122	***Pseudomonas_aeruginosa_CF5_599***	GCF_000481885.1	No	Clinical	Cystic fibrosis	18	86	10	19	12	1538
PA1123	***Pseudomonas_aeruginosa_CF614_523***	GCF_000480355.1	No	Clinical	Cystic fibrosis	17	22	6	15	7	245
PA1124	***Pseudomonas_aeruginosa_CF77_524***	GCF_000480375.1	No	Clinical	Cystic fibrosis	16	5	11	17	14	155
PA1125	***Pseudomonas_aeruginosa_CFSAN084950_12043***	GCF_009648875.1	No	Environment	Plants	18	80	12	19	11	Undefined
PA1126	***Pseudomonas_aeruginosa_Chir_D_144_5975***	GCF_002312195.1	Yes	Environment	Clinical environment: Dental, Hospital	19		10	1	10	Undefined
PA1127	***Pseudomonas_aeruginosa_Chir_D_144_assistant_6892***	GCF_002312685.1	No	Environment	Clinical environment: Dental, Hospital	19	53	8	18	9	Undefined
PA1128	***Pseudomonas_aeruginosa_CL297_7041***	GCF_002193915.1	No	Clinical	Respiratory tract	18	68	13	19	11	2053
PA1129	***Pseudomonas_aeruginosa_CLJ1_7032***	GCF_003032395.1	No	Clinical	Respiratory tract	5		4			2028
PA1130	***Pseudomonas_aeruginosa_CLJ3_5974***	GCF_003057595.1	No	Clinical	Respiratory tract	5		4			2028
PA1131	***Pseudomonas_aeruginosa_CND03_10172***	GCF_003837675.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	3		10	4	10	235
PA1132	***Pseudomonas_aeruginosa_Co380791_10127***	GCF_003836775.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1133	***Pseudomonas_aeruginosa_Co398373_10175***	GCF_003837745.1	No	Environment	Clinical environment: Dental, Hospital	14	52	2	16	2	111
PA1134	***Pseudomonas_aeruginosa_Co399645_10138***	GCF_003837005.1	No	Clinical	Intra-abdominal tract	18	32	13	19	11	3014
PA1135	***Pseudomonas_aeruginosa_COPD2d_5043***	GCF_002021605.1	No	Clinical	Respiratory tract	18	32	12	19	12	643
PA1136	***Pseudomonas_aeruginosa_COPD6a_5006***	GCF_002021645.1	No	Clinical	Respiratory tract	18	102	9	19	12	1631
PA1137	***Pseudomonas_aeruginosa_Cotonu1_10100***	GCF_003836245.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		13	21	13	313
PA1138	***Pseudomonas_aeruginosa_CPHL10299_10119***	GCF_003836625.1	No	Clinical	Gastrointestinal	18	97	13	19	12	647
PA1139	***Pseudomonas_aeruginosa_CPHL10701_10161***	GCF_003837465.1	No	Clinical	Respiratory tract	18	40	11	19	14	2903
PA1140	***Pseudomonas_aeruginosa_CPHL1999_10125***	GCF_003836745.1	Yes	Clinical	Ear	15		12	23	12	244
PA1141	***Pseudomonas_aeruginosa_CPHL2000_10165***	GCF_003837535.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	68	13	19	12	Undefined
PA1142	***Pseudomonas_aeruginosa_CPHL5083_10124***	GCF_003836725.1	No	Clinical	Urinary tract	18	102	13	19	11	1171
PA1143	***Pseudomonas_aeruginosa_CPHL6749_10121***	GCF_003836645.1	Yes	Clinical	Urinary tract	18		9	19	12	882
PA1144	***Pseudomonas_aeruginosa_CPHL8203_10164***	GCF_003837525.1	Yes	Clinical	Urinary tract	18		9	19	5	708

PA1145	***Pseudomonas_aeruginosa_CR1_6461***	GCF_003025345.2	No	Environment	Plants	5		4			3198
PA1146	***Pseudomonas_aeruginosa_D1_10037***	GCF_003834985.1	Yes	Clinical	Gastrointestinal	12		1	14	1	395
PA1147	***Pseudomonas_aeruginosa_D429_Q_isolate_Mi162_2_9940***	GCF_003698835.1	Yes	Clinical	Burn	4		10	3	10	308
PA1148	***Pseudomonas_aeruginosa_D9_3362_10012***	GCF_003834465.1	Yes	Clinical	Respiratory tract	1		12	2	4	253
PA1149	***Pseudomonas_aeruginosa_DHS29_2002***	GCF_000503175.1	No	Clinical	Urinary tract	12	2	1	14	1	395
PA1150	***Pseudomonas_aeruginosa_DK1_substr_NH57388A_6643***	GCF_900069025.1	No	Clinical	Cystic fibrosis	18	78	13	19	11	387
PA1151	***Pseudomonas_aeruginosa_DK2_174***	GCF_000271365.1	No	Clinical	Cystic fibrosis	18	78	13	19	11	386
PA1152	***Pseudomonas_aeruginosa_DLL7525_6931***	GCF_003312935.1	No	Clinical	Gastrointestinal	8	16	10	6	10	309
PA1153	***Pseudomonas_aeruginosa_DN1_5583***	GCF_001722005.2	No	Environment	Soil: Manure, Rocks, Sand, Soil	19	38	10	1	10	316
PA1154	***Pseudomonas_aeruginosa_DUN_001_3B_10085***	GCF_003835945.1	Yes	Clinical	Cystic fibrosis	15		12	23	12	244
PA1155	***Pseudomonas_aeruginosa_DUN_001_4_10083***	GCF_003835905.1	Yes	Clinical	Cystic fibrosis	15		12	23	12	244
PA1156	***Pseudomonas_aeruginosa_DUN_001A_10044***	GCF_003835115.1	Yes	Clinical	Cystic fibrosis	15		12	23	12	244
PA1157	***Pseudomonas_aeruginosa_DUN_003B_10050***	GCF_003835245.1	No	Clinical	Cystic fibrosis	18	97	9	19	12	Undefined
PA1158	***Pseudomonas_aeruginosa_DUN_009B_10077***	GCF_003835775.1	Yes	Clinical	Cystic fibrosis	12		1	14	1	395
PA1159	***Pseudomonas_aeruginosa_DUN_013_10045***	GCF_003835145.1	Yes	Clinical	Cystic fibrosis	18		13	19	12	275
PA1160	***Pseudomonas_aeruginosa_DUN_024_1_10074***	GCF_003835715.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	260
PA1161	***Pseudomonas_aeruginosa_E_500_6222***	GCF_002312415.1	No	Clinical	Respiratory tract	18	93	12	19	12	1239
PA1162	***Pseudomonas_aeruginosa_E1_T4189_10000***	GCF_003834235.1	No	Clinical	Respiratory tract	18	35	12	19	11	3393
PA1163	***Pseudomonas_aeruginosa_E1_WATER_2_9958***	GCF_003833395.1	No	Environment	Farm environment	18	4	9	22	12	348
PA1164	***Pseudomonas_aeruginosa_E2_10011***	GCF_003834455.1	No	Environment	Plants	18	46	13	19	11	Undefined
PA1165	***Pseudomonas_aeruginosa_E2_285***	GCF_000482005.1	No	Environment	Plants	18	46	13	19	11	41
PA1166	***Pseudomonas_aeruginosa_E2_660***	GCF_000297355.1	No	Environment	Plants	18	46	13	19	11	41
PA1167	***Pseudomonas_aeruginosa_E2_DN_2_9957***	GCF_003833385.1	Yes	Environment	Farm environment	13		9	10	12	27
PA1168	***Pseudomonas_aeruginosa_E2758_10592***	GCF_003975105.1	No	Clinical	Eye	18	102	11	19	11	1330
PA1169	***Pseudomonas_aeruginosa_E429_isolate_15108_1_9923***	GCF_003698495.1	Yes	Clinical	Respiratory tract	2		10	5	10	446
PA1170	***Pseudomonas_aeruginosa_E42A_B_isolate_LMG14084_9935***	GCF_003698745.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA1171	***Pseudomonas_aeruginosa_E6130952_7221***	GCF_002085755.1	No	Clinical	Respiratory tract	3	6	10	4	10	235
PA1172	***Pseudomonas_aeruginosa_E80_10733***	GCF_004291075.1	No	Clinical	Cystic fibrosis	17	22	6	15	7	245
PA1173	***Pseudomonas_aeruginosa_E9_4068_10029***	GCF_003834825.1	No	Clinical	Urinary tract	7	15	12	7	12	3390
PA1174	***Pseudomonas_aeruginosa_E90_12001***	GCF_008705235.1	No	Clinical	Cystic fibrosis	18	17	13	19	12	282

PA1175	***Pseudomonas_aeruginosa_EA0A_isolate_39177_9925***	GCF_003698545.1	Yes	Clinical	Eye	13		9	10	12	Undefined
PA1176	***Pseudomonas_aeruginosa_EC22_isolate_AUS52_9941***	GCF_003698855.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	Undefined
PA1177	***Pseudomonas_aeruginosa_Env_1_6932***	GCF_002239565.1	No	Environment	Plants	18	102	9	19	12	Undefined
PA1178	***Pseudomonas_aeruginosa_Env_11_6793***	GCF_002239545.1	No	Environment	Plants	19	8	12	21	4	377
PA1179	***Pseudomonas_aeruginosa_Env_12_6238***	GCF_002239445.1	No	Environment	Plants	18	32	11	19	14	267
PA1180	***Pseudomonas_aeruginosa_Env_14_6756***	GCF_002239425.1	No	Environment	Plants	18	32	13	19	11	1405
PA1181	***Pseudomonas_aeruginosa_Env_16_7060***	GCF_002239535.1	No	Environment	Plants	18	78	13	19	11	116
PA1182	***Pseudomonas_aeruginosa_ENV_205_9833***	GCF_003632235.1	No	Environment	Sewage/Wastewater	19	19	10	21	10	365
PA1183	***Pseudomonas_aeruginosa_ENV_246_9834***	GCF_003632265.1	No	Environment	Sewage/Wastewater	19	19	10	21	10	365
PA1184	***Pseudomonas_aeruginosa_ENV_297_9738***	GCF_003630355.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	35	12	19	12	162
PA1185	***Pseudomonas_aeruginosa_Env_32_6626***	GCF_002239505.1	No	Environment	Plants	18	86	9	19	5	505
PA1186	***Pseudomonas_aeruginosa_ENV_454_9893***	GCF_003633445.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	7	15	7	7	8	2467
PA1187	***Pseudomonas_aeruginosa_Env_47_6425***	GCF_002239485.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	23	13	19	11	164
PA1188	***Pseudomonas_aeruginosa_ENV_480_9892***	GCF_003633435.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	7	15	7	7	8	2467
PA1189	***Pseudomonas_aeruginosa_ENV_551_9856***	GCF_003632705.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	6		8	9	9	1763
PA1190	***Pseudomonas_aeruginosa_ENV_552_9854***	GCF_003632675.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	6		8	9	9	1763
PA1191	***Pseudomonas_aeruginosa_ENV_566_9857***	GCF_003632725.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	6		8	9	9	1763
PA1192	***Pseudomonas_aeruginosa_ENV_567_9895***	GCF_003633495.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	6	1	8	9	9	1763
PA1193	***Pseudomonas_aeruginosa_ENV_568_9891***	GCF_003633405.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	7		7	7	8	2452
PA1194	***Pseudomonas_aeruginosa_ENV_569_9890***	GCF_003633395.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	7		7	7	8	2452
PA1195	***Pseudomonas_aeruginosa_ENV_570_9849***	GCF_003632575.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	7	15	7	7	8	2452
PA1196	***Pseudomonas_aeruginosa_Env_58_6984***	GCF_002239415.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	82	9	19	12	973
PA1197	***Pseudomonas_aeruginosa_Env_62_6520***	GCF_002239465.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	56	6	22	7	1642
PA1198	***Pseudomonas_aeruginosa_ENV_682_9781***	GCF_003631205.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	234
PA1199	***Pseudomonas_aeruginosa_ENV_683_9780***	GCF_003631195.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	82	9	19	12	234
PA1200	***Pseudomonas_aeruginosa_ENV_94_9843***	GCF_003632455.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	19	103	10	21	10	1197
PA1201	***Pseudomonas_aeruginosa_env005_6048***	GCF_002330515.1	Yes	Environment	Other environmental source	15		12	23	12	244

PA1202	***Pseudomonas_aeruginosa_env043_7181***	GCF_002330875.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	16	5	1	17	1	Undefined
PA1203	***Pseudomonas_aeruginosa_env045_6720***	GCF_002330475.1	No	Environment	Other environmental source	18	86	5	19	6	875
PA1204	***Pseudomonas_aeruginosa_env050_5820***	GCF_002330835.1	Yes	Environment	Other environmental source	12		1	14	1	395
PA1205	***Pseudomonas_aeruginosa_env051b_6663***	GCF_002332165.1	Yes	Environment	Other environmental source	12		1	14	1	395
PA1206	***Pseudomonas_aeruginosa_env054_7276***	GCF_002330435.1	Yes	Environment	Other environmental source	13		9	10	12	27
PA1207	***Pseudomonas_aeruginosa_env065a_6545***	GCF_002330425.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	4		10	3	10	308
PA1208	***Pseudomonas_aeruginosa_env065b_6753***	GCF_002330395.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	61	10	21	10	207
PA1209	***Pseudomonas_aeruginosa_env068_6235***	GCF_002330885.1	No	Environment	Other environmental source	18	40	13	19	12	Undefined
PA1210	***Pseudomonas_aeruginosa_env079_6580***	GCF_002330865.1	No	Environment	Other environmental source	14	66	2	16	2	111
PA1211	***Pseudomonas_aeruginosa_env084_6510***	GCF_002330955.1	Yes	Environment	Other environmental source	19		10	21	10	207
PA1212	***Pseudomonas_aeruginosa_env091_7005***	GCF_002330925.1	No	Environment	Other environmental source	16	5	11	17	14	179
PA1213	***Pseudomonas_aeruginosa_env092a_6344***	GCF_002332175.1	Yes	Environment	Other environmental source	13		9	10	12	27
PA1214	***Pseudomonas_aeruginosa_env092b_7158***	GCF_002330385.1	No	Environment	Other environmental source	13	50	9	10	12	27
PA1215	***Pseudomonas_aeruginosa_env097_6693***	GCF_002332125.1	No	Environment	Other environmental source	18	11	8	19	12	Undefined
PA1216	***Pseudomonas_aeruginosa_env099_6951***	GCF_002330815.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	68	13	19	11	285
PA1217	***Pseudomonas_aeruginosa_env100_6566***	GCF_002330805.1	No	Environment	Algae	18	93	11	19	14	500
PA1218	***Pseudomonas_aeruginosa_env101_6678***	GCF_002330775.1	No	Environment	Other environmental source	18	93	12	19	11	3574
PA1219	***Pseudomonas_aeruginosa_env102_6357***	GCF_002330355.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	88	13	19	12	378
PA1220	***Pseudomonas_aeruginosa_env103_7282***	GCF_002330765.1	Yes	Environment	Plants	11		11	13	14	252
PA1221	***Pseudomonas_aeruginosa_env104_6875***	GCF_002330345.1	No	Environment	Plants	18	93	13	19	12	1527
PA1222	***Pseudomonas_aeruginosa_env105_6115***	GCF_002332095.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		13	19	12	1527
PA1223	***Pseudomonas_aeruginosa_env107_6055***	GCF_002330735.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	93	12	19	12	1239
PA1224	***Pseudomonas_aeruginosa_env108_7109***	GCF_002330725.1	Yes	Environment	Other environmental source	11		11	13	14	252
PA1225	***Pseudomonas_aeruginosa_env109b_7167***	GCF_002330695.1	No	Environment	Other environmental source	19	102	8	21	9	815
PA1226	***Pseudomonas_aeruginosa_env110a_6704***	GCF_002330315.1	Yes	Environment	Other environmental source	19		8	21	9	815
PA1227	***Pseudomonas_aeruginosa_env110b_6001***	GCF_002332085.1	Yes	Environment	Other environmental source	19		8	21	9	815
PA1228	***Pseudomonas_aeruginosa_env113a_6335***	GCF_002330305.1	No	Environment	Other environmental source	11	49	11	13	14	252
PA1229	***Pseudomonas_aeruginosa_env113b_6331***	GCF_002332065.1	No	Environment	Other environmental source	4	14	10	3	10	308

PA1230	***Pseudomonas_aeruginosa_env126_5936***	GCF_002330675.1	Yes	Environment	Other environmental source	16		11	17	14	179
PA1231	***Pseudomonas_aeruginosa_env133_7212***	GCF_002332035.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		13	19	11	439
PA1232	***Pseudomonas_aeruginosa_env135_6101***	GCF_002332015.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		13	19	11	439
PA1233	***Pseudomonas_aeruginosa_env137a_6266***	GCF_002330275.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	102	13	19	11	439
PA1234	***Pseudomonas_aeruginosa_env139_6827***	GCF_002330625.1	No	Environment	Other environmental source	18	93	13	20	12	1801
PA1235	***Pseudomonas_aeruginosa_env140_6307***	GCF_002332135.1	Yes	Environment	Other environmental source	18		13	20	12	1801
PA1236	***Pseudomonas_aeruginosa_env142_6523***	GCF_002330255.1	Yes	Environment	Other environmental source	19		10	21	10	207
PA1237	***Pseudomonas_aeruginosa_env144b_6769***	GCF_002326745.1	Yes	Environment	Home environment	18		13	19	11	439
PA1238	***Pseudomonas_aeruginosa_env145a_5972***	GCF_002326725.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	15		12	23	12	244
PA1239	***Pseudomonas_aeruginosa_env146b_7183***	GCF_002326675.1	No	Environment	Other environmental source	18	96	13	19	12	1416
PA1240	***Pseudomonas_aeruginosa_env158_7050***	GCF_002326505.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	97	13	19	11	471
PA1241	***Pseudomonas_aeruginosa_env159a_6735***	GCF_002326455.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	11	19	11	Undefined
PA1242	***Pseudomonas_aeruginosa_env159b_5846***	GCF_002326685.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		11	19	11	Undefined
PA1243	***Pseudomonas_aeruginosa_env165_6320***	GCF_002326445.1	No	Environment	Other environmental source	19	48	10	21	12	Undefined
PA1244	***Pseudomonas_aeruginosa_env169_7278***	GCF_002331995.1	No	Environment	Other environmental source	3	6	10	4	10	235
PA1245	***Pseudomonas_aeruginosa_env172_6388***	GCF_002326435.1	No	Environment	Other environmental source	18	4	9	22	12	348
PA1246	***Pseudomonas_aeruginosa_env179_5964***	GCF_002326425.1	Yes	Environment	Other environmental source	8		10	6	10	309
PA1247	***Pseudomonas_aeruginosa_env187_6439***	GCF_002331985.1	Yes	Environment	Other environmental source	1		12	2	4	253
PA1248	***Pseudomonas_aeruginosa_env189_7152***	GCF_002330605.1	Yes	Environment	Home environment	16		11	17	14	179
PA1249	***Pseudomonas_aeruginosa_env193_6004***	GCF_002326665.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	10	78	5	12	6	274
PA1250	***Pseudomonas_aeruginosa_env199_6734***	GCF_002330235.1	Yes	Environment	Farm environment	10		5	12	6	274
PA1251	***Pseudomonas_aeruginosa_env201_6571***	GCF_002330595.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	94	12	19	11	262
PA1252	***Pseudomonas_aeruginosa_env202_7053***	GCF_002330215.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	102	13	19	12	282
PA1253	***Pseudomonas_aeruginosa_env203_6073***	GCF_002330205.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	86	13	19	12	1226
PA1254	***Pseudomonas_aeruginosa_env204_5860***	GCF_002330175.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	97	9	19	12	258
PA1255	***Pseudomonas_aeruginosa_env207_6940***	GCF_002330585.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		13	19	12	282

PA1256	***Pseudomonas_aeruginosa_env210_6428***	GCF_002326395.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	74	8	19	12	809
PA1257	***Pseudomonas_aeruginosa_env224_7023***	GCF_002330555.1	No	Environment	Other environmental source	18	102	13	19	11	439
PA1258	***Pseudomonas_aeruginosa_env225_6457***	GCF_002326625.1	No	Environment	Algae	18	69	11	19	14	16
PA1259	***Pseudomonas_aeruginosa_env238_6694***	GCF_002326365.1	No	Environment	Home environment	15	32	12	23	12	244
PA1260	***Pseudomonas_aeruginosa_env241a_6636***	GCF_002326605.1	Yes	Environment	Other environmental source	11		11	13	14	252
PA1261	***Pseudomonas_aeruginosa_env241b_6009***	GCF_002330165.1	Yes	Environment	Other environmental source	11		11	13	14	252
PA1262	***Pseudomonas_aeruginosa_env299_7038***	GCF_002330135.1	No	Environment	Other environmental source	12	2	1	14	1	395
PA1263	***Pseudomonas_aeruginosa_env331b_6628***	GCF_002326595.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	9	19	12	Undefined
PA1264	***Pseudomonas_aeruginosa_env334_7163***	GCF_002330525.1	No	Environment	Other environmental source	8	16	10	6	10	309
PA1265	***Pseudomonas_aeruginosa_env345_6600***	GCF_002326355.1	No	Environment	Other environmental source	18	65	6	22	7	485
PA1266	***Pseudomonas_aeruginosa_env396a_6828***	GCF_002326345.1	Yes	Environment	Clinical environment: Dental, Hospital	14		2	16	2	111
PA1267	***Pseudomonas_aeruginosa_env396b_6532***	GCF_002330125.1	Yes	Environment	Clinical environment: Dental, Hospital	18		9	22	12	348
PA1268	***Pseudomonas_aeruginosa_env406b_6148***	GCF_002326585.1	No	Environment	Clinical environment: Dental, Hospital	15	32	12	23	12	244
PA1269	***Pseudomonas_aeruginosa_env408_7331***	GCF_002330505.1	No	Environment	Clinical environment: Dental, Hospital	1	103	12	2	4	253
PA1270	***Pseudomonas_aeruginosa_ENVO281_11902***	GCF_006704735.1	No	Environment	Other environmental source	2	39	10	5	10	446
PA1271	***Pseudomonas_aeruginosa_ENVO304_11900***	GCF_006704685.1	Yes	Environment	Other environmental source	2		10	5	10	446
PA1272	***Pseudomonas_aeruginosa_EPIC_E151_11926***	GCF_006864645.1	No	Clinical	Cystic fibrosis	13	50	9	10	12	27
PA1273	***Pseudomonas_aeruginosa_EPIC_E197_11924***	GCF_006864505.1	No	Clinical	Cystic fibrosis	18	78	13	19	11	514
PA1274	***Pseudomonas_aeruginosa_EPIC_E54_11927***	GCF_006864715.1	No	Clinical	Cystic fibrosis	18	83	11	19	14	527
PA1275	***Pseudomonas_aeruginosa_ER06896_9942***	GCF_003703685.1	No	Clinical	Respiratory tract	19	43	8	18	9	1182
PA1276	***Pseudomonas_aeruginosa_ET02_3996***	GCF_001679905.1	No	Clinical	Gastrointestinal	19	58	13	21	11	2343
PA1277	***Pseudomonas_aeruginosa_F1_DN_2_9962***	GCF_003833465.1	Yes	Environment	Farm environment	16		11	17	14	Undefined
PA1278	***Pseudomonas_aeruginosa_F22031_3096***	GCF_000816985.1	No	Clinical	Bone and Joint	18	64	6	22	7	485
PA1279	***Pseudomonas_aeruginosa_F23197_6110***	GCF_001516245.2	No	Clinical	Cancer	18	81	12	19	11	1295
PA1280	***Pseudomonas_aeruginosa_F34365_6529***	GCF_002724075.1	No	Clinical	Urinary tract	19	57	10	21	10	1076
PA1281	***Pseudomonas_aeruginosa_F462_isolate_CPHL9433_9936***	GCF_003698765.1	No	Environment	Plants	19	54	8	18	9	1920
PA1282	***Pseudomonas_aeruginosa_F5677_6730***	GCF_002946935.1	Yes	Clinical	Cancer	14		2	16	2	111
PA1283	***Pseudomonas_aeruginosa_F63912_7033***	GCF_001594325.2	No	Clinical	Cancer	18	77	9	19	12	198

PA1284	***Pseudomonas_aeruginosa_F9676_2900***	GCF_001077475.1	No	Environment	Plants	18	97	9	19	5	Undefined
PA1285	***Pseudomonas_aeruginosa_FA_HZ1_4011***	GCF_001750705.1	No	Environment	Sewage/Wastewater	13	50	9	10	12	27
PA1286	***Pseudomonas_aeruginosa_FA0A_isolate_Pr335_9938***	GCF_003698795.1	Yes	Environment	Clinical environment: Dental, Hospital	13		9	10	12	27
PA1287	***Pseudomonas_aeruginosa_FDAARGOS_121_6903***	GCF_001471435.1	No	Clinical	Urinary tract	19	51	10	21	10	620
PA1288	***Pseudomonas_aeruginosa_FDAARGOS_505_9955***	GCF_003813005.1	Yes	Clinical	Respiratory tract	16		11	17	14	179
PA1289	***Pseudomonas_aeruginosa_FDAARGOS_532_9952***	GCF_003812165.1	No	Clinical	Respiratory tract	16	5	11	17	14	179
PA1290	***Pseudomonas_aeruginosa_FDAARGOS_610_11151***	GCF_006364795.1	No	Environment	Clinical environment: Dental, Hospital	11	30	11	13	14	252
PA1291	***Pseudomonas_aeruginosa_FFUP_PS_105_6288***	GCF_002188565.1	No	Clinical	Urinary tract	14	52	2	16	2	111
PA1292	***Pseudomonas_aeruginosa_FFUP_PS_144_6558***	GCF_002188535.1	No	Clinical	Urinary tract	16	5	11	17	14	179
PA1293	***Pseudomonas_aeruginosa_FFUP_PS_35_7170***	GCF_002188585.1	Yes	Clinical	Urinary tract	16		11	17	14	179
PA1294	***Pseudomonas_aeruginosa_FFUP_PS_65_7206***	GCF_002188695.1	No	Clinical	Urinary tract	15	32	12	23	12	244
PA1295	***Pseudomonas_aeruginosa_FFUP_PS_690_6970***	GCF_002189115.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA1296	***Pseudomonas_aeruginosa_FFUP_PS_CB5_5766***	GCF_002188505.1	No	Clinical	Respiratory tract	3	6	10	4	10	235
PA1297	***Pseudomonas_aeruginosa_FFUP_PS_CB58_6518***	GCF_002188645.1	No	Clinical	Urinary tract	18	17	13	19	12	282
PA1298	***Pseudomonas_aeruginosa_FMDP001_11958***	GCF_007896855.1	No	Clinical	Respiratory tract	19	102	8	18	9	1249
PA1299	***Pseudomonas_aeruginosa_FRD1_2621***	GCF_000829885.1	No	Clinical	Cystic fibrosis	14	52	2	16	2	111
PA1300	***Pseudomonas_aeruginosa_FRD1_2624***	GCF_000950725.1	No	Clinical	Cystic fibrosis	14	52	2	16	2	111
PA1301	***Pseudomonas_aeruginosa_G1_WATER_2A_9985***	GCF_003833935.1	No	Environment	Farm environment	19	102	8	21	9	1567
PA1302	***Pseudomonas_aeruginosa_G2_10039***	GCF_003835015.1	No	Clinical	Cystic fibrosis	2	39	10	5	10	446
PA1303	***Pseudomonas_aeruginosa_GCID_CRE_0006_10685***	GCF_003977535.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA1304	***Pseudomonas_aeruginosa_GER_MD14_1510_Pae_083_7332***	GCF_003321505.1	No	Environment	Animal	18	102	13	19	11	Undefined
PA1305	***Pseudomonas_aeruginosa_GIMC5015:PAKB6_10430***	GCF_003957825.1	No	Clinical	Respiratory tract	18	32	12	19	12	549
PA1306	***Pseudomonas_aeruginosa_GOM1_11921***	GCF_006802095.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	7	9	19	12	Undefined
PA1307	***Pseudomonas_aeruginosa_H1I_2007***	GCF_000633495.1	No	Environment	Plants	18	78	13	19	12	508
PA1308	***Pseudomonas_aeruginosa_H2_10573***	GCF_003974715.1	No	Clinical	Urinary tract	18	62	9	19	12	1858
PA1309	***Pseudomonas_aeruginosa_H25883_9950***	GCF_003798125.1	No	Clinical	Burn	19	102	10	21	10	1076
PA1310	***Pseudomonas_aeruginosa_H26023_9951***	GCF_003798145.1	No	Clinical	Respiratory tract	1	103	12	2	4	253
PA1311	***Pseudomonas_aeruginosa_H26027_9949***	GCF_003798105.1	No	Clinical	Burn	9	11	9	11	5	17
PA1312	***Pseudomonas_aeruginosa_H27930_5910***	GCF_001516325.2	No	Clinical	Cancer	18	65	6	22	7	389

PA1313	***Pseudomonas_aeruginosa_H5708_6745***	GCF_001516305.2	No	Clinical	Cancer	18	76	6	19	7	3050
PA1314	***Pseudomonas_aeruginosa_HB15_307***	GCF_000215795.4	No	Clinical	Respiratory tract	19	27	12	21	4	560
PA1315	***Pseudomonas_aeruginosa_HB159_10062***	GCF_003835485.1	Yes	Clinical	Urinary tract	15		12	23	12	244
PA1316	***Pseudomonas_aeruginosa_HB392_9983***	GCF_003833905.1	Yes	Clinical	Urinary tract	15		12	23	12	244
PA1317	***Pseudomonas_aeruginosa_HCF100_10566***	GCF_003974575.1	Yes	Clinical	Cystic fibrosis	18		13	19	12	275
PA1318	***Pseudomonas_aeruginosa_HCF19_10544***	GCF_003974115.1	No	Clinical	Cystic fibrosis	18	102	8	19	12	3501
PA1319	***Pseudomonas_aeruginosa_HCF331_10538***	GCF_003973995.1	No	Clinical	Cystic fibrosis	18	78	9	19	12	3697
PA1320	***Pseudomonas_aeruginosa_HCF336_10539***	GCF_003974025.1	No	Clinical	Cystic fibrosis	16	5	11	17	14	155
PA1321	***Pseudomonas_aeruginosa_HCF410_10537***	GCF_003973985.1	No	Clinical	Cystic fibrosis	18	93	13	20	12	Undefined
PA1322	***Pseudomonas_aeruginosa_HCF5_10540***	GCF_003974035.1	No	Clinical	Cystic fibrosis	18	23	13	19	11	Undefined
PA1323	***Pseudomonas_aeruginosa_HCF55_10542***	GCF_003974085.1	No	Clinical	Cystic fibrosis	18	95	8	19	12	172
PA1324	***Pseudomonas_aeruginosa_HCF591_10563***	GCF_003974515.1	No	Clinical	Cystic fibrosis	18	95	12	19	12	Undefined
PA1325	***Pseudomonas_aeruginosa_HCF73_10536***	GCF_003973925.1	Yes	Clinical	Cystic fibrosis	12		1	14	1	395
PA1326	***Pseudomonas_aeruginosa_Hex1T_9517***	GCF_001469435.2	No	Environment	Soil: Manure, Rocks, Sand, Soil	19	8	12	21	4	377
PA1327	***Pseudomonas_aeruginosa_HIAE_PA01_7214***	GCF_003071265.1	No	Clinical	Bacteraemia	18	102	12	19	12	455
PA1328	***Pseudomonas_aeruginosa_HIAE_PA02_6980***	GCF_003055405.1	No	Clinical	Bacteraemia	18	32	13	19	12	381
PA1329	***Pseudomonas_aeruginosa_HIAE_PA05_6966***	GCF_003055585.1	No	Clinical	Bacteraemia	11	49	11	13	14	498
PA1330	***Pseudomonas_aeruginosa_HIAE_PA06_6607***	GCF_003055385.1	No	Clinical	Bacteraemia	18	97	9	19	5	231
PA1331	***Pseudomonas_aeruginosa_HIAE_PA07_6400***	GCF_003055555.1	No	Clinical	Bacteraemia	11	49	11	13	14	252
PA1332	***Pseudomonas_aeruginosa_HIAE_PA08_7210***	GCF_003055325.1	No	Clinical	Respiratory tract	19	102	8	18	9	3573
PA1333	***Pseudomonas_aeruginosa_HIAE_PA09_7098***	GCF_003055265.1	No	Clinical	Bacteraemia	17	22	6	15	7	245
PA1334	***Pseudomonas_aeruginosa_HIAE_PA10_6708***	GCF_003055545.1	No	Clinical	Respiratory tract	18	102	12	19	12	2235
PA1335	***Pseudomonas_aeruginosa_HIAE_PA11_7139***	GCF_003055235.1	No	Clinical	Respiratory tract	15	18	12	23	12	244
PA1336	***Pseudomonas_aeruginosa_HIAE_PA12_6187***	GCF_003055525.1	No	Clinical	Bacteraemia	19	54	8	18	9	10
PA1337	***Pseudomonas_aeruginosa_HIAE_PA13_6929***	GCF_003055275.1	No	Clinical	Bacteraemia	15	32	12	23	12	244
PA1338	***Pseudomonas_aeruginosa_HIAE_PA14_6071***	GCF_003055505.1	No	Clinical	Respiratory tract	18	97	8	19	13	1290
PA1339	***Pseudomonas_aeruginosa_HIAE_PA15_7025***	GCF_003055465.1	No	Clinical	Bacteraemia	18	86	13	19	11	1993
PA1340	***Pseudomonas_aeruginosa_HIAE_PA16_6967***	GCF_003055425.1	No	Clinical	Respiratory tract	19	3	12	20	4	606
PA1341	***Pseudomonas_aeruginosa_HIAE_PA17_6826***	GCF_003055485.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA1342	***Pseudomonas_aeruginosa_HIAE_PA18_6603***	GCF_003055445.1	No	Clinical	Respiratory tract	18	4	9	22	12	348

PA1343	***Pseudomonas_aeruginosa_HIAE_PA19_6880***	GCF_003055365.1	No	Clinical	Respiratory tract	3	6	10	4	10	235
PA1344	***Pseudomonas_aeruginosa_HIAE_PA20_7268***	GCF_003055345.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA1345	***Pseudomonas_aeruginosa_HIAE_PA21_6787***	GCF_003055295.1	No	Clinical	Respiratory tract	1	103	12	2	4	253
PA1346	***Pseudomonas_aeruginosa_HIAE_PA22_6225***	GCF_003055225.1	No	Clinical	Body fluid	18	81	12	19	11	190
PA1347	***Pseudomonas_aeruginosa_HJ2_10552***	GCF_003974295.1	Yes	Clinical	Cystic fibrosis	12		1	14	1	395
PA1348	***Pseudomonas_aeruginosa_HM293_10058***	GCF_003835395.1	Yes	Clinical	Cancer	13		9	10	12	27
PA1349	***Pseudomonas_aeruginosa_HM294_10021***	GCF_003834655.1	Yes	Clinical	Cancer	13		9	10	12	27
PA1350	***Pseudomonas_aeruginosa_HM299_10020***	GCF_003834645.1	Yes	Clinical	Cancer	13			10		27
PA1351	***Pseudomonas_aeruginosa_HM300_10017***	GCF_003834585.1	Yes	Clinical	Cancer	13		9	10	12	27
PA1352	***Pseudomonas_aeruginosa_HM301_10016***	GCF_003834565.1	Yes	Clinical	Cancer	13		9	10	12	27
PA1353	***Pseudomonas_aeruginosa_HM306_10019***	GCF_003834615.1	Yes	Clinical	Cancer	13			10		27
PA1354	***Pseudomonas_aeruginosa_HM307_10018***	GCF_003834605.1	Yes	Clinical	Cancer	13		9	10	12	27
PA1355	***Pseudomonas_aeruginosa_HM308_9984***	GCF_003833925.1	Yes	Clinical	Cancer	13		9	10	12	27
PA1356	***Pseudomonas_aeruginosa_HM324_10014***	GCF_003834525.1	Yes	Clinical	Cancer	13		9	10	12	Undefined
PA1357	***Pseudomonas_aeruginosa_HOU1_11979***	GCF_008245185.1	No	Clinical	Cystic fibrosis	18	80	9	19	12	2855
PA1358	***Pseudomonas_aeruginosa_HUM_242_9853***	GCF_003632635.1	No	Clinical	Ear	6	1	8	9	9	1714
PA1359	***Pseudomonas_aeruginosa_IC1_10168***	GCF_003837605.1	No	Environment	Animal	18	70	12	19	12	Undefined
PA1360	***Pseudomonas_aeruginosa_ICBSVIM_2_7277***	GCF_002351425.1	No	Environment	Home environment	18	84	12	20	11	233
PA1361	***Pseudomonas_aeruginosa_ID4365_2504***	GCF_000647615.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	28	12	21	4	560
PA1362	***Pseudomonas_aeruginosa_IDEXX_Canine4_10126***	GCF_003836765.1	No	Environment	Animal	1	103	12	2	4	253
PA1363	***Pseudomonas_aeruginosa_IDEXX_Canine8_10123***	GCF_003836705.1	No	Environment	Animal	7	15	7	7	8	Undefined
PA1364	***Pseudomonas_aeruginosa_IGB83_2077***	GCF_000647635.1	No	Environment	Plants	18	33	12	19	11	183
PA1365	***Pseudomonas_aeruginosa_IMP_13_10390***	GCF_003950015.1	No	Clinical	Urinary tract	18	81	13	20	12	621
PA1366	***Pseudomonas_aeruginosa_IMP66_11969***	GCF_008033765.1	Yes	Environment	Hydrocarbon contamination	18		9	19	5	132
PA1367	***Pseudomonas_aeruginosa_IMP67_11967***	GCF_008033725.1	Yes	Environment	Hydrocarbon contamination	18		9	19	5	132
PA1368	***Pseudomonas_aeruginosa_IMP68_11968***	GCF_008033745.1	No	Environment	Hydrocarbon contamination	18	86	9	19	5	132
PA1369	***Pseudomonas_aeruginosa_INP_43_12123***	GCF_009905195.1	No	Clinical	Cystic fibrosis	18	74	13	19	11	Undefined
PA1370	***Pseudomonas_aeruginosa_IOMTU_133_3923***	GCF_001548335.1	No	Clinical	Respiratory tract	19	8	12	21	4	1047
PA1371	***Pseudomonas_aeruginosa_isolate_141_5360***	GCF_900147755.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	845
PA1372	***Pseudomonas_aeruginosa_isolate_15111a_3232***	GCF_001374055.1	Yes	Environment	Industrial	14		2	16	2	111

PA1373	***Pseudomonas_aeruginosa_isolate_15111b_3243***	GCF_001374275.1	Yes	Environment	Industrial	14		2	16	2	111
PA1374	***Pseudomonas_aeruginosa_isolate_15111c_3303***	GCF_001375455.1	Yes	Environment	Industrial	1		12	2	4	253
PA1375	***Pseudomonas_aeruginosa_isolate_15121a_3258***	GCF_001374575.1	Yes	Environment	Industrial	1		12	2	4	253
PA1376	***Pseudomonas_aeruginosa_isolate_15121b_3270***	GCF_001374815.1	Yes	Environment	Industrial	1		12	2	4	253
PA1377	***Pseudomonas_aeruginosa_isolate_15121c_3220***	GCF_001373815.1	Yes	Environment	Industrial	1		12	2	4	253
PA1378	***Pseudomonas_aeruginosa_isolate_15211_Gb_3287***	GCF_001375135.1	Yes	Environment	Industrial	1		12	2	4	253
PA1379	***Pseudomonas_aeruginosa_isolate_15211Ba_3244***	GCF_001374295.1	No	Environment	Industrial	15	32	12	23	12	244
PA1380	***Pseudomonas_aeruginosa_isolate_15211Bb_3304***	GCF_001375475.1	Yes	Environment	Industrial	1		12	2	4	253
PA1381	***Pseudomonas_aeruginosa_isolate_15211Ga_3229***	GCF_001373995.1	Yes	Environment	Industrial	1		12	2	4	253
PA1382	***Pseudomonas_aeruginosa_isolate_15211Gc_3233***	GCF_001374075.1	Yes	Environment	Industrial	19		8	18	9	2729
PA1383	***Pseudomonas_aeruginosa_isolate_15221Ba_3271***	GCF_001374835.1	Yes	Environment	Industrial	1		12	2	4	253
PA1384	***Pseudomonas_aeruginosa_isolate_15221Ga_3259***	GCF_001374595.1	No	Environment	Industrial	1	103	12	2	4	253
PA1385	***Pseudomonas_aeruginosa_isolate_15311Ba_3288***	GCF_001375155.1	Yes	Environment	Industrial	1		12	2	4	253
PA1386	***Pseudomonas_aeruginosa_isolate_15311Bb_3231***	GCF_001374035.1	Yes	Environment	Industrial	18		13	19	12	2730
PA1387	***Pseudomonas_aeruginosa_isolate_15311Ga_3221***	GCF_001373835.1	Yes	Environment	Industrial	1		12	2	4	253
PA1388	***Pseudomonas_aeruginosa_isolate_15311Gb_3230***	GCF_001374015.1	Yes	Environment	Industrial	1		12	2	4	253
PA1389	***Pseudomonas_aeruginosa_isolate_15321Ba_3260***	GCF_001374615.1	Yes	Environment	Industrial	1		12	2	4	253
PA1390	***Pseudomonas_aeruginosa_isolate_15321Bb_3272***	GCF_001374855.1	Yes	Environment	Industrial	1		12	2	4	253
PA1391	***Pseudomonas_aeruginosa_isolate_15321Ga_3245***	GCF_001374315.1	No	Environment	Industrial	11	30	11	13	14	252
PA1392	***Pseudomonas_aeruginosa_isolate_15321Gb_3250***	GCF_001374415.1	Yes	Environment	Industrial	1		12	2	4	253
PA1393	***Pseudomonas_aeruginosa_isolate_157_5547***	GCF_900144995.1	Yes	Clinical	Cystic fibrosis	1		12	2	4	253
PA1394	***Pseudomonas_aeruginosa_isolate_1611_5546***	GCF_900147795.1	Yes	Clinical	Cystic fibrosis	1		12	2	4	253
PA1395	***Pseudomonas_aeruginosa_isolate_18_5486***	GCF_900143795.1	No	Clinical	Cystic fibrosis	18	90	13	19	12	2604
PA1396	***Pseudomonas_aeruginosa_isolate_191_5198***	GCF_900145335.1	No	Clinical	Cystic fibrosis	19	61	10	21	10	207
PA1397	***Pseudomonas_aeruginosa_isolate_192_5103***	GCF_900145345.1	No	Clinical	Cystic fibrosis	19	61	10	21	10	207
PA1398	***Pseudomonas_aeruginosa_isolate_195_5167***	GCF_900145365.1	No	Clinical	Cystic fibrosis	18	32	13	19	12	381
PA1399	***Pseudomonas_aeruginosa_isolate_204_5634***	GCF_900145465.1	Yes	Clinical	Cystic fibrosis	18		6	19	7	709
PA1400	***Pseudomonas_aeruginosa_isolate_206_4971***	GCF_900145485.1	No	Clinical	Cystic fibrosis	18	69	13	19	11	676
PA1401	***Pseudomonas_aeruginosa_isolate_207_5292***	GCF_900145495.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	676
PA1402	***Pseudomonas_aeruginosa_isolate_209_5145***	GCF_900145515.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	676

PA1403	***Pseudomonas_aeruginosa_isolate_212_5533***	GCF_900145545.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	676
PA1404	***Pseudomonas_aeruginosa_isolate_214_5172***	GCF_900145565.1	No	Clinical	Cystic fibrosis	18	22	6	19	7	709
PA1405	***Pseudomonas_aeruginosa_isolate_215_5543***	GCF_900145575.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	676
PA1406	***Pseudomonas_aeruginosa_isolate_216_5110***	GCF_900145585.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	2670
PA1407	***Pseudomonas_aeruginosa_isolate_219_5393***	GCF_900145625.1	No	Clinical	Cystic fibrosis	18	86	13	19	11	2670
PA1408	***Pseudomonas_aeruginosa_isolate_224_5610***	GCF_900145665.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	132
PA1409	***Pseudomonas_aeruginosa_isolate_225_4981***	GCF_900145675.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	132
PA1410	***Pseudomonas_aeruginosa_isolate_226_5592***	GCF_900145685.1	No	Clinical	Cystic fibrosis	18	86	9	19	5	132
PA1411	***Pseudomonas_aeruginosa_isolate_228_5469***	GCF_900145705.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	132
PA1412	***Pseudomonas_aeruginosa_isolate_237_5440***	GCF_900145745.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	132
PA1413	***Pseudomonas_aeruginosa_isolate_239_5146***	GCF_900145735.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	132
PA1414	***Pseudomonas_aeruginosa_isolate_240_5453***	GCF_900145755.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	132
PA1415	***Pseudomonas_aeruginosa_isolate_241_5371***	GCF_900145765.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	132
PA1416	***Pseudomonas_aeruginosa_isolate_247_5407***	GCF_900145825.1	No	Clinical	Cystic fibrosis	18	86	9	19	5	132
PA1417	***Pseudomonas_aeruginosa_isolate_25_5463***	GCF_900144115.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	845
PA1418	***Pseudomonas_aeruginosa_isolate_256_5317***	GCF_900145875.1	No	Clinical	Typhoid fever	16	5	11	20	14	179
PA1419	***Pseudomonas_aeruginosa_isolate_257_5408***	GCF_900145885.1	Yes	Clinical	Typhoid fever	16		11	20	14	179
PA1420	***Pseudomonas_aeruginosa_isolate_258_5007***	GCF_900145895.1	Yes	Clinical	Typhoid fever	16		11	20	14	179
PA1421	***Pseudomonas_aeruginosa_isolate_259_5031***	GCF_900145905.1	Yes	Clinical	Typhoid fever	16		11	20	14	179
PA1422	***Pseudomonas_aeruginosa_isolate_2591_4949***	GCF_900147865.1	Yes	Clinical	Typhoid fever	16		11	20	14	179
PA1423	***Pseudomonas_aeruginosa_isolate_260_5738***	GCF_900145915.1	No	Clinical	Typhoid fever	16	5	11	20	14	179
PA1424	***Pseudomonas_aeruginosa_isolate_262_5242***	GCF_900145935.1	Yes	Clinical	Typhoid fever	16		11	20	14	179
PA1425	***Pseudomonas_aeruginosa_isolate_264_5701***	GCF_900145945.1	Yes	Clinical	Typhoid fever	16		11	20	14	179
PA1426	***Pseudomonas_aeruginosa_isolate_265_5029***	GCF_900145955.1	Yes	Clinical	Typhoid fever	16		11	20	14	179
PA1427	***Pseudomonas_aeruginosa_isolate_266_5060***	GCF_900145965.1	No	Clinical	Typhoid fever	16	5	11	20	14	179
PA1428	***Pseudomonas_aeruginosa_isolate_267_5430***	GCF_900145985.1	No	Clinical	Typhoid fever	13	50	9	10	12	27
PA1429	***Pseudomonas_aeruginosa_isolate_268_5704***	GCF_900145995.1	Yes	Clinical	Typhoid fever	13		9	10	12	27
PA1430	***Pseudomonas_aeruginosa_isolate_269_4968***	GCF_900145975.1	No	Clinical	Typhoid fever	13	50	9	10	12	27
PA1431	***Pseudomonas_aeruginosa_isolate_27_5707***	GCF_900143925.1	No	Clinical	Typhoid fever	18	68	13	19	11	291
PA1432	***Pseudomonas_aeruginosa_isolate_270_5626***	GCF_900146005.1	Yes	Clinical	Typhoid fever	13		9	10	12	27

PA1433	***Pseudomonas_aeruginosa_isolate_271_5336***	GCF_900146015.1	Yes	Clinical	Typhoid fever	13		9	10	12	27
PA1434	***Pseudomonas_aeruginosa_isolate_301_4967***	GCF_900146315.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	17
PA1435	***Pseudomonas_aeruginosa_isolate_304_5178***	GCF_900146345.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA1436	***Pseudomonas_aeruginosa_isolate_305_5579***	GCF_900146365.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	17
PA1437	***Pseudomonas_aeruginosa_isolate_307_5055***	GCF_900146375.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA1438	***Pseudomonas_aeruginosa_isolate_315_5340***	GCF_900146445.1	No	Clinical	Cystic fibrosis	19	28	8	21	4	560
PA1439	***Pseudomonas_aeruginosa_isolate_323_5480***	GCF_900146525.1	No	Clinical	Cystic fibrosis	3	6	10	4	10	235
PA1440	***Pseudomonas_aeruginosa_isolate_325_5584***	GCF_900146545.1	No	Clinical	Cystic fibrosis	12	2	1	14	1	395
PA1441	***Pseudomonas_aeruginosa_isolate_33_5570***	GCF_900144225.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	845
PA1442	***Pseudomonas_aeruginosa_isolate_330_5366***	GCF_900146585.1	Yes	Clinical	Cystic fibrosis	18		5	19	6	2677
PA1443	***Pseudomonas_aeruginosa_isolate_333_5520***	GCF_900146615.1	Yes	Clinical	Cystic fibrosis	18		5	19	6	2677
PA1444	***Pseudomonas_aeruginosa_isolate_334_5142***	GCF_900146625.1	Yes	Clinical	Cystic fibrosis	18		5	19	6	2677
PA1445	***Pseudomonas_aeruginosa_isolate_335_5332***	GCF_900146635.1	No	Clinical	Cystic fibrosis	18	78	5	19	6	2677
PA1446	***Pseudomonas_aeruginosa_isolate_336_5037***	GCF_900146645.1	Yes	Clinical	Cystic fibrosis	18		5	19	6	2677
PA1447	***Pseudomonas_aeruginosa_isolate_337_4955***	GCF_900146655.1	Yes	Clinical	Cystic fibrosis	18		5	19	6	2677
PA1448	***Pseudomonas_aeruginosa_isolate_339_5082***	GCF_900146675.1	No	Clinical	Cystic fibrosis	19	39	10	1	12	2555
PA1449	***Pseudomonas_aeruginosa_isolate_34_6533***	GCF_900143785.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	845
PA1450	***Pseudomonas_aeruginosa_isolate_346_5025***	GCF_900146745.1	Yes	Clinical	Cystic fibrosis	1		12	2	4	253
PA1451	***Pseudomonas_aeruginosa_isolate_347_4947***	GCF_900146755.1	Yes	Clinical	Cystic fibrosis	1		12	2	4	253
PA1452	***Pseudomonas_aeruginosa_isolate_348_5438***	GCF_900146765.1	No	Clinical	Cystic fibrosis	1	103	12	2	4	253
PA1453	***Pseudomonas_aeruginosa_isolate_351_5667***	GCF_900146785.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA1454	***Pseudomonas_aeruginosa_isolate_353_5464***	GCF_900146805.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA1455	***Pseudomonas_aeruginosa_isolate_355_5365***	GCF_900146825.1	No	Clinical	Cystic fibrosis	18	72	13	19	10	2684
PA1456	***Pseudomonas_aeruginosa_isolate_356_5210***	GCF_900146835.1	No	Clinical	Cystic fibrosis	11	49	11	13	14	Undefined
PA1457	***Pseudomonas_aeruginosa_isolate_359_5425***	GCF_900146865.1	Yes	Clinical	Cystic fibrosis	18		12	19	4	2584
PA1458	***Pseudomonas_aeruginosa_isolate_36_5046***	GCF_900143815.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	845
PA1459	***Pseudomonas_aeruginosa_isolate_362_5156***	GCF_900146895.1	Yes	Clinical	Cystic fibrosis	18		12	19	4	2584
PA1460	***Pseudomonas_aeruginosa_isolate_363_5591***	GCF_900146905.1	Yes	Clinical	Cystic fibrosis	18		12	19	4	2584
PA1461	***Pseudomonas_aeruginosa_isolate_364_5161***	GCF_900146945.1	Yes	Clinical	Cystic fibrosis	18		12	19	4	2584
PA1462	***Pseudomonas_aeruginosa_isolate_365_5625***	GCF_900146915.1	No	Clinical	Cystic fibrosis	18	86	12	19	4	2584

PA1463	***Pseudomonas_aeruginosa_isolate_370_4980***	GCF_900146965.1	Yes	Clinical	Cystic fibrosis	18		9	19	12	1455
PA1464	***Pseudomonas_aeruginosa_isolate_371_5735***	GCF_900146985.1	No	Clinical	Cystic fibrosis	18	102	9	19	12	1455
PA1465	***Pseudomonas_aeruginosa_isolate_374_5665***	GCF_900147015.1	No	Clinical	Cystic fibrosis	18	86	12	19	4	2584
PA1466	***Pseudomonas_aeruginosa_isolate_375_4972***	GCF_900147035.1	Yes	Clinical	Cystic fibrosis	18		12	19	4	2584
PA1467	***Pseudomonas_aeruginosa_isolate_377_5158***	GCF_900147025.1	Yes	Clinical	Cystic fibrosis	18		12	19	4	2584
PA1468	***Pseudomonas_aeruginosa_isolate_378_5505***	GCF_900147045.1	Yes	Clinical	Cystic fibrosis	18		12	19	4	2584
PA1469	***Pseudomonas_aeruginosa_isolate_383_5465***	GCF_900147095.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	27
PA1470	***Pseudomonas_aeruginosa_isolate_384_5750***	GCF_900147105.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	27
PA1471	***Pseudomonas_aeruginosa_isolate_385_5556***	GCF_900147115.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	27
PA1472	***Pseudomonas_aeruginosa_isolate_396_5131***	GCF_900147225.1	No	Clinical	Cystic fibrosis	18	99	5	19	6	2685
PA1473	***Pseudomonas_aeruginosa_isolate_426_5637***	GCF_900147535.1	No	Clinical	Cystic fibrosis	18	74	8	19	12	809
PA1474	***Pseudomonas_aeruginosa_isolate_432_5426***	GCF_900147585.1	No	Clinical	Cystic fibrosis	18	78	13	19	11	Undefined
PA1475	***Pseudomonas_aeruginosa_isolate_601_5355***	GCF_900148005.1	No	Clinical	Cystic fibrosis	10	78	5	12	6	1068
PA1476	***Pseudomonas_aeruginosa_isolate_61_4958***	GCF_900143965.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	1068
PA1477	***Pseudomonas_aeruginosa_isolate_85_5297***	GCF_900144255.1	Yes	Clinical	Cystic fibrosis	19		8	18	9	1822
PA1478	***Pseudomonas_aeruginosa_isolate_91_4974***	GCF_900144335.1	No	Clinical	Cystic fibrosis	19	54	8	18	9	1822
PA1479	***Pseudomonas_aeruginosa_isolate_92_5054***	GCF_900144345.1	No	Clinical	Cystic fibrosis	18	74	13	19	11	160
PA1480	***Pseudomonas_aeruginosa_isolate_96_5552***	GCF_900144385.1	Yes	Clinical	Cystic fibrosis	18		13	19	12	381
PA1481	***Pseudomonas_aeruginosa_isolate_97_5650***	GCF_900144395.1	Yes	Clinical	Cystic fibrosis	18		13	19	12	381
PA1482	***Pseudomonas_aeruginosa_isolate_ATCC_12903_3251***	GCF_001374435.1	Yes	Environment	Industrial	1		12	2	4	253
PA1483	***Pseudomonas_aeruginosa_isolate_ATCC_13388_3213***	GCF_001373675.1	Yes	Environment	Industrial	1		12	2	4	253
PA1484	***Pseudomonas_aeruginosa_isolate_ATCC_15442_3225***	GCF_001373915.1	Yes	Environment	Industrial	1		12	2	4	253
PA1485	***Pseudomonas_aeruginosa_isolate_ATCC_9027_3278***	GCF_001374975.1	Yes	Environment	Industrial	1		12	2	4	253
PA1486	***Pseudomonas_aeruginosa_isolate_B10W_5627***	GCF_001874465.1	No	Environment	Sewage/Wastewater	4	14	10	3	10	308
PA1487	***Pseudomonas_aeruginosa_isolate_blood_11325***	GCF_901010245.1	No	Clinical	Bacteraemia	18	71	9	19	12	3556
PA1488	***Pseudomonas_aeruginosa_isolate_early_isolate_NN2_clone_C_6774***	GCF_900185255.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	17
PA1489	***Pseudomonas_aeruginosa_isolate_F30658_3634***	GCF_001516265.1	Yes	Clinical	Cancer	14		2	16	2	111
PA1490	***Pseudomonas_aeruginosa_isolate_F9670_3848***	GCF_001542835.1	No	Clinical	Cancer	16	5	11	17	14	155
PA1491	***Pseudomonas_aeruginosa_isolate_H47921_3637***	GCF_001516345.1	No	Clinical	Cancer	18	3	12	19	12	1105
PA1492	***Pseudomonas_aeruginosa_isolate_LRJ19_5155***	GCF_900148305.1	No	Clinical	Cystic fibrosis	18	32	13	19	12	381

PA1493	***Pseudomonas_aeruginosa_isolate_M37351_3639***	GCF_001516385.1	No	Clinical	Cancer	1	103	12	2	4	253
PA1494	***Pseudomonas_aeruginosa_isolate_MGYG_HGUT_02463_12170***	GCF_902387405.1	No	Clinical	Gastrointestinal	19	51	13	21	11	2343
PA1495	***Pseudomonas_aeruginosa_isolate_PA14_4012***	GCF_900005845.1	Yes	Environment	Industrial	1		12	2	4	253
PA1496	***Pseudomonas_aeruginosa_isolate_PcyII_10_5293***	GCF_900149285.1	No	Clinical	Burn	18	97	11	19	14	1233
PA1497	***Pseudomonas_aeruginosa_isolate_RN21_2717***	GCF_001028745.1	No	Clinical	Urinary tract	12	2	1	14	1	395
PA1498	***Pseudomonas_aeruginosa_isolate_RW109_3290***	GCF_001375195.1	Yes	Environment	Industrial	1		12	2	4	253
PA1499	***Pseudomonas_aeruginosa_isolate_RW110_3235***	GCF_001374115.1	No	Environment	Industrial	14	102	2	16	2	111
PA1500	***Pseudomonas_aeruginosa_isolate_RW130_3247***	GCF_001374355.1	No	Environment	Industrial	18	102	9	19	12	641
PA1501	***Pseudomonas_aeruginosa_isolate_RW131_3252***	GCF_001374455.1	Yes	Environment	Industrial	1		12	2	4	253
PA1502	***Pseudomonas_aeruginosa_isolate_RW138_3262***	GCF_001374655.1	Yes	Environment	Industrial	1		12	2	4	253
PA1503	***Pseudomonas_aeruginosa_isolate_RW146_3212***	GCF_001373655.1	Yes	Environment	Industrial	1		12	2	4	253
PA1504	***Pseudomonas_aeruginosa_isolate_RW149_3224***	GCF_001373895.1	Yes	Environment	Industrial	1		12	2	4	253
PA1505	***Pseudomonas_aeruginosa_isolate_RW168_3291***	GCF_001375215.1	Yes	Environment	Industrial	1		12	2	4	253
PA1506	***Pseudomonas_aeruginosa_isolate_RW172_3236***	GCF_001374135.1	Yes	Environment	Industrial	18		13	19	12	2730
PA1507	***Pseudomonas_aeruginosa_isolate_RW176_3248***	GCF_001374375.1	No	Environment	Industrial	19	54	8	18	9	2729
PA1508	***Pseudomonas_aeruginosa_isolate_RW18_3261***	GCF_001374635.1	Yes	Environment	Industrial	1		12	2	4	253
PA1509	***Pseudomonas_aeruginosa_isolate_RW184_3209***	GCF_001373595.1	Yes	Environment	Industrial	1		12	2	4	253
PA1510	***Pseudomonas_aeruginosa_isolate_RW192_3263***	GCF_001374675.1	Yes	Environment	Industrial	1		12	2	4	253
PA1511	***Pseudomonas_aeruginosa_isolate_RW199_3279***	GCF_001374995.1	Yes	Environment	Industrial	1		12	2	4	253
PA1512	***Pseudomonas_aeruginosa_isolate_RW200_3292***	GCF_001375235.1	Yes	Environment	Industrial	1		12	2	4	253
PA1513	***Pseudomonas_aeruginosa_isolate_RW202_3237***	GCF_001374155.1	No	Environment	Industrial	18	66	9	19	12	1342
PA1514	***Pseudomonas_aeruginosa_isolate_RW204_3249***	GCF_001374395.1	No	Environment	Industrial	18	68	13	19	13	645
PA1515	***Pseudomonas_aeruginosa_isolate_RW27_3211***	GCF_001373635.1	Yes	Environment	Industrial	1		12	2	4	253
PA1516	***Pseudomonas_aeruginosa_isolate_RW30_3223***	GCF_001373875.1	Yes	Environment	Industrial	1		12	2	4	253
PA1517	***Pseudomonas_aeruginosa_isolate_RW99_3277***	GCF_001374955.1	Yes	Environment	Industrial	1		12	2	4	253
PA1518	***Pseudomonas_aeruginosa_isolate_T52373_3627***	GCF_001516005.1	No	Clinical	Cancer	18	78	12	19	12	Undefined
PA1519	***Pseudomonas_aeruginosa_isolate_T63266_3628***	GCF_001516105.1	No	Clinical	Cancer	18	86	9	19	5	132
PA1520	***Pseudomonas_aeruginosa_isolate_TSB_1_3210***	GCF_001373615.1	Yes	Environment	Industrial	1		12	2	4	253
PA1521	***Pseudomonas_aeruginosa_isolate_TSB_2_3264***	GCF_001374695.1	Yes	Environment	Industrial	1		12	2	4	253
PA1522	***Pseudomonas_aeruginosa_isolate_TSB_3_3214***	GCF_001373695.1	Yes	Environment	Industrial	1		12	2	4	253

PA1523	***Pseudomonas_aeruginosa_isolate_TSB_4_3227***	GCF_001373955.1	Yes	Environment	Industrial	1		12	2	4	253
PA1524	***Pseudomonas_aeruginosa_isolate_TSB_5_3280***	GCF_001375015.1	Yes	Environment	Industrial	1		12	2	4	253
PA1525	***Pseudomonas_aeruginosa_isolate_TSB_6_3293***	GCF_001375255.1	No	Environment	Industrial	16	5	11	17	14	155
PA1526	***Pseudomonas_aeruginosa_isolate_TSB_7_3238***	GCF_001374175.1	No	Environment	Industrial	18	3	9	19	12	1105
PA1527	***Pseudomonas_aeruginosa_isolate_TSB_8_3298***	GCF_001375355.1	Yes	Environment	Industrial	1		12	2	4	253
PA1528	***Pseudomonas_aeruginosa_isolate_TSB_9_3253***	GCF_001374475.1	Yes	Environment	Industrial	1		12	2	4	253
PA1529	***Pseudomonas_aeruginosa_isolate_TSB_Bead_DWL_Pool_1_3234***	GCF_001374095.1	No	Environment	Industrial	18	93	13	19	12	2730
PA1530	***Pseudomonas_aeruginosa_isolate_TSB_Bead_DWL_Pool_2_3246***	GCF_001374335.1	No	Environment	Industrial	18	65	12	22	12	800
PA1531	***Pseudomonas_aeruginosa_isolate_TSB_Bead_Pool_1_3276***	GCF_001374935.1	Yes	Environment	Industrial	1		12	2	4	253
PA1532	***Pseudomonas_aeruginosa_isolate_TSB_Bead_Pool_2_3289***	GCF_001375175.1	Yes	Environment	Industrial	1		12	2	4	253
PA1533	***Pseudomonas_aeruginosa_isolate_TSB_Pool_3222***	GCF_001373855.1	Yes	Environment	Industrial	1		12	2	4	253
PA1534	***Pseudomonas_aeruginosa_J80UH1OS1_10113***	GCF_003836505.1	No	Environment	Animal	6	1	8	9	9	2227
PA1535	***Pseudomonas_aeruginosa_J9UH1F_10117***	GCF_003836575.1	No	Environment	Animal	11	30	11	13	14	252
PA1536	***Pseudomonas_aeruginosa_JB2_7002***	GCF_003060845.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	19	36	10	21	10	296
PA1537	***Pseudomonas_aeruginosa_JJ692_10015***	GCF_003834545.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA1538	***Pseudomonas_aeruginosa_JJ692_595***	GCF_000481805.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA1539	***Pseudomonas_aeruginosa_JMM_2085***	GCF_000709285.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	42	13	19	12	3489
PA1540	***Pseudomonas_aeruginosa_Jp100_10605***	GCF_003975385.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		11	21	14	2329
PA1541	***Pseudomonas_aeruginosa_Jp1140_10158***	GCF_003837405.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	38	10	1	10	316
PA1542	***Pseudomonas_aeruginosa_Jp1155_10601***	GCF_003975305.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA1543	***Pseudomonas_aeruginosa_Jp1170_10644***	GCF_003976165.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA1544	***Pseudomonas_aeruginosa_Jp1200_10602***	GCF_003975315.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA1545	***Pseudomonas_aeruginosa_Jp1206_10643***	GCF_003976135.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA1546	***Pseudomonas_aeruginosa_Jp1303_10642***	GCF_003976125.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	3	12	20	4	606
PA1547	***Pseudomonas_aeruginosa_Jp222_10603***	GCF_003975325.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		13	21	13	313
PA1548	***Pseudomonas_aeruginosa_Jp224_10159***	GCF_003837415.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316

PA1549	***Pseudomonas_aeruginosa_Jp238_10604***	GCF_003975335.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	13		9	10	12	27
PA1550	***Pseudomonas_aeruginosa_Jp241_10645***	GCF_003976175.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	12	2	1	14	1	395
PA1551	***Pseudomonas_aeruginosa_Jp245_10115***	GCF_003836545.1	Yes	Environment	Animal	16		11	17	14	155
PA1552	***Pseudomonas_aeruginosa_Jp54_10116***	GCF_003836565.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	11		11	13	14	9
PA1553	***Pseudomonas_aeruginosa_Jp60_10646***	GCF_003976185.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	11	30	11	13	14	9
PA1554	***Pseudomonas_aeruginosa_Jp97_10163***	GCF_003837505.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	11	21	14	2329
PA1555	***Pseudomonas_aeruginosa_JYH10_10051***	GCF_003835265.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	85	13	19	12	347
PA1556	***Pseudomonas_aeruginosa_JYH11_10629***	GCF_003975845.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	36	8	21	9	1692
PA1557	***Pseudomonas_aeruginosa_JYH12_10002***	GCF_003834285.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	13	19	12	1332
PA1558	***Pseudomonas_aeruginosa_JYH13_10630***	GCF_003975885.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	7	15	7	7	8	2130
PA1559	***Pseudomonas_aeruginosa_JYH15_10586***	GCF_003974995.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	9		9	11	5	17
PA1560	***Pseudomonas_aeruginosa_JYH16_10007***	GCF_003834385.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	11	19	14	Undefined
PA1561	***Pseudomonas_aeruginosa_JYH17_10628***	GCF_003975835.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	7	15	7	7	8	Undefined
PA1562	***Pseudomonas_aeruginosa_JYH18_10008***	GCF_003834395.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		3	21	3	Undefined
PA1563	***Pseudomonas_aeruginosa_JYH19_10585***	GCF_003974985.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		12	19	12	260
PA1564	***Pseudomonas_aeruginosa_JYH21_10627***	GCF_003975825.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	10	78	5	12	6	274
PA1565	***Pseudomonas_aeruginosa_JYH22_9979***	GCF_003833825.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	11		11	13	14	Undefined
PA1566	***Pseudomonas_aeruginosa_JYH23_10582***	GCF_003974905.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	11	30	11	13	14	Undefined
PA1567	***Pseudomonas_aeruginosa_JYH24_10009***	GCF_003834405.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	6	22	7	1642
PA1568	***Pseudomonas_aeruginosa_JYH25_10584***	GCF_003974945.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	8	21	9	1503
PA1569	***Pseudomonas_aeruginosa_JYH26_9996***	GCF_003834165.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	11	19	14	412

PA1570	***Pseudomonas_aeruginosa_JYH28_9978***	GCF_003833805.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	93	12	19	11	1239
PA1571	***Pseudomonas_aeruginosa_JYH29_10583***	GCF_003974915.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	47	3	21	3	532
PA1572	***Pseudomonas_aeruginosa_JYH6_10004***	GCF_003834325.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	15		12	23	12	Undefined
PA1573	***Pseudomonas_aeruginosa_JYH7_10589***	GCF_003975055.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	15	32	12	23	12	244
PA1574	***Pseudomonas_aeruginosa_JYH8_10055***	GCF_003835335.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	8	18	9	238
PA1575	***Pseudomonas_aeruginosa_JYH9_10587***	GCF_003975005.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	23	13	19	11	164
PA1576	***Pseudomonas_aeruginosa_K34_7_7082***	GCF_003206535.1	No	Clinical	Respiratory tract	18	84	12	20	11	233
PA1577	***Pseudomonas_aeruginosa_Kasamber_5192***	GCF_002003595.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA1578	***Pseudomonas_aeruginosa_KCJK8014_6402***	GCF_003053445.1	No	Environment	Animal	18	26	9	19	12	2853
PA1579	***Pseudomonas_aeruginosa_KCJK8015_7165***	GCF_003053465.1	No	Environment	Animal	18	26	9	19	12	2853
PA1580	***Pseudomonas_aeruginosa_KCJK8016_5927***	GCF_003053485.1	No	Environment	Animal	18	26	9	19	12	2853
PA1581	***Pseudomonas_aeruginosa_KCRI_164A_isolate_RDK04_164A_5790***	GCF_900406855.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	102	13	19	11	1907
PA1582	***Pseudomonas_aeruginosa_KCRI_214_isolate_R0003_214_6411***	GCF_900406875.1	No	Clinical	Respiratory tract	18	78	5	19	6	151
PA1583	***Pseudomonas_aeruginosa_KCRI_242_isolate_R0008_242_6868***	GCF_900406845.1	No	Clinical	Respiratory tract	18	102	10	19	12	1480
PA1584	***Pseudomonas_aeruginosa_KCRI_260_isolate_R0004_260_6277***	GCF_900406865.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	47	10	8	10	357
PA1585	***Pseudomonas_aeruginosa_KCRI_309A_isolate_RDK02_309A_7039***	GCF_900406885.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	15		12	23	12	244
PA1586	***Pseudomonas_aeruginosa_KCRI_310A_isolate_R0008_310A_6804***	GCF_900406825.1	No	Clinical	Burn	18	46	13	19	11	646
PA1587	***Pseudomonas_aeruginosa_KCRI_318_isolate_R0008_318_6936***	GCF_900406835.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	31	10	19	12	1247
PA1588	***Pseudomonas_aeruginosa_KCRI_321A_isolate_R0008_321A_6747***	GCF_900406895.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	15	32	12	23	12	244
PA1589	***Pseudomonas_aeruginosa_KCRI_377_isolate_R0007_377_7311***	GCF_900406935.1	No	Clinical	Burn	18	92	13	19	12	369
PA1590	***Pseudomonas_aeruginosa_KCRI_379A_isolate_RDK06_379A_5812***	GCF_900406945.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	74	8	19	12	809
PA1591	***Pseudomonas_aeruginosa_KCRI_462_isolate_RDK06_462_6637***	GCF_900406955.1	No	Clinical	Burn	18	74	13	19	11	612
PA1592	***Pseudomonas_aeruginosa_KCRI_610_isolate_RDK01_610_7336***	GCF_900406965.1	No	Clinical	Burn	18	74	13	19	11	Undefined
PA1593	***Pseudomonas_aeruginosa_KF702_3207***	GCF_000974565.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	19	102	10	1	10	2735
PA1594	***Pseudomonas_aeruginosa_KRP1_12050***	GCF_009676885.1	No	Environment	Other environmental source	13	50	9	10	12	27

PA1595	***Pseudomonas_aeruginosa_KT1115_12112***	GCF_009833435.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	74	13	19	11	242
PA1596	***Pseudomonas_aeruginosa_KY1_2574***	GCF_000813565.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	7	15	7	7	8	1432
PA1597	***Pseudomonas_aeruginosa_L10_6318***	GCF_002223805.1	No	Environment	Plants	1	103	12	2	4	253
PA1598	***Pseudomonas_aeruginosa_L25_9531***	GCF_003402335.1	No	Environment	Clinical environment: Dental, Hospital	18	81	13	19	12	2963
PA1599	***Pseudomonas_aeruginosa_L28_11988***	GCF_008629865.1	No	Clinical	Respiratory tract	18	102	10	19	12	Undefined
PA1600	***Pseudomonas_aeruginosa_L3_11997***	GCF_008632675.1	No	Clinical	Bacteraemia	18	88	13	19	11	1403
PA1601	***Pseudomonas_aeruginosa_L6_1_3622***	GCF_001483235.1	No	Environment	Hydrocarbon contamination	18	32	11	19	14	267
PA1602	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_10_a1_2580***	GCF_000823945.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1603	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_13_a1_2582***	GCF_000823985.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1604	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_15_a1_2608***	GCF_000824505.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1605	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_16_a1_2584***	GCF_000824025.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1606	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_18_a1_2586***	GCF_000824065.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1607	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_19_a1_2609***	GCF_000824525.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1608	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_20_a1_2587***	GCF_000824085.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1609	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_22_a1_2610***	GCF_000824545.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1610	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_26_a1_2592***	GCF_000824185.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1611	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_28_a1_2593***	GCF_000824205.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1612	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_3_a1_2605***	GCF_000824445.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1613	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_31_a1_2595***	GCF_000824245.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1614	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_32_a1_2596***	GCF_000824265.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1615	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_33_a1_2597***	GCF_000824285.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1616	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_35_a1_2598***	GCF_000824305.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146

PA1617	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_36_a1_2599***	GCF_000824325.1	No	Clinical	Cystic fibrosis	17	86	11	22	14	146
PA1618	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_37_a1_2618***	GCF_000824685.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1619	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_39_a1_2601***	GCF_000824365.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1620	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_5_a1_2606***	GCF_000824465.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1621	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_6_a1_2607***	GCF_000824485.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1622	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_8_a1_2578***	GCF_000823905.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1623	***Pseudomonas_aeruginosa_LES_CF_sputum_CF03_contigs_9_a1_2579***	GCF_000823925.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1624	***Pseudomonas_aeruginosa_LiA131_2005_10162***	GCF_003837485.1	No	Environment	Animal	19	102	10	21	10	620
PA1625	***Pseudomonas_aeruginosa_LiA133_2003_10114***	GCF_003836525.1	No	Environment	Animal	6	1	8	9	9	3764
PA1626	***Pseudomonas_aeruginosa_LiA145_2005_10156***	GCF_003837365.1	No	Environment	Animal	18	97	13	19	11	471
PA1627	***Pseudomonas_aeruginosa_LiA161_2005_10112***	GCF_003836465.1	No	Environment	Animal	18	93	12	19	12	260
PA1628	***Pseudomonas_aeruginosa_LiA179_2006_10111***	GCF_003836455.1	No	Environment	Animal	19	102	13	21	13	1400
PA1629	***Pseudomonas_aeruginosa_LiA18_2003_10108***	GCF_003836405.1	Yes	Environment	Animal	12		1	14	1	Undefined
PA1630	***Pseudomonas_aeruginosa_LiA50_2005_10154***	GCF_003837325.1	No	Environment	Animal	16	5	11	17	14	155
PA1631	***Pseudomonas_aeruginosa_LiA63_2006_10107***	GCF_003836385.1	Yes	Environment	Animal	11		11	13	14	252
PA1632	***Pseudomonas_aeruginosa_LiA91_2004_10160***	GCF_003837435.1	Yes	Environment	Animal	19		10	21	10	620
PA1633	***Pseudomonas_aeruginosa_LiA96_2004_10152***	GCF_003837285.1	Yes	Environment	Animal	19		10	21	10	620
PA1634	***Pseudomonas_aeruginosa_LIM1209_7229***	GCF_003204515.1	No	Clinical	Bacteraemia	17	22	13	15	13	277
PA1635	***Pseudomonas_aeruginosa_LiP11_10067***	GCF_003835575.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1636	***Pseudomonas_aeruginosa_LiP12_10064***	GCF_003835525.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1637	***Pseudomonas_aeruginosa_LiP14_10065***	GCF_003835545.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1638	***Pseudomonas_aeruginosa_LiP1d_10032***	GCF_003834885.1	No	Clinical	Cystic fibrosis	4	14	10	3	10	308
PA1639	***Pseudomonas_aeruginosa_LiP2b_10030***	GCF_003834835.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1640	***Pseudomonas_aeruginosa_LiP2c_10028***	GCF_003834805.1	No	Clinical	Cystic fibrosis	17	86	11	22	14	146
PA1641	***Pseudomonas_aeruginosa_LiP5_10027***	GCF_003834785.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1642	***Pseudomonas_aeruginosa_LiP6_10069***	GCF_003835595.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146
PA1643	***Pseudomonas_aeruginosa_LiP8_10068***	GCF_003835585.1	Yes	Clinical	Cystic fibrosis	17		11	22	14	146

PA1644	***Pseudomonas_aeruginosa_LiP9_10031***	GCF_003834865.1	No	Clinical	Cystic fibrosis	17	86	11	22	14	146
PA1645	***Pseudomonas_aeruginosa_LMG2107_10106***	GCF_003836355.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	55	10	21	10	Undefined
PA1646	***Pseudomonas_aeruginosa_LMG5031_10150***	GCF_003837245.1	No	Environment	Plants	5		4			Undefined
PA1647	***Pseudomonas_aeruginosa_LV_6231***	GCF_003347525.1	No	Environment	Plants	15	32	9	23	12	1227
PA1648	***Pseudomonas_aeruginosa_LW_10696***	GCF_004010895.1	No	Clinical	Respiratory tract	19	43	8	18	9	1182
PA1649	***Pseudomonas_aeruginosa_Lw1047_10153***	GCF_003837305.1	No	Clinical	Bacteraemia	18	76	13	19	12	2409
PA1650	***Pseudomonas_aeruginosa_M10_10721***	GCF_004123535.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	32	12	19	12	549
PA1651	***Pseudomonas_aeruginosa_M1608_7239***	GCF_001516365.2	Yes	Clinical	Cancer	1		12	2	4	253
PA1652	***Pseudomonas_aeruginosa_m183_6493***	GCF_002794745.1	No	Environment	Plants	18	102		19		162
PA1653	***Pseudomonas_aeruginosa_M26_7294***	GCF_002189505.1	No	Clinical	Urinary tract	18	97	9	19	12	882
PA1654	***Pseudomonas_aeruginosa_M53_10726***	GCF_004123635.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1655	***Pseudomonas_aeruginosa_M54_10720***	GCF_004123525.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1656	***Pseudomonas_aeruginosa_M55_10719***	GCF_004123515.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1657	***Pseudomonas_aeruginosa_M55212_6119***	GCF_002927235.1	No	Clinical	Cancer	14	52	2	16	2	111
PA1658	***Pseudomonas_aeruginosa_M56_10718***	GCF_004123475.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	8	18	9	Undefined
PA1659	***Pseudomonas_aeruginosa_M57_10717***	GCF_004123445.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1660	***Pseudomonas_aeruginosa_M58_10716***	GCF_004123435.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1661	***Pseudomonas_aeruginosa_M59_10714***	GCF_004123415.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1662	***Pseudomonas_aeruginosa_M60_10725***	GCF_004123625.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1663	***Pseudomonas_aeruginosa_M61_10715***	GCF_004123425.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1664	***Pseudomonas_aeruginosa_M62_10724***	GCF_004123615.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1665	***Pseudomonas_aeruginosa_M63_10711***	GCF_004123325.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1666	***Pseudomonas_aeruginosa_M64_10723***	GCF_004123565.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1667	***Pseudomonas_aeruginosa_M65_10722***	GCF_004123545.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined

PA1668	***Pseudomonas_aeruginosa_M66_10712***	GCF_004123335.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	18	9	Undefined
PA1669	***Pseudomonas_aeruginosa_M67_10713***	GCF_004123345.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	43	8	18	9	Undefined
PA1670	***Pseudomonas_aeruginosa_M7_3990***	GCF_001619935.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	76	13	19	11	Undefined
PA1671	***Pseudomonas_aeruginosa_M74707_6548***	GCF_002927095.1	No	Clinical	Urinary tract	10	78	5	12	6	274
PA1672	***Pseudomonas_aeruginosa_MCF104_10571***	GCF_003974685.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	3003
PA1673	***Pseudomonas_aeruginosa_MCF149_10578***	GCF_003974825.1	No	Clinical	Cystic fibrosis	18	83	9	19	12	2407
PA1674	***Pseudomonas_aeruginosa_MCF182_10576***	GCF_003974795.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	3003
PA1675	***Pseudomonas_aeruginosa_MCF206_10581***	GCF_003974895.1	No	Clinical	Cystic fibrosis	18	102	12	19	12	3003
PA1676	***Pseudomonas_aeruginosa_MCF430_10580***	GCF_003974885.1	No	Clinical	Cystic fibrosis	18	78	9	19	12	181
PA1677	***Pseudomonas_aeruginosa_MED01_11125***	GCF_005863515.1	Yes	Clinical	Gastrointestinal	14		2	16	2	111
PA1678	***Pseudomonas_aeruginosa_MED02_11123***	GCF_005863485.1	Yes	Clinical	Gastrointestinal	14		2	16	2	111
PA1679	***Pseudomonas_aeruginosa_MED03_11124***	GCF_005863495.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	14		2	16	2	111
PA1680	***Pseudomonas_aeruginosa_MED04_11126***	GCF_005863555.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	14		2	16	2	111
PA1681	***Pseudomonas_aeruginosa_MED05_11129***	GCF_005863605.1	Yes	Clinical	Gastrointestinal	14		2	16	2	111
PA1682	***Pseudomonas_aeruginosa_MED06_11127***	GCF_005863585.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1683	***Pseudomonas_aeruginosa_MED07_11128***	GCF_005863595.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1684	***Pseudomonas_aeruginosa_MED08_11130***	GCF_005863615.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1685	***Pseudomonas_aeruginosa_MED09_11131***	GCF_005863625.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1686	***Pseudomonas_aeruginosa_MED10_11132***	GCF_005863685.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1687	***Pseudomonas_aeruginosa_MED11_11136***	GCF_005863765.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1688	***Pseudomonas_aeruginosa_MED12_11135***	GCF_005863735.1	Yes	Clinical	Gastrointestinal	14		2	16	2	111
PA1689	***Pseudomonas_aeruginosa_MED13_11133***	GCF_005863695.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1690	***Pseudomonas_aeruginosa_MED14_11134***	GCF_005863725.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1691	***Pseudomonas_aeruginosa_MED15_11137***	GCF_005863785.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA1692	***Pseudomonas_aeruginosa_MED16_11138***	GCF_005863795.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1693	***Pseudomonas_aeruginosa_MED17_11140***	GCF_005863835.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1694	***Pseudomonas_aeruginosa_MED18_11139***	GCF_005863805.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1695	***Pseudomonas_aeruginosa_MED19_11141***	GCF_005863855.1	Yes	Clinical	Bacteraemia	14		2	16	2	111

PA1696	***Pseudomonas_aeruginosa_MED20_11143***	GCF_005863895.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1697	***Pseudomonas_aeruginosa_MED21_11142***	GCF_005863885.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1698	***Pseudomonas_aeruginosa_MED22_11144***	GCF_005863925.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1699	***Pseudomonas_aeruginosa_MED23_11146***	GCF_005863955.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1700	***Pseudomonas_aeruginosa_MED24_11145***	GCF_005863945.1	Yes	Clinical	Gastrointestinal	14		2	16	2	111
PA1701	***Pseudomonas_aeruginosa_MED25_11147***	GCF_005863975.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA1702	***Pseudomonas_aeruginosa_MED26_11148***	GCF_005863995.1	No	Clinical	Gastrointestinal	14	52	2	16	2	111
PA1703	***Pseudomonas_aeruginosa_MED27_11149***	GCF_005864015.1	No	Clinical	Bacteraemia	14	52	2	16	2	111
PA1704	***Pseudomonas_aeruginosa_Mex2_10130***	GCF_003836835.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	58	10	21	10	Undefined
PA1705	***Pseudomonas_aeruginosa_MH38_2079***	GCF_000689435.1	No	Clinical	Urinary tract	14	52	2	16	2	111
PA1706	***Pseudomonas_aeruginosa_Mi159_10104***	GCF_003836315.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	86	9	19	5	132
PA1707	***Pseudomonas_aeruginosa_Mi162_10303***	GCF_003841045.1	Yes	Clinical	Burn	14		2	16	2	111
PA1708	***Pseudomonas_aeruginosa_MMK2018_11103***	GCF_004685005.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	84	12	20	11	233
PA1709	***Pseudomonas_aeruginosa_MRSN_317_2627***	GCF_000982125.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	24	12	21	4	137
PA1710	***Pseudomonas_aeruginosa_MRSN_321_2628***	GCF_000982155.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	86		19		663
PA1711	***Pseudomonas_aeruginosa_MRSN11278_10515***	GCF_003969955.1	No	Clinical	Respiratory tract	19	10	8	18	9	829
PA1712	***Pseudomonas_aeruginosa_MRSN11281_10516***	GCF_003969965.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	86	5	19	6	875
PA1713	***Pseudomonas_aeruginosa_MRSN11285_10520***	GCF_003970055.1	No	Clinical	Urinary tract	19	54	8	18	9	3030
PA1714	***Pseudomonas_aeruginosa_MRSN11286_10523***	GCF_003970625.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	93	9	19	12	2387
PA1715	***Pseudomonas_aeruginosa_MRSN11536_10522***	GCF_003970615.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	81	13	20	12	621
PA1716	***Pseudomonas_aeruginosa_MRSN11538_10514***	GCF_003969915.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	78	9	19	12	1229
PA1717	***Pseudomonas_aeruginosa_MRSN11976_10524***	GCF_003970635.1	No	Clinical	Respiratory tract	14	52	2	16	2	111
PA1718	***Pseudomonas_aeruginosa_MRSN12280_6456***	GCF_003028335.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	3	6	10	4	10	Undefined
PA1719	***Pseudomonas_aeruginosa_MRSN12282_10521***	GCF_003970065.1	No	Clinical	Respiratory tract	18	4	9	22	12	348
PA1720	***Pseudomonas_aeruginosa_MRSN12283_10511***	GCF_003969865.1	No	Clinical	Urinary tract	18	46	13	19	11	646
PA1721	***Pseudomonas_aeruginosa_MRSN12365_10512***	GCF_003969875.1	Yes	Clinical	Respiratory tract	1		12	2	4	253

PA1722	***Pseudomonas_aeruginosa_MRSN12368_10519***	GCF_003970005.1	No	Clinical	Bacteraemia	17	102	6	15	7	1685
PA1723	***Pseudomonas_aeruginosa_MRSN12914_10510***	GCF_003969855.1	No	Clinical	Urinary tract	19	47	10	8	10	357
PA1724	***Pseudomonas_aeruginosa_MRSN1344_10518***	GCF_003969985.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	70	12	19	12	3003
PA1725	***Pseudomonas_aeruginosa_MRSN13488_10517***	GCF_003969975.1	No	Clinical	Urinary tract	18	74	8	19	12	1414
PA1726	***Pseudomonas_aeruginosa_MRSN1356_10509***	GCF_003969825.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	44	8	19	9	3031
PA1727	***Pseudomonas_aeruginosa_MRSN1380_10507***	GCF_003969785.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	97	9	19	12	241
PA1728	***Pseudomonas_aeruginosa_MRSN1388_10491***	GCF_003969475.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	3	9	19	12	1105
PA1729	***Pseudomonas_aeruginosa_MRSN14981_10493***	GCF_003969495.1	No	Clinical	Respiratory tract	18	102	9	19	12	3004
PA1730	***Pseudomonas_aeruginosa_MRSN15566_10508***	GCF_003969795.1	No	Clinical	Urinary tract	18	80	9	19	12	2855
PA1731	***Pseudomonas_aeruginosa_MRSN15678_10492***	GCF_003969485.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	3		10	4	10	235
PA1732	***Pseudomonas_aeruginosa_MRSN15753_10506***	GCF_003969775.1	No	Clinical	Respiratory tract	10	78	5	12	6	274
PA1733	***Pseudomonas_aeruginosa_MRSN1583_10490***	GCF_003969445.1	No	Clinical	Respiratory tract	18	93	11	19	11	3005
PA1734	***Pseudomonas_aeruginosa_MRSN1601_10489***	GCF_003969415.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	32	10	19	12	3032
PA1735	***Pseudomonas_aeruginosa_MRSN1612_10504***	GCF_003969725.1	No	Clinical	Ear	19	61	10	21	10	207
PA1736	***Pseudomonas_aeruginosa_MRSN1613_10487***	GCF_003969395.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	68	13	19	13	2952
PA1737	***Pseudomonas_aeruginosa_MRSN1617_10488***	GCF_003969405.1	No	Clinical	Respiratory tract	18	12	11	20	14	390
PA1738	***Pseudomonas_aeruginosa_MRSN16344_10503***	GCF_003969715.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	80	13	19	12	3033
PA1739	***Pseudomonas_aeruginosa_MRSN16345_10486***	GCF_003969365.1	No	Clinical	Urinary tract	18	99	11	19	14	211
PA1740	***Pseudomonas_aeruginosa_MRSN16383_10485***	GCF_003969355.1	No	Clinical	Respiratory tract	18	102	11	19	14	3006
PA1741	***Pseudomonas_aeruginosa_MRSN16740_10483***	GCF_003969305.1	No	Clinical	Respiratory tract	18	102	8	19	9	633
PA1742	***Pseudomonas_aeruginosa_MRSN16744_10482***	GCF_003969295.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	8	16	10	6	10	309
PA1743	***Pseudomonas_aeruginosa_MRSN16847_10505***	GCF_003969735.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	1	103	12	2	4	253
PA1744	***Pseudomonas_aeruginosa_MRSN1688_10484***	GCF_003969315.1	No	Clinical	Urinary tract	18	32	12	19	12	699
PA1745	***Pseudomonas_aeruginosa_MRSN1739_10502***	GCF_003969695.1	No	Clinical	Bacteraemia	18	81	13	19	11	463
PA1746	***Pseudomonas_aeruginosa_MRSN17849_10480***	GCF_003969255.1	No	Clinical	Respiratory tract	19	102	8	21	9	2065

PA1747	***Pseudomonas_aeruginosa_MRSN18560_10693***	GCF_003978035.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	78	9	19	5	3007
PA1748	***Pseudomonas_aeruginosa_MRSN18562_10501***	GCF_003969655.1	No	Clinical	Respiratory tract	18	63	9	19	12	3034
PA1749	***Pseudomonas_aeruginosa_MRSN18754_10463***	GCF_003968625.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	93		19		166
PA1750	***Pseudomonas_aeruginosa_MRSN18803_10691***	GCF_003977965.1	No	Clinical	Respiratory tract	18	78	9	19	12	2132
PA1751	***Pseudomonas_aeruginosa_MRSN18855_10689***	GCF_003977945.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	93	9	19	12	3035
PA1752	***Pseudomonas_aeruginosa_MRSN18970_10481***	GCF_003969265.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	95	9	19	12	192
PA1753	***Pseudomonas_aeruginosa_MRSN18971_2086***	GCF_000710625.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	95	9	19	12	192
PA1754	***Pseudomonas_aeruginosa_MRSN1899_10478***	GCF_003969195.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	97	13	19	12	1074
PA1755	***Pseudomonas_aeruginosa_MRSN1902_10479***	GCF_003969225.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	32	12	19	12	3008
PA1756	***Pseudomonas_aeruginosa_MRSN1906_10476***	GCF_003969165.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	15	32	12	23	12	244
PA1757	***Pseudomonas_aeruginosa_MRSN1925_10499***	GCF_003969635.1	No	Clinical	Respiratory tract	16	5	11	17	14	155
PA1758	***Pseudomonas_aeruginosa_MRSN1948_10475***	GCF_003969155.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	9		9	11	5	845
PA1759	***Pseudomonas_aeruginosa_MRSN19711_10452***	GCF_003968385.1	No	Clinical	Respiratory tract	19	102		21		2865
PA1760	***Pseudomonas_aeruginosa_MRSN20176_10474***	GCF_003969105.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	102	10	1	10	316
PA1761	***Pseudomonas_aeruginosa_MRSN20190_10453***	GCF_003968395.1	No	Clinical	Respiratory tract	18	100	13	19	12	3036
PA1762	***Pseudomonas_aeruginosa_MRSN2101_10472***	GCF_003969075.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	32	12	19	12	827
PA1763	***Pseudomonas_aeruginosa_MRSN2108_10690***	GCF_003977955.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	7	15	7	7	8	3037
PA1764	***Pseudomonas_aeruginosa_MRSN2144_10688***	GCF_003977935.1	No	Clinical	Urinary tract	16	5	11	17	14	179
PA1765	***Pseudomonas_aeruginosa_MRSN23861_10473***	GCF_003969095.1	No	Clinical	Respiratory tract	18	17	13	19	12	282
PA1766	***Pseudomonas_aeruginosa_MRSN2444_10470***	GCF_003969055.1	No	Clinical	Respiratory tract	18	79	9	19	12	654
PA1767	***Pseudomonas_aeruginosa_MRSN25623_10500***	GCF_003969645.1	No	Clinical	Respiratory tract	18	102	12	19	12	3038
PA1768	***Pseudomonas_aeruginosa_MRSN25678_10462***	GCF_003968615.1	No	Clinical	Urinary tract	7	15	7	7	8	3039
PA1769	***Pseudomonas_aeruginosa_MRSN25762_10469***	GCF_003969035.1	No	Clinical	Respiratory tract	9	11	9	11	5	17
PA1770	***Pseudomonas_aeruginosa_MRSN26263_10498***	GCF_003969615.1	No	Clinical	Respiratory tract	18	35	9	19	12	3009
PA1771	***Pseudomonas_aeruginosa_MRSN29192_10468***	GCF_003968985.1	No	Clinical	Urinary tract	18	96	11	19	11	3010

PA1772	***Pseudomonas_aeruginosa_MRSN30858_10497***	GCF_003969575.1	No	Clinical	Respiratory tract	19	102	10	21	10	2142
PA1773	***Pseudomonas_aeruginosa_MRSN315_10451***	GCF_003968375.1	No	Clinical	Respiratory tract	18	102	13	19	11	108
PA1774	***Pseudomonas_aeruginosa_MRSN317_10692***	GCF_003977995.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	24	12	21	4	137
PA1775	***Pseudomonas_aeruginosa_MRSN321_10461***	GCF_003968585.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	86	9	19	12	663
PA1776	***Pseudomonas_aeruginosa_MRSN346179_10496***	GCF_003969565.1	No	Clinical	Respiratory tract	18	86	12	19	12	3011
PA1777	***Pseudomonas_aeruginosa_MRSN351791_10495***	GCF_003969555.1	No	Clinical	Urinary tract	11	49	11	13	14	252
PA1778	***Pseudomonas_aeruginosa_MRSN3587_10471***	GCF_003969065.1	No	Clinical	Urinary tract	18	102	13	19	11	164
PA1779	***Pseudomonas_aeruginosa_MRSN358800_10513***	GCF_003969885.1	No	Clinical	Respiratory tract	18	40	13	19	12	3040
PA1780	***Pseudomonas_aeruginosa_MRSN3705_10467***	GCF_003968965.1	No	Clinical	Respiratory tract	5		4			2031
PA1781	***Pseudomonas_aeruginosa_MRSN373401_10466***	GCF_003968955.1	No	Clinical	Urinary tract	18	85	13	19	12	347
PA1782	***Pseudomonas_aeruginosa_MRSN390231_10465***	GCF_003968935.1	No	Clinical	Respiratory tract	18	69		19		2572
PA1783	***Pseudomonas_aeruginosa_MRSN401528_10686***	GCF_003977895.1	No	Clinical	Urinary tract	18	35	11	19	14	3042
PA1784	***Pseudomonas_aeruginosa_MRSN435288_10460***	GCF_003968565.1	No	Clinical	Respiratory tract	18	17	8	19	12	3012
PA1785	***Pseudomonas_aeruginosa_MRSN436311_10464***	GCF_003968895.1	No	Clinical	Urinary tract	19	54	8	18	9	3013
PA1786	***Pseudomonas_aeruginosa_MRSN443463_10450***	GCF_003968325.1	No	Clinical	Respiratory tract	18	68	13	19	11	2851
PA1787	***Pseudomonas_aeruginosa_MRSN4841_10448***	GCF_003968305.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA1788	***Pseudomonas_aeruginosa_MRSN5498_10449***	GCF_003968315.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	32	13	19	11	3014
PA1789	***Pseudomonas_aeruginosa_MRSN5508_10459***	GCF_003968535.1	No	Clinical	Body fluid	18	25	13	19	12	3002
PA1790	***Pseudomonas_aeruginosa_MRSN5519_10447***	GCF_003968295.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	3		10	4	10	235
PA1791	***Pseudomonas_aeruginosa_MRSN552_10446***	GCF_003968275.1	No	Clinical	Urinary tract	18	35	13	19	12	1654
PA1792	***Pseudomonas_aeruginosa_MRSN5524_10444***	GCF_003968225.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA1793	***Pseudomonas_aeruginosa_MRSN5539_10445***	GCF_003968235.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	3		10	4	10	235
PA1794	***Pseudomonas_aeruginosa_MRSN6241_10441***	GCF_003968155.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	5		4			3043
PA1795	***Pseudomonas_aeruginosa_MRSN6678_10442***	GCF_003968165.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	3		10	4	10	235
PA1796	***Pseudomonas_aeruginosa_MRSN6695_10440***	GCF_003968135.1	No	Clinical	Urinary tract	18	93	13	19	12	497
PA1797	***Pseudomonas_aeruginosa_MRSN6739_10458***	GCF_003968525.1	No	Clinical	Urinary tract	18	97	13	19	11	3015
PA1798	***Pseudomonas_aeruginosa_MRSN7014_10438***	GCF_003968115.1	No	Clinical	Respiratory tract	18	93	12	19	12	1129

PA1799	***Pseudomonas_aeruginosa_MRSN8130_10457***	GCF_003968495.1	No	Clinical	Bacteraemia	2	39	10	5	10	446
PA1800	***Pseudomonas_aeruginosa_MRSN8136_10439***	GCF_003968125.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	32	13	19	12	381
PA1801	***Pseudomonas_aeruginosa_MRSN8139_10436***	GCF_003968045.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	60	8	21	9	1503
PA1802	***Pseudomonas_aeruginosa_MRSN8141_10456***	GCF_003968475.1	Yes	Clinical	Respiratory tract	5		4			3043
PA1803	***Pseudomonas_aeruginosa_MRSN8912_10437***	GCF_003968055.1	No	Clinical	Urinary tract	19	47	3	21	3	532
PA1804	***Pseudomonas_aeruginosa_MRSN9718_10455***	GCF_003968445.1	No	Clinical	Urinary tract	19	39	12	21	12	1601
PA1805	***Pseudomonas_aeruginosa_MRSN9873_10454***	GCF_003968425.1	No	Clinical	Urinary tract	18	35	9	19	12	3045
PA1806	***Pseudomonas_aeruginosa_MRSN994_10435***	GCF_003968035.1	No	Clinical	Respiratory tract	13	50	9	10	12	27
PA1807	***Pseudomonas_aeruginosa_MSB2949_10093***	GCF_003836085.1	Yes	Clinical	Cystic fibrosis	15		12	23	12	244
PA1808	***Pseudomonas_aeruginosa_MSH10_10632***	GCF_003975915.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		13	19	11	689
PA1809	***Pseudomonas_aeruginosa_MSH10_603***	GCF_000481965.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	74	13	19	11	689
PA1810	***Pseudomonas_aeruginosa_MSH3_10588***	GCF_003975025.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	74	13	19	11	689
PA1811	***Pseudomonas_aeruginosa_MSH3_604***	GCF_000481985.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	74	13	19	11	689
PA1812	***Pseudomonas_aeruginosa_MTB_1_210***	GCF_000504045.1	No	Environment	Hydrocarbon contamination	19	102	8	21	9	2689
PA1813	***Pseudomonas_aeruginosa_MW3a_2006***	GCF_000590905.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	10	21	10	296
PA1814	***Pseudomonas_aeruginosa_N002_241***	GCF_000287815.1	No	Environment	Hydrocarbon contamination	18	102		19		Undefined
PA1815	***Pseudomonas_aeruginosa_N17_1_3988***	GCF_001606045.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	86	13	19	12	2362
PA1816	***Pseudomonas_aeruginosa_NA04_7242***	GCF_002204155.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	96	13	19	12	3765
PA1817	***Pseudomonas_aeruginosa_NCGM1900_2620***	GCF_000829275.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA1818	***Pseudomonas_aeruginosa_NCGM1984_2619***	GCF_000829255.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA1819	***Pseudomonas_aeruginosa_NCGM257_3921***	GCF_001547955.1	No	Clinical	Urinary tract	19	47	10	8	10	357
PA1820	***Pseudomonas_aeruginosa_NCMG1179_677***	GCF_000291745.1	No	Clinical	Respiratory tract	18	7	9	19	12	1285
PA1821	***Pseudomonas_aeruginosa_NCTC10299_12152***	GCF_901482505.1	No	Clinical	Gastrointestinal	18	93	13	19	12	Undefined
PA1822	***Pseudomonas_aeruginosa_NCTC10782_5991***	GCF_900455355.1	No	Clinical	Urinary tract	18	32	9	19	12	Undefined
PA1823	***Pseudomonas_aeruginosa_NCTC12903_11167***	GCF_900636755.1	No	Clinical	Bacteraemia	16	5	11	17	14	155
PA1824	***Pseudomonas_aeruginosa_NCTC13359_11326***	GCF_901472545.1	No	Environment	Other environmental source	11	30	11	13	14	252
PA1825	***Pseudomonas_aeruginosa_NCTC13715_11168***	GCF_900636975.1	No	Clinical	Urinary tract	19	47	3	21	3	773

PA1826	***Pseudomonas_aeruginosa_NCTC13716_6010***	GCF_900455455.1	No	Clinical	Respiratory tract	14	52	2	16	2	111
PA1827	***Pseudomonas_aeruginosa_NCTC13717_5931***	GCF_900455365.1	No	Clinical	Bacteraemia	18	84	12	20	11	233
PA1828	***Pseudomonas_aeruginosa_NCTC13719_6717***	GCF_900455415.1	No	Clinical	Bacteraemia	19	47	10	8	10	357
PA1829	***Pseudomonas_aeruginosa_NCTC13921_6847***	GCF_900455535.1	No	Clinical	Respiratory tract	17	22	13	15	13	277
PA1830	***Pseudomonas_aeruginosa_NCTC6750_6271***	GCF_900461635.1	No	Clinical	Urinary tract	18	97	9	19	12	882
PA1831	***Pseudomonas_aeruginosa_NICED_PA_01_12128***	GCF_009939155.1	No	Clinical	Gastrointestinal	19	102	8	18	9	1203
PA1832	***Pseudomonas_aeruginosa_NN5_10560***	GCF_003974455.1	No	Clinical	Cystic fibrosis	15	32	12	23	12	244
PA1833	***Pseudomonas_aeruginosa_NUBRI_P_11108***	GCF_004790695.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	14	83	2	16	2	111
PA1834	***Pseudomonas_aeruginosa_Ocean_1155_5897***	GCF_002237405.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA1835	***Pseudomonas_aeruginosa_Ocean_1170_6005***	GCF_002263545.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	38	10	1	10	316
PA1836	***Pseudomonas_aeruginosa_Ocean_1175_6075***	GCF_002237425.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		10	1	10	316
PA1837	***Pseudomonas_aeruginosa_Ocean_238_7079***	GCF_002263685.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	13	50	9	10	12	27
PA1838	***Pseudomonas_aeruginosa_OENV015_11901***	GCF_006704695.1	Yes	Environment	Other environmental source	2		10	5	10	298
PA1839	***Pseudomonas_aeruginosa_OENV043_11899***	GCF_006704675.1	Yes	Environment	Other environmental source	2		10	5	10	446
PA1840	***Pseudomonas_aeruginosa_OENV069_11898***	GCF_006704665.1	Yes	Environment	Other environmental source	2		10	5	10	446
PA1841	***Pseudomonas_aeruginosa_OENV139_11897***	GCF_006704645.1	Yes	Environment	Other environmental source	2		10	5	10	446
PA1842	***Pseudomonas_aeruginosa_Ortho_1_6543***	GCF_002312335.1	No	Environment	Clinical environment: Dental, Hospital	19	61	10	21	10	Undefined
PA1843	***Pseudomonas_aeruginosa_OY15_10534***	GCF_003973905.1	No	Clinical	Cystic fibrosis	18	86	13	19	12	998
PA1844	***Pseudomonas_aeruginosa_P1885_10590***	GCF_003975085.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	7	15		7		Undefined
PA1845	***Pseudomonas_aeruginosa_P2_L230_95_2510***	GCF_000760505.1	No	Clinical	Eye	18	102	13	19	12	Undefined
PA1846	***Pseudomonas_aeruginosa_P2404_10597***	GCF_003975215.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	8		10	6	10	309
PA1847	***Pseudomonas_aeruginosa_P2733_10638***	GCF_003976035.1	No	Clinical	Respiratory tract	18	101	8	19	9	379
PA1848	***Pseudomonas_aeruginosa_P27b_7290***	GCF_002285195.1	Yes	Environment	Plants	18		13	19	11	553
PA1849	***Pseudomonas_aeruginosa_P28a_7341***	GCF_002326325.1	No	Environment	Plants	18	93	13	19	11	553
PA1850	***Pseudomonas_aeruginosa_P28b_6206***	GCF_002326535.1	Yes	Environment	Plants	18		13	19	11	553
PA1851	***Pseudomonas_aeruginosa_P37_5699***	GCF_002025525.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	8	21	9	1146

PA1852	***Pseudomonas_aeruginosa_P38_11999***	GCF_008632775.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	102	13	19	12	1212
PA1853	***Pseudomonas_aeruginosa_P47_5200***	GCF_002025555.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	21	9	1146
PA1854	***Pseudomonas_aeruginosa_P49_5653***	GCF_002025515.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		8	21	9	1146
PA1855	***Pseudomonas_aeruginosa_P7_L633_96_2509***	GCF_000760495.1	No	Clinical	Eye	19	102	10	1	10	316
PA1856	***Pseudomonas_aeruginosa_PA_032_10388***	GCF_003940675.1	No	Environment	Clinical environment: Dental, Hospital	3	6	10	4	10	235
PA1857	***Pseudomonas_aeruginosa_PA_038_10369***	GCF_003936385.1	No	Environment	Clinical environment: Dental, Hospital	18	25	9	19	5	664
PA1858	***Pseudomonas_aeruginosa_PA_041_10375***	GCF_003936965.1	Yes	Environment	Clinical environment: Dental, Hospital	18		9	19	5	664
PA1859	***Pseudomonas_aeruginosa_PA_058_10389***	GCF_003944895.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1860	***Pseudomonas_aeruginosa_PA_059_10386***	GCF_003940635.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1861	***Pseudomonas_aeruginosa_PA_060_10362***	GCF_003935835.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1862	***Pseudomonas_aeruginosa_PA_061_10387***	GCF_003940665.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1863	***Pseudomonas_aeruginosa_PA_064_10373***	GCF_003936925.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1864	***Pseudomonas_aeruginosa_PA_112_10368***	GCF_003936325.1	Yes	Environment	Clinical environment: Dental, Hospital	18		5	19	6	859
PA1865	***Pseudomonas_aeruginosa_PA_113_10378***	GCF_003937395.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1866	***Pseudomonas_aeruginosa_PA_114_10377***	GCF_003937375.1	No	Environment	Clinical environment: Dental, Hospital	18	45	13	20	12	571
PA1867	***Pseudomonas_aeruginosa_PA_117_10374***	GCF_003936935.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1868	***Pseudomonas_aeruginosa_PA_118_10382***	GCF_003939695.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1869	***Pseudomonas_aeruginosa_PA_178_10380***	GCF_003939105.1	Yes	Environment	Clinical environment: Dental, Hospital	18		5	19	6	859
PA1870	***Pseudomonas_aeruginosa_PA_179_10381***	GCF_003939685.1	Yes	Environment	Clinical environment: Dental, Hospital	18		5	19	6	859
PA1871	***Pseudomonas_aeruginosa_PA_180_10367***	GCF_003936295.1	No	Environment	Clinical environment: Dental, Hospital	18	102	5	19	6	859
PA1872	***Pseudomonas_aeruginosa_PA_182_10365***	GCF_003936245.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571

PA1873	***Pseudomonas_aeruginosa_PA_185_10372***	GCF_003936905.1	Yes	Environment	Clinical environment: Dental, Hospital	18		5	19	6	859
PA1874	***Pseudomonas_aeruginosa_PA_187_10371***	GCF_003936865.1	Yes	Environment	Clinical environment: Dental, Hospital	3		10	4	10	235
PA1875	***Pseudomonas_aeruginosa_PA_254_10370***	GCF_003936835.1	Yes	Environment	Clinical environment: Dental, Hospital	3		10	4	10	235
PA1876	***Pseudomonas_aeruginosa_PA_283_10366***	GCF_003936255.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1877	***Pseudomonas_aeruginosa_PA_286_10363***	GCF_003936225.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1878	***Pseudomonas_aeruginosa_PA_289_10385***	GCF_003940625.1	Yes	Environment	Clinical environment: Dental, Hospital	18		13	20	12	571
PA1879	***Pseudomonas_aeruginosa_PA_294_10384***	GCF_003940585.1	No	Environment	Clinical environment: Dental, Hospital	3	6	10	4	10	235
PA1880	***Pseudomonas_aeruginosa_PA_304_10383***	GCF_003940575.1	Yes	Environment	Clinical environment: Dental, Hospital	3		10	4	10	235
PA1881	***Pseudomonas_aeruginosa_PA_50010278_12081***	GCF_009791355.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19		3	21	3	773
PA1882	***Pseudomonas_aeruginosa_PA_81_10357***	GCF_003866475.1	No	Clinical	Cystic fibrosis	19	47	10	8	10	357
PA1883	***Pseudomonas_aeruginosa_PA_CL501_10962***	GCF_004372585.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1884	***Pseudomonas_aeruginosa_PA_CL502_10961***	GCF_004372535.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1885	***Pseudomonas_aeruginosa_PA_CL504_10960***	GCF_004372525.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1886	***Pseudomonas_aeruginosa_PA_CL505_10959***	GCF_004372505.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1887	***Pseudomonas_aeruginosa_PA_CL506b_10957***	GCF_004372485.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1888	***Pseudomonas_aeruginosa_PA_CL507_10958***	GCF_004372495.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1889	***Pseudomonas_aeruginosa_PA_CL509_10975***	GCF_004372825.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	179
PA1890	***Pseudomonas_aeruginosa_PA_CL510_10955***	GCF_004372435.1	No	Environment	Clinical environment: Dental, Hospital	16	5	11	17	14	179
PA1891	***Pseudomonas_aeruginosa_PA_CL511_10954***	GCF_004372415.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	179
PA1892	***Pseudomonas_aeruginosa_PA_CL512_10953***	GCF_004372395.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	179
PA1893	***Pseudomonas_aeruginosa_PA_CL514_10952***	GCF_004372375.1	No	Environment	Clinical environment: Dental, Hospital	18	12	11	20	14	390

PA1894	***Pseudomonas_aeruginosa_PA_CL515_10973***	GCF_004372805.1	Yes	Environment	Clinical environment: Dental, Hospital	18		11	20	14	390
PA1895	***Pseudomonas_aeruginosa_PA_CL516_10972***	GCF_004372775.1	Yes	Environment	Clinical environment: Dental, Hospital	18		11	20	14	Undefined
PA1896	***Pseudomonas_aeruginosa_PA_CL517_10971***	GCF_004372745.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	179
PA1897	***Pseudomonas_aeruginosa_PA_CL518_10970***	GCF_004372725.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	179
PA1898	***Pseudomonas_aeruginosa_PA_CL519_10951***	GCF_004372345.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	179
PA1899	***Pseudomonas_aeruginosa_PA_CL521a_10949***	GCF_004372315.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	155
PA1900	***Pseudomonas_aeruginosa_PA_CL521b_10948***	GCF_004372295.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	155
PA1901	***Pseudomonas_aeruginosa_PA_CL524_10969***	GCF_004372705.1	Yes	Environment	Clinical environment: Dental, Hospital	16		11	17	14	155
PA1902	***Pseudomonas_aeruginosa_PA_CL527_10967***	GCF_004372675.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	Undefined
PA1903	***Pseudomonas_aeruginosa_PA_CL528_10968***	GCF_004372695.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1904	***Pseudomonas_aeruginosa_PA_CL529_10946***	GCF_004372255.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1905	***Pseudomonas_aeruginosa_PA_CL534a_10945***	GCF_004372235.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1906	***Pseudomonas_aeruginosa_PA_CL534x_11101***	GCF_004378765.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1907	***Pseudomonas_aeruginosa_PA_CL542a_10932***	GCF_004371955.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1908	***Pseudomonas_aeruginosa_PA_CL542b_10933***	GCF_004371965.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1909	***Pseudomonas_aeruginosa_PA_CL545b_10943***	GCF_004372185.1	No	Environment	Clinical environment: Dental, Hospital	18	13	12	19	11	186
PA1910	***Pseudomonas_aeruginosa_PA_CL547b_10944***	GCF_004372195.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	Undefined
PA1911	***Pseudomonas_aeruginosa_PA_CL549_10942***	GCF_004372145.1	Yes	Environment	Clinical environment: Dental, Hospital	18		12	19	11	186
PA1912	***Pseudomonas_aeruginosa_PA_D1_3998***	GCF_001721745.1	No	Clinical	Respiratory tract	19	47	10	21	10	1971
PA1913	***Pseudomonas_aeruginosa_PA_D16_4001***	GCF_001721805.1	Yes	Clinical	Respiratory tract	19		10	21	10	1971
PA1914	***Pseudomonas_aeruginosa_PA_D2_3999***	GCF_001721765.1	Yes	Clinical	Respiratory tract	19		10	21	10	1971
PA1915	***Pseudomonas_aeruginosa_PA_D21_4006***	GCF_001722045.1	Yes	Clinical	Respiratory tract	19		10	21	10	1971

PA1916	***Pseudomonas_aeruginosa_PA_D22_4002***	GCF_001721825.1	Yes	Clinical	Respiratory tract	19		10	21	10	1971
PA1917	***Pseudomonas_aeruginosa_PA_D25_4003***	GCF_001721845.1	Yes	Clinical	Respiratory tract	19		10	21	10	1971
PA1918	***Pseudomonas_aeruginosa_PA_D5_4005***	GCF_001722025.1	Yes	Clinical	Respiratory tract	19		10	21	10	1971
PA1919	***Pseudomonas_aeruginosa_PA_D9_4000***	GCF_001721785.1	Yes	Clinical	Respiratory tract	19		10	21	10	1971
PA1920	***Pseudomonas_aeruginosa_PA_HTX1_10359***	GCF_003933495.1	Yes	Clinical	Bacteraemia	8		10	6	10	309
PA1921	***Pseudomonas_aeruginosa_PA_HTX2_10358***	GCF_003933315.1	No	Clinical	Bacteraemia	8	16	10	6	10	309
PA1922	***Pseudomonas_aeruginosa_PA_NM_015_11883***	GCF_006704355.1	Yes	Clinical	Respiratory tract	2		10	5	10	298
PA1923	***Pseudomonas_aeruginosa_PA_NM_069_11880***	GCF_006704275.1	Yes	Clinical	Respiratory tract	2		10	5	10	298
PA1924	***Pseudomonas_aeruginosa_PA_NM_074_11881***	GCF_006704285.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA1925	***Pseudomonas_aeruginosa_PA_NM_079_11879***	GCF_006704255.1	Yes	Clinical	Respiratory tract	2		10	5	10	298
PA1926	***Pseudomonas_aeruginosa_PA_NM_088_11878***	GCF_006704245.1	Yes	Clinical	Bacteraemia	2		10	5	10	298
PA1927	***Pseudomonas_aeruginosa_PA_ST235_2505***	GCF_000737795.1	No	Clinical	Bacteraemia	3	6	10	4	10	235
PA1928	***Pseudomonas_aeruginosa_PA_W1_9972***	GCF_003833685.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	6	1	8	9	9	2548
PA1929	***Pseudomonas_aeruginosa_PA_W10_9971***	GCF_003833665.1	No	Clinical	Burn	19	102	10	21	10	1158
PA1930	***Pseudomonas_aeruginosa_PA_W11_10325***	GCF_003841745.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	67	9	19	12	399
PA1931	***Pseudomonas_aeruginosa_PA_W12_10312***	GCF_003841235.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		11	20	14	Undefined
PA1932	***Pseudomonas_aeruginosa_PA_W13_10311***	GCF_003841205.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	102	8	21	9	701
PA1933	***Pseudomonas_aeruginosa_PA_W14_9993***	GCF_003834105.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		13	19	12	381
PA1934	***Pseudomonas_aeruginosa_PA_W15_10324***	GCF_003841715.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		9	19	5	132
PA1935	***Pseudomonas_aeruginosa_PA_W16_9974***	GCF_003833715.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	74	8	19	12	909
PA1936	***Pseudomonas_aeruginosa_PA_W17_10321***	GCF_003841635.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	8	16	10	6	10	Undefined
PA1937	***Pseudomonas_aeruginosa_PA_W18_10322***	GCF_003841645.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	12		1	14	1	395
PA1938	***Pseudomonas_aeruginosa_PA_W19_10310***	GCF_003841185.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	64		22		485
PA1939	***Pseudomonas_aeruginosa_PA_W2_10329***	GCF_003841815.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	102	12	19	11	1014
PA1940	***Pseudomonas_aeruginosa_PA_W20_10323***	GCF_003841705.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	8		10	6	10	309

PA1941	***Pseudomonas_aeruginosa_PA_W21_9992***	GCF_003834085.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19		10	21	10	296
PA1942	***Pseudomonas_aeruginosa_PA_W23_9973***	GCF_003833705.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	102	12	19	12	2235
PA1943	***Pseudomonas_aeruginosa_PA_W24_9994***	GCF_003834125.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	2		10	5	10	446
PA1944	***Pseudomonas_aeruginosa_PA_W25_10316***	GCF_003841565.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	13		9	10	12	27
PA1945	***Pseudomonas_aeruginosa_PA_W26_10319***	GCF_003841615.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	44	10	19	10	408
PA1946	***Pseudomonas_aeruginosa_PA_W27_10318***	GCF_003841605.1	Yes	Clinical	Urinary tract	18		10	19	10	408
PA1947	***Pseudomonas_aeruginosa_PA_W28_9990***	GCF_003834025.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	15	32	12	23	12	244
PA1948	***Pseudomonas_aeruginosa_PA_W29_9967***	GCF_003833585.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	93	5	19	6	2685
PA1949	***Pseudomonas_aeruginosa_PA_W3_9997***	GCF_003834185.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	12		1	14	1	395
PA1950	***Pseudomonas_aeruginosa_PA_W30_10306***	GCF_003841095.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	9		9	11	5	17
PA1951	***Pseudomonas_aeruginosa_PA_W31_9989***	GCF_003834015.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	12		1	14	1	395
PA1952	***Pseudomonas_aeruginosa_PA_W32_9966***	GCF_003833565.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	3		10	4	10	235
PA1953	***Pseudomonas_aeruginosa_PA_W33_9970***	GCF_003833645.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	85	13	19	12	347
PA1954	***Pseudomonas_aeruginosa_PA_W34_10315***	GCF_003841525.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	36	10	21	10	296
PA1955	***Pseudomonas_aeruginosa_PA_W35_10317***	GCF_003841575.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		9	19	5	132
PA1956	***Pseudomonas_aeruginosa_PA_W36_9965***	GCF_003833545.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	9		9	11	5	17
PA1957	***Pseudomonas_aeruginosa_PA_W37_9969***	GCF_003833625.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		6	19	7	170
PA1958	***Pseudomonas_aeruginosa_PA_W38_9968***	GCF_003833605.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	13	50	9	10	12	449
PA1959	***Pseudomonas_aeruginosa_PA_W39_9988***	GCF_003834005.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	12	2	1	14	1	395
PA1960	***Pseudomonas_aeruginosa_PA_W4_9977***	GCF_003833785.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	8		10	6	10	309
PA1961	***Pseudomonas_aeruginosa_PA_W41_10309***	GCF_003841165.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	13		9	10	12	27

PA1962	***Pseudomonas_aeruginosa_PA_W42_9986***	GCF_003833955.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	12		1	14	1	395
PA1963	***Pseudomonas_aeruginosa_PA_W43_9991***	GCF_003834035.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	16		11	17	14	179
PA1964	***Pseudomonas_aeruginosa_PA_W44_9963***	GCF_003833485.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	92	13	19	11	2808
PA1965	***Pseudomonas_aeruginosa_PA_W45_9959***	GCF_003833425.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	13		9	10	12	27
PA1966	***Pseudomonas_aeruginosa_PA_W46_9964***	GCF_003833525.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	103	10	21	10	1197
PA1967	***Pseudomonas_aeruginosa_PA_W47_10308***	GCF_003841145.1	Yes	Clinical	Burn	2		10	5	10	446
PA1968	***Pseudomonas_aeruginosa_PA_W48_10314***	GCF_003841515.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	15	32	12	23	12	244
PA1969	***Pseudomonas_aeruginosa_PA_W5_9976***	GCF_003833765.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	12		1	14	1	395
PA1970	***Pseudomonas_aeruginosa_PA_W6_10327***	GCF_003841775.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	97	9	19	12	882
PA1971	***Pseudomonas_aeruginosa_PA_W7_10313***	GCF_003841305.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	1	103	12	2	4	253
PA1972	***Pseudomonas_aeruginosa_PA_W8_10326***	GCF_003841755.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	97	13	19	12	2123
PA1973	***Pseudomonas_aeruginosa_PA1_497***	GCF_000496605.2	No	Clinical	Respiratory tract	18	88	13	19	12	782
PA1974	***Pseudomonas_aeruginosa_PA1_6054***	GCF_002866765.1	Yes	Clinical	Respiratory tract	19		10	8	10	357
PA1975	***Pseudomonas_aeruginosa_Pa1014_9910***	GCF_003670025.1	No	Clinical	Bacteraemia	18	84	12	20	11	233
PA1976	***Pseudomonas_aeruginosa_PA103_2044***	GCF_000611975.2	No	Clinical	Respiratory tract	2	39	10	5	10	298
PA1977	***Pseudomonas_aeruginosa_Pa1060_9907***	GCF_003669975.1	Yes	Clinical	Urinary tract	18		12	20	11	233
PA1978	***Pseudomonas_aeruginosa_Pa1076_9658***	GCF_003611405.1	No	Clinical	Urinary tract	8	16	10	6	10	309
PA1979	***Pseudomonas_aeruginosa_Pa1078_9899***	GCF_003669815.1	Yes	Clinical	Respiratory tract	8		10	6	10	309
PA1980	***Pseudomonas_aeruginosa_PA1088_5724***	GCF_001792835.1	No	Clinical	Urinary tract	17	22	13	15	13	277
PA1981	***Pseudomonas_aeruginosa_Pa1123_9902***	GCF_003669875.1	Yes	Clinical	Urinary tract	18		12	20	11	233
PA1982	***Pseudomonas_aeruginosa_Pa1175_9911***	GCF_003670055.1	Yes	Clinical	Urinary tract	18		12	20	11	233
PA1983	***Pseudomonas_aeruginosa_PA11803_5097***	GCF_001792875.1	No	Clinical	Bacteraemia	17	22	13	15	13	277
PA1984	***Pseudomonas_aeruginosa_Pa1207_5865***	GCF_002208645.1	No	Clinical	Respiratory tract	16	5	11	17	14	155
PA1985	***Pseudomonas_aeruginosa_PA12117_4952***	GCF_001806505.1	No	Clinical	Bacteraemia	17	22	13	15	13	277
PA1986	***Pseudomonas_aeruginosa_PA121617_3995***	GCF_001679685.1	No	Clinical	Respiratory tract	18	102	6	22	7	389
PA1987	***Pseudomonas_aeruginosa_PA123_12070***	GCF_009727505.1	No	Clinical	Eye	18	68	13	19	12	218

PA1988	***Pseudomonas_aeruginosa_Pa124_6251***	GCF_002192475.1	No	Clinical	Respiratory tract	8	16	10	6	10	309
PA1989	***Pseudomonas_aeruginosa_Pa1242_6732***	GCF_002205375.1	No	Clinical	Bacteraemia	17	22	13	15	13	277
PA1990	***Pseudomonas_aeruginosa_PA126_12071***	GCF_009727515.1	No	Clinical	Eye	18	44	10	19	9	2726
PA1991	***Pseudomonas_aeruginosa_PA127_12072***	GCF_009727535.1	Yes	Clinical	Eye	18		13	19	12	218
PA1992	***Pseudomonas_aeruginosa_Pa127_6938***	GCF_002205355.1	Yes	Clinical	Respiratory tract	8		10	6	10	309
PA1993	***Pseudomonas_aeruginosa_Pa1354_9905***	GCF_003669925.1	Yes	Clinical	Body fluid	18		12	20	11	233
PA1994	***Pseudomonas_aeruginosa_PA149_6789***	GCF_003332625.1	No	Clinical	Eye	18	79	9	19	12	Undefined
PA1995	***Pseudomonas_aeruginosa_PA157_6754***	GCF_003332575.1	No	Clinical	Eye	18	78	13	19	11	386
PA1996	***Pseudomonas_aeruginosa_PA162_12069***	GCF_009727485.1	Yes	Clinical	Eye	2		10	5	10	298
PA1997	***Pseudomonas_aeruginosa_PA169_12068***	GCF_009727465.1	No	Clinical	Eye	19	102	10	21	10	1027
PA1998	***Pseudomonas_aeruginosa_PA17_7087***	GCF_003332795.1	No	Clinical	Eye	18	76	13	19	11	Undefined
PA1999	***Pseudomonas_aeruginosa_PA171_6657***	GCF_003332565.1	No	Clinical	Eye	18	97	13	19	11	471
PA2000	***Pseudomonas_aeruginosa_PA175_6553***	GCF_003332455.1	No	Clinical	Eye	8	16	10	6	10	309
PA2001	***Pseudomonas_aeruginosa_Pa1780_9909***	GCF_003670015.1	Yes	Clinical	Urinary tract	18		12	20	11	233
PA2002	***Pseudomonas_aeruginosa_PA181_12067***	GCF_009727425.1	No	Clinical	Eye	15	32	12	23	12	244
PA2003	***Pseudomonas_aeruginosa_Pa1810_9904***	GCF_003669905.1	Yes	Clinical	Urinary tract	18		12	20	11	233
PA2004	***Pseudomonas_aeruginosa_PA182_12064***	GCF_009727385.1	Yes	Clinical	Eye	13		9	10	12	27
PA2005	***Pseudomonas_aeruginosa_PA188_12065***	GCF_009727395.1	Yes	Clinical	Eye	18		11	19	11	491
PA2006	***Pseudomonas_aeruginosa_PA189_12063***	GCF_009727345.1	No	Clinical	Eye	18	86	11	19	11	491
PA2007	***Pseudomonas_aeruginosa_PA193_12062***	GCF_009727335.1	No	Clinical	Eye	18	79	13	19	12	760
PA2008	***Pseudomonas_aeruginosa_PA198_12061***	GCF_009727325.1	No	Clinical	Eye	4	14	10	3	10	308
PA2009	***Pseudomonas_aeruginosa_PA1RG_3201***	GCF_001293085.1	No	Environment	Clinical environment: Dental, Hospital	18	88	13	19	12	782
PA2010	***Pseudomonas_aeruginosa_PA2_6803***	GCF_002866725.1	No	Clinical	Respiratory tract	4	14	10	3	10	308
PA2011	***Pseudomonas_aeruginosa_PA206_12059***	GCF_009727245.1	No	Clinical	Eye	7	15	7	7	8	Undefined
PA2012	***Pseudomonas_aeruginosa_PA21_ST175_262***	GCF_000342145.1	No	Clinical	Bacteraemia	18	65	6	22	7	175
PA2013	***Pseudomonas_aeruginosa_PA217_12057***	GCF_009727225.1	No	Clinical	Eye	19	102	12	21	4	1047
PA2014	***Pseudomonas_aeruginosa_PA218_12058***	GCF_009727235.1	No	Clinical	Eye	18	79	13	19	12	3083
PA2015	***Pseudomonas_aeruginosa_PA219_12054***	GCF_009727125.1	Yes	Clinical	Eye	4		10	3	10	308
PA2016	***Pseudomonas_aeruginosa_PA220_12056***	GCF_009727165.1	Yes	Clinical	Eye	19		10	1	10	316
PA2017	***Pseudomonas_aeruginosa_PA221_12055***	GCF_009727135.1	No	Clinical	Eye	19	38	10	1	10	316

PA2018	***Pseudomonas_aeruginosa_Pa2441_9657***	GCF_003611395.1	Yes	Clinical	Body fluid	15		12	23	12	244
PA2019	***Pseudomonas_aeruginosa_Pa2562_9906***	GCF_003669955.1	No	Clinical	Body fluid	18	84	12	20	11	233
PA2020	***Pseudomonas_aeruginosa_Pa2568_9908***	GCF_003669995.1	Yes	Clinical	Body fluid	18		12	20	11	233
PA2021	***Pseudomonas_aeruginosa_PA298_11122***	GCF_005305005.1	No	Clinical	Gastrointestinal	17	22	13	15	13	277
PA2022	***Pseudomonas_aeruginosa_PA3_7102***	GCF_002866785.1	No	Clinical	Respiratory tract	18	84	12	20	11	233
PA2023	***Pseudomonas_aeruginosa_PA31_6374***	GCF_003332785.1	Yes	Clinical	Eye	4		10	3	10	308
PA2024	***Pseudomonas_aeruginosa_PA32_6820***	GCF_003332735.1	Yes	Clinical	Eye	4		10	3	10	308
PA2025	***Pseudomonas_aeruginosa_PA33_7092***	GCF_003332715.1	Yes	Clinical	Eye	4		10	3	10	308
PA2026	***Pseudomonas_aeruginosa_PA34_6359***	GCF_002591765.1	No	Clinical	Respiratory tract	18	86	9	19	5	Undefined
PA2027	***Pseudomonas_aeruginosa_PA34_9522***	GCF_003332705.2	No	Clinical	Eye	19	48	3	21	3	1284
PA2028	***Pseudomonas_aeruginosa_PA3448_5236***	GCF_001802735.1	No	Clinical	Bacteraemia	17	22	13	15	13	277
PA2029	***Pseudomonas_aeruginosa_Pa347_9901***	GCF_003669855.1	No	Clinical	Body fluid	18	95	13	19	13	1207
PA2030	***Pseudomonas_aeruginosa_PA35_5777***	GCF_003332755.1	No	Clinical	Eye	4	14	10	3	10	308
PA2031	***Pseudomonas_aeruginosa_PA37_6567***	GCF_003332665.1	Yes	Clinical	Eye	4		10	3	10	308
PA2032	***Pseudomonas_aeruginosa_PA4_7118***	GCF_002866745.1	No	Clinical	Respiratory tract	18	63	10	19	12	1858
PA2033	***Pseudomonas_aeruginosa_PA40_7076***	GCF_003332655.1	No	Clinical	Eye	18	86	8	19	9	2966
PA2034	***Pseudomonas_aeruginosa_Pa423_9655***	GCF_003611345.1	Yes	Clinical	Respiratory tract	8		10	6	10	309
PA2035	***Pseudomonas_aeruginosa_PA45_289***	GCF_000359565.1	No	Clinical	Bacteraemia	18	95	12	19	12	266
PA2036	***Pseudomonas_aeruginosa_PA4722_12122***	GCF_009901795.1	No	Clinical	Gastrointestinal	17	22	13	15	13	277
PA2037	***Pseudomonas_aeruginosa_PA5_7006***	GCF_002866685.1	No	Clinical	Respiratory tract	19	47	10	8	10	357
PA2038	***Pseudomonas_aeruginosa_Pa58_6334***	GCF_002192495.1	No	Clinical	Respiratory tract	4	14	10	3	10	308
PA2039	***Pseudomonas_aeruginosa_PA59_12042***	GCF_009497675.1	No	Environment	Animal	18	91	12	19	12	260
PA2040	***Pseudomonas_aeruginosa_PA59_6015***	GCF_003332415.1	No	Clinical	Cystic fibrosis	18	86	6	19	7	649
PA2041	***Pseudomonas_aeruginosa_PA6_6099***	GCF_002866805.1	Yes	Clinical	Respiratory tract	4		10	3	10	308
PA2042	***Pseudomonas_aeruginosa_PA64_6176***	GCF_003332385.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	775
PA2043	***Pseudomonas_aeruginosa_Pa64_7022***	GCF_002915615.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	20	13	21	11	1560
PA2044	***Pseudomonas_aeruginosa_PA66_5826***	GCF_003332375.1	Yes	Clinical	Cystic fibrosis	18		6	19	7	649
PA2045	***Pseudomonas_aeruginosa_PA7_119***	GCF_000017205.1	No	Clinical	Unknown	5		4			1195
PA2046	***Pseudomonas_aeruginosa_PA77_7182***	GCF_002211545.1	No	Clinical	Bacteraemia	4	14	10	3	10	308
PA2047	***Pseudomonas_aeruginosa_PA7790_5368***	GCF_001870265.1	No	Clinical	Respiratory tract	17	22	13	15	13	277

PA2048	***Pseudomonas_aeruginosa_Pa792_9654***	GCF_003611335.1	No	Clinical	Intra-abdominal tract	15	32	12	23	12	244
PA2049	***Pseudomonas_aeruginosa_Pa795_9656***	GCF_003611355.1	Yes	Clinical	Body fluid	15		12	23	12	244
PA2050	***Pseudomonas_aeruginosa_PA82_5867***	GCF_003332645.1	No	Clinical	Eye	19	102	10	21	10	1027
PA2051	***Pseudomonas_aeruginosa_PA8281_5357***	GCF_001792855.1	No	Clinical	Respiratory tract	17	22	13	15	13	277
PA2052	***Pseudomonas_aeruginosa_Pa84_6035***	GCF_002205335.1	No	Clinical	Respiratory tract	18	102	13	19	12	3569
PA2053	***Pseudomonas_aeruginosa_Pa885_9900***	GCF_003669825.1	Yes	Clinical	Respiratory tract	8		10	6	10	309
PA2054	***Pseudomonas_aeruginosa_PA92_6202***	GCF_003332475.1	No	Clinical	Cystic fibrosis	18	72	9	19	5	775
PA2055	***Pseudomonas_aeruginosa_PA99_2045***	GCF_000611995.2	No	Clinical	Urinary tract	18	81	13	19	11	463
PA2056	***Pseudomonas_aeruginosa_PABL001_9628***	GCF_003412325.1	No	Clinical	Bacteraemia	18	102	9	19	12	447
PA2057	***Pseudomonas_aeruginosa_PABL002_9626***	GCF_003412285.1	Yes	Clinical	Bacteraemia	1		12	2	4	253
PA2058	***Pseudomonas_aeruginosa_PABL003_9627***	GCF_003412295.1	No	Clinical	Bacteraemia	18	97	9	19	12	258
PA2059	***Pseudomonas_aeruginosa_PABL004_9612***	GCF_003411985.1	No	Clinical	Bacteraemia	18	32	6	19	7	1734
PA2060	***Pseudomonas_aeruginosa_PABL011_9625***	GCF_003412275.1	No	Clinical	Bacteraemia	9	11	9	11	5	845
PA2061	***Pseudomonas_aeruginosa_PABL012_9632***	GCF_003429185.1	No	Clinical	Bacteraemia	18	29	9	19	5	Undefined
PA2062	***Pseudomonas_aeruginosa_PABL013_9624***	GCF_003412255.1	No	Clinical	Bacteraemia	19	102	10	21	10	296
PA2063	***Pseudomonas_aeruginosa_PABL014_9623***	GCF_003412225.1	No	Clinical	Bacteraemia	19	61	10	21	10	207
PA2064	***Pseudomonas_aeruginosa_PABL016_9621***	GCF_003412165.1	No	Clinical	Bacteraemia	19	38	10	1	10	2555
PA2065	***Pseudomonas_aeruginosa_PABL017_9633***	GCF_003429205.1	No	Clinical	Bacteraemia	18	102	13	19	11	2167
PA2066	***Pseudomonas_aeruginosa_PABL019_9620***	GCF_003412155.1	Yes	Clinical	Bacteraemia	18		13	19	11	1506
PA2067	***Pseudomonas_aeruginosa_PABL022_9618***	GCF_003412125.1	Yes	Clinical	Bacteraemia	2		10	5	10	298
PA2068	***Pseudomonas_aeruginosa_PABL023_9598***	GCF_003411725.1	No	Clinical	Bacteraemia	18	86	13	19	12	1226
PA2069	***Pseudomonas_aeruginosa_PABL024_9603***	GCF_003411815.1	No	Clinical	Bacteraemia	18	102	9	19	12	991
PA2070	***Pseudomonas_aeruginosa_PABL026_9580***	GCF_003411355.1	No	Clinical	Bacteraemia	18	93	13	19	11	108
PA2071	***Pseudomonas_aeruginosa_PABL028_9604***	GCF_003411845.1	No	Clinical	Bacteraemia	18	79	12	19	11	Undefined
PA2072	***Pseudomonas_aeruginosa_PABL031_9611***	GCF_003411975.1	No	Clinical	Bacteraemia	18	81	13	19	11	463
PA2073	***Pseudomonas_aeruginosa_PABL034_9608***	GCF_003411905.1	Yes	Clinical	Bacteraemia	18		9	22	12	348
PA2074	***Pseudomonas_aeruginosa_PABL037_9605***	GCF_003411875.1	No	Clinical	Bacteraemia	14	52	2	16	2	111
PA2075	***Pseudomonas_aeruginosa_PABL038_9568***	GCF_003411125.1	No	Clinical	Bacteraemia	14	52	2	16	2	111
PA2076	***Pseudomonas_aeruginosa_PABL041_9585***	GCF_003411465.1	No	Clinical	Bacteraemia	1	103	12	2	4	253
PA2077	***Pseudomonas_aeruginosa_PABL042_9573***	GCF_003411235.1	No	Clinical	Bacteraemia	16	5	11	17	14	179

PA2078	***Pseudomonas_aeruginosa_PABL043_9587***	GCF_003411505.1	No	Clinical	Bacteraemia	5		4			1195
PA2079	***Pseudomonas_aeruginosa_PABL045_9591***	GCF_003411585.1	No	Clinical	Bacteraemia	18	98	13	19	11	1506
PA2080	***Pseudomonas_aeruginosa_PABL046_9588***	GCF_003411535.1	No	Clinical	Bacteraemia	18	76	6	19	7	3050
PA2081	***Pseudomonas_aeruginosa_PABL047_9602***	GCF_003411805.1	No	Clinical	Bacteraemia	15	32	12	23	12	244
PA2082	***Pseudomonas_aeruginosa_PABL048_9601***	GCF_003411785.2	Yes	Clinical	Bacteraemia	2		10	5	10	298
PA2083	***Pseudomonas_aeruginosa_PABL049_9599***	GCF_003411745.1	No	Clinical	Bacteraemia	15	32	12	23	12	244
PA2084	***Pseudomonas_aeruginosa_PABL052_9597***	GCF_003411705.1	No	Clinical	Bacteraemia	18	32		19		381
PA2085	***Pseudomonas_aeruginosa_PABL055_9589***	GCF_003411555.1	No	Clinical	Bacteraemia	18	7	9	19	12	1285
PA2086	***Pseudomonas_aeruginosa_PABL058_9551***	GCF_003410785.1	Yes	Clinical	Bacteraemia	16		11	17	14	179
PA2087	***Pseudomonas_aeruginosa_PABL059_9566***	GCF_003411095.1	Yes	Clinical	Bacteraemia	18		9	22	12	348
PA2088	***Pseudomonas_aeruginosa_PABL061_9579***	GCF_003411345.1	No	Clinical	Bacteraemia	18	97	9	19	5	232
PA2089	***Pseudomonas_aeruginosa_PABL062_9560***	GCF_003410975.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA2090	***Pseudomonas_aeruginosa_PABL066_9582***	GCF_003411415.1	No	Clinical	Bacteraemia	18	4	9	22	12	348
PA2091	***Pseudomonas_aeruginosa_PABL068_9576***	GCF_003411275.1	No	Clinical	Bacteraemia	19	102	8	21	9	Undefined
PA2092	***Pseudomonas_aeruginosa_PABL069_9577***	GCF_003411285.1	No	Clinical	Bacteraemia	18	4	9	22	12	348
PA2093	***Pseudomonas_aeruginosa_PABL070_9575***	GCF_003411265.1	No	Clinical	Bacteraemia	18	64	6	22	7	485
PA2094	***Pseudomonas_aeruginosa_PABL072_9556***	GCF_003410875.1	No	Clinical	Bacteraemia	2	39	10	5	10	446
PA2095	***Pseudomonas_aeruginosa_PABL073_9548***	GCF_003410715.1	No	Clinical	Bacteraemia	10	78	5	12	6	274
PA2096	***Pseudomonas_aeruginosa_PABL076_9550***	GCF_003410765.1	No	Clinical	Bacteraemia	18	97	9	19	5	1058
PA2097	***Pseudomonas_aeruginosa_PABL077_9570***	GCF_003411165.1	No	Clinical	Bacteraemia	18	76	13	19	11	2053
PA2098	***Pseudomonas_aeruginosa_PABL078_9571***	GCF_003411185.1	No	Clinical	Bacteraemia	18	78	13	19	12	589
PA2099	***Pseudomonas_aeruginosa_PABL080_9567***	GCF_003411115.1	No	Clinical	Bacteraemia	18	102	11	19	14	1337
PA2100	***Pseudomonas_aeruginosa_PABL083_9562***	GCF_003411005.1	Yes	Clinical	Bacteraemia	3		10	4	10	235
PA2101	***Pseudomonas_aeruginosa_PABL085_9559***	GCF_003410935.1	No	Clinical	Bacteraemia	19	103	13	21	11	2406
PA2102	***Pseudomonas_aeruginosa_PABL089_9545***	GCF_003410645.1	Yes	Clinical	Bacteraemia	18		9	22	12	348
PA2103	***Pseudomonas_aeruginosa_PABL090_9537***	GCF_003410505.1	No	Clinical	Bacteraemia	18	84	12	20	11	233
PA2104	***Pseudomonas_aeruginosa_PABL092_9533***	GCF_003410435.1	Yes	Clinical	Bacteraemia	18		10	19	10	639
PA2105	***Pseudomonas_aeruginosa_PABL096_9629***	GCF_003412355.1	No	Clinical	Bacteraemia	18	73	9	19	5	254
PA2106	***Pseudomonas_aeruginosa_PABL097_9547***	GCF_003410705.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2107	***Pseudomonas_aeruginosa_PABL100_9544***	GCF_003410635.1	No	Clinical	Bacteraemia	18	17	13	19	12	Undefined

PA2108	***Pseudomonas_aeruginosa_PABL102_9541***	GCF_003410585.1	No	Clinical	Bacteraemia	18	11	8	19	12	1394
PA2109	***Pseudomonas_aeruginosa_PABL103_9538***	GCF_003410515.1	No	Clinical	Bacteraemia	19	39	10	21	10	319
PA2110	***Pseudomonas_aeruginosa_PABL104_9540***	GCF_003410565.1	No	Clinical	Bacteraemia	18	66	10	19	10	639
PA2111	***Pseudomonas_aeruginosa_PABL105_9534***	GCF_003410445.1	Yes	Clinical	Bacteraemia	9		9	11	5	17
PA2112	***Pseudomonas_aeruginosa_PABL106_9539***	GCF_003410555.1	No	Clinical	Bacteraemia	3	6	10	4	10	235
PA2113	***Pseudomonas_aeruginosa_PABL107_9535***	GCF_003410475.1	No	Clinical	Bacteraemia	19	8	12	21	4	377
PA2114	***Pseudomonas_aeruginosa_PABL108_9536***	GCF_003410485.1	No	Clinical	Bacteraemia	8	16	10	6	10	309
PA2115	***Pseudomonas_aeruginosa_PAC08_5361***	GCF_002002365.1	No	Clinical	Urinary tract	19	58	10	21	10	1076
PA2116	***Pseudomonas_aeruginosa_PAC106A_11035***	GCF_004374005.1	No	Clinical	Cystic fibrosis	18	86	9	19	5	132
PA2117	***Pseudomonas_aeruginosa_PAC107A_11036***	GCF_004374065.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	17
PA2118	***Pseudomonas_aeruginosa_PAC10A_11031***	GCF_004373965.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA2119	***Pseudomonas_aeruginosa_PAC115A_10996***	GCF_004373255.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA2120	***Pseudomonas_aeruginosa_PAC117A_11032***	GCF_004373975.1	Yes	Clinical	Cystic fibrosis	18		10	19	10	853
PA2121	***Pseudomonas_aeruginosa_PAC117B_11012***	GCF_004373575.1	No	Clinical	Cystic fibrosis	10	78	5	12	6	2834
PA2122	***Pseudomonas_aeruginosa_PAC13A_11027***	GCF_004373875.1	Yes	Clinical	Cystic fibrosis	18		10	19	10	853
PA2123	***Pseudomonas_aeruginosa_PAC13B_11034***	GCF_004373995.1	No	Clinical	Cystic fibrosis	18	83	10	19	10	853
PA2124	***Pseudomonas_aeruginosa_PAC14B_11011***	GCF_004373565.1	Yes	Clinical	Cystic fibrosis	12		1	14	1	395
PA2125	***Pseudomonas_aeruginosa_PAC15A_11010***	GCF_004373545.1	No	Clinical	Cystic fibrosis	18	44	13	19	11	884
PA2126	***Pseudomonas_aeruginosa_PAC15B_11009***	GCF_004373515.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	Undefined
PA2127	***Pseudomonas_aeruginosa_PAC17_5026***	GCF_002002765.1	No	Clinical	Bacteraemia	3	6	10	4	10	235
PA2128	***Pseudomonas_aeruginosa_PAC17A_11008***	GCF_004373505.1	No	Clinical	Cystic fibrosis	18	78	13	19	11	Undefined
PA2129	***Pseudomonas_aeruginosa_PAC18B_11006***	GCF_004373455.1	Yes	Clinical	Cystic fibrosis	18		6	19	7	170
PA2130	***Pseudomonas_aeruginosa_PAC22A_11001***	GCF_004373355.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2131	***Pseudomonas_aeruginosa_PAC31A_11097***	GCF_004378725.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	471
PA2132	***Pseudomonas_aeruginosa_PAC38A_10989***	GCF_004373125.1	No	Clinical	Cystic fibrosis	10	78	5	12	6	Undefined
PA2133	***Pseudomonas_aeruginosa_PAC38B_11016***	GCF_004373655.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	Undefined
PA2134	***Pseudomonas_aeruginosa_PAC42A_11020***	GCF_004373745.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	471
PA2135	***Pseudomonas_aeruginosa_PAC44A_11099***	GCF_004378745.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA2136	***Pseudomonas_aeruginosa_PAC44C_10998***	GCF_004373305.1	Yes	Clinical	Cystic fibrosis	9		9	11	5	17
PA2137	***Pseudomonas_aeruginosa_PAC46A_11061***	GCF_004374525.1	No	Clinical	Cystic fibrosis	18	23	13	19	11	499

PA2138	***Pseudomonas_aeruginosa_PAC56A_11007***	GCF_004373475.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	Undefined
PA2139	***Pseudomonas_aeruginosa_PAC56B_11025***	GCF_004373845.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	Undefined
PA2140	***Pseudomonas_aeruginosa_PAC61A_11045***	GCF_004374205.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	499
PA2141	***Pseudomonas_aeruginosa_PAC76A_10986***	GCF_004373035.1	No	Clinical	Cystic fibrosis	18	81	13	19	12	Undefined
PA2142	***Pseudomonas_aeruginosa_PAC78B_11004***	GCF_004373415.1	Yes	Clinical	Cystic fibrosis	18		6	19	7	170
PA2143	***Pseudomonas_aeruginosa_PAC79A_11028***	GCF_004373885.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	132
PA2144	***Pseudomonas_aeruginosa_PAC79B_11029***	GCF_004373915.1	Yes	Clinical	Cystic fibrosis	18		9	19	5	132
PA2145	***Pseudomonas_aeruginosa_PAC80A_10992***	GCF_004373175.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	471
PA2146	***Pseudomonas_aeruginosa_PAC93B_11037***	GCF_004374075.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	27
PA2147	***Pseudomonas_aeruginosa_PAC93C_11038***	GCF_004374085.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	27
PA2148	***Pseudomonas_aeruginosa_PAC95A_10982***	GCF_004372985.1	No	Clinical	Cystic fibrosis	18	78	6	19	7	170
PA2149	***Pseudomonas_aeruginosa_PAC97A_10980***	GCF_004372925.1	No	Clinical	Cystic fibrosis	18	93	8	19	13	Undefined
PA2150	***Pseudomonas_aeruginosa_PAC98C_11019***	GCF_004373725.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	471
PA2151	***Pseudomonas_aeruginosa_PAC98D_10990***	GCF_004373135.1	No	Clinical	Cystic fibrosis	18	97	13	19	11	471
PA2152	***Pseudomonas_aeruginosa_PAC9A_11033***	GCF_004373985.1	No	Clinical	Cystic fibrosis	18	78		19		Undefined
PA2153	***Pseudomonas_aeruginosa_PACS2_84***	GCF_000168335.1	No	Clinical	Cystic fibrosis	18	11	8	19	12	1394
PA2154	***Pseudomonas_aeruginosa_PADK2_CF510_376***	GCF_000259025.1	No	Clinical	Cystic fibrosis	18	78	13	19	11	386
PA2155	***Pseudomonas_aeruginosa_Pae_CF6701l_2633***	GCF_001007215.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2156	***Pseudomonas_aeruginosa_Pae_CF6702o_2666***	GCF_001023985.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2157	***Pseudomonas_aeruginosa_Pae_CF6702q_2689***	GCF_001024445.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2158	***Pseudomonas_aeruginosa_Pae_CF6703c_2655***	GCF_001023765.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2159	***Pseudomonas_aeruginosa_Pae_CF6703i_2673***	GCF_001024125.1	No	Clinical	Cystic fibrosis	10	78	5	12	6	274
PA2160	***Pseudomonas_aeruginosa_Pae_CF6705e_2706***	GCF_001024775.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2161	***Pseudomonas_aeruginosa_Pae_CF6705q_2824***	GCF_001036815.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2162	***Pseudomonas_aeruginosa_Pae_CF6707d_2723***	GCF_001034755.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2163	***Pseudomonas_aeruginosa_Pae_CF6707t_2853***	GCF_001037395.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2164	***Pseudomonas_aeruginosa_Pae_CF6709b_2750***	GCF_001035305.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2165	***Pseudomonas_aeruginosa_Pae_CF6709n_2762***	GCF_001035535.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2166	***Pseudomonas_aeruginosa_Pae_CF6710e_2773***	GCF_001035765.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2167	***Pseudomonas_aeruginosa_Pae_CF6710l_3103***	GCF_001035885.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274

PA2168	***Pseudomonas_aeruginosa_Pae_CF6710m_2780***	GCF_001035925.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2169	***Pseudomonas_aeruginosa_Pae_CF6710n_2781***	GCF_001035945.1	No	Clinical	Cystic fibrosis	10	78	5	12	6	274
PA2170	***Pseudomonas_aeruginosa_Pae_CF6711t_2807***	GCF_001036485.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2171	***Pseudomonas_aeruginosa_Pae_CF6712d_2808***	GCF_001036495.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2172	***Pseudomonas_aeruginosa_Pae_CF6712h_2813***	GCF_001036585.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2173	***Pseudomonas_aeruginosa_Pae_CF6712j_2815***	GCF_001036645.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2174	***Pseudomonas_aeruginosa_PAE006_11982***	GCF_008386455.1	No	Clinical	Respiratory tract	18	95	12	19	12	3348
PA2175	***Pseudomonas_aeruginosa_Pae100_7256***	GCF_002216425.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		11	19	14	110
PA2176	***Pseudomonas_aeruginosa_Pae102_6011***	GCF_002216485.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		11	19	14	110
PA2177	***Pseudomonas_aeruginosa_Pae110_10151***	GCF_003837265.1	No	Environment	Other environmental source	18	93	11	19	14	110
PA2178	***Pseudomonas_aeruginosa_Pae110_6843***	GCF_002216345.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	93	11	19	14	110
PA2179	***Pseudomonas_aeruginosa_Pae111_7123***	GCF_002216335.1	No	Environment	Farm environment	18	68	13	19	11	1605
PA2180	***Pseudomonas_aeruginosa_Pae112_7021***	GCF_002216325.1	No	Environment	Farm environment	18	95	12	19	12	1129
PA2181	***Pseudomonas_aeruginosa_Pae113_10697***	GCF_004053835.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	54	8	18	9	3137
PA2182	***Pseudomonas_aeruginosa_Pae113_5830***	GCF_002216355.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	95	9	19	11	Undefined
PA2183	***Pseudomonas_aeruginosa_Pae12_10704***	GCF_004053975.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	15	18	12	23	12	244
PA2184	***Pseudomonas_aeruginosa_Pae160_7099***	GCF_002216465.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	8	16	10	6	10	309
PA2185	***Pseudomonas_aeruginosa_PAE1880_10732***	GCF_004213525.1	No	Clinical	Urinary tract	9	11	9	11	5	17
PA2186	***Pseudomonas_aeruginosa_Pae21_10708***	GCF_004054065.1	No	Clinical	Urinary tract	18	11	8	19	12	1394
PA2187	***Pseudomonas_aeruginosa_Pae22_10709***	GCF_004054095.1	No	Clinical	Respiratory tract	11	30	11	13	14	252
PA2188	***Pseudomonas_aeruginosa_Pae29_10703***	GCF_004053955.1	No	Clinical	Respiratory tract	19	47	10	8	10	357
PA2189	***Pseudomonas_aeruginosa_Pae39_10706***	GCF_004054035.1	No	Clinical	Respiratory tract	18	70	9	19	12	3079
PA2190	***Pseudomonas_aeruginosa_Pae42_10698***	GCF_004053845.1	Yes	Clinical	Respiratory tract	19		10	8	10	357
PA2191	***Pseudomonas_aeruginosa_Pae66_10707***	GCF_004054045.1	No	Clinical	Bone and Joint	19	38	3	21	3	3078
PA2192	***Pseudomonas_aeruginosa_Pae70_10705***	GCF_004053985.1	No	Clinical	Urinary tract	18	44	13	19	12	275
PA2193	***Pseudomonas_aeruginosa_Pae74_10701***	GCF_004053935.1	No	Clinical	Respiratory tract	15	32	12	23	12	244
PA2194	***Pseudomonas_aeruginosa_Pae81_10700***	GCF_004053865.1	No	Clinical	Urinary tract	19	54	8	18	9	3080
PA2195	***Pseudomonas_aeruginosa_Pae83_10702***	GCF_004053945.1	Yes	Clinical	Respiratory tract	18		9	19	12	3079

PA2196	***Pseudomonas_aeruginosa_Pae85_5932***	GCF_002216405.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	17	22	13	15	13	1128
PA2197	***Pseudomonas_aeruginosa_PaEB1_7175***	GCF_002216505.1	No	Environment	Sewage/Wastewater	18	93		19		262
PA2198	***Pseudomonas_aeruginosa_PaEB6_5895***	GCF_002216445.1	No	Environment	Sewage/Wastewater	18	78	13	19	12	508
PA2199	***Pseudomonas_aeruginosa_PAG_2088***	GCF_000743405.1	No	Clinical	Bacteraemia	16	5	11	17	14	155
PA2200	***Pseudomonas_aeruginosa_PAH13_7651***	GCF_002283295.1	No	Environment	Clinical environment: Dental, Hospital	17	22	13	15	13	277
PA2201	***Pseudomonas_aeruginosa_PAL01_5797***	GCF_003143795.1	No	Clinical	Respiratory tract	14	52	2	16	2	111
PA2202	***Pseudomonas_aeruginosa_PAL11_7136***	GCF_003143815.1	No	Clinical	Respiratory tract	3	6	10	4	10	235
PA2203	***Pseudomonas_aeruginosa_PAN3_7650***	GCF_002263535.1	No	Environment	Clinical environment: Dental, Hospital	17	22	13	15	13	277
PA2204	***Pseudomonas_aeruginosa_PAO1_107***	GCF_000006765.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	32	12	19	12	549
PA2205	***Pseudomonas_aeruginosa_PAO1161_10710***	GCF_004102665.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	32	12	19	12	549
PA2206	***Pseudomonas_aeruginosa_PAS10_6688***	GCF_002201325.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA2207	***Pseudomonas_aeruginosa_PAS2_5875***	GCF_002201295.1	No	Clinical	Bacteraemia	19	102	10	21	10	1076
PA2208	***Pseudomonas_aeruginosa_PAS4_6100***	GCF_002201405.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA2209	***Pseudomonas_aeruginosa_PAS5_6728***	GCF_002201225.1	No	Clinical	Bacteraemia	3	6	10	4	10	235
PA2210	***Pseudomonas_aeruginosa_PAS6_6028***	GCF_002201255.1	Yes	Clinical	Urinary tract	3		10	4	10	235
PA2211	***Pseudomonas_aeruginosa_PAS8_6190***	GCF_002201385.1	Yes	Clinical	Respiratory tract	19		10	21	10	1076
PA2212	***Pseudomonas_aeruginosa_PAS9_7267***	GCF_002201375.1	Yes	Clinical	Bacteraemia	3		10	4	10	235
PA2213	***Pseudomonas_aeruginosa_PASGNDM345_6255***	GCF_002104615.1	No	Clinical	Respiratory tract	4	14	10	3	10	308
PA2214	***Pseudomonas_aeruginosa_PASGNDM544_6199***	GCF_002134885.1	No	Clinical	Respiratory tract	4	14	10	3	10	308
PA2215	***Pseudomonas_aeruginosa_PASGNDM571_6592***	GCF_002134845.1	Yes	Clinical	Urinary tract	4		10	3	10	308
PA2216	***Pseudomonas_aeruginosa_PASGNDM583_6563***	GCF_002134835.1	Yes	Clinical	Urinary tract	4		10	3	10	308
PA2217	***Pseudomonas_aeruginosa_PASGNDM586_7075***	GCF_002134915.1	Yes	Clinical	Urinary tract	4		10	3	10	308
PA2218	***Pseudomonas_aeruginosa_PASGNDM587_6805***	GCF_002134895.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	4		10	3	10	308
PA2219	***Pseudomonas_aeruginosa_PASGNDM590_5769***	GCF_002134975.1	Yes	Clinical	Urinary tract	4		10	3	10	308
PA2220	***Pseudomonas_aeruginosa_PASGNDM591_6102***	GCF_002134965.1	Yes	Clinical	Urinary tract	4		10	3	10	308
PA2221	***Pseudomonas_aeruginosa_PASGNDM592_5821***	GCF_002134905.1	Yes	Clinical	Urinary tract	4		10	3	10	308
PA2222	***Pseudomonas_aeruginosa_PASGNDM593_6784***	GCF_002134985.1	Yes	Clinical	Urinary tract	4		10	3	10	308
PA2223	***Pseudomonas_aeruginosa_PASGNDM699_7104***	GCF_002104595.1	Yes	Clinical	Respiratory tract	4		10	3	10	308

PA2224	***Pseudomonas_aeruginosa_PASP010_11920***	GCF_006705085.1	No	Clinical	Bacteraemia	2	39	10	5	10	446
PA2225	***Pseudomonas_aeruginosa_PASP063_11919***	GCF_006705075.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2226	***Pseudomonas_aeruginosa_PASP107_11918***	GCF_006705065.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2227	***Pseudomonas_aeruginosa_PASP118_11917***	GCF_006705045.1	Yes	Clinical	Bacteraemia	2		10	5	10	298
PA2228	***Pseudomonas_aeruginosa_PASP145_11915***	GCF_006704985.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2229	***Pseudomonas_aeruginosa_PASP163_11914***	GCF_006704975.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2230	***Pseudomonas_aeruginosa_PASP170_11916***	GCF_006704995.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2231	***Pseudomonas_aeruginosa_PASP174_11913***	GCF_006704955.1	No	Clinical	Bacteraemia	2	39	10	5	10	446
PA2232	***Pseudomonas_aeruginosa_PASP199_11912***	GCF_006704945.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2233	***Pseudomonas_aeruginosa_PASP363_11911***	GCF_006704895.1	Yes	Clinical	Bacteraemia	2		10	5	10	298
PA2234	***Pseudomonas_aeruginosa_PASP368_11910***	GCF_006704885.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2235	***Pseudomonas_aeruginosa_PASP375_11909***	GCF_006704875.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2236	***Pseudomonas_aeruginosa_PASP418_11908***	GCF_006704865.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2237	***Pseudomonas_aeruginosa_PASP614_11907***	GCF_006704815.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2238	***Pseudomonas_aeruginosa_PB350_6610***	GCF_002812905.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA2239	***Pseudomonas_aeruginosa_PB353_6129***	GCF_002812865.1	No	Clinical	Urinary tract	18	102	13	19	12	Undefined
PA2240	***Pseudomonas_aeruginosa_PB354_7065***	GCF_002812885.1	Yes	Clinical	Urinary tract	18		13	19	12	Undefined
PA2241	***Pseudomonas_aeruginosa_PB367_7067***	GCF_002812925.1	No	Clinical	Respiratory tract	3	6	10	4	10	235
PA2242	***Pseudomonas_aeruginosa_PB368_7201***	GCF_002812845.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	39	10	21	10	319
PA2243	***Pseudomonas_aeruginosa_PB369_7191***	GCF_002812825.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19		10	21	10	319
PA2244	***Pseudomonas_aeruginosa_PD1_10570***	GCF_003974645.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	564
PA2245	***Pseudomonas_aeruginosa_PDR_2511***	GCF_000783275.1	No	Clinical	Urinary tract	7	15	12	7	12	3390
PA2246	***Pseudomonas_aeruginosa_PFK10_7600***	GCF_000505805.1	No	Environment	Sewage/Wastewater	18	93		20		575
PA2247	***Pseudomonas_aeruginosa_PhDW6_10105***	GCF_003836345.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	90	13	19	11	553
PA2248	***Pseudomonas_aeruginosa_PK6_7601***	GCF_000505825.1	No	Environment	Hydrocarbon contamination	18	69		19		514
PA2249	***Pseudomonas_aeruginosa_PMM38_10095***	GCF_003836135.1	No	Clinical	Respiratory tract	19	47	3	21	3	773
PA2250	***Pseudomonas_aeruginosa_PN586_35_w_10171***	GCF_003837665.1	No	Clinical	Urinary tract	14	52	2	16	2	111
PA2251	***Pseudomonas_aeruginosa_PPF_1_6589***	GCF_002287725.2	Yes	Environment	Clinical environment: Dental, Hospital	19		10	1	10	Undefined

PA2252	***Pseudomonas_aeruginosa_PPF_13_5940***	GCF_002312625.1	Yes	Environment	Clinical environment: Dental, Hospital	19		8	18	9	Undefined
PA2253	***Pseudomonas_aeruginosa_PPF_18_6586***	GCF_002312675.1	Yes	Environment	Clinical environment: Dental, Hospital	19		10	21	10	Undefined
PA2254	***Pseudomonas_aeruginosa_PPF_19_6654***	GCF_002312295.1	Yes	Environment	Clinical environment: Dental, Hospital	19		10	21	10	2503
PA2255	***Pseudomonas_aeruginosa_PPF_2_6351***	GCF_002312215.1	Yes	Environment	Clinical environment: Dental, Hospital	19		10	1	10	Undefined
PA2256	***Pseudomonas_aeruginosa_PPF_20_7309***	GCF_002312275.1	Yes	Environment	Clinical environment: Dental, Hospital	19		8	18	9	Undefined
PA2257	***Pseudomonas_aeruginosa_PPF_7_6077***	GCF_002312585.1	Yes	Environment	Clinical environment: Dental, Hospital	19		10	1	10	Undefined
PA2258	***Pseudomonas_aeruginosa_PS00100_9943***	GCF_003703855.1	No	Environment	Other environmental source	19	43	8	18	9	1182
PA2259	***Pseudomonas_aeruginosa_Ps04_5778***	GCF_002915235.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	74	13	19	11	676
PA2260	***Pseudomonas_aeruginosa_Ps1_3316***	GCF_001420535.1	No	Clinical	Urinary tract	18	45	13	19	11	644
PA2261	***Pseudomonas_aeruginosa_PS1_9947***	GCF_003725635.1	No	Clinical	Urinary tract	19	47	3	21	3	773
PA2262	***Pseudomonas_aeruginosa_PS1793_11896***	GCF_006704595.1	Yes	Clinical	Respiratory tract	2		10	5	10	298
PA2263	***Pseudomonas_aeruginosa_PS1796_11895***	GCF_006704575.1	Yes	Clinical	Respiratory tract	2		10	5	10	298
PA2264	***Pseudomonas_aeruginosa_PS1797_11894***	GCF_006704565.1	Yes	Clinical	Respiratory tract	2		10	5	10	298
PA2265	***Pseudomonas_aeruginosa_PS1875_11893***	GCF_006704555.1	Yes	Clinical	Bacteraemia	2		10	5	10	298
PA2266	***Pseudomonas_aeruginosa_PS1882_11892***	GCF_006704545.1	Yes	Clinical	Bacteraemia	2		10	5	10	298
PA2267	***Pseudomonas_aeruginosa_PS1884_11890***	GCF_006704485.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2268	***Pseudomonas_aeruginosa_PS1893_11889***	GCF_006704475.1	Yes	Clinical	Urinary tract	2		10	5	10	298
PA2269	***Pseudomonas_aeruginosa_PS1934_11891***	GCF_006704495.1	Yes	Clinical	Urinary tract	2		10	5	10	298
PA2270	***Pseudomonas_aeruginosa_PS1946_11887***	GCF_006704445.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2271	***Pseudomonas_aeruginosa_PS1948_11884***	GCF_006704365.1	Yes	Clinical	Urinary tract	2		10	5	10	446
PA2272	***Pseudomonas_aeruginosa_PS1955_11886***	GCF_006704385.1	Yes	Clinical	Bacteraemia	2		10	5	10	298
PA2273	***Pseudomonas_aeruginosa_PS1977_11882***	GCF_006704345.1	Yes	Clinical	Bacteraemia	2		10	5	10	446
PA2274	***Pseudomonas_aeruginosa_Ps2_3315***	GCF_001420525.1	No	Clinical	Urinary tract	18	45	13	19	11	2190
PA2275	***Pseudomonas_aeruginosa_PS2027_11885***	GCF_006704375.1	Yes	Clinical	Bacteraemia	2		10	5	10	298
PA2276	***Pseudomonas_aeruginosa_PS3_2513***	GCF_000786565.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	53	8	18	9	926
PA2277	***Pseudomonas_aeruginosa_PT12_10547***	GCF_003974185.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	10	21	10	296

PA2278	***Pseudomonas_aeruginosa_PT31M_10099***	GCF_003836225.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	9	11	9	11	5	17
PA2279	***Pseudomonas_aeruginosa_PT6_10577***	GCF_003974805.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	25	9	19	12	447
PA2280	***Pseudomonas_aeruginosa_PUPa3_10182***	GCF_003838485.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	97	9	19	12	241
PA2281	***Pseudomonas_aeruginosa_PUPa3_2080***	GCF_000698765.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	97	9	19	12	241
PA2282	***Pseudomonas_aeruginosa_RB_48_2005***	GCF_000568115.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	32	12	19	12	549
PA2283	***Pseudomonas_aeruginosa_RD1_3_12124***	GCF_009911735.1	No	Environment	Other environmental source	18	86	11	19	11	257
PA2284	***Pseudomonas_aeruginosa_RM1_6781***	GCF_002927195.1	No	Clinical	Respiratory tract	18	65	6	22	7	175
PA2285	***Pseudomonas_aeruginosa_RNS_PA1_3991***	GCF_001623945.1	Yes	Clinical	Gastrointestinal	3		10	4	10	235
PA2286	***Pseudomonas_aeruginosa_RNS_PA46_3992***	GCF_001623955.1	No	Clinical	Burn	3	6	10	4	10	235
PA2287	***Pseudomonas_aeruginosa_RNS_PA92_6546***	GCF_002406335.1	No	Clinical	Burn	3	6	10	4	10	235
PA2288	***Pseudomonas_aeruginosa_RNS_PAE05_3993***	GCF_001623985.1	No	Environment	Clinical environment: Dental, Hospital	3	6	10	4	10	235
PA2289	***Pseudomonas_aeruginosa_RNS_PAE08_6631***	GCF_002406345.1	No	Environment	Clinical environment: Dental, Hospital	3	6	10	4	10	235
PA2290	***Pseudomonas_aeruginosa_RP73_192***	GCF_000414035.1	No	Clinical	Cystic fibrosis	18	102	9	19	12	198
PA2291	***Pseudomonas_aeruginosa_Rsan_ver_10177***	GCF_003837775.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	86	13	19	12	998
PA2292	***Pseudomonas_aeruginosa_S122_C02_RS_6446***	GCF_002136245.1	No	Clinical	Respiratory tract	3	6	10	4	10	235
PA2293	***Pseudomonas_aeruginosa_S137_C02_RS_6638***	GCF_002136195.1	Yes	Clinical	Respiratory tract	18		13	20	12	621
PA2294	***Pseudomonas_aeruginosa_S143_C02_RS_6904***	GCF_002136515.1	Yes	Clinical	Respiratory tract	18		13	20	12	621
PA2295	***Pseudomonas_aeruginosa_S14b_6337***	GCF_002326525.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	97	13	19	12	Undefined
PA2296	***Pseudomonas_aeruginosa_S1e_7215***	GCF_002326305.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	198
PA2297	***Pseudomonas_aeruginosa_S1f_6658***	GCF_002330065.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	77	9	19	12	198
PA2298	***Pseudomonas_aeruginosa_S1g_6514***	GCF_002326275.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	198
PA2299	***Pseudomonas_aeruginosa_S1h_6791***	GCF_002326265.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	198
PA2300	***Pseudomonas_aeruginosa_S20b_6800***	GCF_002326195.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	92	8	19	12	2027
PA2301	***Pseudomonas_aeruginosa_S21a_6840***	GCF_002326515.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	11	30	11	13	14	984
PA2302	***Pseudomonas_aeruginosa_S220_C06_RS_6572***	GCF_002136495.1	Yes	Clinical	Respiratory tract	18		13	20	12	621
PA2303	***Pseudomonas_aeruginosa_S2239_15_10102***	GCF_003836275.1	No	Clinical	Cystic fibrosis	18	102	11	19	14	110
PA2304	***Pseudomonas_aeruginosa_S247_C06_RS_5800***	GCF_002136205.1	Yes	Clinical	Respiratory tract	18		13	20	12	621
PA2305	***Pseudomonas_aeruginosa_S252_C06_RS_6039***	GCF_002136215.1	Yes	Clinical	Respiratory tract	18		6	22	7	175

PA2306	***Pseudomonas_aeruginosa_S25b_2_5878***	GCF_002326085.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	68	13	19	13	645
PA2307	***Pseudomonas_aeruginosa_S292_C06_RS_5841***	GCF_002136165.1	Yes	Clinical	Respiratory tract	18		6	22	7	175
PA2308	***Pseudomonas_aeruginosa_S35004_591***	GCF_000481725.1	No	Clinical	Bacteraemia	16	5	11	17	14	179
PA2309	***Pseudomonas_aeruginosa_S39_C01_BS_6008***	GCF_002136285.1	Yes	Clinical	Bacteraemia	3		10	4	10	235
PA2310	***Pseudomonas_aeruginosa_S422_C09_BS_5934***	GCF_002136135.1	Yes	Clinical	Bacteraemia	18		6	22	7	175
PA2311	***Pseudomonas_aeruginosa_S426_C09_BS_7010***	GCF_002136125.1	Yes	Clinical	Bacteraemia	18		6	22	7	175
PA2312	***Pseudomonas_aeruginosa_S432_C09_RS_7094***	GCF_002136115.1	Yes	Clinical	Respiratory tract	18		6	22	7	175
PA2313	***Pseudomonas_aeruginosa_S434_C09_BS_6366***	GCF_002136065.1	Yes	Clinical	Bacteraemia	18		6	22	7	175
PA2314	***Pseudomonas_aeruginosa_S435_C09_BS_6798***	GCF_002136075.1	Yes	Clinical	Bacteraemia	18		6	22	7	175
PA2315	***Pseudomonas_aeruginosa_S440_C09_BS_5806***	GCF_002136445.1	Yes	Clinical	Bacteraemia	18		6	22	7	175
PA2316	***Pseudomonas_aeruginosa_S442_C09_BS_6162***	GCF_002136055.1	Yes	Clinical	Bacteraemia	18		6	22	7	175
PA2317	***Pseudomonas_aeruginosa_S443_C09_RS_6969***	GCF_002136015.1	Yes	Clinical	Respiratory tract	18		6	22	7	175
PA2318	***Pseudomonas_aeruginosa_S461_C10_RS_5920***	GCF_002136455.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA2319	***Pseudomonas_aeruginosa_S49_C01_BS_7011***	GCF_002136525.1	Yes	Clinical	Bacteraemia	3		10	4	10	235
PA2320	***Pseudomonas_aeruginosa_S518_C10_BS_6862***	GCF_002135995.1	No	Clinical	Bacteraemia	18	65	6	22	7	175
PA2321	***Pseudomonas_aeruginosa_S53_C01_BS_6946***	GCF_002136295.1	No	Clinical	Bacteraemia	19	47	3	21	3	532
PA2322	***Pseudomonas_aeruginosa_S54485_10063***	GCF_003835495.1	Yes	Clinical	Urinary tract	4		10	3	10	308
PA2323	***Pseudomonas_aeruginosa_S54485_596***	GCF_000481825.1	No	Clinical	Urinary tract	4	14	10	3	10	308
PA2324	***Pseudomonas_aeruginosa_S558_C10_BS_5984***	GCF_002136005.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA2325	***Pseudomonas_aeruginosa_S567_C10_BS_6501***	GCF_002135965.1	No	Clinical	Bacteraemia	12	2	1	14	1	395
PA2326	***Pseudomonas_aeruginosa_S57_C01_BS_6087***	GCF_002136535.1	Yes	Clinical	Bacteraemia	19		3	21	3	532
PA2327	***Pseudomonas_aeruginosa_S61_C01_BS_6021***	GCF_002136275.1	Yes	Clinical	Bacteraemia	14		2	16	2	111
PA2328	***Pseudomonas_aeruginosa_S611_C13_RS_6838***	GCF_002135955.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA2329	***Pseudomonas_aeruginosa_S619_C13_RS_6824***	GCF_002135925.1	Yes	Clinical	Respiratory tract	18		12	19	12	260
PA2330	***Pseudomonas_aeruginosa_S625_C13_RS_6911***	GCF_002135915.1	Yes	Clinical	Respiratory tract	18		12	19	12	260
PA2331	***Pseudomonas_aeruginosa_S626_C13_RS_6955***	GCF_002135885.1	No	Clinical	Respiratory tract	16	5	11	17	14	179
PA2332	***Pseudomonas_aeruginosa_S650_C13_BS_7179***	GCF_002135875.1	No	Clinical	Bacteraemia	18	84	12	19	12	260
PA2333	***Pseudomonas_aeruginosa_S658_C13_RS_5789***	GCF_002135845.1	Yes	Clinical	Respiratory tract	18		6	22	7	175
PA2334	***Pseudomonas_aeruginosa_S668_C14_BS_6743***	GCF_002135835.1	Yes	Clinical	Bacteraemia	18		13	20	12	621
PA2335	***Pseudomonas_aeruginosa_S669_C14_BS_6408***	GCF_002135795.1	No	Clinical	Bacteraemia	18	84	12	20	11	233

PA2336	***Pseudomonas_aeruginosa_S708_C14_RS_7198***	GCF_002136415.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA2337	***Pseudomonas_aeruginosa_S742_C15_BS_5948***	GCF_002135805.1	No	Clinical	Bacteraemia	14	52	2	16	2	111
PA2338	***Pseudomonas_aeruginosa_S749_C15_RS_6438***	GCF_002135755.1	No	Clinical	Respiratory tract	14	52	2	16	2	111
PA2339	***Pseudomonas_aeruginosa_S769_C16_RS_7296***	GCF_002135705.1	No	Clinical	Respiratory tract	18	81	13	20	12	621
PA2340	***Pseudomonas_aeruginosa_S782_C16_RS_5922***	GCF_002135715.1	Yes	Clinical	Respiratory tract	18		13	20	12	621
PA2341	***Pseudomonas_aeruginosa_S787_C16_RS_5998***	GCF_002136375.1	Yes	Clinical	Respiratory tract	18		13	20	12	621
PA2342	***Pseudomonas_aeruginosa_S794_C17_BS_5810***	GCF_002135675.1	Yes	Clinical	Bacteraemia	4		10	3	10	308
PA2343	***Pseudomonas_aeruginosa_S811_C17_BS_6582***	GCF_002135615.1	Yes	Clinical	Bacteraemia	18		13	20	12	621
PA2344	***Pseudomonas_aeruginosa_S819_C17_BS_6661***	GCF_002135685.1	Yes	Clinical	Bacteraemia	4		10	3	10	308
PA2345	***Pseudomonas_aeruginosa_S823_C17_RS_6185***	GCF_002135635.1	Yes	Clinical	Respiratory tract	3		10	4	10	235
PA2346	***Pseudomonas_aeruginosa_S827_C17_BS_6477***	GCF_002136365.1	Yes	Clinical	Bacteraemia	4		10	3	10	308
PA2347	***Pseudomonas_aeruginosa_S829_C17_RS_5883***	GCF_002135625.1	Yes	Clinical	Respiratory tract	18		13	20	12	621
PA2348	***Pseudomonas_aeruginosa_S830_C17_BS_5986***	GCF_002136355.1	No	Clinical	Bacteraemia	4	14	10	3	10	308
PA2349	***Pseudomonas_aeruginosa_S854_C18_BS_6989***	GCF_002136335.1	Yes	Clinical	Bacteraemia	3		10	4	10	235
PA2350	***Pseudomonas_aeruginosa_S86968_6031***	GCF_001515845.2	Yes	Clinical	Cancer	16		11	17	14	155
PA2351	***Pseudomonas_aeruginosa_S8b_1_6625***	GCF_002326245.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	2105
PA2352	***Pseudomonas_aeruginosa_S8b_3_5901***	GCF_002326205.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	86	9	19	12	2105
PA2353	***Pseudomonas_aeruginosa_SC1_10532***	GCF_003973885.1	No	Clinical	Cystic fibrosis	7	15	7	7	8	Undefined
PA2354	***Pseudomonas_aeruginosa_SCH_ABX04_5128***	GCF_002001305.1	Yes	Clinical	Cystic fibrosis	13		9	10	12	27
PA2355	***Pseudomonas_aeruginosa_SCH_ABX05_5199***	GCF_002001265.1	No	Clinical	Cystic fibrosis	18	87	5	19	6	Undefined
PA2356	***Pseudomonas_aeruginosa_SCH_ABX08_5466***	GCF_002005765.1	No	Clinical	Cystic fibrosis	13	50	9	10	12	27
PA2357	***Pseudomonas_aeruginosa_SCH_ABX09_5112***	GCF_002001225.1	No	Clinical	Cystic fibrosis	18	97	9	19	12	241
PA2358	***Pseudomonas_aeruginosa_SCH_ABX14_5011***	GCF_001990445.1	No	Clinical	Cystic fibrosis	9	11	9	11	5	17
PA2359	***Pseudomonas_aeruginosa_SCH_ABX19_5979***	GCF_002154915.1	No	Clinical	Cystic fibrosis	18	11	8	19	12	Undefined
PA2360	***Pseudomonas_aeruginosa_SCV20265_215***	GCF_000510305.1	No	Clinical	Cystic fibrosis	18	102	13	19	11	299
PA2361	***Pseudomonas_aeruginosa_SD9_5325***	GCF_002025565.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	102	8	21	9	Undefined
PA2362	***Pseudomonas_aeruginosa_SG17M_2042***	GCF_000568215.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	9	11	9	11	5	17
PA2363	***Pseudomonas_aeruginosa_Site_7_6815***	GCF_002312135.1	Yes	Environment	Clinical environment: Dental, Hospital	19			21		Undefined
PA2364	***Pseudomonas_aeruginosa_SJTD_1_385***	GCF_000271985.2	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	72	9	19	12	2619

PA2365	***Pseudomonas_aeruginosa_SJU_R10_1_6384***	GCF_002329935.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		11	19	14	Undefined
PA2366	***Pseudomonas_aeruginosa_SJU_R10_2_7044***	GCF_002285345.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		11	19	14	Undefined
PA2367	***Pseudomonas_aeruginosa_SJU_R10_3_7318***	GCF_002329925.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	11	19	14	Undefined
PA2368	***Pseudomonas_aeruginosa_SJU_R8_2_7126***	GCF_002329975.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	86	13	19	12	Undefined
PA2369	***Pseudomonas_aeruginosa_SJU_R8_3_6045***	GCF_002329965.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		13	19	12	Undefined
PA2370	***Pseudomonas_aeruginosa_SJU_S6_1_5859***	GCF_002329905.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		8	19	9	Undefined
PA2371	***Pseudomonas_aeruginosa_SJU_S6_2_6052***	GCF_002329885.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		8	19	9	Undefined
PA2372	***Pseudomonas_aeruginosa_SJU_S6_3_6336***	GCF_002285355.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	72	8	19	9	Undefined
PA2373	***Pseudomonas_aeruginosa_SJU_S72_1_6042***	GCF_002329845.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	97	9	19	12	1669
PA2374	***Pseudomonas_aeruginosa_SJU_S72_2_6701***	GCF_002329815.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	1669
PA2375	***Pseudomonas_aeruginosa_SJU_S72_3_6909***	GCF_002329805.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	1669
PA2376	***Pseudomonas_aeruginosa_SJU_S79_1_6123***	GCF_002329775.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	198
PA2377	***Pseudomonas_aeruginosa_SJU_S79_2_6315***	GCF_002330005.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	198
PA2378	***Pseudomonas_aeruginosa_SJU_S79_3_6029***	GCF_002329765.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	198
PA2379	***Pseudomonas_aeruginosa_SJU_S9_1_7292***	GCF_002330045.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		8	19	9	Undefined
PA2380	***Pseudomonas_aeruginosa_SJU_S9_2_6158***	GCF_002330015.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		8	19	9	Undefined
PA2381	***Pseudomonas_aeruginosa_SJU_S9_3_6561***	GCF_002329865.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		8	19	9	Undefined
PA2382	***Pseudomonas_aeruginosa_SJU_W20_1_6598***	GCF_002329735.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		6	22	7	1665
PA2383	***Pseudomonas_aeruginosa_SJU_W20_2_6177***	GCF_002285375.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	65	6	22	7	1665
PA2384	***Pseudomonas_aeruginosa_SJU_W20_3_6786***	GCF_002329725.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		6	22	7	1665
PA2385	***Pseudomonas_aeruginosa_SJU_W4_1_7030***	GCF_002330095.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		9	19	5	167
PA2386	***Pseudomonas_aeruginosa_SJU_W4_2_6535***	GCF_002330075.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18		9	19	5	167
PA2387	***Pseudomonas_aeruginosa_SJU_W4_3_5834***	GCF_002516415.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	97	9	19	5	167
PA2388	***Pseudomonas_aeruginosa_SMC1595_10554***	GCF_003974335.1	Yes	Clinical	Cystic fibrosis	18		9	19	12	399
PA2389	***Pseudomonas_aeruginosa_SMC1596_10531***	GCF_003973825.1	No	Clinical	Cystic fibrosis	18	86	12	19	12	1097

PA2390	***Pseudomonas_aeruginosa_SMC4386_3621***	GCF_001482885.1	No	Clinical	Eye	18	78	13	19	11	2012
PA2391	***Pseudomonas_aeruginosa_SMC4386_delta_CRISPR_Cas_3619***	GCF_001482865.1	No	Clinical	Eye	18	78	13	19	11	2012
PA2392	***Pseudomonas_aeruginosa_SMC4389_3620***	GCF_001482875.1	No	Clinical	Eye	18	79	9	19	12	654
PA2393	***Pseudomonas_aeruginosa_SMC5451_10529***	GCF_003973805.1	No	Clinical	Cystic fibrosis	18	78	12	19	12	Undefined
PA2394	***Pseudomonas_aeruginosa_So098_10143***	GCF_003837105.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	15		12	23	12	244
PA2395	***Pseudomonas_aeruginosa_SP2230_10393***	GCF_003952285.1	No	Clinical	Bacteraemia	19	47	10	8	10	357
PA2396	***Pseudomonas_aeruginosa_SP4371_10392***	GCF_003950255.1	No	Clinical	Bacteraemia	19	47	10	8	10	357
PA2397	***Pseudomonas_aeruginosa_SP4527_10694***	GCF_003991465.1	No	Clinical	Bacteraemia	19	47	10	8	10	357
PA2398	***Pseudomonas_aeruginosa_SP4528_9945***	GCF_003716765.1	No	Clinical	Respiratory tract	19	47	10	8	10	357
PA2399	***Pseudomonas_aeruginosa_SS1_10550***	GCF_003974255.1	Yes	Clinical	Cystic fibrosis	18		6	19	7	170
PA2400	***Pseudomonas_aeruginosa_ST260_2576***	GCF_000817865.1	No	Clinical	Bacteraemia	18	102	12	19	12	260
PA2401	***Pseudomonas_aeruginosa_ST773_12047***	GCF_009664165.1	No	Clinical	Urinary tract	19	47	3	21	3	773
PA2402	***Pseudomonas_aeruginosa_Stone_130_226***	GCF_000478465.2	No	Clinical	Burn	18	4	9	22	12	348
PA2403	***Pseudomonas_aeruginosa_SWPA15J_NSWPA15a_10128***	GCF_003836805.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	86	8	19	9	Undefined
PA2404	***Pseudomonas_aeruginosa_T2584_10636***	GCF_003976005.1	Yes	Clinical	Respiratory tract	18		12	19	12	260
PA2405	***Pseudomonas_aeruginosa_T3044_10633***	GCF_003975935.1	No	Clinical	Respiratory tract	17	22	13	15	13	277
PA2406	***Pseudomonas_aeruginosa_T3354_10635***	GCF_003975965.1	No	Clinical	Respiratory tract	18	84	12	20	11	233
PA2407	***Pseudomonas_aeruginosa_T3382_10591***	GCF_003975095.1	No	Clinical	Respiratory tract	18	86	11	19	11	491
PA2408	***Pseudomonas_aeruginosa_T3677_10634***	GCF_003975955.1	No	Clinical	Respiratory tract	19	48	10	8	10	357
PA2409	***Pseudomonas_aeruginosa_T38079_5952***	GCF_001515915.2	Yes	Clinical	Cancer	16		11	17	14	155
PA2410	***Pseudomonas_aeruginosa_T3979_10637***	GCF_003976025.1	Yes	Clinical	Respiratory tract	18		13	19	12	381
PA2411	***Pseudomonas_aeruginosa_T4242_10593***	GCF_003975125.1	No	Clinical	Respiratory tract	18	81	13	19	11	3420
PA2412	***Pseudomonas_aeruginosa_T6313_6490***	GCF_002927155.1	No	Clinical	Bacteraemia	16	5	11	17	14	179
PA2413	***Pseudomonas_aeruginosa_TC4411_11970***	GCF_008033805.1	Yes	Clinical	Urinary tract	18		12	19	12	549
PA2414	***Pseudomonas_aeruginosa_TNCF_106_4963***	GCF_001765865.1	No	Clinical	Cystic fibrosis	18	10	11	20	14	Undefined
PA2415	***Pseudomonas_aeruginosa_TNCF_109_5527***	GCF_001765915.1	No	Clinical	Cystic fibrosis	18	10	11	20	14	390
PA2416	***Pseudomonas_aeruginosa_TNCF_151_5624***	GCF_001766115.1	Yes	Clinical	Cystic fibrosis	18		11	20	14	390
PA2417	***Pseudomonas_aeruginosa_TNCF_155_1_5709***	GCF_001765995.1	No	Clinical	Cystic fibrosis	18	10	11	20	14	1923
PA2418	***Pseudomonas_aeruginosa_TNCF_167_5657***	GCF_001766075.1	No	Clinical	Cystic fibrosis	18	10	11	20	14	Undefined

PA2419	***Pseudomonas_aeruginosa_TNCF_176_5207***	GCF_001766135.1	Yes	Clinical	Cystic fibrosis	18		11	20	14	Undefined
PA2420	***Pseudomonas_aeruginosa_TNCF_23_5568***	GCF_001765595.1	Yes	Clinical	Cystic fibrosis	18		11	20	14	Undefined
PA2421	***Pseudomonas_aeruginosa_TNCF_32_5379***	GCF_001766145.1	No	Clinical	Cystic fibrosis	18	10	11	20	14	390
PA2422	***Pseudomonas_aeruginosa_TNCF_42_5109***	GCF_001765645.1	Yes	Clinical	Cystic fibrosis	18		11	20	14	390
PA2423	***Pseudomonas_aeruginosa_TNCF_49M_5351***	GCF_001765715.1	Yes	Clinical	Cystic fibrosis	18		11	20	14	390
PA2424	***Pseudomonas_aeruginosa_TNCF_76_5125***	GCF_001765805.1	Yes	Clinical	Cystic fibrosis	18		11	20	14	390
PA2425	***Pseudomonas_aeruginosa_Tu61_10122***	GCF_003836685.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	54	8	18	9	2032
PA2426	***Pseudomonas_aeruginosa_Tu863_10148***	GCF_003837195.1	No	Clinical	Ear	7	15	7	7	8	2042
PA2427	***Pseudomonas_aeruginosa_TuD199_10097***	GCF_003836175.1	No	Clinical	Respiratory tract	19	38	10	1	10	316
PA2428	***Pseudomonas_aeruginosa_TUEPA7472_6436***	GCF_003324555.1	No	Clinical	Bacteraemia	4	14	10	3	10	308
PA2429	***Pseudomonas_aeruginosa_U0272B_10098***	GCF_003836205.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	242
PA2430	***Pseudomonas_aeruginosa_U0288B_10330***	GCF_003858115.1	Yes	Clinical	Cystic fibrosis	18		13	19	12	381
PA2431	***Pseudomonas_aeruginosa_U0310A_10146***	GCF_003837165.1	No	Clinical	Cystic fibrosis	18	86	6	19	7	649
PA2432	***Pseudomonas_aeruginosa_U0330A_10089***	GCF_003836025.1	No	Clinical	Cystic fibrosis	18	93	12	19	12	266
PA2433	***Pseudomonas_aeruginosa_U1i_6349***	GCF_002326055.1	No	Environment	Home environment	1	103	12	2	4	253
PA2434	***Pseudomonas_aeruginosa_U1j_3_6311***	GCF_002326165.1	Yes	Environment	Home environment	4		10	3	10	308
PA2435	***Pseudomonas_aeruginosa_U1o_2_6702***	GCF_002326045.1	Yes	Environment	Home environment	1		12	2	4	253
PA2436	***Pseudomonas_aeruginosa_U2504_10013***	GCF_003834495.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA2437	***Pseudomonas_aeruginosa_U2504_594***	GCF_000481785.1	No	Clinical	Urinary tract	3	6	10	4	10	235
PA2438	***Pseudomonas_aeruginosa_U2816_10594***	GCF_003975135.1	Yes	Clinical	Urinary tract	18		9	19	12	270
PA2439	***Pseudomonas_aeruginosa_U350_10087***	GCF_003835985.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	242
PA2440	***Pseudomonas_aeruginosa_U397A_10145***	GCF_003837145.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	242
PA2441	***Pseudomonas_aeruginosa_U413A_10086***	GCF_003835955.1	No	Clinical	Cystic fibrosis	18	79	10	19	10	988
PA2442	***Pseudomonas_aeruginosa_U421_10092***	GCF_003836075.1	No	Clinical	Cystic fibrosis	18	102	13	19	11	Undefined
PA2443	***Pseudomonas_aeruginosa_U435_10090***	GCF_003836035.1	Yes	Clinical	Cystic fibrosis	10		5	12	6	274
PA2444	***Pseudomonas_aeruginosa_U451_10142***	GCF_003837085.1	Yes	Clinical	Cystic fibrosis	18		13	19	11	242
PA2445	***Pseudomonas_aeruginosa_U454A_10084***	GCF_003835915.1	Yes	Clinical	Cystic fibrosis	18		6	19	7	649
PA2446	***Pseudomonas_aeruginosa_U5a_2_5775***	GCF_002326025.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	19	38	12	21	4	1339
PA2447	***Pseudomonas_aeruginosa_U5b_2_6379***	GCF_002325985.1	Yes	Environment	Soil: Manure, Rocks, Sand, Soil	18		9	19	12	258
PA2448	***Pseudomonas_aeruginosa_UCBPP_PA14_109***	GCF_000014625.1	No	Clinical	Burn	1	103	12	2	4	253

PA2449	***Pseudomonas_aeruginosa_UDL_597***	GCF_000481845.1	No	Clinical	Urinary tract	18	86	13	19	12	2621
PA2450	***Pseudomonas_aeruginosa_UM_01_2646***	GCF_001013395.1	No	Clinical	Bacteraemia	18	76		19		Undefined
PA2451	***Pseudomonas_aeruginosa_UMB0501_12092***	GCF_009807255.1	No	Clinical	Urinary tract	14	66	2	16	2	111
PA2452	***Pseudomonas_aeruginosa_UMB0801_12104***	GCF_009807625.1	No	Clinical	Urinary tract	18	4	9	22	12	348
PA2453	***Pseudomonas_aeruginosa_UMB0802_12097***	GCF_009807355.1	Yes	Clinical	Urinary tract	18		9	22	12	348
PA2454	***Pseudomonas_aeruginosa_UMB1204_12100***	GCF_009807525.1	No	Clinical	Urinary tract	18	32	9	19	5	708
PA2455	***Pseudomonas_aeruginosa_UMB151_12099***	GCF_009807515.1	No	Clinical	Urinary tract	18	102	9	19	12	Undefined
PA2456	***Pseudomonas_aeruginosa_UMB2231_12098***	GCF_009807395.1	Yes	Clinical	Urinary tract	18		13	19	12	3323
PA2457	***Pseudomonas_aeruginosa_UMB2253_12096***	GCF_009807295.1	No	Clinical	Genital Tract	18	96	13	19	12	3323
PA2458	***Pseudomonas_aeruginosa_UMB2261_12094***	GCF_009807275.1	Yes	Clinical	Genital Tract	18		13	19	12	3323
PA2459	***Pseudomonas_aeruginosa_UMB2738_11971***	GCF_008086145.1	No	Clinical	Urinary tract	8	16	10	6	10	309
PA2460	***Pseudomonas_aeruginosa_UMB4740_12101***	GCF_009807535.1	No	Clinical	Genital Tract	18	46	13	19	11	152
PA2461	***Pseudomonas_aeruginosa_UMB6995_12093***	GCF_009807265.1	Yes	Clinical	Urinary tract	9		9	11	5	17
PA2462	***Pseudomonas_aeruginosa_UMB7567_12095***	GCF_009807285.1	No	Clinical	Urinary tract	18	78	13	19	11	Undefined
PA2463	***Pseudomonas_aeruginosa_UMB7777_12102***	GCF_009807545.1	Yes	Clinical	Urinary tract	9		9	11	5	17
PA2464	***Pseudomonas_aeruginosa_UQCCR_393788042_K_AB94_6154***	GCF_002088215.1	No	Clinical	Bacteraemia	19	47	3	21	3	532
PA2465	***Pseudomonas_aeruginosa_Urg_5_6664***	GCF_002312645.1	Yes	Environment	Clinical environment: Dental, Hospital	19		10	21	10	2503
PA2466	***Pseudomonas_aeruginosa_Urg_7_6210***	GCF_002312315.1	Yes	Environment	Clinical environment: Dental, Hospital	19		10	21	10	2503
PA2467	***Pseudomonas_aeruginosa_Us411_10157***	GCF_003837375.1	No	Clinical	Urinary tract	18	102	8	19	12	1394
PA2468	***Pseudomonas_aeruginosa_USDA_ARS_USMARC_41639_3640***	GCF_001518975.1	No	Environment	Animal	18	32	9	19	12	Undefined
PA2469	***Pseudomonas_aeruginosa_VA_134_3846***	GCF_001447845.1	No	Clinical	Burn	18	93	12	19	12	3090
PA2470	***Pseudomonas_aeruginosa_VD171_7248***	GCF_002312795.1	No	Clinical	Respiratory tract	18	97	13	19	11	Undefined
PA2471	***Pseudomonas_aeruginosa_VD329_6512***	GCF_002312505.1	Yes	Clinical	Respiratory tract	18			19		Undefined
PA2472	***Pseudomonas_aeruginosa_VD564_6275***	GCF_002312495.1	Yes	Clinical	Respiratory tract	18			19		Undefined
PA2473	***Pseudomonas_aeruginosa_VD609_7051***	GCF_002312705.1	Yes	Clinical	Respiratory tract	18		13	19	11	Undefined
PA2474	***Pseudomonas_aeruginosa_VD706_7176***	GCF_002312765.1	Yes	Clinical	Respiratory tract	18		13	19	11	Undefined
PA2475	***Pseudomonas_aeruginosa_VET_120_9721***	GCF_003629995.1	No	Environment	Animal	18	97	13	19	12	1074
PA2476	***Pseudomonas_aeruginosa_VET_124_9894***	GCF_003633465.1	No	Environment	Animal	7	15	7	7	8	2471
PA2477	***Pseudomonas_aeruginosa_VET_125_9708***	GCF_003629755.1	No	Environment	Animal	18	102	12	19	12	487

PA2478	***Pseudomonas_aeruginosa_VET_21_9752***	GCF_003630635.1	No	Environment	Animal	12	2	1	14	1	395
PA2479	***Pseudomonas_aeruginosa_VET_22_9706***	GCF_003629695.1	No	Environment	Animal	18	78	6	19	7	170
PA2480	***Pseudomonas_aeruginosa_VET_23_9673***	GCF_003629045.1	No	Environment	Animal	18	74	13	19	11	242
PA2481	***Pseudomonas_aeruginosa_VET_24_9877***	GCF_003633125.1	No	Environment	Animal	19	102	10	21	10	319
PA2482	***Pseudomonas_aeruginosa_VET_25_9695***	GCF_003629485.1	No	Environment	Animal	17	22	6	15	7	245
PA2483	***Pseudomonas_aeruginosa_VET_26_9675***	GCF_003629085.1	No	Environment	Animal	18	102	9	19	12	270
PA2484	***Pseudomonas_aeruginosa_VET_27_9886***	GCF_003633295.1	No	Environment	Animal	19	61	13	21	13	313
PA2485	***Pseudomonas_aeruginosa_VET_29_9743***	GCF_003630455.1	No	Environment	Animal	18	102	13	19	11	164
PA2486	***Pseudomonas_aeruginosa_VET_31_9869***	GCF_003632965.1	No	Environment	Animal	18	10	11	20	14	390
PA2487	***Pseudomonas_aeruginosa_VET_32_9739***	GCF_003630365.1	No	Environment	Animal	9	11	9	11	5	845
PA2488	***Pseudomonas_aeruginosa_VET_33_9667***	GCF_003628935.1	Yes	Environment	Animal	18		13	19	11	2450
PA2489	***Pseudomonas_aeruginosa_VET_34_9668***	GCF_003628945.1	No	Environment	Animal	18	32	13	19	11	2450
PA2490	***Pseudomonas_aeruginosa_VET_36_9670***	GCF_003628985.1	No	Environment	Animal	18	32	13	19	11	2450
PA2491	***Pseudomonas_aeruginosa_VET_39_D2_9789***	GCF_003631365.1	No	Environment	Animal	18	79	13	19	11	2462
PA2492	***Pseudomonas_aeruginosa_VET_40_9737***	GCF_003630335.1	No	Environment	Animal	18	94	13	19	12	497
PA2493	***Pseudomonas_aeruginosa_VET_41_9688***	GCF_003629345.1	No	Environment	Animal	18	72	13	19	12	2469
PA2494	***Pseudomonas_aeruginosa_VET_46_9703***	GCF_003629655.1	No	Environment	Animal	18	46	13	19	11	646
PA2495	***Pseudomonas_aeruginosa_VET_47_9797***	GCF_003631515.1	No	Environment	Animal	18	31	13	19	11	591
PA2496	***Pseudomonas_aeruginosa_VET_49_9791***	GCF_003631405.1	No	Environment	Animal	18	79	12	19	11	190
PA2497	***Pseudomonas_aeruginosa_VET_53_9698***	GCF_003629545.1	No	Environment	Animal	17	22	13	15	13	1128
PA2498	***Pseudomonas_aeruginosa_VET_58_9896***	GCF_003633515.1	No	Environment	Animal	6	1	8	9	9	1744
PA2499	***Pseudomonas_aeruginosa_VNMU089_12121***	GCF_009887995.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		13	19	12	218
PA2500	***Pseudomonas_aeruginosa_VNMU141_12120***	GCF_009887745.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		12	19	12	260
PA2501	***Pseudomonas_aeruginosa_VNMU143_12119***	GCF_009887715.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19		12	21	4	1047
PA2502	***Pseudomonas_aeruginosa_VNMU144_12115***	GCF_009887625.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19		12	21	4	1047
PA2503	***Pseudomonas_aeruginosa_VNMU145_12117***	GCF_009887695.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	47	10	8	10	2592
PA2504	***Pseudomonas_aeruginosa_VNMU148_12118***	GCF_009887705.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18		9	19	5	664

PA2505	***Pseudomonas_aeruginosa_VNMU149_12116***	GCF_009887645.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	15	102	12	23	12	244
PA2506	***Pseudomonas_aeruginosa_VRFPA01_7586***	GCF_000335395.2	No	Clinical	Bacteraemia	5		4			Undefined
PA2507	***Pseudomonas_aeruginosa_VRFPA02_7587***	GCF_000399805.1	No	Clinical	Bacteraemia	14	79		16		111
PA2508	***Pseudomonas_aeruginosa_VRFPA03_7591***	GCF_000467675.1	No	Clinical	Eye	19	102		1		Undefined
PA2509	***Pseudomonas_aeruginosa_VRFPA04_230***	GCF_000473745.2	No	Clinical	Eye	19	14	12	21	4	823
PA2510	***Pseudomonas_aeruginosa_VRFPA07_2003***	GCF_000506805.1	No	Clinical	Gastrointestinal	19	61	13	21	13	313
PA2511	***Pseudomonas_aeruginosa_VRFPA08_2004***	GCF_000506885.1	No	Clinical	Urinary tract	19	14		21		823
PA2512	***Pseudomonas_aeruginosa_W_101_9631***	GCF_003413835.1	No	Environment	Sewage/Wastewater	18	67	8	19	10	Undefined
PA2513	***Pseudomonas_aeruginosa_W13a_2_6703***	GCF_002326115.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	13	19	12	647
PA2514	***Pseudomonas_aeruginosa_W15Apr4_10600***	GCF_003975285.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19		13	21	13	313
PA2515	***Pseudomonas_aeruginosa_W15Aug23_10641***	GCF_003976105.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	6	19	7	Undefined
PA2516	***Pseudomonas_aeruginosa_W15Dec14_10599***	GCF_003975245.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	11	102	11	13	14	Undefined
PA2517	***Pseudomonas_aeruginosa_W15Dec4_10596***	GCF_003975205.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	17	22	13	15	13	277
PA2518	***Pseudomonas_aeruginosa_W15Okt31_10639***	GCF_003976065.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	16		11	17	14	Undefined
PA2519	***Pseudomonas_aeruginosa_W16407_6873***	GCF_001516165.2	No	Clinical	Cancer	15	32	12	23	12	244
PA2520	***Pseudomonas_aeruginosa_W1c_6097***	GCF_002326125.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	102	11	19	14	1337
PA2521	***Pseudomonas_aeruginosa_W1d_6994***	GCF_002325965.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	15		12	23	12	244
PA2522	***Pseudomonas_aeruginosa_W1j_7113***	GCF_002325945.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	1		12	2	4	253
PA2523	***Pseudomonas_aeruginosa_W21b_2_7036***	GCF_002326095.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	97	13	19	11	471
PA2524	***Pseudomonas_aeruginosa_W25637_6866***	GCF_002927035.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA2525	***Pseudomonas_aeruginosa_W36662_7266***	GCF_001516185.2	No	Clinical	Cancer	9	11	9	11	5	17
PA2526	***Pseudomonas_aeruginosa_W45909_5913***	GCF_001516205.2	No	Clinical	Cancer	13	50	9	10	12	27
PA2527	***Pseudomonas_aeruginosa_W5a_2_6644***	GCF_002325925.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	44	13	19	12	275
PA2528	***Pseudomonas_aeruginosa_W5Aug16_10110***	GCF_003836445.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	12	13	19	12	959

PA2529	***Pseudomonas_aeruginosa_W5Aug28_10598***	GCF_003975225.1	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	9		9	11	5	17
PA2530	***Pseudomonas_aeruginosa_W60856_6659***	GCF_001516225.2	No	Clinical	Cancer	18	13	13	19	12	959
PA2531	***Pseudomonas_aeruginosa_W70322_6250***	GCF_002927215.1	No	Clinical	Bacteraemia	18	12	13	19	12	282
PA2532	***Pseudomonas_aeruginosa_W91453_5888***	GCF_002927135.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA2533	***Pseudomonas_aeruginosa_WH_SGI_V_07181_3362***	GCF_001449725.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19		10	21	10	319
PA2534	***Pseudomonas_aeruginosa_WH_SGI_V_07182_3405***	GCF_001450585.1	No	Clinical	Ear	18	32	12	19	12	699
PA2535	***Pseudomonas_aeruginosa_WH_SGI_V_07248_3517***	GCF_001452825.1	No	Clinical	Burn	19	57	10	21	10	1076
PA2536	***Pseudomonas_aeruginosa_WH_SGI_V_07251_3567***	GCF_001453825.1	No	Clinical	Respiratory tract	2	39	10	5	10	446
PA2537	***Pseudomonas_aeruginosa_WH_SGI_V_07252_7630***	GCF_001452885.1	No	Clinical	Respiratory tract	19	19	8	18	9	2030
PA2538	***Pseudomonas_aeruginosa_WH_SGI_V_07254_3522***	GCF_001452915.1	No	Clinical	Burn	18	4	11	22	14	348
PA2539	***Pseudomonas_aeruginosa_WH_SGI_V_07255_3568***	GCF_001453835.1	Yes	Clinical	Burn	19		13	21	13	313
PA2540	***Pseudomonas_aeruginosa_WH_SGI_V_07259_3570***	GCF_001453885.1	Yes	Clinical	Burn	14		2	16	2	111
PA2541	***Pseudomonas_aeruginosa_WH_SGI_V_07261_3525***	GCF_001452985.1	No	Clinical	Burn	5		4			2031
PA2542	***Pseudomonas_aeruginosa_WH_SGI_V_07263_3527***	GCF_001453015.1	No	Clinical	Burn	19	20	8	18	9	1203
PA2543	***Pseudomonas_aeruginosa_WH_SGI_V_07268_3603***	GCF_001454595.1	Yes	Clinical	Burn	3		10	4	10	235
PA2544	***Pseudomonas_aeruginosa_WH_SGI_V_07276_3575***	GCF_001454045.1	Yes	Clinical	Burn	3		10	4	10	235
PA2545	***Pseudomonas_aeruginosa_WH_SGI_V_07277_3576***	GCF_001454065.1	No	Clinical	Burn	19	39	10	21	10	319
PA2546	***Pseudomonas_aeruginosa_WH_SGI_V_07278_3572***	GCF_001453915.1	No	Clinical	Burn	18	46	13	19	12	2034
PA2547	***Pseudomonas_aeruginosa_WH_SGI_V_07280_3604***	GCF_001454625.1	No	Clinical	Cystic fibrosis	18	88	10	19	12	2035
PA2548	***Pseudomonas_aeruginosa_WH_SGI_V_07287_3607***	GCF_001454675.1	No	Environment	Plants	5		4			2039
PA2549	***Pseudomonas_aeruginosa_WH_SGI_V_07290_3579***	GCF_001454125.1	No	Clinical	Burn	15	32	12	23	12	244
PA2550	***Pseudomonas_aeruginosa_WH_SGI_V_07293_3581***	GCF_001454165.1	Yes	Clinical	Burn	19		12	21	4	671
PA2551	***Pseudomonas_aeruginosa_WH_SGI_V_07295_3583***	GCF_001454205.1	No	Clinical	Burn	4	14	10	3	10	308
PA2552	***Pseudomonas_aeruginosa_WH_SGI_V_07296_3584***	GCF_001454225.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA2553	***Pseudomonas_aeruginosa_WH_SGI_V_07297_3585***	GCF_001454235.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	2	39	10	5	10	446
PA2554	***Pseudomonas_aeruginosa_WH_SGI_V_07299_3566***	GCF_001453805.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	32	12	19	12	549
PA2555	***Pseudomonas_aeruginosa_WH_SGI_V_07306_3587***	GCF_001454285.1	No	Clinical	Burn	19	61	13	21	13	Undefined
PA2556	***Pseudomonas_aeruginosa_WH_SGI_V_07309_3588***	GCF_001454305.1	No	Clinical	Burn	3	6	10	4	10	235

PA2557	***Pseudomonas_aeruginosa_WH_SGI_V_07311_7632***	GCF_001454745.1	Yes	Clinical	Burn	15		12	23	12	244
PA2558	***Pseudomonas_aeruginosa_WH_SGI_V_07312_3914***	GCF_001454335.1	No	Clinical	Ear	7	15	7	7	8	2042
PA2559	***Pseudomonas_aeruginosa_WH_SGI_V_07318_3611***	GCF_001454755.1	No	Clinical	Burn	19	47	3	21	3	532
PA2560	***Pseudomonas_aeruginosa_WH_SGI_V_07323_3596***	GCF_001454465.1	No	Clinical	Burn	14	52	2	16	2	111
PA2561	***Pseudomonas_aeruginosa_WH_SGI_V_07383_3438***	GCF_001451245.1	No	Environment	Other environmental source	18	10	11	19	14	640
PA2562	***Pseudomonas_aeruginosa_WS136_2577***	GCF_000820805.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	78	11	19	14	3597
PA2563	***Pseudomonas_aeruginosa_WS394_2512***	GCF_000786485.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	3	6	10	4	10	235
PA2564	***Pseudomonas_aeruginosa_WW_12000***	GCF_008693305.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	1	103	12	2	4	253
PA2565	***Pseudomonas_aeruginosa_X13273_590***	GCF_000481705.1	No	Clinical	Bacteraemia	4	14	10	3	10	308
PA2566	***Pseudomonas_aeruginosa_X24509_10006***	GCF_003834355.1	No	Clinical	Urinary tract	18	83	11	19	14	527
PA2567	***Pseudomonas_aeruginosa_X24509_598***	GCF_000481865.1	No	Clinical	Urinary tract	18	83	11	19	14	527
PA2568	***Pseudomonas_aeruginosa_X78812_6522***	GCF_001542795.2	No	Clinical	Cancer	18	96	11	19	11	257
PA2569	***Pseudomonas_aeruginosa_X9820_6393***	GCF_002724095.1	No	Clinical	Cancer	10	78	5	12	6	209
PA2570	***Pseudomonas_aeruginosa_XMG_378***	GCF_000265035.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	95	11	19	11	2438
PA2571	***Pseudomonas_aeruginosa_Y31_6550***	GCF_003369775.1	No	Clinical	Respiratory tract	18	95	10	19	12	Undefined
PA2572	***Pseudomonas_aeruginosa_Y71_9532***	GCF_003408495.1	No	Clinical	Respiratory tract	17	102	6	15	7	245
PA2573	***Pseudomonas_aeruginosa_Y82_7124***	GCF_003369755.1	No	Clinical	Respiratory tract	14	52	2	16	2	111
PA2574	***Pseudomonas_aeruginosa_Y89_7172***	GCF_003369735.1	No	Clinical	Respiratory tract	17	102	6	15	7	245
PA2575	***Pseudomonas_aeruginosa_YL84_2501***	GCF_000524595.1	No	Environment	Soil: Manure, Rocks, Sand, Soil	18	97	13	19	12	Undefined
PA2576	***Pseudomonas_aeruginosa_Zw115_10567***	GCF_003974605.1	No	Clinical	Cystic fibrosis	18	32	12	19	12	699
PA2577	***Pseudomonas_aeruginosa_Zw31_10548***	GCF_003974195.1	No	Clinical	Cystic fibrosis	18	86	9	19	5	287
PA2578	***Pseudomonas_aeruginosa_Zw49_10569***	GCF_003974625.1	No	Clinical	Cystic fibrosis	18	93	13	20	12	Undefined
PA2579	***Pseudomonas_aeruginosa_Zw64_10549***	GCF_003974205.1	No	Clinical	Cystic fibrosis	18	42	13	19	11	499
PA2580	***Pseudomonas_aeruginosa_Zw70_10545***	GCF_003974135.1	Yes	Clinical	Cystic fibrosis	18		12	19	12	699
PA2581	***Pseudomonas_aeruginosa_Zw75_2_10557***	GCF_003974395.1	No	Clinical	Cystic fibrosis	18	95	10	19	12	1050
PA2582	***Pseudomonas_aeruginosa_Zw9_10568***	GCF_003974615.1	No	Clinical	Cystic fibrosis	19	28	12	21	4	671
PA2583	***SGHG 14778***	In-house collection	No	Clinical	Unknown	10	78	5	12	6	274
PA2584	***SGHG 14838***	In-house collection	No	Clinical	Unknown	8	16	10	6	10	309
PA2585	***SGHG 14986***	In-house collection	No	Clinical	Unknown	18	65	6	22	7	389

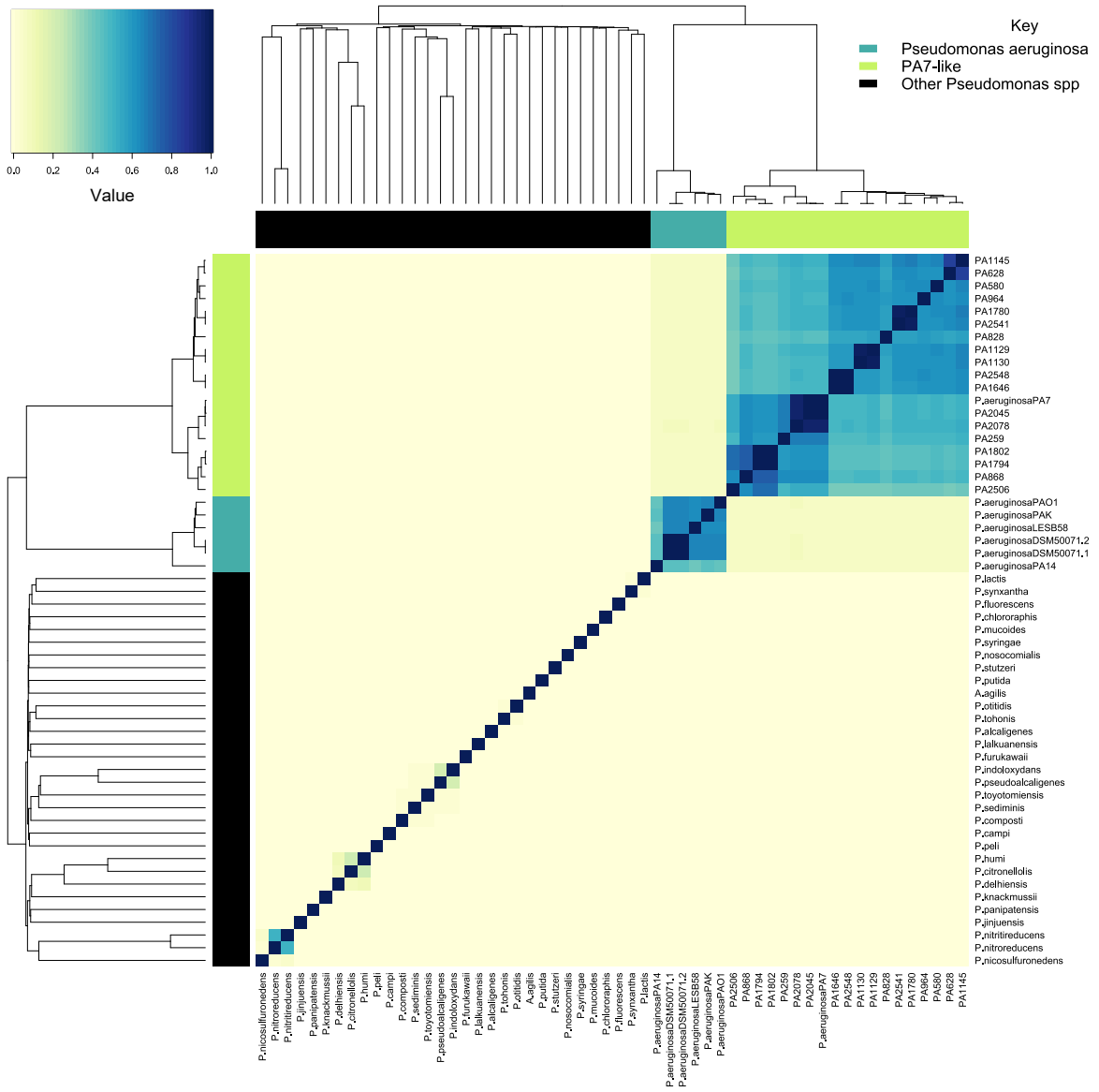
PA2586	***SGHG 14992***	In-house collection	No	Clinical	Unknown	18	81	13	19	12	760
PA2587	***SGHG G2969***	In-house collection	No	Clinical	Unknown	18	88	10	19	12	2100
PA2588	***Pseudomonas_aeruginosa_WH_SGI_V_07050_3348***	GCF_001449435.1	No	Clinical	Respiratory tract	6	1	8	9	9	2020
PA2589	***Pseudomonas_aeruginosa_WH_SGI_V_07166_3350***	GCF_001449485.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	54	8	18	9	1990
PA2590	***Pseudomonas_aeruginosa_WH_SGI_V_07167_3351***	GCF_001449505.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	19	47	10	8	10	357
PA2591	***Pseudomonas_aeruginosa_WH_SGI_V_07247_3516***	GCF_001452805.1	Yes	Clinical	Burn	3		10	4	10	235
PA2592	***Pseudomonas_aeruginosa_WH_SGI_V_07249_3518***	GCF_001452835.1	No	Clinical	Burn	12	2	1	14	1	395
PA2593	***Pseudomonas_aeruginosa_WH_SGI_V_07250_3519***	GCF_001452865.1	No	Clinical	Bacteraemia	16	5	11	17	14	155
PA2594	***Pseudomonas_aeruginosa_WH_SGI_V_07253_3521***	GCF_001452905.1	No	Clinical	Burn	18	71	13	19	12	292
PA2595	***Pseudomonas_aeruginosa_WH_SGI_V_07260_3524***	GCF_001452965.1	No	Clinical	Respiratory tract	18	102	12	19	12	260
PA2596	***Pseudomonas_aeruginosa_WH_SGI_V_07265_3526***	GCF_001452995.1	No	Clinical	Respiratory tract	19	54	8	18	9	2032
PA2597	***Pseudomonas_aeruginosa_WH_SGI_V_07266_3574***	GCF_001453985.1	No	Clinical	Respiratory tract	18	31	10	19	12	2033
PA2598	***Pseudomonas_aeruginosa_WH_SGI_V_07267_3528***	GCF_001453025.1	Yes	Clinical	Respiratory tract	18		9	22	12	Undefined
PA2599	***Pseudomonas_aeruginosa_WH_SGI_V_07284_3577***	GCF_001454085.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	102	10	1	10	316
PA2600	***Pseudomonas_aeruginosa_WH_SGI_V_07286_3578***	GCF_001454095.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	19	55		21		2038
PA2601	***Pseudomonas_aeruginosa_WH_SGI_V_07291_3580***	GCF_001454145.1	No	Clinical	Bacteraemia	18	84	12	20	11	233
PA2602	***Pseudomonas_aeruginosa_WH_SGI_V_07294_3582***	GCF_001454175.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	86	9	19	5	132
PA2603	***Pseudomonas_aeruginosa_WH_SGI_V_07300_3586***	GCF_001454265.1	No	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	18	90	13	19	11	Undefined
PA2604	***Pseudomonas_aeruginosa_WH_SGI_V_07305_3609***	GCF_001454725.1	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	9	11	9	11	5	17
PA2605	***Pseudomonas_aeruginosa_WH_SGI_V_07310_3589***	GCF_001454325.1	No	Clinical	Burn	18	102	6	19	7	2041
PA2606	***Pseudomonas_aeruginosa_WH_SGI_V_07313_3591***	GCF_001454365.1	No	Clinical	Respiratory tract	19	38	10	1	10	316
PA2607	***Pseudomonas_aeruginosa_WH_SGI_V_07316_3593***	GCF_001454395.1	No	Clinical	Urinary tract	18	68		19		2044
PA2608	***Pseudomonas_aeruginosa_WH_SGI_V_07317_3594***	GCF_001454415.1	No	Clinical	Respiratory tract	18	70	12	19	12	2045
PA2609	***Pseudomonas_aeruginosa_WH_SGI_V_07322_3595***	GCF_001454445.1	No	Clinical	Bacteraemia	14	52	2	16	2	111
PA2610	***Pseudomonas_aeruginosa_WH_SGI_V_07324_3597***	GCF_001454485.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA2611	***Pseudomonas_aeruginosa_WH_SGI_V_07325_3598***	GCF_001454495.1	Yes	Clinical	Urinary tract	14		2	16	2	111
PA2612	***Pseudomonas_aeruginosa_WH_SGI_V_07327_3614***	GCF_001454825.1	Yes	Clinical	Respiratory tract	14		2	16	2	111

PA2613	***Pseudomonas_aeruginosa_WH_SGI_V_07328_3599***	GCF_001454515.1	Yes	Clinical	Respiratory tract	14		2	16	2	111
PA2614	***Pseudomonas_aeruginosa_WH_SGI_V_07329_3600***	GCF_001454545.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	14		2	16	2	111
PA2615	***Pseudomonas_aeruginosa_WH_SGI_V_07330_3601***	GCF_001454565.1	Yes	Clinical	Abscess/Skin/Tissue/Ulcer/Wound	14		2	16	2	111
PA2616	***Pseudomonas_aeruginosa_WH_SGI_V_07368_3382***	GCF_001450115.1	No	Clinical	Respiratory tract	19	28	12	21	4	671
PA2617	***EA7-1***	In-house collection	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	15		12	23	12	244
PA2618	***EA7-3***	In-house collection	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	15		12	23	12	244
PA2619	***EA7-4***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	15	32	12	23	12	244
PA2620	***EA8-1***	In-house collection	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	1		12	2	4	253
PA2621	***EA8-8***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	1	103	12	2	4	253
PA2622	***EA14-1***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	1	103	12	2	4	253
PA2623	***EA14-2***	In-house collection	Yes	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	1		12	2	4	253
PA2624	***EA16-1***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	62	9	19	12	698
PA2625	***EA21-4***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	16	5	11	17	14	179
PA2626	***EA26-1***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	93	13	19	11	439
PA2627	***EA27-1***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	93		19		847
PA2628	***EA28-7***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	16	5	11	17	14	179
PA2629	***EA29-1***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	97	11	19	14	1233
PA2630	***EA35-5***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	65	6	22	7	485
PA2631	***EA41-7***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	86	13	19	12	1226
PA2632	***EA43-2***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	6	1	8	9	9	1328
PA2633	***EA44-1***	In-house collection	No	Environment	Water: Lakes, Oceans, Ponds, Puddles, Rivers	18	97	9	19	12	882
PA2634	***AZPAE15042_IHMA87_PA7like***	In-house collection	yes	Clinical	Urinary tract	5		4		n/a	2211

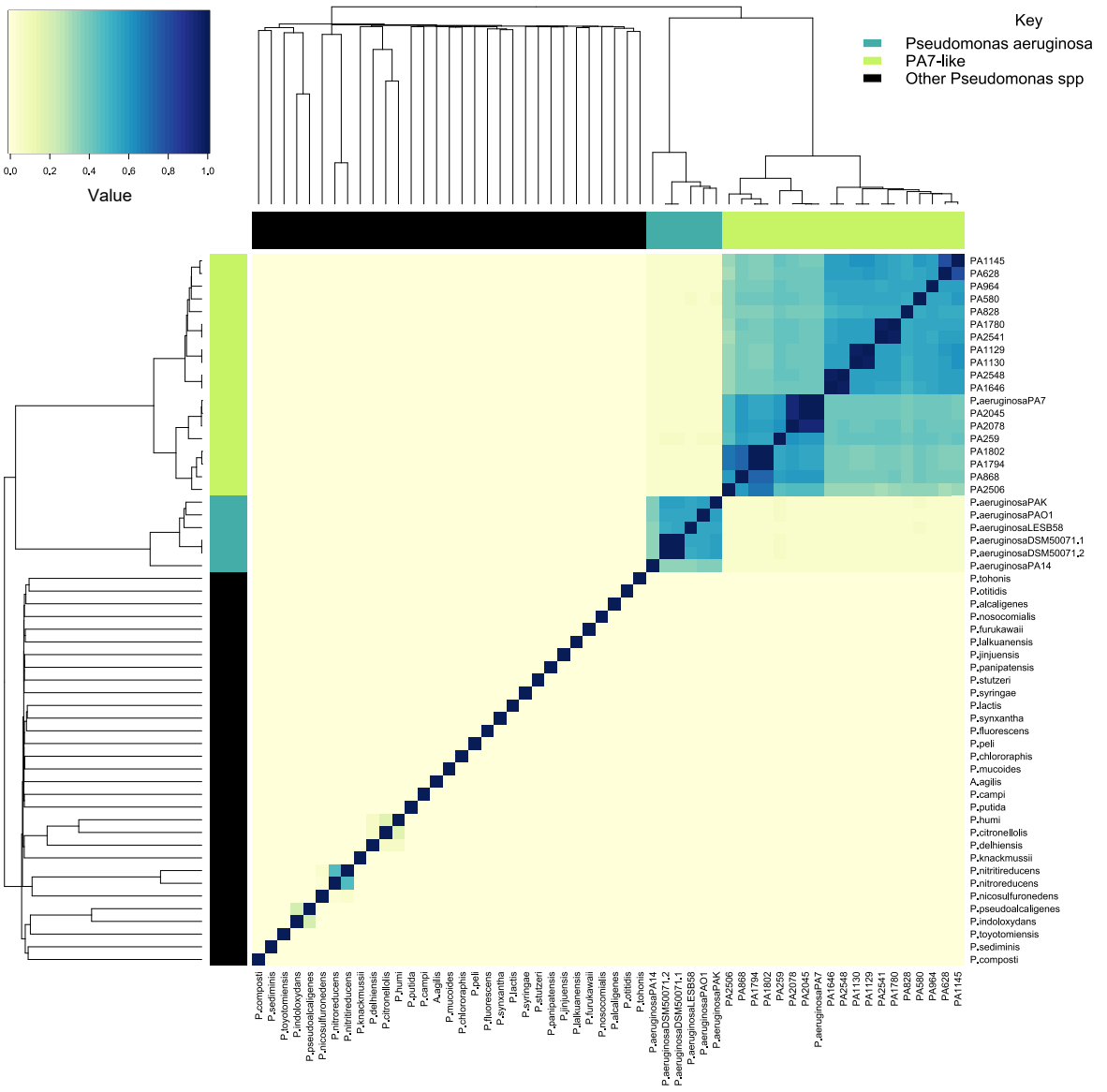
Appendix - Table 4: Protein sequences of the 16 ribosomal proteins used in robust clustering taken from the PAO1 genome (NP_252950.1)

Product _Gene	*Genbank ID*	*Protein sequence*
L2_rplB	NP_252950.1	MAIVKCKPTSAGRRFVVKVVNQELHKGAPYAPLLEKKSKSGGRN NNGRITTRHIGGGHKQHYRLVDFRRNKDGIPAIVERVEYDPNRTA HIALLKYADGERRYIIAPKGVAAGDQLISGIGAPIKAGNSMPLRNIP VGSTVHGIELKPGKGAQIARSAGASAQLVAREGAYVTLRLRSGE MRKVLAECRATLGEVSNSEHSLRSLGKAGATRWRGVRPTVRGV AMNPVDHPHGGGEGRTSAGRHPVSPWGLQTKGKKTRSNKRTD NMIVRRRK
L3_rplC	NP_252953.1	MTIGVVGRKCGMTRIFTEEGVSIPVTVIEVEPNRVTQFKTEETDGY RAVQVTAGERRASRVTKAQAGHFAKANVAAGRGVWEFRLGEEQ YAAGDQITVDLFQAGQMVDVTGESKGKGFAGTIKRWNFRGQDN THGNSVSHRVPGSIGQCQTPGRVFKGKKMSGHLGAERVTVQSL EIVRVDAERNLLLVKGAVPGATGGDVIVRPAAKARG
L4_rplD	NP_252952.1	MQLNVNGAQAIEVSERTFGGEFNETLVHQAVVAYMAGGRQGSK AQKTRSEVSGGGKKPWRQKGTGRARAGTIRSPIWRGGGTTFAA KPRSHEQKLNKKMYRAALRSILAELVRLDRLVVVADFAVDAPKTK GLVAKLDTLGLKDVLIVTDGVDENLYLAARNLAHVDVRDVQGSDP VSLIAYDKVLVTVSAVKKFEELLG
L5_rplE	NP_252941.1	MARLKEIYRKEIAPKLKEELQLANVMEVPRVTKITLNMGLGEAVGD KKIIENAVADLEKITGQKPVVTYARKSIAGFKIREGWPIGVKVTLRS DRMYEFLDRLLSISLPRVRDFRGLNAKSFDGRGNYSMGVKEQIIF PEIDYDKIDALRGLDITLTTTARTDDEGRALLRAFKFPFRN
L6_rplF	NP_252938.1	MSRVAKNPVKLPAGVEIKLAGQQLSIKGAKGALELKVHPSVEVIQ DSGELRFAARNGDQQTRAMAGTTRALVNNMVVGVSQGFERKLQ LVGVGYKAQAKGQVLSLSLGFSHPVDYELPAGIVAETPSQTDILIK GIDKQLVGQVAAEIRDFRPPEPYKGKGVRYADEVVRRKEAKKK
L14_rplN	NP_252943.1	MIQTQSMLDVADNSGARRVMCIKVLGGSHRRYAGIGDIIKVTVKE AIPRGKVKKGQVMTAVVVRTKHGVRRTDGSIIRFDGNAAVLLNNK QEPIGTRIFGPVTRELRTEKFMKIVSLAPEVL
L15_rplO	NP_252934.1	MQLNDLRSAPGARREKHRPGRGIGSGLGKTGGRGHKGLTSRSG GKVAPGFEGGQQPLHRRLPKFGFVSLKAMDRAEVRTSELAKVEG DVVSLQTLKDANLINQHVQRVKVMLSGEVGRAVTLKGIAATKGAR AAIEAAGGKFED
L16_rplP	NP_252946.1	MLQPKRTKFRKQMTGHNRGLAHRGSKVSFGEYALKATSRGRLT ARQIESARRALTRHVKRGGKIWIRVFPDKPVTKKPLEVRMGKGKG GVEYWVAQIQPGKVLYEIEGVSEELAREAFALAAAKLPLATSFVK RTVM
L18_rplR	NP_252937.1	MSVKKETRLRRARKARLKMRELETVRLCVYRSSQHIYAQVIAADG GKVLASASTLDKDLREGATGNIDAAKKVGQLVAERAKAAGVTQV AFDRSGFKYHGRVKALADAAREGGLEF

L22_rplV	NP_252948.1	MEVAAKLSGARISAQKARLVADQIRGKKVGEALNLLAFSSKKAAEI MKKVLESAVANAEHNEGADVDDLKVSTVFVNEGRSLKRIMPRAK GRADRIVKRSCHITVKVADK
L24_rplX	NP_252942.1	MQKIRRDDEVIVIAGKDKGKRGKVLKVLADDRLVVGGVNLIKRHT KPNPMLGQQGGIVEKEAPLHVSNVAIFNTETSKADRVGFKVEDG KKIRVFKSTQKPVQA
S3_rpsC	NP_252947.1	MGQKVHPNGIRLGIVKEHTSVWYADRKNYADYLFADLKVREYLQ DKLKSASVSRIDIHRPAQTARITIHTARPGIVIGKKGEDVEKLRQDL TKQMGVPVHINIEEIRKPELDAMLVAQSVAQQLERRVMFRRAMK RAVQNAMRIGAKGIKIQVSGRLGGAEIARTEWYREGRVPLHTLRA DIDYATYEAHTTYGVIGVKVWIFKGEVIGGRQEELKPVAPAPRKKA AR
S8_rpsH	NP_252939.1	MSMQDPLADMLTRIRNAQMAEKTVVSMPSSKLKAAVAKVLKDEG YIADFQISSEVKPQLSIELKYFEGKPVIEEVKRISRPGLRQYKSVEQ LPKVRGGLGVSIVSTNKGVMTDRAARAAGVGGEVLCTVF
S10_rpsJ	NP_252954.1	MQNQQIRIRLKAFDHRLIDQSTQEIVETAKRTGAQVRGPIPLPTRK ERFTVLISPHVNKDARDQYEIRTHKRVLDIVQPTDKTVDALMKLDL AAGVEVQISLG
S17_rpsQ	NP_252944.1	MAEAQKTVRTLTGRVVSDKMDKTVTVLIERRVKHPIYGKYVKRST KLHAHDESNQCRIGDLVTIRETRPLAKTKAWTLVDIVERAVEV
S19_rpsS	NP_252949.1	MPRSLKKGPFIDLHLLKKVEVAVEKNDRKPIKTWSRRSMILPHMV GLTIAVHNGRQHVPVLVNEDMVGHKLGEFAATRTYRGHAADKKA KR



Appendix - Figure 1: Jaccard similarity index of genomic signatures of PA7-like and Pseudomonas spp. based on a k-mer size of 51. The dendrogram is based on the similarity of the heatmap which visualises a matrix of Jaccard similarity index values between strains. Annotations alongside the rows and columns indicate the species of the strain. Raw data for heatmaps is displayed in Appendix - Table 29.



Appendix - Figure 2: Jaccard similarity index of genomic signatures of PA7-like and Pseudomonas spp. based on a k-mer size of 71. The dendrogram is based on the similarity of the heatmap which visualises a matrix of Jaccard similarity index values between strains. Annotations alongside the rows and columns indicate the species of the strain. Raw data for heatmaps is displayed in Appendix - Table 30.

Appendix - Table 5: Comparison of the area under the curve for PA7-like and PA strains grown in Biolog PM1 plate. The area under the curve is reported as the median with the interquartile range and statistical comparison are determined by a Mann-Whitney U test following confirmation of a significant difference ($p \leq 0.05$) between the two group by a Kruskal-Wallis test.

Position	Substrate	Group	Mdn	IQR	U	p-value
A01	Negative Control	PA PA7-like	0.57 0.59	0.62 0.10	492	0.858
A02	L-Arabinose	PA PA7-like	284.91 234.84	714.58 419.63	555	0.523
A03	N-Acetyl-D-Glucosamine	PA PA7-like	6078.88 6674.59	3080.27 6647.26	546	0.605
A04	D-Saccharic Acid	PA PA7-like	0.25 0.32	13.84 4.52	506	1.000
A05	Succinic Acid	PA PA7-like	9659.02 9794.53	3074.50 2249.12	546	0.607
A06	D-Galactose	PA PA7-like	0.00 0.19	0.53 10.07	403.5	0.141
A07	L-Aspartic Acid	PA PA7-like	9133.28 9833.39	2711.03 1857.01	388	0.124
A08	L-Proline	PA PA7-like	9444.52 8922.88	782.26 1524.56	574	0.379
A09	D-Alanine	PA PA7-like	3500.74 6151.35	5030.12 4836.92	343	0.032
A10	D-Trehalose	PA PA7-like	139.48 77.07	567.74 2184.92	498.5	0.927
A11	D-Mannose	PA PA7-like	5.07 8.70	92.56 92.28	495	0.888
A12	Dulcitol	PA PA7-like	172.35 179.74	143.74 319.40	518	0.880
B01	D-Serine	PA PA7-like	282.77 536.91	440.47 375.76	394	0.144
B02	D-Sorbitol	PA PA7-like	2.14 1.03	32.01 40.10	518	0.874
B03	Glycerol	PA PA7-like	7424.97 6648.02	1315.55 1459.88	767	0.000
B04	L-Fucose	PA PA7-like	0.03 0.04	9.26 2.66	505.5	1.000
B05	D-Glucuronic Acid	PA PA7-like	0.00 0.00	4.30 0.03	592	0.213
B06	D-Gluconic Acid	PA PA7-like	10113.36 10015.36	1376.62 1281.88	531	0.750
B07	D,L-α-Glycerol-Phosphate	PA PA7-like	345.03 256.40	450.13 1946.63	522	0.839
B08	D-Xylose	PA PA7-like	812.30 683.41	905.20 943.13	548.5	0.582
B09	L-Lactic Acid	PA PA7-like	8878.65 9052.20	1781.50 1319.87	517	0.891
B10	Formic Acid	PA PA7-like	472.62 237.34	836.94 1223.02	503	0.974
B11	D-Mannitol	PA PA7-like	7808.28 7895.51	1253.80 840.89	546	0.607
B12	L-Glutamic Acid	PA PA7-like	9936.28 9906.70	950.75 839.57	488	0.820
C01	D-Glucose-6-Phosphate	PA PA7-like	14.47 0.00	96.26 21.09	634	0.088
C02	D-Galactonic Acid-γ-Lactone	PA PA7-like	0.00 0.00	3.76 5.42	511.5	0.941
C03	D,L-Malic Acid	PA PA7-like	10100.28 9942.01	1784.71 1313.14	527	0.790
C04	D-Ribose	PA	1356.03	1581.73	485	0.790

		PA7-like	1356.14	1656.60		
C05	Tween 20	PA	7732.36	1503.64	593	0.259
		PA7-like	7629.00	1794.26		
C06	L-Rhamnose	PA	0.00	8.53	474	0.655
		PA7-like	0.00	11.68		
C07	D-Fructose	PA	7260.44	2257.15	531	0.750
		PA7-like	6837.75	1960.76		
C08	Acetic Acid	PA	6172.23	2986.04	436	0.365
		PA7-like	6346.17	2277.14		
C09	α-D-Glucose	PA	8920.54	1340.72	631	0.103
		PA7-like	8689.41	789.52		
C10	Maltose	PA	0.17	23.53	454	0.478
		PA7-like	0.31	32.49		
C11	D-Melibiose	PA	2.48	54.31	482.5	0.760
		PA7-like	7.32	75.79		
C12	Thymidine	PA	92.77	242.62	467	0.613
		PA7-like	169.16	277.18		
D01	L-Asparagine	PA	9879.22	1508.58	569	0.416
		PA7-like	9574.58	1144.63		
D02	D-Aspartic Acid	PA	0.17	22.97	542.5	0.609
		PA7-like	0.00	13.23		
D03	D-Glucosaminic Acid	PA	0.84	33.07	516	0.897
		PA7-like	0.38	40.48		
D04	1,2-Propanediol	PA	203.91	809.33	611	0.165
		PA7-like	11.80	253.08		
D05	Tween 40	PA	8566.48	1606.01	606	0.194
		PA7-like	8209.53	1981.91		
D06	α-Keto-Glutaric Acid	PA	9455.22	1516.33	580	0.338
		PA7-like	9244.61	758.94		
D07	α-Keto-Butyric Acid	PA	1681.43	1709.66	547.5	0.591
		PA7-like	1660.79	2392.17		
D08	α-Methyl-D-Galactoside	PA	1.20	44.68	542.5	0.625
		PA7-like	0.15	45.18		
D09	α-D-Lactose	PA	1.12	12.18	511	0.951
		PA7-like	0.90	11.28		
D10	Lactulose	PA	0.00	7.82	469	0.604
		PA7-like	0.06	2.38		
D11	Sucrose	PA	3.24	49.49	487.5	0.807
		PA7-like	0.85	63.49		
D12	Uridine	PA	1155.05	2110.49	406	0.194
		PA7-like	2330.76	2771.26		
E01	L-Glutamine	PA	10378.68	1296.46	608	0.185
		PA7-like	10075.44	1318.29		
E02	m-Tartaric Acid	PA	0.06	3.76	459.5	0.519
		PA7-like	0.16	24.79		
E03	D-Glucose-1-Phosphate	PA	0.97	70.53	439	0.360
		PA7-like	20.32	100.48		
E04	D-Fructose-6-Phosphate	PA	0.81	21.68	504	0.983
		PA7-like	0.94	7.05		
E05	Tween 80	PA	8296.38	1250.13	652	0.056
		PA7-like	7803.55	952.51		
E06	α-Hydroxy Glutaric Acid-γ-Lactone	PA	1.74	65.73	469.5	0.625
		PA7-like	6.81	129.51		
E07	α-Hydroxy Butyric Acid	PA	2045.83	2312.39	551	0.562
		PA7-like	1910.81	2599.75		
E08	ß-Methyl-D-Glucoside	PA	0.93	17.28	479	0.719
		PA7-like	3.53	62.21		
E09	Adonitol	PA	3.01	55.29	572	0.369
		PA7-like	0.00	101.82		
E10	Maltotriose	PA	206.12	504.05	533	0.726
		PA7-like	114.53	531.96		
E11	2-Deoxy Adenosine	PA	0.00	0.16	451	0.375
		PA7-like	0.00	1.99		

E12	Adenosine	PA PA7-like	847.31 917.97	1520.57 3528.78	491	0.849
F01	Glycyl-L-Aspartic Acid	PA PA7-like	47.16 225.82	330.91 510.56	427	0.300
F02	Citric Acid	PA PA7-like	8676.92 8840.67	1229.11 984.94	487	0.810
F03	myo-Inositol	PA PA7-like	0.36 0.44	53.38 30.27	495	0.885
F04	D-Threonine	PA PA7-like	19.89 27.84	262.58 952.66	481.5	0.748
F05	Fumaric Acid	PA PA7-like	10281.29 9792.89	1441.69 1523.34	576	0.365
F06	Bromo Succinic Acid	PA PA7-like	5356.28 5309.94	2992.62 1420.50	451	0.478
F07	Propionic Acid	PA PA7-like	9328.80 8694.73	2111.05 3064.68	627	0.115
F08	Mucic Acid	PA PA7-like	1.02 0.09	43.50 8.96	557	0.482
F09	Glycolic Acid	PA PA7-like	0.17 0.00	13.90 37.58	519	0.861
F10	Glyoxylic Acid	PA PA7-like	0.00 0.00	0.01 2.84	430.5	0.237
F11	D-Cellobiose	PA PA7-like	6.84 1.85	219.41 219.01	487	0.801
F12	Inosine	PA PA7-like	4114.66 5011.61	4246.18 4518.15	506	1.000
G01	Glycyl-L-Glutamic Acid	PA PA7-like	288.90 499.26	612.29 1432.30	376.5	0.091
G02	Tricarballylic Acid	PA PA7-like	7.48 12.42	226.00 313.94	483	0.761
G03	L-Serine	PA PA7-like	560.82 3033.24	2587.12 2695.70	279.5	0.003
G04	L-Threonine	PA PA7-like	603.03 1259.51	1781.94 2767.92	408.5	0.203
G05	L-Alanine	PA PA7-like	7788.13 8070.57	1990.74 1561.09	447	0.446
G06	L-Alanyl-Glycine	PA PA7-like	312.08 215.35	926.63 1033.40	484	0.777
G07	Acetoacetic Acid	PA PA7-like	287.96 375.37	641.12 1392.34	428	0.308
G08	N-Acetyl-ß-D-Mannosamine	PA PA7-like	0.36 0.00	77.74 127.66	515	0.906
G09	Mono Methyl Succinate	PA PA7-like	1817.48 4631.29	3392.05 4210.99	236	0.000
G10	Methyl Pyruvate	PA PA7-like	5107.28 4331.49	2842.74 2689.34	490	0.840
G11	D-Malic Acid	PA PA7-like	619.67 651.12	1212.86 1365.99	493	0.870
G12	L-Malic Acid	PA PA7-like	10602.53 9936.92	1025.48 1854.00	567	0.431
H01	Glycyl-L-Proline	PA PA7-like	6049.29 5944.43	6447.80 6313.10	536	0.701
H02	p-Hydroxy Phenyl Acetic Acid	PA PA7-like	10205.60 9728.27	2298.27 2243.79	623	0.127
H03	m-Hydroxy Phenyl Acetic Acid	PA PA7-like	0.00 0.00	151.64 202.87	489	0.807
H04	Tyramine	PA PA7-like	9210.85 8305.88	1698.41 2561.62	612	0.167
H05	D-Psicose	PA PA7-like	401.94 352.21	1029.07 695.66	535	0.703
H06	L-Lyxose	PA PA7-like	1671.02 1263.76	2107.49 1876.46	535	0.703
H07	Glucuronamide	PA	0.00	82.19	448	0.403

		PA7-like	2.17	93.11		
H08	Pyruvic Acid	PA	3859.70	4862.59	354	0.047
		PA7-like	6586.10	3199.60		
H09	L-Galactonic Acid-γ-Lactone	PA	0.00	96.17	464	0.558
		PA7-like	0.58	169.34		
H10	D-Galacturonic Acid	PA	0.06	273.41	538.5	0.649
		PA7-like	0.00	262.06		
H11	Phenylethylamine	PA	0.00	244.80	432	0.300
		PA7-like	0.09	273.75		
H12	2-Aminoethanol	PA	3515.38	4102.48	365	0.065
		PA7-like	6160.44	4361.71		

Appendix - Alignment 1: Alignment of the pvdI(2) *sequences of PA7 to the NCTC 12903 strain. Amino acids are coloured according to amino acid physiochemical property.*


cov pid 1701 8 1800
1 NCTC_12903_pvdI(2) 100.0% 100.0%
2 PA7_pvdI(2) 100.0% 96.5%
cov pid 1801 9 1900
1 NCTC_12903_pvdI(2) 100.0% 100.0%
2 PA7_pvdI(2) 100.0% 96.5%
cov pid 1901 0 2000
1 NCTC_12903_pvdI(2) 100.0% 100.0%
2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2001 1 2100
1 NCTC_12903_pvdI(2) 100.0% 100.0%
2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2101 2 2200
1 NCTC_12903_pvdI(2) 100.0% 100.0%
2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2201 3 2300
1 NCTC_12903_pvdI(2) 100.0% 100.0%
2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2301 4 2400
1 NCTC_12903_pvdI(2) 100.0% 100.0%
2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2401 5 2500
1 NCTC_12903_pvdI(2) 100.0% 100.0%
2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2501 6 2600
1 NCTC_12903_pvdI(2) 100.0% 100.0%
2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2601 7 2700
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2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2701 8 2800
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2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2801 9 2900
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2 PA7_pvdI(2) 100.0% 96.5%
cov pid 2901 0 3000
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2 PA7_pvdI(2) 100.0% 96.5%
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2 PA7_pvdI(2) 100.0% 96.5%
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2 PA7_pvdI(2) 100.0% 96.5%
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2 PA7_pvdI(2) 100.0% 96.5%
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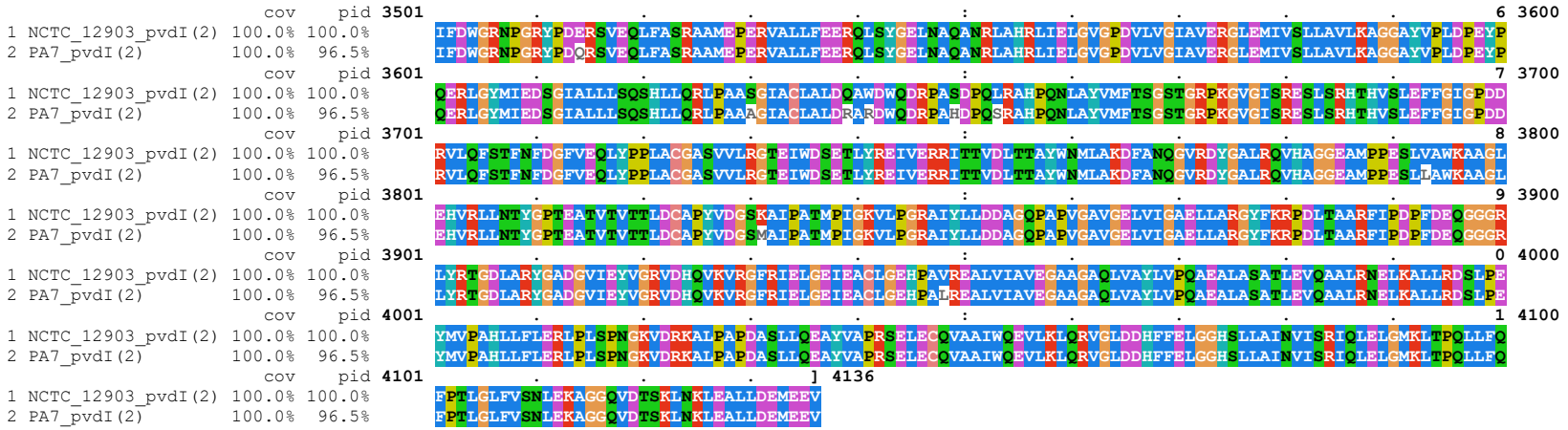
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2 PA7_pvdI(2) 100.0% 96.5% IFDWGRNPGRYPDQRSVEQLFASRAAMEPERVALLFEERQLSYGELNAQANRLAHRLIELGVGPDVLVGIAVERGLEMIVSLLAVLKAGGAYVPLDPEYP
cov pid 3601 7 3700
1 NCTC_12903_pvdI(2) 100.0% 100.0% QERLGYMIEDSGIALLLSQSHLLQRLPAASGIACLALDQAWDWQDRPASDPQLRAHPQNLAYVMFTSGSTGRPKGVGISRESLSRHTHVSLEFFGIGPDD
2 PA7_pvdI(2) 100.0% 96.5% QERLGYMIEDSGIALLLSQSHLLQRLPAAAGIACLALDRARDWQDRPAHDPQSRAHPQNLAYVMFTSGSTGRPKGVGISRESLSRHTHVSLEFFGIGPDD
cov pid 3701 8 3800
1 NCTC_12903_pvdI(2) 100.0% 100.0% RVLQESTFNFDGFVEQLYPPLACGASVVLRGTEIWDSETLYREIVERRITTVDLTTAYWNMLAKDFANQGVRDYGALRQVHAGGEAMPPESLVAWKAAGL
2 PA7_pvdI(2) 100.0% 96.5% RVLQESTFNFDGFVEQLYPPLACGASVVLRGTEIWDSETLYREIVERRITTVDLTTAYWNMLAKDFANQGVRDYGALRQVHAGGEAMPPESLLAWKAAGL
cov pid 3801 9 3900
1 NCTC_12903_pvdI(2) 100.0% 100.0% EHVRLLNTYGPTEATVTVTTLDCAPYVDGSKAIPATMPIGKVLPGRAIYLLDDAGQPAPVGAVGELVIGAELLARGYFKRPDLTAARFIPDPFDEQGGGR
2 PA7_pvdI(2) 100.0% 96.5% EHVRLLNTYGPTEATVTVTTLDCAPYVDGSMAIPATMPIGKVLPGRAIYLLDDAGQPAPVGAVGELVIGAELLARGYFKRPDLTAARFIPDPFDEQGGGR
cov pid 3901 0 4000
1 NCTC_12903_pvdI(2) 100.0% 100.0% LYRTGDLARYGADGVIEYVGRVDHQVKVRGFRIELGEIEACLGEHPAVREALVIAVEGAAGAQLVAYLVPQAEALASATLEVQAALRNELKALLRDSLPE
2 PA7_pvdI(2) 100.0% 96.5% LYRTGDLARYGADGVIEYVGRVDHQVKVRGFRIELGEIEACLGEHPALREALVIAVEGAAGAQLVAYLVPQAEALASATLEVQAALRNELKALLRDSLPE
cov pid 4001 1 4100
1 NCTC_12903_pvdI(2) 100.0% 100.0% YMVPAHLLFLERLPLSPNGKVDRKALPAPDASLLQEAYVAPRSELEQVAAIWQEVLKLQRVGLDDHFFELGGHSLLAINVISRIQLELGMKLTPQLLFQ
2 PA7_pvdI(2) 100.0% 96.5% YMVPAHLLFLERLPLSPNGKVDRKALPAPDASLLQEAYVAPRSELEQVAAIWQEVLKLQRVGLDDHFFELGGHSLLAINVISRIQLELGMKLTPQLLFQ
cov pid 4101] 4136
1 NCTC_12903_pvdI(2) 100.0% 100.0% FPTLGLFVSNLEKAGGQVDTSKLNKLEALLDEMEEV
2 PA7_pvdI(2) 100.0% 96.5% FPTLGLFVSNLEKAGGQVDTSKLNKLEALLDEMEEV

Appendix - Alignment 2: Alignment of the pvdJ(2) *sequences of PA7 to the NCTC 12903 strain. Amino acids are coloured according to amino acid physiochemical property.*


cov pid 1701 8 1800
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 1801 9 1900
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 1901 0 2000
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 2001 1 2100
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 2101 2 2200
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 2201 3 2300
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 2301 4 2400
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 2401 5 2500
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 2501 6 2600
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 2601 7 2700
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 2701 8 2800
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2 PA7_pvdJ(2) 100.0% 96.7%
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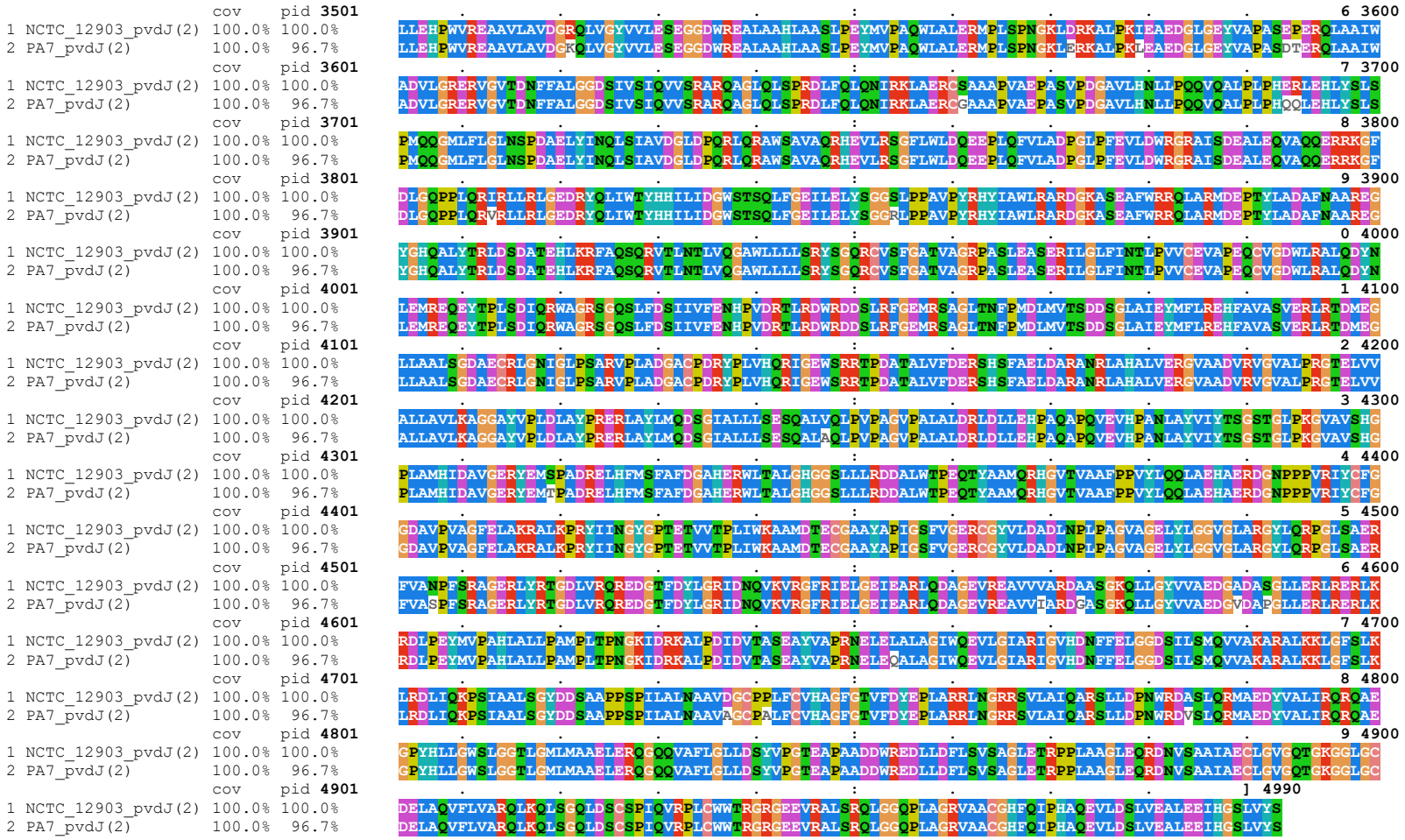
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 2901 0 3000
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 3001 1 3100
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 3101 2 3200
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 3201 3 3300
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 3301 4 3400
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 3401 5 3500
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%


cov pid 3501
6 3600
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 3601
7 3700
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 3701
8 3800
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 3801
9 3900
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 3901
0 4000
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4001
1 4100
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4101
2 4200
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4201
3 4300
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4301
4 4400
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4401
5 4500
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4501
6 4600
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4601
7 4700
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4701
8 4800
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4801
9 4900
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%
cov pid 4901
] 4990
1 NCTC_12903_pvdJ(2) 100.0% 100.0%
2 PA7_pvdJ(2) 100.0% 96.7%

Appendix - Table 6: Sampling locations of strains isolated on PA-CN agar from environmental samples.

Sample number	Sample type	Sampling Site	GPS coordinates	Isolate number	Oxidase Test	Gram Stain	Sequencing ID
ENV003	Leaves	University of East Anglia Broads	52.617144,1.228656	ENV003.1	+	gram negative bacilli	
ENV008	Leaves	University of East Anglia Broads	52.616254,1.233498	ENV008.1	+	gram negative bacilli	
		University of East Anglia Broads	52.616686,1.233542	ENV008.2	+	gram negative bacilli	
ENV009	Plants	University of East Anglia Broads	52.616686,1.233542	ENV009.1	+	gram negative bacilli	*Pseudomonas synxantha*
		University of East Anglia Broads	52.618276,1.233587	ENV009.2	+	gram negative bacilli	
ENV011	Leaves	University of East Anglia Broads	52.618276,1.233587	ENV011.1	+	gram negative bacilli	
ENV013	Plants	University of East Anglia Broads	52.61965,1.232565	ENV013.1	+	gram negative bacilli	
				ENV013.2	+	gram negative bacilli	
MH001	Leaves	Mousehold Heath	52.645362,1.319807	MH001.1	-	gram negative bacilli	
MH003	Leaves	Mousehold Heath	52.646467,1.316653	MH003.1	-	gram negative bacilli	
MH004	Plants	Mousehold Heath	52.64679,1.316564	MH004.1	-	gram negative bacilli	
				MH004.2	-	gram negative bacilli	
				MH004.3	-	gram negative bacilli	
MH008	Plants	Mousehold Heath	52.644715,1.309502	MH008.1	-	gram negative bacilli	
MH009	Leaves	Mousehold Heath	52.643718,1.309502	MH009.1	+	gram negative bacilli	*Pseudomonas putida*
				MH009.2	-	gram negative cocci	
MH013	Plants	Mousehold Heath	52.643583,1.312922	MH013.1	-	gram negative bacilli	
				MH013.2	-	gram negative bacilli	
MH015	Plants	Mousehold Heath	52.643286,1.315276	MH015.1	-	gram negative bacilli	
MH016	Leaves	Mousehold Heath	52.643772,1.317186	MH016.1	-	gram negative bacilli	
				MH016.2	+	gram negative bacilli	
				MH016.3	-	unclear	
MH018	Leaves	Mousehold Heath	52.645065,1.319407	MH018.1	-	gram negative bacilli	*Eschericia sp. E4742*
MH020	Plants	Mousehold Heath	52.645766,1.317542	MH020.1	+	gram negative bacilli	
MM001	Marsh	Marston Marsh	52.601216,1.274498	MM001.1	+	gram negative bacilli	
				MM001.2	+	gram negative bacilli	
MM002	Water	Marston Marsh	52.600676,1.273965	MM002.1	+	gram negative bacilli	
				MM002.2	-	gram negative bacilli	
				MM002.3	-	gram negative bacilli	
				MM002.4	-	gram negative bacilli	
MM003	Water	Marston Marsh	52.600892,1.273077	MM003.1	+	gram negative bacilli	
MM005	Water	Marston Marsh	52.601269,1.271389	MM005.1	+	gram negative bacilli	
				MM005.2	-	gram negative bacilli	
				MM005.3	-	gram negative bacilli	
MM007	Water	Marston Marsh	52.601108,1.265569	MM007.1	+	gram negative bacilli	
				MM007.2	+	gram negative bacilli	
MM008	Marsh	Marston Marsh	52.600434,1.263037	MM008.1	+	gram negative bacilli	*Pseudomonas putida*
MM009	Marsh	Marston Marsh	52.600892,1.261927	MM009.1	+	gram negative bacilli	*Pseudomonas sp. Leaf58*
				MM009.2	+	gram negative bacilli	
				MM009.3	-	gram negative bacilli	
MM011	Marsh	Marston Marsh	52.60259,1.265614	MM011.1	-	gram negative bacilli	
MM012	Marsh	Marston Marsh	52.60259,1.26708	MM012.1	+	gram negative bacilli	
FW024	Water	Foxely Woods	52.768071,1.038971	FW024.1	-	gram negative bacilli	
				FW024.2	-	gram negative bacilli	

SP004	Water	Sparham Pools	52.717861,1.073162	SP004.1	-	gram negative bacilli
SP006	Water	Sparham Pools	52.717295,1.073429	SP006.1	+	gram negative bacilli
				SP006.2	+	gram negative bacilli
				SP006.3	-	gram negative bacilli
SP011	Water	Sparham Pools	52.718373,1.068443	SP011.1	+	gram negative bacilli
SP013	Water	Sparham Pools	52.719693,1.067419	SP013.1	+	gram negative bacilli
				SP013.2	-	gram negative bacilli
MM004	Soil	Marston Marsh	52.601216,1.271922	MM004.1	+	gram negative bacilli
				MM004.4	+	gram negative bacilli
				MM004.5	+	gram negative bacilli
MM006	Soil	Marston Marsh	52.602051,1.268812	MM006.1	+	gram negative bacilli
				MM006.2	+	gram negative bacilli
MM010	Soil	Marston Marsh	52.601566,1.263571	MM010.1	-	gram negative bacilli
				MM010.2	-	gram negative bacilli
				MM010.5	-	gram negative bacilli
MM014	Plants	Marston Marsh	52.603803,1.2701	MM014.1	+	gram negative bacilli
				MM014.2	-	gram negative bacilli
				MM014.4	-	gram negative bacilli
DW001	Soil	Danby Woods	52.603426,1.276142	DW001.1	+	gram negative bacilli
DW002	Leaves	Danby Woods	52.60321,1.275831	DW002.1	+	gram negative bacilli
				DW002.3	-	gram negative bacilli
				DW002.4	+	gram negative bacilli
				DW002.5	-	gram negative cocci
DW003	Soil	Danby Woods	52.603291,1.275386	DW003.1	+	gram negative bacilli
				DW003.2	+	gram negative bacilli
				DW003.4	+	gram negative bacilli
				DW003.5	-	gram negative bacilli
DW004	Plants	Danby Woods	52.604369,1.275298	DW004.1	+	gram negative bacilli
				DW004.3	-	gram negative bacilli
				DW004.4	-	gram negative bacilli
DW005	Soil	Danby Woods	52.604584,1.275564	DW005.1	-	gram positive cocci
				DW005.2	+	gram negative bacilli
				DW005.4	-	gram negative bacilli
				DW005.6	-	gram negative bacilli
				DW005.7	-	gram negative bacilli
DW006	Soil	Danby Woods	52.604099,1.276364	DW006.1	-	gram negative bacilli
				DW006.2	-	gram negative cocci
				DW006.3	-	gram negative bacilli
				DW006.6	-	gram negative bacilli
				DW006.7	-	gram negative bacilli
DW007	Soil	Danby Woods	52.604234,1.276897	DW007.1	+	gram negative bacilli
				DW007.2	+	gram negative bacilli
				DW007.3	+	gram negative bacilli
				DW007.6	-	gram negative bacilli
SP015	Water	Sparham Pools	52.717456,1.066929	SP015.1	-	gram negative bacilli
				SP015.2	+	gram negative bacilli
HG001	Water	Horsey Gap	52.767316,1.640753	HG001.1	-	gram negative bacilli

				HG001.2	-	gram negative bacilli	
				HG001.3	-	gram negative bacilli	
				HG004.2	-	gram negative bacilli	
DW008	Soil	Danby Woods	52.603345,1.276497	DW008.1	+	gram negative bacilli	
				DW008.2	+	gram negative bacilli	
DW009	Soil	Danby Woods	52.603021,1.275964	DW009.1	+	gram negative bacilli	
				DW009.2	-	gram negative bacilli	
DW010	Soil	Danby Woods	52.602967,1.276319	DW010.1	+	gram negative bacilli	
				DW010.2	-	gram negative coccii	
DW011	Soil	Danby Woods	52.602779,1.277385	DW011.1	-	gram negative bacilli	
DW013	Soil	Danby Woods	52.60356,1.277385	DW013.1	+	gram negative bacilli	
				DW013.2	-	gram negative bacilli	
DW014	Soil	Danby Woods	52.603291,1.276675	DW014.1	-	gram negative cocci	
				DW014.2	+	gram negative bacilli	
DW015	Soil	Danby Woods	52.602752,1.276453	DW015.1	+	gram negative bacilli	
				DW015.2	-	gram negative bacilli	
FW001	Soil	Foxely Woods	52.762142,1.03545	FW001.1	+	gram negative bacilli	
FW002	Soil	Foxely Woods	52.762465,1.037277	FW002.1	-	gram negative bacilli	
FW003	Plants	Foxely Woods	52.763058,1.039505	FW003.1	+	gram negative bacilli	
FW004	Plants	Foxely Woods	52.760848,1.043516	FW004.1	+	gram negative bacilli	
				FW004.2	+	gram negative bacilli	
				FW004.3	-	gram negative bacilli	
FW006	Leaves	Foxely Woods	52.762088,1.048106	FW006.1	-	gram negative bacilli	
				FW006.2	+	gram negative bacilli	
FW009	Soil	Foxely Woods	52.763489,1.04873	FW009.1	-	gram negative bacilli	
FW010	Leaves	Foxely Woods	52.764055,1.048017	FW010.1	-	gram negative bacilli	
				FW010.2	-	gram negative bacilli	
FW011	Plants	Foxely Woods	52.764459,1.047571	FW011.1	-	gram negative bacilli	
				FW011.2	-	gram negative bacilli	
FW012	Soil	Foxely Woods	52.764918,1.046992	FW012.1	-	gram negative bacilli	
				FW013.2	-	gram negative bacilli	
FW014	Leaves	Foxely Woods	52.765214,1.045343	FW014.1	-	gram negative bacilli	
				FW014.2	-	gram negative bacilli	
FW017	Leaves	Foxely Woods	52.76322,1.045611	FW017.1	-	gram positive cocci	
				FW017.2	-	gram negative bacilli	
FW018	Plants	Foxely Woods	52.761495,1.045967	FW018.1	+	gram negative bacilli	
				FW018.2	-	gram negative bacilli	
FW020	Plants	Foxely Woods	52.760632,1.042937	FW020.1	+	gram negative bacilli	
				FW020.2	+	gram negative bacilli	
FW021	Leaves	Foxely Woods	52.766966,1.042357	FW021.1	-	gram negative bacilli	
				FW021.2	-	gram negative bacilli	
FW023	Leaves	Foxely Woods	52.76772,1.039951	FW023.2	+	gram negative bacilli	*Pseudomonas putida*
SP002	Leaves	Sparham Pools	52.720367,1.070535	SP002.1	-	gram negative bacilli	
				SP002.2	-	gram negative bacilli	
SP010	Soil	Sparham Pools	52.717295,1.069867	SP010.1	+	gram negative bacilli	
				SP010.2	+	gram negative bacilli	
LWR001	Soil	Lower Wood	52.536344,1.152327	LWR001.1	+	gram negative bacilli	

LWR003	Soil	Lower Wood	52.539362,1.153834	LWR003.1	-	gram negative bacilli	
LWR004	Soil	Lower Wood	52.539551,1.154189	LWR004.1	+	gram negative bacilli	
				LWR004.2	+	gram negative bacilli	
LWR005	Leaves	Lower Wood	52.539794,1.155253	LWR005.1	+	gram negative bacilli	
				LWR005.2	-	gram negative cocci	
LWR006	Soil	Lower Wood	52.539174,1.157558	LWR006.1	-	gram negative bacilli	
LWR007	Leaves	Lower Wood	52.539147,1.158178	LWR007.1	-	gram negative bacilli	
				LWR007.2	-	gram negative bacilli	
				LWR007.3	-	gram negative bacilli	
				LWR007.4	-	gram negative bacilli	
				LWR007.6	-	gram negative bacilli	
LWR009	Soil	Lower Wood	52.53823,1.16035	LWR009.1	+	gram negative bacilli	
LWR010	Soil	Lower Wood	52.536586,1.15809	LWR010.1	+	gram negative bacilli	
LWR011	Plants	Lower Wood	52.536937,1.15215	LWR011.1	-	gram negative bacilli	
				LWR011.2	+	gram negative bacilli	*Pseudomonas aeruginosa*
LWR012	Soil	Lower Wood	52.536074,1.15277	LWR012.1	+	gram negative bacilli	
				LWR012.2	-	gram negative bacilli	
				LWR012.3	-	gram negative bacilli	
HG003	Soil	Horsey Gap	52.766319,1.642001	HG003.1	+	gram negative bacilli	
				HG003.2	+	gram negative bacilli	
UBM001	Marsh/ Fen	Upton Broad and Marshes	52.668486,1.518877	UBM001.1	+	gram negative bacilli	
				UBM001.2	+	gram negative bacilli	
				UBM001.4	+	gram negative cocci	
				UBM001.6	+	gram negative bacilli	
UBM002	Marsh/ Fen	Upton Broad and Marshes	52.668351,1.519722	UBM002.1	+	gram negative bacilli	
				UBM002.2	+	gram negative bacilli	
				UBM002.3	+	gram negative bacilli	
				UBM002.5	+	gram negative bacilli	
UBM003	Marsh/ Fen	Upton Broad and Marshes	52.668351,1.5199	UBM003.1	+	gram negative cocci	
				UBM003.2	+	gram negative cocci	
				UBM003.4	+	gram negative bacilli	
UBM005	Marsh/ Fen	Upton Broad and Marshes	52.668189,1.521278	UBM005.1	+	gram negative bacilli	
UBM007	Marsh/ Fen	Upton Broad and Marshes	52.668297,1.525191	UBM007.1	+	gram negative bacilli	
				UBM007.2	+	gram negative bacilli	
				UBM007.3	+	gram negative cocci	
UBM008	Marsh/ Fen	Upton Broad and Marshes	52.668109,1.525369	UBM008.1	+	gram negative bacilli	
				UBM008.2	+	gram negative bacilli	
UBM010	Marsh/ Fen	Upton Broad and Marshes	52.668216,1.526748	UBM010.1	+	gram negative bacilli	
				UBM010.2	+	gram negative bacilli	
				UBM010.4	+	gram negative bacilli	
UBM011	Marsh/ Fen	Upton Broad and Marshes	52.66889,1.527281	UBM011.1	+	gram negative bacilli	
				UBM011.2	+	gram negative bacilli	
UBM012	Marsh/ Fen	Upton Broad and Marshes	52.670642,1.527281	UBM012.1	+	gram negative bacilli	
UBM013	Marsh/ Fen	Upton Broad and Marshes	52.671208,1.527148	UBM013.1	+	gram negative bacilli	
UBM015	Marsh/ Fen	Upton Broad and Marshes	52.673229,1.531728	UBM015.1	-	gram negative bacilli	
UBM018	Marsh/ Fen	Upton Broad and Marshes	52.672636,1.525725	UBM018.1	+	gram negative bacilli	
				UBM018.2	+	gram negative bacilli	

				UBM018.3	+	gram negative bacilli	
				UBM018.4	-	gram negative bacilli	
				UBM018.5	+	gram negative bacilli	
UBM019	Marsh/ Fen	Upton Broad and Marshes	52.669402,1.52 0077	UBM019.1	+	gram negative bacilli	
RLF001	Marsh/ Fen	Redgrave and Lopham Fen	52.381266,1.01 5399	RLF001.1	-	gram negative bacilli	
RLF005	Plants	Redgrave and Lopham Fen	52.382533,1.01 774	RLF005.1	+	gram negative bacilli	
				RLF005.3	-	unclear	
RLF006	Marsh/ Fen	Redgrave and Lopham Fen	52.382317,1.01 8889	RLF006.1	+	gram negative bacilli	
				RLF006.3	+	gram negative bacilli	
				RLF006.5	+	gram negative bacilli	
RLF007	Plants	Redgrave and Lopham Fen	52.381563,1.02 2203	RLF007.1	-	gram negative cocci	
				RLF007.2	-	gram negative bacilli	
RLF011	Water	Redgrave and Lopham Fen	52.378463,1.02 5605	RLF011.1	+	gram negative bacilli	
				RLF011.2	+	gram negative bacilli	
RLF012	Water	Redgrave and Lopham Fen	52.378275,1.02 2689	RLF012.1	+	gram negative bacilli	
RLF013	Water	Redgrave and Lopham Fen	52.377035,1.01 8094	RLF013.1	+	gram negative bacilli	
RLF014	Water	Redgrave and Lopham Fen	52.376954,1.01 7961	RLF014.1	+	gram negative bacilli	
				RLF014.2	+	gram negative bacilli	
				RLF014.4	-	unclear	
RLF008	Fungi	Redgrave and Lopham Fen	52.381482,1.02 2115	RLF008.1 small	-	gram negative bacilli	
				RLF008.1 large	-	gram negative bacilli	
RLF015	Marsh/ Fen	Redgrave and Lopham Fen	52.376038,1.00 961	RLF015.1	-	gram negative bacilli	
				RLF015.2	+	gram negative bacilli	
				RLF015.3	-	gram negative bacilli	
RLF016	Water	Redgrave and Lopham Fen	52.374421,1.00 3244	RLF016.1	+	gram negative bacilli	
				RLF016.2	+	gram negative bacilli	
				RLF016.3	+	gram negative bacilli	
				RLF016.4	+	gram negative bacilli	
				RLF016.5	-	unclear	
				RLF016.6	+	gram negative bacilli	
RLF017	Marsh/ Fen	Redgrave and Lopham Fen	52.37469,1.003 244	RLF017.1	+	gram negative bacilli	
				RLF017.2	+	gram negative bacilli	
				RLF017.3	+	gram negative bacilli	
RLF018	Marsh/ Fen	Redgrave and Lopham Fen	52.375067,1.00 3027	RLF018.1	+	gram negative bacilli	
RLF019	Marsh/ Fen	Redgrave and Lopham Fen	52.375337,1.00 2673	RLF019.1	+	gram negative bacilli	
				RLF019.2	+	gram negative bacilli	
				RLF019.3	+	gram negative bacilli	
				RLF019.4	+	gram negative bacilli	
				RLF019.5	-	gram negative diplococci	
				RLF019.6	+	gram negative bacilli	
RLF021	Marsh/ Fen	Redgrave and Lopham Fen	52.375606,1.00 0597	RLF021.1	+	gram negative bacilli	
				RLF021.2	+	gram negative bacilli	
				RLF021.3	+	gram negative bacilli	
RLF023	Marsh/ Fen	Redgrave and Lopham Fen	52.375526,0.99 9713	RLF023.1	+	gram negative bacilli	
				RLF023.2	+	gram negative bacilli	
				RLF023.3	+	gram negative bacilli	
RLF024	Marsh/ Fen	Redgrave and Lopham Fen	52.375526,0.99 9359	RLF024.1	+	gram negative bacilli	*Pseudomonas sp. CCOS 191*

				RLF024.2	+	gram negative bacilli
RLF025	Marsh/ Fen	Redgrave and Lopham Fen	52.375121,0.998829	RLF025.1	+	gram negative bacilli
				RLF025.4	+	gram negative bacilli
RLF026	Marsh/ Fen	Redgrave and Lopham Fen	52.37469,0.999183	RLF026.1	-	gram negative bacilli
RLF027	Fungi	Redgrave and Lopham Fen	52.374852,0.999051	RLF027.1	+	gram negative bacilli
				RLF027.4	-	gram negative cocci
				RLF027.6	+	gram negative bacilli
				RLF027.9	-	gram negative bacilli
				RLF027.7	+	gram negative bacilli
RLF030	Marsh/ Fen	Redgrave and Lopham Fen	52.378059,1.009522	RLF030.1	+	gram negative bacilli
				RLF030.2	+	gram negative bacilli
				RLF030.4	+	gram negative bacilli
				RLF030.5 small	-	gram negative bacilli
				RLF030.5 large	-	gram negative bacilli
RLF031	Marsh/ Fen	Redgrave and Lopham Fen	52.37814,1.009434	RLF031.1 small	-	gram negative bacilli
				RLF031.1 large	-	gram negative bacilli

Appendix - Table 7: Metadata for strains isolated from samples provided by the Environment Agency.

Sample	Sample Type	Sampling Site	Isolate number	Sequencing ID
EA1	Water	Allonby	EA1.1	
			EA1.2	
			EA1.3	
			EA1.4	
			EA1.5	
EA2	Water	Birling Gap	EA2.1	
			EA2.2	
			EA2.3	
			EA2.4	
			EA2.5	
			EA2.6	
EA3	Water	Blue Anchor West	EA3.1	
			EA3.2	
			EA3.4	
EA4	Water	Blythe South Beach	EA4.1	
EA5	Water	Croyde Bay	EA5.1	
			EA5.2	
			EA5.3	
EA6	Water	Dunster Beach	EA6.2	
			EA6.4	
EA7	Water	Formby	EA7.1	*Pseudomonas aeruginosa*
			EA7.2	
			EA7.3	*Pseudomonas aeruginosa*
			EA7.4	*Pseudomonas aeruginosa*
EA8	Water	Heacham	EA8.1	*Pseudomonas aeruginosa*
			EA8.2	
			EA8.3	
			EA8.4	
			EA8.5	
			EA8.6	
			EA8.7	
			EA8.8	*Pseudomonas aeruginosa*
EA9	Water	Lowestoft (North of Claremount Pier)	EA9.1	
			EA9.5	
			EA9.7	
			EA9.8	
EA10	Water	Lynmouth Beach	EA10.1	
			EA10.2	
			EA10.3	
			EA10.4	
EA11	Water	Minehead Terminus	EA11.1	
			EA11.2	
			EA11.3	
			EA11.4	

			EA11.5	
			EA11.6	
EA12	Water	Porlock Weir	EA12.1	
			EA12.2	
			EA12.4	
EA13	Water	Ryde	EA13.1	
			EA13.2	
			EA13.3	
			EA13.5	
EA14	Water	Seascale	EA14.1	*Pseudomonas aeruginosa*
			EA14.2	*Pseudomonas aeruginosa*
			EA14.3	
			EA14.5	
EA15	Water	West Kirby	EA15.2	
			EA15.3	
			EA15.4	
			EA15.5	
EA16	Water	Beadnell	EA16.1	*Pseudomonas aeruginosa*
			EA16.2	
			EA16.3	
			EA16.4	
			EA16.5	
EA17	Water	Chapel St Leonards	EA17.1	
			EA17.2	
			EA17.3	
			EA17.4	
EA18	Water	Colwick coutnry Park (West Lake)	EA18.1	
			EA18.2	
			EA18.3	
			EA18.4	
EA19	Water	Keynes Cotsworld Country Park and Beach	EA19.1	
			EA19.2	
EA20	Water	Compton Bay	EA20.1	
			EA20.3	
EA21	Water	Dovercourt	EA21.1	
			EA21.2	
			EA21.3	
			EA21.4	*Pseudomonas aeruginosa*
EA22	Water	Danes Dyke, Flamborough	EA22.1	
			EA22.2	
			EA22.3	
			EA22.4	
EA23	Water	Fresham Great Pond	EA23.1	
			EA23.2	
			EA23.3	
			EA23.4	
			EA23.5	

EA24	Water	Westgate Bay	EA24.1	
			EA24.2	
			EA24.3	
			EA24.4	
EA25	Water	Gorleston Beach	EA25.1	
			EA25.2	
			EA25.3	
EA26	Water	Hemsby Beach	EA26.1	*Pseudomonas aeruginosa*
			EA26.2	
			EA26.3	
			EA26.4	
			EA26.5	
			EA26.6	
			EA26.7	
			EA26.8	
			EA26.10	
EA27	Water	Hunstanton Main Beach	EA27.1	*Pseudomonas aeruginosa*
			EA27.2	
			EA27.3	
EA28	Water	Henleaze Lake	EA28.1	
			EA28.2	
			EA28.3	
			EA28.4	
			EA28.7	*Pseudomonas aeruginosa*
EA29	Water	Hornsea	EA29.1	*Pseudomonas aeruginosa*
			EA29.2	
			EA29.3	
			EA29.4	
			EA29.5	
EA30	Water	Jaywick	EA30.2	
			EA30.3	
			EA30.4	
EA31	Water	Hunstanton Beach (Old Hunstanton)	EA31.1	
			EA31.2	
			EA31.3	
			EA31.4	
EA32	Water	Lowesoft (South of Claremont Pier)	EA32.1	
			EA32.3	
			EA32.4	
EA33	Water	Mundesley	EA33.1	
			EA33.3	
EA34	Water	Runswick Bay	EA34.1	
			EA34.2	
			EA34.3	
			EA34.4	
			EA34.5	
			EA34.6	

EA35	Water	Sheerness	EA35.1	
			EA35.2	
			EA35.3	
			EA35.4	
			EA35.5	*Pseudomonas aeruginosa*
EA37	Water	Shell Bay North	EA37.1	
			EA37.3	
			EA37.4	
EA38	Water	Sheringham	EA38.1	
			EA38.2	
			EA38.3	
			EA38.4	
EA39	Water	St Mildred's Bay	EA39.1	
			EA39.3	
			EA39.5	
EA40	Water	Spittal	EA40.1	
			EA40.2	
EA41	Water	Sutton-on-Sea	EA41.2	
			EA41.3	
			EA41.4	
			EA41.5	
			EA41.7	*Pseudomonas aeruginosa*
EA42	Water	Wells Beach	EA42.1	
			EA42.2	
			EA42.3	
			EA42.4	
EA43	Water	West Runton Beach	EA43.1	
			EA43.2	*Pseudomonas aeruginosa*
			EA43.3	
EA44	Water	Wharfe at Cromwheel, Ilkley	EA44.1	*Pseudomonas aeruginosa*
			EA44.2	
			EA44.3	
			EA44.4	
EA45	Water	Westward Ho	EA45.1	
			EA45.2	
			EA45.3	
			EA45.4	
EA46	Water	Windermere, Fellfoot	EA46.1	
			EA46.2	
			EA46.3	
EA47	Water	Windermere, Lakeside YMCA	EA47.1	
			EA47.2	
			EA47.3	
			EA47.4	
EA48	Water	Windermere, Millerground Landing	EA48.1	
			EA48.2	
			EA48.3	

EA49	Water	Windermere, Rayrigg Meadow	EA49.1 EA49.2
EA50	Water	Reighton	EA50.1 EA50.2 EA50.3 EA50.4

Appendix - Table 8: Mann-Whitney U test comparing pairwise F_{ST} *values observed between Groups 1 and 2. Significant p-values (*$p \leq 0.05$*) are highlighted in* ***bold****.*

	group1	***group2***	***U***	***p.adj***
With overlapping core groups	Within Group 1	Within Group 2	695	**0.001**
	Within Group 1	Between Group 1 and Group 2	5230	**7.06×10^{-8}**
	Within Group 2	Between Group 1 and Group2	1908	0.870
Without overlapping core groups	Within Group 1	Within Group 2	6	**2.49×10^{-10}**
	Within Group 1	Between Group 1 and Group 2	2604	**3.84×10^{-14}**
	Within Group 2	Between Group 1 and Group2	363	**0.002**

Appendix - Table 9: Fisher's exact test comparing the distribution of isolates across core groups from specified sources. Resulting p-values were calculated after the removal of clonally linked strains and adjusted using the Benjamini-Hochberg correction with significant p-values ($p \leq 0.05$) indicated in ***bold.***

	Core Group	Number of isolates in core group	Percentage of isolates in source	Percentage of isolates not in source	Fisher's test adjusted p-value	Wald Test	Wald p-value
Abscess/Skin/Tissue/Ulcer/Wound	*Core1*	16	6.25	93.75	1.000	0.24	0.808
	Core2	27	7.41	92.59	1.000	0.09	0.926
	Core3	21	0.00	100.00	0.993	0.00	0.999
	Core4	45	4.44	95.56	0.993	0.86	0.392
	Core5	19	0.00	100.00	0.993	0.00	1.000
	Core6	19	10.53	89.47	0.993	0.43	0.668
	Core7	23	13.04	86.96	0.993	0.91	0.361
	Core8	25	12.00	88.00	0.993	0.76	0.445
	Core9	10	10.00	90.00	0.993	0.25	0.804
	Core10	19	5.26	94.74	1.000	0.42	0.672
	Core11	30	6.67	93.33	1.000	0.25	0.803
	Core12	28	10.71	89.29	0.993	0.56	0.576
	Core13	31	3.23	96.77	0.993	0.94	0.349
	Core14	22	9.09	90.91	0.993	0.21	0.832
	Core15	40	7.50	92.50	1.000	0.09	0.928
	Core16	32	3.13	96.88	0.993	0.97	0.332
	Core17	45	0.00	100.00	0.506	0.00	0.999
	Core18	52	5.77	94.23	1.000	0.57	0.567
	Core19	715	8.67	91.33	0.993	1.08	0.279
	Core20	47	8.51	91.49	1.000	0.16	0.871
	Core21	146	8.90	91.10	0.993	0.48	0.630
	Core22	46	4.35	95.65	0.993	0.89	0.374
	Core23	39	17.95	82.05	0.506	2.28	**0.023**
Bacteraemia	*Core1*	16	6.25	93.75	1.000	0.40	0.688
	Core2	27	3.70	96.30	0.777	0.95	0.341
	Core3	21	19.05	80.95	0.473	1.54	0.124
	Core4	45	11.11	88.89	0.785	0.46	0.644
	Core5	19	31.58	68.42	0.070	3.10	**0.002**
	Core6	19	15.79	84.21	0.725	0.99	0.320
	Core7	23	0.00	100.00	0.660	0.07	0.944
	Core8	25	36.00	64.00	**0.007**	4.16	**0.000**
	Core9	10	0.00	100.00	0.785	0.00	1.000
	Core10	19	0.00	100.00	0.725	0.00	0.999
	Core11	30	6.67	93.33	1.000	0.47	0.635
	Core12	28	3.57	96.43	0.777	0.99	0.322
	Core13	31	6.45	93.55	1.000	0.52	0.601
	Core14	22	9.09	90.91	1.000	0.01	0.992
	Core15	40	22.50	77.50	0.079	2.83	**0.005**
	Core16	32	18.75	81.25	0.473	1.85	0.064
	Core17	45	15.56	84.44	0.548	1.49	0.136
	Core18	52	3.85	96.15	0.725	1.30	0.193

	Core19	715	6.43	93.57	0.183	3.44	**0.001**
	Core20	47	10.64	89.36	0.785	0.36	0.720
	Core21	146	9.59	90.41	1.000	0.19	0.847
	Core22	46	15.22	84.78	0.548	1.43	0.153
	Core23	39	12.82	87.18	0.725	0.80	0.424
Cystic Fibrosis	*Core1*	16	6.25	93.75	0.743	0.82	0.414
	Core2	27	3.70	96.30	0.505	1.37	0.170
	Core3	21	4.76	95.24	0.505	1.11	0.269
	Core4	45	2.22	97.78	0.106	1.92	0.055
	Core5	19	5.26	94.74	0.581	1.00	0.317
	Core6	19	0.00	100.00	0.463	0.00	1.000
	Core7	23	4.35	95.65	0.505	1.20	0.229
	Core8	25	4.00	96.00	0.505	1.29	0.196
	Core9	10	0.00	100.00	0.509	0.00	1.000
	Core10	19	21.05	78.95	0.505	0.98	0.327
	Core11	30	33.33	66.67	0.058	3.07	**0.002**
	Core12	28	28.57	71.43	0.169	2.30	**0.021**
	Core13	31	6.45	93.55	0.535	1.11	0.266
	Core14	22	4.55	95.45	0.505	1.16	0.248
	Core15	40	7.50	92.50	0.505	1.09	0.278
	Core16	32	9.38	90.63	0.791	0.67	0.506
	Core17	45	8.89	91.11	0.581	0.89	0.375
	Core18	52	1.92	98.08	0.075	2.07	**0.038**
	Core19	715	18.18	81.82	0.058	5.15	**0.000**
	Core20	47	19.15	80.85	0.505	1.18	0.240
	Core21	146	6.16	93.84	0.075	2.60	**0.009**
	Core22	46	15.22	84.78	0.725	0.38	0.707
	Core23	39	5.13	94.87	0.463	1.46	0.144
Respiratory Tract	*Core1*	16	12.50	87.50	1.000	0.44	0.657
	Core2	27	22.22	77.78	0.880	0.78	0.434
	Core3	21	38.10	61.90	0.265	2.53	**0.012**
	Core4	45	22.22	77.78	0.880	1.02	0.309
	Core5	19	21.05	78.95	0.880	0.52	0.604
	Core6	19	10.53	89.47	1.000	0.71	0.477
	Core7	23	0.00	100.00	0.265	0.18	0.854
	Core8	25	24.00	76.00	0.880	0.99	0.323
	Core9	10	10.00	90.00	1.000	0.56	0.577
	Core10	19	15.79	84.21	1.000	0.10	0.921
	Core11	30	13.33	86.67	1.000	0.49	0.625
	Core12	28	25.00	75.00	0.880	1.19	0.235
	Core13	31	9.68	90.32	0.880	1.03	0.301
	Core14	22	13.64	86.36	1.000	0.38	0.704
	Core15	40	17.50	82.50	1.000	0.15	0.881
	Core16	32	31.25	68.75	0.399	2.18	**0.029**
	Core17	45	24.44	75.56	0.880	1.41	0.157
	Core18	52	19.23	80.77	0.880	0.51	0.609
	Core19	715	15.52	84.48	0.880	1.10	0.271
	Core20	47	21.28	78.72	0.880	0.87	0.387

	Core21	146	13.01	86.99	0.880	1.23	0.218
	Core22	46	17.39	82.61	1.000	0.14	0.888
	Core23	39	10.26	89.74	0.880	1.07	0.285
Urinary Tract	*Core1*	16	0.00	100.00	1.000	0.00	1.000
	Core2	27	7.41	92.59	1.000	0.33	0.743
	Core3	21	4.76	95.24	1.000	0.70	0.486
	Core4	45	28.89	71.11	**0.000**	4.27	**0.000**
	Core5	19	10.53	89.47	1.000	0.20	0.843
	Core6	19	10.53	89.47	1.000	0.20	0.843
	Core7	23	13.04	86.96	1.000	0.63	0.525
	Core8	25	8.00	92.00	1.000	0.21	0.832
	Core9	10	0.00	100.00	1.000	0.00	1.000
	Core10	19	5.26	94.74	1.000	0.59	0.555
	Core11	30	13.33	86.67	1.000	0.78	0.435
	Core12	28	7.14	92.86	1.000	0.38	0.702
	Core13	31	6.45	93.55	1.000	0.53	0.593
	Core14	22	22.73	77.27	0.564	2.10	**0.035**
	Core15	40	7.50	92.50	1.000	0.38	0.704
	Core16	32	12.50	87.50	1.000	0.65	0.519
	Core17	45	8.89	91.11	1.000	0.08	0.938
	Core18	52	7.69	92.31	1.000	0.39	0.699
	Core19	715	8.11	91.89	1.000	1.41	0.158
	Core20	47	8.51	91.49	1.000	0.17	0.865
	Core21	146	12.33	87.67	1.000	1.36	0.174
	Core22	46	2.17	97.83	0.905	1.52	0.128
	Core23	39	7.69	92.31	1.000	0.33	0.739
Clinical environment: Dental, Hospital	*Core1*	16	6.25	93.75	0.894	1.37	0.171
	Core2	27	3.70	96.30	0.950	0.85	0.396
	Core3	21	0.00	100.00	1.000	0.00	1.000
	Core4	45	8.89	91.11	0.184	3.41	**0.001**
	Core5	19	0.00	100.00	1.000	0.00	1.000
	Core6	19	0.00	100.00	1.000	0.00	1.000
	Core7	23	0.00	100.00	1.000	0.00	0.997
	Core8	25	0.00	100.00	1.000	0.00	0.999
	Core9	10	0.00	100.00	1.000	0.00	1.000
	Core10	19	5.26	94.74	0.894	1.20	0.231
	Core11	30	0.00	100.00	1.000	0.00	1.000
	Core12	28	0.00	100.00	1.000	0.00	1.000
	Core13	31	3.23	96.77	0.950	0.71	0.477
	Core14	22	9.09	90.91	0.609	2.44	**0.014**
	Core15	40	5.00	95.00	0.834	1.63	0.103
	Core16	32	3.13	96.88	0.950	0.68	0.497
	Core17	45	2.22	97.78	1.000	0.33	0.738
	Core18	52	1.92	98.08	1.000	0.19	0.852
	Core19	715	0.70	99.30	0.828	2.50	**0.012**
	Core20	47	4.26	95.74	0.856	1.41	0.160
	Core21	146	0.68	99.32	1.000	0.90	0.369
	Core22	46	0.00	100.00	1.000	0.00	0.999

	Core23	39	2.56	97.44	0.997	0.48	0.632
Plants	*Core1*	16	0.00	100.00	1.000	0.01	0.996
	Core2	27	3.70	96.30	1.000	0.77	0.442
	Core3	21	0.00	100.00	1.000	0.00	0.998
	Core4	45	0.00	100.00	1.000	0.01	0.989
	Core5	19	0.00	100.00	1.000	0.00	1.000
	Core6	19	0.00	100.00	1.000	0.00	1.000
	Core7	23	4.35	95.65	1.000	0.93	0.353
	Core8	25	0.00	100.00	1.000	0.02	0.986
	Core9	10	0.00	100.00	1.000	0.00	0.997
	Core10	19	0.00	100.00	1.000	0.00	1.000
	Core11	30	0.00	100.00	1.000	0.01	0.996
	Core12	28	3.57	96.43	1.000	0.73	0.464
	Core13	31	0.00	100.00	1.000	0.00	0.999
	Core14	22	4.55	95.45	1.000	0.97	0.330
	Core15	40	0.00	100.00	1.000	0.00	0.999
	Core16	32	0.00	100.00	1.000	0.00	1.000
	Core17	45	0.00	100.00	1.000	0.01	0.989
	Core18	52	3.85	96.15	1.000	1.15	0.250
	Core19	715	2.52	97.48	1.000	2.14	**0.032**
	Core20	47	0.00	100.00	1.000	0.00	1.000
	Core21	146	0.68	99.32	1.000	0.98	0.326
	Core22	46	0.00	100.00	1.000	nan	nan
	Core23	39	2.56	97.44	1.000	0.40	0.691
Soil: Manure, Rocks, Sand, Soil	*Core1*	16	12.50	87.50	0.564	2.15	**0.031**
	Core2	27	0.00	100.00	1.000	0.01	0.996
	Core3	21	0.00	100.00	1.000	0.00	0.999
	Core4	45	0.00	100.00	1.000	0.00	1.000
	Core5	19	0.00	100.00	1.000	0.00	1.000
	Core6	19	0.00	100.00	1.000	0.00	1.000
	Core7	23	13.04	86.96	0.564	2.71	**0.007**
	Core8	25	0.00	100.00	1.000	0.01	0.990
	Core9	10	0.00	100.00	1.000	0.00	1.000
	Core10	19	0.00	100.00	1.000	0.00	1.000
	Core11	30	0.00	100.00	1.000	0.00	1.000
	Core12	28	0.00	100.00	1.000	0.00	0.999
	Core13	31	3.23	96.77	1.000	0.17	0.867
	Core14	22	0.00	100.00	1.000	0.01	0.996
	Core15	40	2.50	97.50	1.000	0.09	0.925
	Core16	32	0.00	100.00	1.000	0.00	1.000
	Core17	45	0.00	100.00	1.000	0.00	1.000
	Core18	52	0.00	100.00	1.000	0.01	0.990
	Core19	715	4.20	95.80	0.564	3.15	**0.002**
	Core20	47	0.00	100.00	1.000	0.00	0.999
	Core21	146	2.74	97.26	1.000	0.00	0.999
	Core22	46	0.00	100.00	1.000	0.00	1.000
	Core23	39	0.00	100.00	1.000	0.01	0.996
Animal	*Core1*	16	0.00	100.00	1.000	0.00	1.000

	Core2	27	3.70	96.30	1.000	0.31	0.755
	Core3	21	0.00	100.00	1.000	0.00	0.998
	Core4	45	0.00	100.00	0.955	0.00	1.000
	Core5	19	0.00	100.00	1.000	0.00	0.999
	Core6	19	5.26	94.74	1.000	0.05	0.959
	Core7	23	13.04	86.96	0.843	1.70	0.089
	Core8	25	0.00	100.00	1.000	0.00	1.000
	Core9	10	40.00	60.00	**0.023**	3.94	**0.000**
	Core10	19	0.00	100.00	1.000	0.00	0.999
	Core11	30	3.33	96.67	1.000	0.42	0.673
	Core12	28	0.00	100.00	1.000	0.00	1.000
	Core13	31	3.23	96.77	1.000	0.46	0.648
	Core14	22	4.55	95.45	1.000	0.10	0.920
	Core15	40	5.00	95.00	1.000	0.00	0.998
	Core16	32	0.00	100.00	1.000	0.00	0.999
	Core17	45	4.44	95.56	1.000	0.18	0.860
	Core18	52	5.77	94.23	1.000	0.26	0.799
	Core19	715	6.85	93.15	0.843	3.06	**0.002**
	Core20	47	2.13	97.87	1.000	0.89	0.374
	Core21	146	3.42	96.58	1.000	0.92	0.359
	Core22	46	2.17	97.83	1.000	0.87	0.386
	Core23	39	0.00	100.00	1.000	0.00	0.999
Water: Lakes, Oceans, Ponds, Puddles, Rivers	*Core1*	16	18.75	81.25	0.585	1.31	0.189
	Core2	27	14.81	85.19	0.705	0.37	0.712
	Core3	21	0.00	100.00	0.586	0.00	1.000
	Core4	45	0.00	100.00	0.207	0.00	1.000
	Core5	19	10.53	89.47	0.956	0.57	0.565
	Core6	19	10.53	89.47	0.956	0.57	0.565
	Core7	23	13.04	86.96	0.810	0.66	0.509
	Core8	25	0.00	100.00	0.536	nan	nan
	Core9	10	30.00	70.00	0.368	2.12	**0.034**
	Core10	19	5.26	94.74	1.000	0.57	0.565
	Core11	30	10.00	90.00	1.000	0.18	0.860
	Core12	28	10.71	89.29	0.956	0.30	0.762
	Core13	31	16.13	83.87	0.585	0.74	0.458
	Core14	22	9.09	90.91	1.000	0.73	0.466
	Core15	40	5.00	95.00	0.801	0.90	0.371
	Core16	32	0.00	100.00	0.368	0.01	0.990
	Core17	45	8.89	91.11	1.000	0.57	0.568
	Core18	52	25.00	75.00	**0.046**	3.39	**0.001**
	Core19	715	9.37	90.63	0.956	0.37	0.713
	Core20	47	2.13	97.87	0.368	1.53	0.126
	Core21	146	13.70	86.30	0.536	1.13	0.259
	Core22	46	13.04	86.96	0.801	0.94	0.346
	Core23	39	10.26	89.74	0.956	0.86	0.391

Appendix - Table 10: Significant SNPs with an association to a niche specific clade. Significance (p ≤ 1.00 × 10^{-6}) was determined using the lrt p-value identified using Pyseer with the number of strains containing the gene also described. The clinical and environmental percentage is calculated as the number of strains from a clinical or environmental lineage that contain the SNP against the total number of strains containing the SNP. SNPs were identified using the PAO1 type strain as a reference for calling and are underlined in the table.

Position in PAO1	Reference	Query	p-value	Clinical (%)	Environment (%)	Core4	Core8	Core16	Core9	Core13	Core18	Total number of strains
2961328	G	A	1.13E-40	35.2	64.8	45	0	0	0	31	52	128
4510007	C	T	3.06E-35	87.5	12.5	45	25	0	10	0	0	80
1603008	G	A	7.87E-31	23.1	76.9	0	25	0	0	31	52	108
3728929	T	C	7.87E-31	23.1	76.9	0	25	0	0	31	52	108
5427504	G	A	7.87E-31	88.5	11.5	45	0	32	10	0	0	87
3231002	C	T	6.49E-24	96.6	3.4	0	25	32	0	0	2	59
308052	T	C	1.58E-23	86.4	13.6	45	25	0	10	0	1	81
5029352	A	G	1.58E-23	86.4	13.6	45	25	0	10	0	1	81
6144163	T	C	1.58E-23	86.4	13.6	45	25	0	10	0	1	81
175357	C	T	1.82E-22	96.6	3.4	0	25	32	0	0	2	59
6206318	C	T	1.02E-21	96.6	3.4	0	25	32	0	0	2	59
5900398	G	A	1.65E-21	90.5	9.5	0	25	32	0	0	6	63
5832440	G	A	2.59E-21	81.4	18.6	0	25	32	10	0	3	70
309957	AGCG	GGCA	1.25E-19	97.2	2.8	45	25	0	0	0	2	72
5388185	G	A	1.68E-19	95.9	4.1	45	25	0	0	0	3	73
309764	TCT	CCC	6.59E-19	97.2	2.8	45	25	0	0	0	2	72
3268548	C	T	8.53E-19	95.9	4.1	45	25	0	0	0	3	73
3363877	T	C	8.70E-19	82.6	17.4	0	25	32	10	0	2	69
3199941	T	C	1.10E-18	95.9	4.1	45	25	0	0	0	3	73
3200727	C	T	1.10E-18	95.9	4.1	45	25	0	0	0	3	73
587433	G	A	1.39E-18	35.7	64.3	45	0	0	0	31	50	126

587470	G	A	1.39E-18	35.7	64.3	45	0	0	0	31	50	126
4958695	TAG	CAA	1.69E-18	95.9	4.1	45	25	0	0	0	3	73
853961	C	T	1.76E-18	97.2	2.8	45	25	0	0	0	2	72
2956354	C	T	1.76E-18	97.2	2.8	45	25	0	0	0	2	72
1059597	G	T	3.20E-18	86.4	13.6	45	25	0	10	0	1	81
1824485	G	A	3.20E-18	86.4	13.6	45	25	0	10	0	1	81
3069881	C	T	3.56E-18	97.2	2.8	45	25	0	0	0	2	72
3121631	G	C	3.56E-18	97.2	2.8	45	25	0	0	0	2	72
3121669	AGC	GCA	3.56E-18	97.2	2.8	45	25	0	0	0	2	72
3121770	C	T	3.56E-18	97.2	2.8	45	25	0	0	0	2	72
3320688	G	A	3.56E-18	97.2	2.8	45	25	0	0	0	2	72
5522946	G	A	5.07E-18	96.6	3.4	0	25	32	0	0	2	59
986426	C	T	9.41E-18	92.1	7.9	45	25	0	0	0	6	76
1670090	C	T	9.41E-18	92.1	7.9	45	25	0	0	0	6	76
1791160	A	G	9.41E-18	92.1	7.9	45	25	0	0	0	6	76
2834325	G	A	9.41E-18	92.1	7.9	45	25	0	0	0	6	76
3393309	C	T	9.41E-18	92.1	7.9	45	25	0	0	0	6	76
3470896	C	T	9.41E-18	92.1	7.9	45	25	0	0	0	6	76
622163	CGCCG	TGCCA	1.12E-17	93.4	6.6	0	25	32	0	0	4	61
5384641	C	T	1.12E-17	97.2	2.8	45	25	0	0	0	2	72
2975623	T	A	2.33E-17	96.6	3.4	0	25	32	0	0	2	59
5419656	T	C	3.07E-17	96.3	3.8	45	0	32	0	0	3	80
1898280	G	A	3.15E-17	87.5	12.5	45	0	32	10	0	1	88
206559	C	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
389044	C	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
390129	C	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
633055	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1035618	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153

1038642	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1214604	G	A	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1222836	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1222848	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1732911	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1774434	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1774914	G	A	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1858519	T	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1950313	AAAGA	GAAGG	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
1950323	TGCA	GGCG	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
2017729	GAGG	CAGC	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
2091607	G	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
2214816	GA	AG	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
2919189	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
2999087	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
3046168	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
3190309	A	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
3190360	G	A	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
3206090	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
3574807	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
4253627	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
4256422	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
4256726	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
4407334	C	T	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
4425655	A	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
4427735	A	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
4520190	C	A	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
4973667	C	A	7.77E-17	45.8	54.2	45	25	0	0	31	52	153

4980808	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5005065	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5017327	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5087963	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5110285	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5200871	C	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5244161	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5297549	A	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5305480	G	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5322546	G	A	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5459541	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5467607	C	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5490071	C	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5757184	C	A	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5863025	GA	AC	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5863037	C	A	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5909170	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5910865	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5943662	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
5944983	G	A	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
6003919	A	G	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
6240003	T	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
6257526	A	C	7.77E-17	45.8	54.2	45	25	0	0	31	52	153
19316	A	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
114371	T	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
169492	A	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
182673	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
343756	A	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42

353689	A	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
457620	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
591816	C	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
643910	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1011522	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1059627	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1157062	A	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1157154	T	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1157491	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1157681	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1157688	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1157752	C	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1157797	C	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1157857	T	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1157887	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1158164	C	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1158200	T	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1158281	T	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1158302	T	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1158329	GTAG	ATAA	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1158452	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1158509	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1200040	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1680063	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1897082	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1897285	C	CT	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1949543	A	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1949823	T	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42

1971845	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
2033084	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
2033120	A	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
2065072	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
2976723	C	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
3144526	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
3234835	T	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
3293626	G	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
3306141	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
3367261	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
3627997	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
3677383	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
3776352	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
4025328	T	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
4134308	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
4204914	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
4407474	G	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
5012222	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
5302995	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
5502844	A	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
5563325	A	G	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
5629424	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
5775785	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
5918482	C	T	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
6004651	G	A	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
6182252	T	C	7.77E-17	76.2	23.8	0	0	32	10	0	0	42
1602951	T	C	8.03E-17	21.6	78.4	0	25	0	10	31	50	116
2975617	C	T	8.82E-17	82.6	17.4	0	25	32	10	0	2	69

364882	G	A	9.74E-17	97.2	2.8	45	25	0	0	0	2	72
570219	G	A	9.74E-17	97.2	2.8	45	25	0	0	0	2	72
570231	C	T	9.74E-17	97.2	2.8	45	25	0	0	0	2	72
2216035	T	C	9.74E-17	97.2	2.8	45	25	0	0	0	2	72
5725742	T	C	9.74E-17	97.2	2.8	45	25	0	0	0	2	72
5522695	A	G	1.36E-16	82.6	17.4	0	25	32	10	0	2	69
1080267	G	A	1.50E-16	86.4	13.6	45	25	0	10	0	1	81
5340863	A	C	2.04E-16	26.0	74.0	0	0	32	10	31	50	123
1077261	T	G	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
1153217	C	T	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
1731514	C	T	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
2936525	C	T	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
3041060	C	T	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
5029552	G	A	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
5029604	G	A	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
5888603	A	G	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
5976715	A	G	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
6065454	G	A	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
6247022	G	A	2.04E-16	97.2	2.8	45	25	0	0	0	2	72
3803203	G	A	2.24E-16	82.6	17.4	0	25	32	10	0	2	69
5991504	A	G	2.25E-16	23.6	76.4	0	25	0	0	31	50	106
677735	A	G	4.15E-16	95.0	5.0	0	25	32	0	0	3	60
6189798	G	A	4.18E-16	96.6	3.4	0	25	32	0	0	2	59
938316	A	G	4.39E-16	23.8	76.2	0	25	0	0	31	49	105
683129	C	T	5.80E-16	93.4	6.6	0	25	32	0	0	4	61
705855	C	T	6.92E-16	96.6	3.4	0	25	32	1	0	1	59
5860960	C	T	1.01E-15	36.0	64.0	45	0	0	0	31	49	125
4085227	GGTG	CTGA	1.36E-15	81.4	18.6	0	25	32	10	0	3	70

6121895	G	A	1.51E-15	22.9	77.1	0	25	0	1	31	52	109
894870	G	A	1.72E-15	90.5	9.5	0	25	32	0	0	6	63
3336291	C	T	1.88E-15	85.1	14.9	0	25	32	9	0	1	67
630881	G	A	3.13E-15	87.5	12.5	45	0	32	10	0	1	88
547314	TGA	GTGG	3.16E-15	88.6	11.4	45	25	0	9	0	0	79
1769632	G	A	5.34E-15	97.2	2.8	45	25	0	0	0	2	72
5202730	T	G	5.84E-15	21.7	78.3	0	25	0	10	31	49	115
5009594	G	A	1.00E-14	97.5	2.5	45	0	32	0	0	2	79
300373	T	C	1.25E-14	42.1	57.9	45	0	0	10	0	52	107
366833	G	C	1.25E-14	42.1	57.9	45	0	0	10	0	52	107
572892	A	G	1.25E-14	42.1	57.9	45	0	0	10	0	52	107
1900960	T	C	1.25E-14	42.1	57.9	45	0	0	10	0	52	107
4354870	A	G	1.25E-14	42.1	57.9	45	0	0	10	0	52	107
5968021	A	G	1.25E-14	42.1	57.9	45	0	0	10	0	52	107
58538	T	C	1.25E-14	64.8	35.2	0	25	32	0	31	0	88
1580113	T	C	1.25E-14	64.8	35.2	0	25	32	0	31	0	88
3786240	T	C	1.25E-14	64.8	35.2	0	25	32	0	31	0	88
4357430	G	A	1.25E-14	64.8	35.2	0	25	32	0	31	0	88
1734040	CT	TC	1.49E-14	97.2	2.8	45	25	0	0	0	2	72
3746084	G	A	1.49E-14	97.2	2.8	45	25	0	0	0	2	72
2177156	G	A	2.37E-14	96.6	3.4	0	25	32	0	0	2	59
2928308	C	A	2.98E-14	97.2	2.8	45	25	0	0	0	2	72
4821380	G	A	3.08E-14	36.3	63.7	45	0	0	0	31	48	124
587458	A	G	3.28E-14	33.1	66.9	45	0	0	9	31	51	136
5081734	G	A	3.40E-14	97.2	2.8	45	25	0	0	0	2	72
6028884	A	G	3.79E-14	23.6	76.4	0	25	0	0	31	50	106
5022391	G	A	5.88E-14	97.2	2.8	45	25	0	0	0	2	72
664168	C	T	6.26E-14	93.4	6.6	0	25	32	0	0	4	61

5425615	T	C	7.10E-14	33.1	66.9	45	0	0	10	31	50	136
3072047	A	G	7.52E-14	26.0	74.0	0	0	32	10	31	50	123
5051232	G	A	7.86E-14	97.2	2.8	45	25	0	0	0	2	72
2970781	G	A	8.51E-14	21.6	78.4	0	25	0	10	31	50	116
4775528	G	A	8.88E-14	97.2	2.8	45	25	0	0	0	2	72
2013237	C	T	8.91E-14	89.1	10.9	0	25	32	0	0	7	64
1722167	C	T	9.42E-14	94.6	5.4	45	25	0	0	0	4	74
3186886	GGCA	AGCC	1.12E-13	23.6	76.4	0	25	0	0	31	50	106
1059783	G	A	1.42E-13	85.4	14.6	45	25	0	10	0	2	82
2791691	G	A	1.77E-13	97.2	2.8	45	25	0	0	0	2	72
5862804	A	G	1.79E-13	36.0	64.0	45	0	0	0	31	49	125
57169	T	C	1.88E-13	58.2	41.8	0	25	32	10	31	0	98
3677885	T	C	1.88E-13	58.2	41.8	0	25	32	10	31	0	98
4936745	G	A	2.07E-13	97.2	2.8	45	25	0	0	0	2	72
5342441	T	C	2.07E-13	97.2	2.8	45	25	0	0	0	2	72
593348	G	T	2.10E-13	97.2	2.8	45	25	0	0	0	2	72
3039883	G	A	2.10E-13	97.2	2.8	45	25	0	0	0	2	72
5048543	C	T	2.10E-13	97.2	2.8	45	25	0	0	0	2	72
3008294	C	T	2.74E-13	97.2	2.8	45	25	0	0	0	2	72
3276703	G	A	2.78E-13	94.6	5.4	45	25	0	0	0	4	74
3277930	CGGC	GGGT	2.78E-13	94.6	5.4	45	25	0	0	0	4	74
3685386	T	C	2.78E-13	94.6	5.4	45	25	0	0	0	4	74
5553835	C	T	2.78E-13	94.6	5.4	45	25	0	0	0	4	74
5564144	C	T	2.78E-13	94.6	5.4	45	25	0	0	0	4	74
2592746	A	G	2.92E-13	97.2	2.8	45	25	0	0	0	2	72
5774202	C	A	2.92E-13	97.2	2.8	45	25	0	0	0	2	72
545878	T	G	3.30E-13	48.1	51.9	45	0	32	0	31	52	160
546135	A	T	3.30E-13	48.1	51.9	45	0	32	0	31	52	160

2092320	G	T	3.30E-13	48.1	51.9	45	0	32	0	31	52	160
4285413	A	G	3.30E-13	48.1	51.9	45	0	32	0	31	52	160
5112484	G	A	3.30E-13	48.1	51.9	45	0	32	0	31	52	160
247326	C	T	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
566029	C	T	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
1130479	C	T	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
1391741	T	C	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
1565358	C	T	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
2875925	G	A	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
3129266	T	C	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
3148643	A	G	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
3244413	C	T	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
3310250	G	A	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
3418591	C	T	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
3741473	G	A	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
4391426	C	T	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
4422270	G	A	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
4492147	T	C	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
4749880	A	G	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
5037122	C	T	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
5040366	ACCG	CCT	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
5062594	T	C	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
5106512	G	A	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
5136087	G	A	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
5243282	G	A	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
5251713	A	G	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
5334963	G	A	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
5426722	C	T	3.30E-13	71.4	28.6	0	25	0	10	0	0	35

6252947	T	C	3.30E-13	71.4	28.6	0	25	0	10	0	0	35
404659	A	G	4.14E-13	33.8	66.2	45	0	0	10	31	47	133
6162712	C	T	4.30E-13	96.3	3.8	45	0	32	0	0	3	80
5364802	G	A	4.32E-13	95.0	5.0	0	25	32	0	0	3	60
1989879	A	G	4.35E-13	36.0	64.0	45	0	0	0	31	49	125
4984811	G	A	4.63E-13	97.2	2.8	45	25	0	0	0	2	72
5818702	C	T	4.97E-13	97.2	2.8	45	25	0	0	0	2	72
3658431	C	T	5.00E-13	96.6	3.4	45	25	14	0	0	3	87
4740061	C	T	5.06E-13	94.6	5.4	45	25	0	0	0	4	74
1622828	G	A	5.36E-13	87.7	12.3	0	25	32	0	0	8	65
1170973	C	T	5.89E-13	97.2	2.8	45	25	0	0	0	2	72
1078884	C	T	6.37E-13	28.1	71.9	0	0	32	0	31	51	114
3749699	G	A	6.56E-13	95.9	4.1	45	25	0	0	0	3	73
5086531	C	T	6.58E-13	97.2	2.8	45	25	0	0	0	2	72
4096	C	T	7.96E-13	95.9	4.1	45	25	0	0	0	3	73
4113709	C	T	8.02E-13	97.2	2.8	45	25	0	0	0	2	72
5704478	C	T	8.02E-13	97.2	2.8	45	25	0	0	0	2	72
3350923	G	A	8.40E-13	97.2	2.8	45	25	0	0	0	2	72
2650636	C	G	8.47E-13	97.2	2.8	45	25	0	0	0	2	72
3509614	C	T	8.69E-13	97.2	2.8	45	25	0	0	0	2	72
5240008	C	T	9.01E-13	95.9	4.1	45	25	0	0	0	3	73
5421259	A	C	9.22E-13	21.7	78.3	0	25	0	10	31	49	115
1042928	G	A	9.48E-13	86.5	13.5	45	0	32	10	0	2	89
1578240	T	C	1.06E-12	33.3	66.7	45	0	0	10	31	49	135
6065082	G	A	1.07E-12	92.1	7.9	45	25	0	0	0	6	76
1404649	G	C	1.09E-12	95.0	5.0	0	25	32	0	0	3	60
1521624	CGCG	TGCA	1.11E-12	97.2	2.8	45	25	0	0	0	2	72
1425764	G	A	1.25E-12	95.9	4.1	45	25	0	0	0	3	73

1531100	C	T	1.25E-12	95.9	4.1	45	25	0	0	0	3	73
1190269	G	A	1.27E-12	95.0	5.0	0	25	32	0	0	3	60
5420067	G	C	1.29E-12	97.5	2.5	45	0	32	0	0	2	79
5420425	G	A	1.29E-12	97.5	2.5	45	0	32	0	0	2	79
565243	C	G	1.32E-12	95.9	4.1	45	25	0	0	0	3	73
4541352	T	C	1.42E-12	21.7	78.3	0	25	0	10	31	49	115
5381023	A	G	1.54E-12	33.3	66.7	45	0	0	9	31	50	135
3270061	A	G	1.76E-12	97.2	2.8	45	25	0	0	0	2	72
3270229	G	A	1.76E-12	97.2	2.8	45	25	0	0	0	2	72
5000869	C	G	1.76E-12	97.2	2.8	45	25	0	0	0	2	72
3133091	G	A	1.78E-12	97.2	2.8	45	25	0	0	0	2	72
5241268	G	A	1.78E-12	97.2	2.8	45	25	0	0	0	2	72
5769909	G	A	1.78E-12	97.2	2.8	45	25	0	0	0	2	72
3319797	G	A	1.83E-12	95.9	4.1	45	25	0	0	0	3	73
4191377	G	A	2.04E-12	97.2	2.8	45	25	0	0	0	2	72
5522895	C	T	2.09E-12	95.0	5.0	0	25	32	0	0	3	60
4856	G	A	2.27E-12	97.2	2.8	45	25	0	0	0	2	72
5553692	C	A	2.27E-12	97.2	2.8	45	25	0	0	0	2	72
2190417	C	T	2.28E-12	90.9	9.1	45	25	0	0	0	7	77
3351887	G	A	2.28E-12	90.9	9.1	45	25	0	0	0	7	77
6020723	G	A	2.28E-12	90.9	9.1	45	25	0	0	0	7	77
162580	T	C	2.34E-12	26.0	74.0	0	0	32	10	31	50	123
1002209	C	T	2.34E-12	97.2	2.8	45	25	0	0	0	2	72
1271133	G	A	2.34E-12	97.2	2.8	45	25	0	0	0	2	72
5010290	CGCT	TGCC	2.34E-12	97.2	2.8	45	25	0	0	0	2	72
6242894	C	T	2.38E-12	97.5	2.5	45	0	32	0	0	2	79
1076838	C	T	2.58E-12	95.9	4.1	45	25	0	0	0	3	73
5123326	G	C	2.58E-12	95.9	4.1	45	25	0	0	0	3	73

6173234	CGCCGCCCTG	C	2.58E-12	95.9	4.1	45	25	0	0	0	3	73
6028874	A	G	2.79E-12	21.6	78.4	0	25	0	10	31	50	116
5876011	T	C	2.87E-12	90.9	9.1	45	25	0	0	0	7	77
4282096	A	C	3.22E-12	97.2	2.8	45	25	0	0	0	2	72
5597521	T	C	3.22E-12	97.2	2.8	45	25	0	0	0	2	72
5829778	C	T	3.32E-12	91.9	8.1	0	25	32	0	0	5	62
4328160	G	T	3.94E-12	97.2	2.8	45	25	0	0	0	2	72
4328546	C	T	3.94E-12	97.2	2.8	45	25	0	0	0	2	72
3280482	G	A	3.96E-12	91.9	8.1	0	25	32	0	0	5	62
5754091	G	A	4.14E-12	97.2	2.8	45	25	0	0	0	2	72
5763967	G	A	4.23E-12	91.9	8.1	0	25	32	0	0	5	62
3433771	T	C	4.29E-12	24.0	76.0	0	25	0	0	31	48	104
554584	C	G	4.43E-12	97.2	2.8	45	25	0	0	0	2	72
3041600	C	T	4.43E-12	97.2	2.8	45	25	0	0	0	2	72
3806375	G	A	4.69E-12	93.4	6.6	0	25	32	0	0	4	61
5244212	C	T	4.76E-12	94.6	5.4	45	25	0	0	0	4	74
5795774	G	T	4.84E-12	95.9	4.1	45	25	0	0	0	3	73
535069	A	G	5.02E-12	90.9	9.1	45	25	0	0	0	7	77
3127088	G	A	5.02E-12	90.9	9.1	45	25	0	0	0	7	77
1078145	A	C	5.26E-12	95.9	4.1	45	25	0	0	0	3	73
1146953	C	T	5.73E-12	88.6	11.4	45	25	0	0	0	9	79
3408444	A	C	5.93E-12	90.9	9.1	45	25	0	0	0	7	77
3590503	T	C	6.05E-12	97.2	2.8	45	25	0	0	0	2	72
3729001	GCG	TCA	6.05E-12	97.2	2.8	45	25	0	0	0	2	72
1837582	C	T	6.27E-12	89.1	10.9	0	25	32	0	0	7	64
2564232	G	A	6.34E-12	93.3	6.7	45	25	0	0	0	5	75
3363850	G	A	6.83E-12	95.0	5.0	0	25	32	1	0	2	60
3363868	G	A	6.83E-12	95.0	5.0	0	25	32	1	0	2	60

5237232	C	T	6.84E-12	36.3	63.7	45	0	0	0	31	48	124
5800937	G	A	6.91E-12	95.9	4.1	45	25	0	0	0	3	73
6110672	G	A	7.27E-12	97.5	2.5	45	0	32	0	0	2	79
5744792	G	C	7.50E-12	95.9	4.1	45	25	0	0	0	3	73
1700224	C	A	7.60E-12	90.9	9.1	45	25	0	0	0	7	77
1843093	G	A	7.60E-12	90.9	9.1	45	25	0	0	0	7	77
1843343	T	A	7.60E-12	90.9	9.1	45	25	0	0	0	7	77
3300650	G	A	7.60E-12	90.9	9.1	45	25	0	0	0	7	77
4386444	G	A	7.90E-12	97.5	2.5	45	0	32	0	0	2	79
3870968	C	G	8.44E-12	97.5	2.5	45	0	32	1	0	1	79
1495486	G	A	8.47E-12	97.2	2.8	45	25	0	0	0	2	72
382475	G	A	8.83E-12	97.2	2.8	45	25	0	0	0	2	72
1907075	G	A	8.83E-12	97.2	2.8	45	25	0	0	0	2	72
4779706	C	T	8.83E-12	97.2	2.8	45	25	0	0	0	2	72
4779871	G	A	8.83E-12	97.2	2.8	45	25	0	0	0	2	72
4935530	AGCCT	GGCCC	8.83E-12	97.2	2.8	45	25	0	0	0	2	72
174880	G	A	1.04E-11	97.2	2.8	45	25	0	0	0	2	72
2938199	G	A	1.04E-11	97.2	2.8	45	25	0	0	0	2	72
2938403	C	T	1.04E-11	97.2	2.8	45	25	0	0	0	2	72
555328	C	T	1.06E-11	97.2	2.8	45	25	0	0	0	2	72
1743551	C	T	1.06E-11	97.2	2.8	45	25	0	0	0	2	72
559620	A	G	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
1080425	C	T	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
1080850	C	T	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
1083122	C	T	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
1708937	G	A	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
1755955	C	T	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
2936184	C	T	1.12E-11	97.2	2.8	45	25	0	0	0	2	72

2940039	A	C	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
2940051	C	T	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
2940657	C	T	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
2940758	GTTCA	ATTCG	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
2942522	G	A	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
5026078	C	T	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
5782874	C	A	1.12E-11	97.2	2.8	45	25	0	0	0	2	72
3018460	G	C	1.23E-11	95.9	4.1	45	25	0	0	0	3	73
3336731	G	A	1.23E-11	95.9	4.1	45	25	0	0	0	3	73
5989696	G	A	1.23E-11	95.9	4.1	45	25	0	0	0	3	73
5807502	G	A	1.32E-11	21.6	78.4	0	25	0	10	31	50	116
3586437	G	A	1.32E-11	97.5	2.5	45	0	32	0	0	2	79
3778291	TC	CT	1.33E-11	86.5	13.5	45	0	32	10	0	2	89
3778334	C	T	1.33E-11	86.5	13.5	45	0	32	10	0	2	89
2203134	G	A	1.41E-11	97.2	2.8	45	25	0	0	0	2	72
2209573	G	A	1.41E-11	97.2	2.8	45	25	0	0	0	2	72
1602900	C	T	1.52E-11	36.6	63.4	45	0	0	0	31	47	123
3258926	C	T	1.67E-11	97.2	2.8	45	25	0	0	0	2	72
4997268	T	C	1.72E-11	84.3	15.7	45	25	0	10	0	3	83
4289311	C	T	1.95E-11	22.5	77.5	0	25	0	10	31	45	111
1837480	G	A	2.20E-11	77.0	23.0	0	25	32	10	0	7	74
3913602	A	G	2.21E-11	87.7	12.3	0	25	32	0	0	8	65
685673	C	T	2.41E-11	95.0	5.0	0	25	32	0	0	3	60
3043057	T	C	3.01E-11	95.9	4.1	45	25	0	0	0	3	73
540967	G	A	3.02E-11	95.9	4.1	45	25	0	0	0	3	73
3827607	G	A	3.20E-11	81.4	18.6	0	25	32	10	0	3	70
1573524	C	T	3.37E-11	93.3	6.7	45	25	0	0	0	5	75
1072368	G	A	3.40E-11	97.2	2.8	45	25	0	0	0	2	72

1867312	T	C	3.40E-11	97.2	2.8	45	25	0	0	0	2	72
2741412	G	A	3.40E-11	97.2	2.8	45	25	0	0	0	2	72
3853752	G	A	3.40E-11	97.2	2.8	45	25	0	0	0	2	72
6004801	G	A	3.50E-11	95.9	4.1	45	25	0	0	0	3	73
6004927	G	A	3.50E-11	95.9	4.1	45	25	0	0	0	3	73
2140724	C	T	3.77E-11	93.4	6.6	0	25	32	0	0	4	61
5805367	C	T	3.99E-11	21.6	78.4	0	25	0	10	31	50	116
6024566	C	T	4.17E-11	90.9	9.1	45	25	0	0	0	7	77
1568211	T	C	4.46E-11	95.0	5.0	0	25	32	0	0	3	60
630668	A	G	4.48E-11	21.6	78.4	0	25	0	10	31	50	116
3667733	C	G	4.95E-11	23.8	76.2	0	25	0	0	31	49	105
4141169	G	A	5.17E-11	95.9	4.1	45	25	0	0	0	3	73
6244967	C	G	5.51E-11	95.9	4.1	45	25	0	0	0	3	73
2194766	C	T	5.85E-11	95.9	4.1	45	25	0	0	0	3	73
3341752	C	T	5.85E-11	95.9	4.1	45	25	0	0	0	3	73
628527	T	C	5.93E-11	95.9	4.1	45	25	0	0	0	3	73
994605	C	T	6.19E-11	37.5	62.5	45	0	0	0	31	44	120
5370414	T	C	6.37E-11	21.6	78.4	0	25	0	10	31	50	116
6128982	A	G	6.86E-11	23.4	76.6	0	25	0	1	31	50	107
5414320	C	T	7.52E-11	97.5	2.5	45	0	32	0	0	2	79
1856717	G	A	7.60E-11	95.9	4.1	45	25	0	0	0	3	73
5733029	G	A	8.02E-11	93.4	6.6	0	25	32	0	0	4	61
5851781	T	C	8.36E-11	23.1	76.9	0	25	0	1	31	51	108
3433939	A	G	8.39E-11	24.0	76.0	0	25	0	0	31	48	104
3830441	T	C	8.45E-11	93.4	6.6	0	25	32	0	0	4	61
1120289	C	T	9.43E-11	97.2	2.8	45	25	0	0	0	2	72
1290123	C	T	1.01E-10	93.3	6.7	45	25	0	0	0	5	75
4886311	G	A	1.01E-10	93.3	6.7	45	25	0	0	0	5	75

547167	GC	AT	1.01E-10	95.9	4.1	45	25	0	0	0	3	73
5424473	A	G	1.03E-10	33.3	66.7	45	0	0	10	31	49	135
5424959	T	C	1.03E-10	33.3	66.7	45	0	0	10	31	49	135
6121134	A	G	1.11E-10	21.6	78.4	0	25	0	9	31	51	116
4971094	A	G	1.20E-10	95.9	4.1	45	25	0	0	0	3	73
2017369	C	T	1.23E-10	34.1	65.9	45	0	0	10	31	46	132
5093677	A	G	1.30E-10	42.5	57.5	45	0	0	10	0	51	106
5151966	A	G	1.30E-10	42.5	57.5	45	0	0	10	0	51	106
3784676	T	C	1.30E-10	64.0	36.0	0	25	32	0	31	1	89
3930866	G	A	1.33E-10	97.5	2.5	45	0	32	0	0	2	79
1810171	C	T	1.37E-10	97.5	2.5	45	0	32	0	0	2	79
5020988	CTGGCG	GTAGCA	1.43E-10	95.9	4.1	45	25	0	0	0	3	73
5080781	T	G	1.48E-10	97.2	2.8	45	25	0	0	0	2	72
5421212	A	G	1.53E-10	21.6	78.4	0	25	0	10	31	50	116
4085248	G	A	1.83E-10	82.6	17.4	0	25	32	9	0	3	69
455835	T	C	2.04E-10	23.6	76.4	0	25	0	0	31	50	106
3040880	C	T	2.09E-10	95.9	4.1	45	25	0	0	0	3	73
3373773	G	A	2.09E-10	95.9	4.1	45	25	0	0	0	3	73
5788992	G	A	2.09E-10	95.9	4.1	45	25	0	0	0	3	73
5951007	A	G	2.09E-10	95.9	4.1	45	25	0	0	0	3	73
2180835	T	C	2.25E-10	21.6	78.4	0	25	0	8	31	52	116
1125346	G	A	2.25E-10	95.9	4.1	45	25	0	0	0	3	73
5074336	C	T	2.38E-10	87.7	12.3	0	25	32	1	0	7	65
6125563	C	T	2.41E-10	90.6	9.4	45	0	32	8	0	0	85
5494853	G	A	2.47E-10	97.5	2.5	45	0	32	0	0	2	79
3017908	C	A	2.52E-10	89.7	10.3	45	25	0	0	0	8	78
1817766	C	T	2.62E-10	95.9	4.1	45	25	0	0	0	3	73
3318453	C	T	2.81E-10	23.8	76.2	0	25	0	0	31	49	105

5120923	G	A	2.98E-10	95.9	4.1	45	25	0	0	0	3	73
6129079	A	G	3.00E-10	21.6	78.4	0	25	0	8	31	52	116
167670	G	A	3.03E-10	46.9	53.1	45	0	0	0	0	51	96
3358187	A	G	3.03E-10	46.9	53.1	45	0	0	0	0	51	96
3789954	T	C	3.03E-10	46.9	53.1	45	0	0	0	0	51	96
3793952	C	T	3.03E-10	46.9	53.1	45	0	0	0	0	51	96
3448887	T	C	3.03E-10	57.6	42.4	0	25	32	10	31	1	99
3762506	C	T	3.05E-10	97.2	2.8	45	25	0	0	0	2	72
4565621	A	G	3.05E-10	97.2	2.8	45	25	0	0	0	2	72
5422198	C	T	3.14E-10	21.9	78.1	0	25	0	10	31	48	114
5229548	C	T	3.55E-10	94.6	5.4	45	25	0	0	0	4	74
3161774	T	C	3.59E-10	26.0	74.0	0	0	32	10	31	50	123
3161768	TCCATGTCG G	T	3.59E-10	97.2	2.8	45	25	0	0	0	2	72
3351572	C	G	3.59E-10	97.2	2.8	45	25	0	0	0	2	72
1074879	CTT	TTC	3.75E-10	95.9	4.1	45	25	0	0	0	3	73
1083986	G	A	3.75E-10	95.9	4.1	45	25	0	0	0	3	73
5085683	A	G	3.75E-10	95.9	4.1	45	25	0	0	0	3	73
5778322	T	C	3.75E-10	95.9	4.1	45	25	0	0	0	3	73
5965829	C	T	3.75E-10	95.9	4.1	45	25	0	0	0	3	73
3252050	G	A	4.01E-10	97.2	2.8	45	25	0	0	0	2	72
3616816	A	C	4.01E-10	97.2	2.8	45	25	0	0	0	2	72
3790554	A	G	4.01E-10	97.2	2.8	45	25	0	0	0	2	72
1928917	G	A	4.48E-10	97.5	2.5	45	0	32	0	0	2	79
5405873	T	C	4.70E-10	21.6	78.4	0	25	0	10	31	50	116
5417348	A	G	4.70E-10	21.6	78.4	0	25	0	10	31	50	116
5894647	C	A	4.72E-10	95.9	4.1	45	25	0	0	0	3	73
1836624	TGGC	CGGT	4.92E-10	97.5	2.5	45	0	32	0	0	2	79
584580	ATT	GTC	5.08E-10	36.3	63.7	45	0	0	0	31	48	124

2993230	C	T	5.23E-10	94.6	5.4	45	25	0	0	0	4	74
1164167	A	G	5.34E-10	93.3	6.7	45	25	0	0	0	5	75
3349414	G	A	5.38E-10	93.3	6.7	45	25	0	0	0	5	75
951575	C	T	5.39E-10	96.6	3.4	0	25	32	0	0	2	59
4468790	C	T	5.52E-10	95.9	4.1	45	25	0	0	0	3	73
5474655	T	C	5.58E-10	21.6	78.4	0	25	0	10	31	50	116
4773665	A	G	5.58E-10	26.2	73.8	0	0	32	10	31	49	122
5893296	C	T	6.21E-10	95.0	5.0	0	25	32	0	0	3	60
2204744	G	A	6.23E-10	95.9	4.1	45	25	0	0	0	3	73
3203968	C	A	6.34E-10	22.1	77.9	0	25	0	10	31	47	113
599581	T	C	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
1230187	T	C	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
1949287	TCAGA	CCAGG	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
1950967	A	G	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
1951165	G	A	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
1951378	G	A	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
2735749	G	A	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
3190189	G	A	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
3763298	T	C	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
4306769	T	C	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
4555539	G	A	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
4555752	GC	AG	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
4555785	AAT	GAG	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
4555793	T	C	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
4555840	C	G	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
4558793	T	C	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
5279235	A	T	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
5813145	T	C	6.41E-10	46.1	53.9	45	25	0	0	31	51	152

5944521	G	A	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
5944989	G	A	6.41E-10	46.1	53.9	45	25	0	0	31	51	152
457539	A	G	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
1155961	A	G	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
1615504	T	C	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
1780257	G	A	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
1808024	A	G	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
1949789	A	G	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
1949876	A	G	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
3296489	A	G	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
3591631	T	C	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
4283865	T	C	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
4614683	A	G	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
4777606	G	A	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
4780282	C	T	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
6230717	G	C	6.41E-10	74.4	25.6	0	0	32	10	0	1	43
502540	G	A	6.52E-10	90.9	9.1	45	25	0	0	0	7	77
5409591	T	C	6.56E-10	96.6	3.4	0	25	32	0	0	2	59
1149089	G	A	6.71E-10	92.1	7.9	45	25	0	0	0	6	76
2492175	C	T	6.71E-10	97.2	2.8	45	25	0	0	0	2	72
2492231	C	G	6.71E-10	97.2	2.8	45	25	0	0	0	2	72
5046771	C	T	7.33E-10	92.1	7.9	45	25	0	0	0	6	76
3310948	GCCC	ACCT	7.48E-10	95.9	4.1	45	25	0	0	0	3	73
5135786	CCCCA	TCCCG	7.92E-10	95.9	4.1	45	25	0	0	0	3	73
626895	T	C	8.23E-10	21.9	78.1	0	25	0	8	31	50	114
3046373	A	G	8.46E-10	95.9	4.1	45	25	0	0	0	3	73
5441384	T	C	8.89E-10	94.6	5.4	45	25	0	0	0	4	74
3555959	G	A	9.07E-10	97.2	2.8	45	25	0	0	0	2	72

3291801	C	T	9.74E-10	91.9	8.1	0	25	32	0	0	5	62
966101	A	T	1.04E-09	21.6	78.4	0	25	0	10	31	50	116
4997610	G	A	1.04E-09	95.9	4.1	45	25	0	1	0	2	73
4997997	G	A	1.04E-09	95.9	4.1	45	25	0	1	0	2	73
4998165	T	C	1.04E-09	95.9	4.1	45	25	0	1	0	2	73
3322499	G	A	1.06E-09	94.6	5.4	45	25	0	0	0	4	74
5467785	C	T	1.07E-09	94.6	5.4	45	25	0	0	0	4	74
5120938	C	T	1.08E-09	84.3	15.7	45	25	0	10	0	3	83
681978	G	A	1.08E-09	86.4	13.6	0	25	32	0	0	9	66
6018707	G	C	1.09E-09	94.6	5.4	45	25	0	0	0	4	74
3118062	G	A	1.11E-09	94.6	5.4	45	25	0	0	0	4	74
5710327	G	C	1.11E-09	95.9	4.1	45	25	0	0	0	3	73
1776615	T	C	1.14E-09	87.5	12.5	45	25	0	9	0	1	80
5658312	A	C	1.20E-09	26.4	73.6	0	0	32	10	31	48	121
1901050	T	C	1.22E-09	81.4	18.6	0	25	32	10	0	3	70
5556251	G	A	1.26E-09	93.3	6.7	45	25	0	0	0	5	75
1392885	T	C	1.28E-09	84.3	15.7	45	25	0	10	0	3	83
3119255	G	A	1.28E-09	95.9	4.1	45	25	0	0	0	3	73
1722566	C	T	1.36E-09	95.9	4.1	45	25	0	0	0	3	73
4290527	A	G	1.38E-09	34.9	65.1	45	0	0	10	31	43	129
1260622	A	G	1.39E-09	26.2	73.8	0	0	32	10	31	49	122
267679	T	C	1.39E-09	28.7	71.3	0	25	0	10	0	52	87
440449	G	T	1.39E-09	28.7	71.3	0	25	0	10	0	52	87
441054	T	C	1.39E-09	28.7	71.3	0	25	0	10	0	52	87
1707741	A	C	1.39E-09	28.7	71.3	0	25	0	10	0	52	87
3032715	A	G	1.39E-09	28.7	71.3	0	25	0	10	0	52	87
3957123	T	C	1.39E-09	28.7	71.3	0	25	0	10	0	52	87
4269210	A	G	1.39E-09	28.7	71.3	0	25	0	10	0	52	87

4369172	A	G	1.39E-09	28.7	71.3	0	25	0	10	0	52	87
6165492	A	C	1.39E-09	28.7	71.3	0	25	0	10	0	52	87
3694579	G	A	1.39E-09	71.3	28.7	45	0	32	0	31	0	108
4379957	G	A	1.39E-09	71.3	28.7	45	0	32	0	31	0	108
4381223	G	A	1.39E-09	71.3	28.7	45	0	32	0	31	0	108
5146805	T	TC	1.39E-09	71.3	28.7	45	0	32	0	31	0	108
5146899	A	G	1.39E-09	71.3	28.7	45	0	32	0	31	0	108
5146976	G	C	1.39E-09	71.3	28.7	45	0	32	0	31	0	108
1260290	G	A	1.39E-09	95.9	4.1	45	25	0	0	0	3	73
4872369	C	T	1.39E-09	95.9	4.1	45	25	0	0	0	3	73
5314788	G	A	1.39E-09	95.9	4.1	45	25	0	0	0	3	73
3319959	C	A	1.42E-09	92.1	7.9	45	25	0	0	0	6	76
5294062	C	T	1.49E-09	78.1	21.9	0	25	32	10	0	6	73
5839417	T	C	1.50E-09	26.2	73.8	0	0	32	10	31	49	122
3203556	G	A	1.51E-09	24.3	75.7	0	25	0	0	31	47	103
4773860	T	C	1.57E-09	94.6	5.4	45	25	0	0	0	4	74
2972033	G	A	1.63E-09	36.3	63.7	45	0	0	0	31	48	124
1017194	A	G	1.63E-09	95.9	4.1	45	25	0	0	0	3	73
1082112	G	A	1.65E-09	84.3	15.7	45	25	0	10	0	3	83
5967673	G	A	1.65E-09	84.3	15.7	45	25	0	10	0	3	83
340876	C	T	1.65E-09	97.2	2.8	45	25	0	2	0	0	72
400062	T	A	1.69E-09	36.3	63.7	45	0	0	0	31	48	124
964226	C	T	1.70E-09	23.6	76.4	0	25	0	0	31	50	106
964286	C	T	1.70E-09	23.6	76.4	0	25	0	0	31	50	106
964302	G	A	1.70E-09	23.6	76.4	0	25	0	0	31	50	106
964307	G	C	1.70E-09	23.6	76.4	0	25	0	0	31	50	106
964446	G	C	1.70E-09	23.6	76.4	0	25	0	0	31	50	106
3299914	G	A	1.71E-09	93.3	6.7	45	25	0	0	0	5	75

3932739	C	T	1.83E-09	89.7	10.3	45	25	0	0	0	8	78
3336296	C	T	1.84E-09	90.5	9.5	0	25	32	6	0	0	63
1266455	G	T	1.93E-09	95.9	4.1	45	25	0	0	0	3	73
587554	A	G	1.97E-09	33.6	66.4	45	0	0	9	31	49	134
5111618	G	A	2.13E-09	89.7	10.3	45	25	0	0	0	8	78
2210926	G	A	2.15E-09	94.6	5.4	45	25	0	0	0	4	74
6028426	T	C	2.20E-09	22.7	77.3	0	25	0	10	31	44	110
112817	C	T	2.30E-09	95.9	4.1	45	25	0	0	0	3	73
1767246	C	T	2.32E-09	90.9	9.1	45	25	0	0	0	7	77
5242434	G	A	2.37E-09	92.1	7.9	45	25	0	0	0	6	76
1629508	G	A	2.39E-09	94.6	5.4	45	25	0	0	0	4	74
2142948	ACCAGGGCGGAGGGGAC	GCCTGGGAAAAAGGG	2.52E-09	94.6	5.4	45	25	0	0	0	4	74
3161863	C	T	2.56E-09	97.2	2.8	45	25	0	0	0	2	72
4566393	G	C	2.56E-09	97.2	2.8	45	25	0	0	0	2	72
5920515	C	T	2.59E-09	96.3	3.8	45	0	32	0	0	3	80
5710589	C	T	2.66E-09	97.2	2.8	45	25	0	0	0	2	72
2608484	CAA	TAG	2.72E-09	95.9	4.1	45	25	0	0	0	3	73
4023001	G	A	3.06E-09	95.9	4.1	45	25	0	0	0	3	73
4328847	T	A	3.06E-09	95.9	4.1	45	25	0	0	0	3	73
2559407	G	A	3.08E-09	93.3	6.7	45	25	0	0	0	5	75
3729942	G	A	3.08E-09	93.3	6.7	45	25	0	0	0	5	75
2765737	G	A	3.17E-09	95.9	4.1	45	25	0	0	0	3	73
682200	C	T	3.18E-09	86.4	13.6	0	25	32	0	0	9	66
5209567	G	A	3.25E-09	85.6	14.4	45	0	32	10	0	3	90
5903328	G	A	3.34E-09	91.9	8.1	0	25	32	0	0	5	62
1038495	C	T	3.43E-09	95.9	4.1	45	25	0	0	0	3	73
4121113	C	T	3.61E-09	96.3	3.8	45	0	32	3	0	0	80

2176765	C	T	3.85E-09	94.6	5.4	45	25	0	0	0	4	74
3504540	G	A	3.98E-09	95.9	4.1	45	25	0	0	0	3	73
1522779	C	T	4.04E-09	89.7	10.3	45	25	0	0	0	8	78
2838642	G	A	4.08E-09	93.4	6.6	0	25	32	0	0	4	61
2975034	G	A	4.12E-09	95.9	4.1	45	25	0	0	0	3	73
1956793	C	T	4.14E-09	97.5	2.5	45	0	32	0	0	2	79
630062	C	T	4.41E-09	94.6	5.4	45	25	0	0	0	4	74
1727213	C	T	4.42E-09	89.7	10.3	45	25	0	0	0	8	78
1838325	C	T	4.58E-09	95.9	4.1	45	25	0	0	0	3	73
3199911	G	A	4.62E-09	93.3	6.7	45	25	0	0	0	5	75
964243	A	G	4.74E-09	23.8	76.2	0	25	0	0	31	49	105
5863298	C	T	4.75E-09	93.3	6.7	45	25	0	0	0	5	75
2115687	C	T	4.76E-09	95.9	4.1	45	25	0	2	0	1	73
1389534	C	T	4.83E-09	95.9	4.1	45	25	0	0	0	3	73
4775234	G	A	4.83E-09	95.9	4.1	45	25	0	0	0	3	73
2210179	C	G	4.90E-09	42.5	57.5	45	0	0	10	0	51	106
1133867	C	T	4.92E-09	87.5	12.5	45	25	0	0	0	10	80
2931645	G	A	5.15E-09	93.3	6.7	45	25	0	0	0	5	75
4543557	C	T	5.30E-09	95.9	4.1	45	25	0	0	0	3	73
1681038	C	T	5.34E-09	93.4	6.6	0	25	32	0	0	4	61
4976338	G	A	5.52E-09	89.7	10.3	45	25	0	0	0	8	78
1271277	G	A	5.55E-09	95.9	4.1	45	25	0	0	0	3	73
6215049	G	A	5.88E-09	87.5	12.5	45	25	0	0	0	10	80
3433819	AC	GT	5.89E-09	24.3	75.7	0	25	0	0	31	47	103
3909041	A	G	6.16E-09	21.7	78.3	0	25	0	9	31	50	115
5019576	T	C	6.21E-09	92.1	7.9	45	25	0	0	0	6	76
5019590	G	A	6.21E-09	92.1	7.9	45	25	0	0	0	6	76
2756252	GTC	G	6.23E-09	95.9	4.1	45	25	0	0	0	3	73

841417	C	T	6.24E-09	93.9	6.1	45	0	32	0	0	5	82
5789268	G	A	6.38E-09	92.1	7.9	45	25	0	0	0	6	76
1725201	C	T	6.50E-09	89.7	10.3	45	25	0	0	0	8	78
6028372	C	A	6.55E-09	25.0	75.0	0	25	0	0	31	44	100
652022	G	A	6.61E-09	85.1	14.9	0	25	32	0	0	10	67
5969160	T	C	7.05E-09	28.1	71.9	0	0	32	10	31	41	114
4827242	G	A	7.08E-09	94.6	5.4	45	25	0	0	0	4	74
503796	C	T	7.88E-09	95.9	4.1	45	25	0	0	0	3	73
5202931	A	G	7.94E-09	43.8	56.3	45	25	0	10	31	49	160
1881914	CCCC	TCCT	7.94E-09	91.4	8.6	0	0	32	0	0	3	35
2569169	G	A	7.94E-09	91.4	8.6	0	0	32	0	0	3	35
4204038	C	T	7.94E-09	91.4	8.6	0	0	32	0	0	3	35
4275416	T	C	7.94E-09	91.4	8.6	0	0	32	0	0	3	35
5826551	C	T	8.38E-09	93.9	6.1	45	0	32	0	0	5	82
5543831	ACGTCCA	GCGCCCG	8.45E-09	26.2	73.8	0	0	32	10	31	49	122
5888000	G	A	8.51E-09	95.9	4.1	45	25	0	0	0	3	73
5858485	G	A	8.58E-09	91.9	8.1	0	25	32	0	0	5	62
1761348	C	G	8.82E-09	84.3	15.7	45	25	0	10	0	3	83
5437410	A	G	8.82E-09	93.3	6.7	45	25	0	0	0	5	75
2937003	C	G	8.91E-09	95.9	4.1	45	25	0	0	0	3	73
2939917	T	C	8.91E-09	95.9	4.1	45	25	0	0	0	3	73
5787956	G	A	8.91E-09	95.9	4.1	45	25	0	0	0	3	73
5244059	G	A	9.43E-09	93.3	6.7	45	25	0	0	0	5	75
5244092	C	T	9.43E-09	93.3	6.7	45	25	0	0	0	5	75
467579	C	T	9.62E-09	97.5	2.5	45	1	32	0	0	2	80
5440025	T	C	9.63E-09	96.3	3.8	45	0	32	0	0	3	80
3681025	G	A	9.79E-09	89.7	10.3	45	25	0	0	0	8	78
3729927	G	A	1.02E-08	82.4	17.6	45	25	0	10	0	5	85

4282315	A	G	1.06E-08	26.7	73.3	0	0	32	10	31	47	120
3705242	C	T	1.06E-08	87.5	12.5	45	25	0	0	0	10	80
1957264	G	A	1.06E-08	97.5	2.5	45	0	32	0	0	2	79
5425148	A	G	1.08E-08	33.6	66.4	45	0	0	10	31	48	134
3758385	C	A	1.12E-08	32.5	67.5	0	25	0	0	0	52	77
3956601	C	T	1.12E-08	32.5	67.5	0	25	0	0	0	52	77
6216709	A	G	1.12E-08	32.5	67.5	0	25	0	0	0	52	77
3862488	C	T	1.13E-08	97.5	2.5	45	0	32	0	0	2	79
3433959	G	A	1.14E-08	24.3	75.7	0	25	0	0	31	47	103
4107991	G	C	1.14E-08	93.3	6.7	45	25	0	0	0	5	75
964193	A	G	1.15E-08	22.6	77.4	0	24	0	0	31	51	106
3605651	G	A	1.15E-08	42.5	57.5	45	0	0	10	0	51	106
4124342	A	G	1.15E-08	42.5	57.5	45	0	0	10	0	51	106
4212223	G	A	1.15E-08	42.5	57.5	45	0	0	10	0	51	106
4212310	C	T	1.15E-08	64.0	36.0	0	25	32	0	31	1	89
3415819	A	G	1.15E-08	88.6	11.4	45	25	0	0	0	9	79
2984343	C	T	1.17E-08	95.9	4.1	45	25	0	0	0	3	73
2492744	G	A	1.19E-08	94.6	5.4	45	25	0	0	0	4	74
4314015	G	A	1.21E-08	95.9	4.1	45	25	0	0	0	3	73
4316825	T	A	1.21E-08	95.9	4.1	45	25	0	0	0	3	73
1146321	T	C	1.22E-08	93.3	6.7	45	25	0	0	0	5	75
1039160	C	T	1.23E-08	83.3	16.7	45	25	0	10	0	4	84
5769720	C	T	1.25E-08	94.6	5.4	45	25	0	0	0	4	74
357283	C	T	1.27E-08	92.1	7.9	45	25	0	0	0	6	76
2017050	G	A	1.29E-08	46.1	53.9	45	25	0	0	31	51	152
2019330	C	T	1.29E-08	46.1	53.9	45	25	0	0	31	51	152
2546895	A	G	1.29E-08	46.1	53.9	45	25	0	0	31	51	152
2967760	A	G	1.29E-08	46.1	53.9	45	25	0	0	31	51	152

3190576	C	T	1.29E-08	46.1	53.9	45	25	0	0	31	51	152
3193737	C	T	1.29E-08	46.1	53.9	45	25	0	0	31	51	152
4410225	G	A	1.29E-08	46.1	53.9	45	25	0	0	31	51	152
5135776	T	C	1.29E-08	46.1	53.9	45	25	0	0	31	51	152
1615174	G	A	1.29E-08	74.4	25.6	0	0	32	10	0	1	43
5301918	C	T	1.29E-08	74.4	25.6	0	0	32	10	0	1	43
5890920	C	T	1.41E-08	95.9	4.1	45	25	0	0	0	3	73
4751470	C	T	1.45E-08	89.7	10.3	45	25	0	0	0	8	78
4424020	T	C	1.46E-08	94.6	5.4	45	25	0	0	0	4	74
13761	G	T	1.47E-08	94.6	5.4	45	25	0	0	0	4	74
5646318	C	A	1.52E-08	94.6	5.4	45	25	0	0	0	4	74
275301	T	A	1.52E-08	95.9	4.1	45	25	0	0	0	3	73
1132184	G	A	1.52E-08	95.9	4.1	45	25	0	0	0	3	73
41006	CC	AT	1.53E-08	89.7	10.3	45	25	0	0	0	8	78
3725317	C	T	1.55E-08	91.9	8.1	0	25	32	0	0	5	62
2928240	C	T	1.60E-08	94.6	5.4	45	25	0	0	0	4	74
812168	C	T	1.64E-08	94.1	5.9	0	0	32	0	0	2	34
3873395	G	A	1.64E-08	94.1	5.9	0	0	32	0	0	2	34
3936049	G	A	1.64E-08	94.1	5.9	0	0	32	0	0	2	34
5876	C	A	1.65E-08	89.1	10.9	0	25	32	0	0	7	64
3202527	G	A	1.70E-08	96.3	3.8	45	0	32	0	0	3	80
1075992	C	G	1.72E-08	25.3	74.7	0	25	0	0	31	43	99
4721803	C	T	1.73E-08	90.5	9.5	0	25	32	0	0	6	63
4375006	G	A	1.73E-08	95.9	4.1	45	25	0	0	0	3	73
5123269	G	A	1.74E-08	94.6	5.4	45	25	0	0	0	4	74
1579309	C	T	1.74E-08	95.9	4.1	45	25	0	0	0	3	73
3474237	G	A	1.84E-08	95.9	4.1	45	25	0	0	0	3	73
3746336	T	C	1.87E-08	46.9	53.1	45	0	0	0	0	51	96

2753059	GT	AC	1.91E-08	93.9	6.1	45	0	32	0	0	5	82
4423824	G	A	1.96E-08	94.6	5.4	45	25	0	0	0	4	74
1075386	C	T	2.03E-08	95.9	4.1	45	25	0	0	0	3	73
1075434	C	T	2.03E-08	95.9	4.1	45	25	0	0	0	3	73
5842394	G	A	2.03E-08	95.9	4.1	45	25	0	0	0	3	73
1034977	A	G	2.05E-08	40.7	59.3	0	25	32	0	31	52	140
408288	A	G	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
447703	C	T	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
489660	C	T	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
823007	T	C	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
833579	C	T	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
1024564	C	T	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
1165053	T	C	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
1264412	C	T	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
1284680	C	T	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
1596703	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
1633065	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
1685661	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
1960894	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
3343567	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
3403367	G	GT	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
4394633	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
4487758	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
4822486	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
4926900	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
5083126	C	T	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
5105211	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
5152191	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55

5532470	C	T	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
5605827	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
5676779	A	G	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
5912506	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
6180201	G	A	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
6181614	C	T	2.05E-08	81.8	18.2	45	0	0	10	0	0	55
563308	C	T	2.09E-08	94.6	5.4	45	25	0	0	0	4	74
3443441	C	A	2.10E-08	95.9	4.1	45	25	0	0	0	3	73
2236720	A	G	2.13E-08	42.5	57.5	45	0	0	10	0	51	106
5194080	G	A	2.18E-08	95.9	4.1	45	25	0	0	0	3	73
5194152	A	T	2.18E-08	95.9	4.1	45	25	0	0	0	3	73
5194470	CT	TC	2.18E-08	95.9	4.1	45	25	0	0	0	3	73
5284490	C	A	2.18E-08	95.9	4.1	45	25	0	0	0	3	73
5568195	C	T	2.23E-08	80.5	19.5	45	25	0	10	0	7	87
3617793	G	A	2.24E-08	95.9	4.1	45	25	0	0	0	3	73
5794016	G	A	2.25E-08	80.3	19.7	0	25	32	10	0	4	71
1038174	G	A	2.26E-08	94.6	5.4	45	25	0	0	0	4	74
5942632	C	T	2.26E-08	94.6	5.4	45	25	0	0	0	4	74
4616377	C	T	2.29E-08	84.3	15.7	45	25	0	10	0	3	83
3153710	C	T	2.31E-08	24.3	75.7	0	25	0	0	31	47	103
1075050	A	C	2.31E-08	89.7	10.3	45	25	0	0	0	8	78
5133582	C	T	2.31E-08	89.7	10.3	45	25	0	0	0	8	78
6024796	G	A	2.31E-08	89.7	10.3	45	25	0	0	0	8	78
3583080	T	G	2.42E-08	43.5	56.5	45	25	0	10	31	50	161
6001771	T	C	2.42E-08	43.5	56.5	45	25	0	10	31	50	161
508441	C	T	2.42E-08	94.1	5.9	0	0	32	0	0	2	34
3689310	G	A	2.42E-08	94.1	5.9	0	0	32	0	0	2	34
3965486	C	T	2.42E-08	94.1	5.9	0	0	32	0	0	2	34

4476788	A	C	2.42E-08	94.1	5.9	0	0	32	0	0	2	34
4485625	C	G	2.42E-08	94.1	5.9	0	0	32	0	0	2	34
6143241	G	A	2.42E-08	94.1	5.9	0	0	32	0	0	2	34
1454735	C	T	2.48E-08	94.6	5.4	45	25	0	0	0	4	74
3185948	GACC	AACT	2.60E-08	93.3	6.7	45	25	0	0	0	5	75
3149155	G	C	2.69E-08	23.6	76.4	0	25	0	0	31	50	106
1148873	C	T	2.95E-08	90.9	9.1	45	25	0	0	0	7	77
4931729	C	CCGG	3.03E-08	24.3	75.7	0	25	0	0	31	47	103
1517662	G	A	3.22E-08	94.6	5.4	45	25	0	0	0	4	74
4963708	A	G	3.35E-08	43.5	56.5	45	25	0	10	31	50	161
175712	G	A	3.35E-08	94.1	5.9	0	0	32	0	0	2	34
677552	G	A	3.35E-08	94.1	5.9	0	0	32	0	0	2	34
683518	C	T	3.35E-08	94.1	5.9	0	0	32	0	0	2	34
4766408	G	A	3.35E-08	94.1	5.9	0	0	32	0	0	2	34
1077062	A	T	3.63E-08	94.6	5.4	45	25	0	0	0	4	74
3712120	G	A	3.65E-08	93.3	6.7	45	25	0	0	0	5	75
5568303	G	A	3.68E-08	93.3	6.7	45	25	0	0	0	5	75
189770	T	C	3.92E-08	42.9	57.1	45	0	0	10	0	50	105
589991	C	T	3.95E-08	35.2	64.8	45	0	0	10	31	42	128
1072898	A	C	4.03E-08	95.9	4.1	45	25	0	0	0	3	73
1072942	C	T	4.03E-08	95.9	4.1	45	25	0	0	0	3	73
1073009	CCTTTCT	TCTTCC	4.03E-08	95.9	4.1	45	25	0	0	0	3	73
1073079	A	G	4.03E-08	95.9	4.1	45	25	0	0	0	3	73
2984157	C	T	4.03E-08	95.9	4.1	45	25	0	0	0	3	73
3142499	A	G	4.03E-08	95.9	4.1	45	25	0	0	0	3	73
3142612	C	T	4.03E-08	95.9	4.1	45	25	0	0	0	3	73
4290013	T	C	4.14E-08	22.1	77.9	0	25	0	10	31	47	113
4290043	G	T	4.14E-08	93.9	6.1	45	0	32	0	0	5	82

6216784	A	G	4.26E-08	43.8	56.3	45	25	0	10	31	49	160
3605642	G	A	4.26E-08	46.9	53.1	45	0	0	0	0	51	96
3608489	A	G	4.26E-08	46.9	53.1	45	0	0	0	0	51	96
4942056	G	A	4.26E-08	46.9	53.1	45	0	0	0	0	51	96
3601167	G	A	4.26E-08	91.4	8.6	0	0	32	0	0	3	35
3601320	C	T	4.26E-08	91.4	8.6	0	0	32	0	0	3	35
5924943	C	T	4.26E-08	91.4	8.6	0	0	32	0	0	3	35
5995719	A	G	4.38E-08	21.7	78.3	0	25	0	10	31	49	115
967222	T	C	4.58E-08	21.7	78.3	0	25	0	10	31	49	115
3183420	T	C	4.61E-08	46.1	53.9	45	25	0	0	31	51	152
3287399	T	C	4.61E-08	46.1	53.9	45	25	0	0	31	51	152
3293671	A	G	4.61E-08	46.1	53.9	45	25	0	0	31	51	152
3480177	T	C	4.61E-08	46.1	53.9	45	25	0	0	31	51	152
4194262	T	C	4.61E-08	46.1	53.9	45	25	0	0	31	51	152
5559555	G	A	4.61E-08	46.1	53.9	45	25	0	0	31	51	152
1899379	A	G	4.61E-08	28.6	71.4	0	0	32	0	31	49	112
3310948	G	A	4.61E-08	74.4	25.6	0	0	32	10	0	1	43
4603014	G	A	4.61E-08	74.4	25.6	0	0	32	10	0	1	43
4603162	G	A	4.61E-08	74.4	25.6	0	0	32	10	0	1	43
40982	A	G	4.75E-08	29.9	70.1	0	0	32	0	31	44	107
5421922	T	C	4.80E-08	23.8	76.2	0	25	0	0	31	49	105
3153064	G	A	4.82E-08	29.4	70.6	0	0	32	0	31	46	109
522890	C	T	4.85E-08	89.7	10.3	45	25	0	0	0	8	78
3189422	A	G	5.02E-08	22.3	77.7	0	25	0	10	31	46	112
1837495	A	G	5.14E-08	86.4	13.6	0	25	32	0	0	9	66
1031836	C	T	5.18E-08	94.6	5.4	45	25	0	0	0	4	74
6210919	G	A	5.22E-08	91.9	8.1	0	25	32	0	0	5	62
4448092	A	G	5.27E-08	46.1	53.9	45	25	0	0	31	51	152

3366968	G	A	5.29E-08	97.5	2.5	45	0	32	0	0	2	79
3751517	G	A	5.29E-08	97.5	2.5	45	0	32	0	0	2	79
3639148	T	C	5.33E-08	43.5	56.5	45	25	0	10	31	50	161
5706990	T	C	5.33E-08	43.5	56.5	45	25	0	10	31	50	161
4041405	G	T	5.33E-08	94.1	5.9	0	0	32	0	0	2	34
5972229	G	A	5.33E-08	94.1	5.9	0	0	32	0	0	2	34
5319798	GGC	AGT	5.48E-08	94.6	5.4	45	25	0	0	0	4	74
3856157	G	A	5.50E-08	93.3	6.7	45	25	0	0	0	5	75
314526	G	T	5.57E-08	93.4	6.6	0	25	32	0	0	4	61
4026170	T	C	5.62E-08	43.5	56.5	45	25	0	10	31	50	161
1851986	G	A	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
2032937	C	T	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
2106921	C	T	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
2107065	G	A	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
2128559	C	T	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
5270927	G	A	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
6061784	C	T	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
6122441	C	T	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
6122498	G	A	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
6126120	G	A	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
6176406	G	A	5.62E-08	94.1	5.9	0	0	32	0	0	2	34
246647	T	C	5.73E-08	93.3	6.7	45	25	0	0	0	5	75
1151701	C	T	5.93E-08	94.6	5.4	45	25	0	0	0	4	74
5891008	G	A	5.98E-08	94.6	5.4	45	25	0	0	0	4	74
545751	A	G	5.99E-08	26.4	73.6	0	0	32	10	31	48	121
3782616	C	T	6.01E-08	64.0	36.0	0	25	32	0	31	1	89
565474	T	C	6.01E-08	83.3	16.7	45	25	0	10	0	4	84
994493	A	G	6.07E-08	21.1	78.9	0	24	0	10	31	49	114

3372332	G	A	6.22E-08	94.6	5.4	45	25	0	0	0	4	74
588874	A	G	6.29E-08	79.2	20.8	0	25	32	10	0	5	72
2022099	A	G	6.48E-08	43.5	56.5	45	25	0	10	31	50	161
4484416	A	G	6.48E-08	43.5	56.5	45	25	0	10	31	50	161
6001172	A	C	6.48E-08	43.5	56.5	45	25	0	10	31	50	161
368822	C	T	6.48E-08	94.1	5.9	0	0	32	0	0	2	34
1629602	G	A	6.48E-08	94.1	5.9	0	0	32	0	0	2	34
1708364	G	A	6.48E-08	94.1	5.9	0	0	32	0	0	2	34
2853706	G	A	6.48E-08	94.1	5.9	0	0	32	0	0	2	34
3284301	C	T	6.48E-08	94.1	5.9	0	0	32	0	0	2	34
3412405	G	A	6.48E-08	94.1	5.9	0	0	32	0	0	2	34
3819516	G	A	6.48E-08	94.1	5.9	0	0	32	0	0	2	34
3819953	T	G	6.48E-08	94.1	5.9	0	0	32	0	0	2	34
4481027	C	T	6.48E-08	94.1	5.9	0	0	32	0	0	2	34
4086022	G	A	6.52E-08	85.1	14.9	0	25	32	0	0	10	67
5045987	A	G	6.66E-08	22.1	77.9	0	25	0	10	31	47	113
3198463	T	C	6.68E-08	94.6	5.4	45	25	0	0	0	4	74
683730	G	A	6.73E-08	87.7	12.3	0	25	32	0	0	8	65
198677	A	G	6.87E-08	69.4	30.6	0	25	0	10	0	1	36
207130	C	T	6.87E-08	69.4	30.6	0	25	0	10	0	1	36
1155428	T	C	6.87E-08	69.4	30.6	0	25	0	10	0	1	36
1155448	A	G	6.87E-08	69.4	30.6	0	25	0	10	0	1	36
1826110	C	G	6.87E-08	69.4	30.6	0	25	0	10	0	1	36
2207340	T	C	6.87E-08	69.4	30.6	0	25	0	10	0	1	36
3149362	T	C	6.87E-08	69.4	30.6	0	25	0	10	0	1	36
4931084	A	G	6.87E-08	69.4	30.6	0	25	0	10	0	1	36
5136106	T	C	6.87E-08	69.4	30.6	0	25	0	10	0	1	36
1075098	T	C	7.16E-08	29.9	70.1	0	0	32	0	31	44	107

2932299	C	T	7.17E-08	92.1	7.9	45	25	0	0	0	6	76
4778707	C	T	7.18E-08	92.1	7.9	45	25	0	0	0	6	76
3507269	G	A	7.33E-08	91.4	8.6	0	0	32	0	0	3	35
5502353	G	A	7.33E-08	91.4	8.6	0	0	32	0	0	3	35
4360496	TTCT	CTCG	7.40E-08	73.1	26.9	0	25	32	10	0	11	78
2242793	A	G	7.54E-08	46.1	53.9	45	25	0	0	31	51	152
5889761	A	C	7.54E-08	46.1	53.9	45	25	0	0	31	51	152
5896485	T	C	7.54E-08	46.1	53.9	45	25	0	0	31	51	152
5910235	G	T	7.54E-08	46.1	53.9	45	25	0	0	31	51	152
5862870	C	G	7.54E-08	74.4	25.6	0	0	32	10	0	1	43
196398	G	C	7.62E-08	36.9	63.1	45	0	0	0	31	46	122
4866422	C	T	7.69E-08	94.6	5.4	45	25	0	0	0	4	74
1884425	G	A	7.76E-08	26.7	73.3	0	0	32	10	31	47	120
612261	T	C	7.82E-08	42.5	57.5	45	0	0	10	0	51	106
3159170	G	A	7.82E-08	64.0	36.0	0	25	32	0	31	1	89
1134615	G	A	7.93E-08	92.1	7.9	45	25	0	0	0	6	76
2206397	G	T	8.08E-08	90.9	9.1	45	25	0	0	0	7	77
964377	A	G	8.14E-08	22.9	77.1	0	25	0	2	31	51	109
2747293	T	G	8.18E-08	28.6	71.4	0	0	32	0	31	49	112
4811605	C	T	8.31E-08	94.6	5.4	45	25	0	0	0	4	74
981370	G	A	8.34E-08	95.9	4.1	45	25	0	0	0	3	73
3666488	T	C	8.44E-08	42.9	57.1	45	0	0	10	0	50	105
6169220	T	C	8.44E-08	42.9	57.1	45	0	0	10	0	50	105
1867285	G	C	8.44E-08	84.3	15.7	45	25	0	10	0	3	83
6001136	T	C	8.45E-08	95.9	4.1	45	25	0	0	0	3	73
622174	CC	AA	8.76E-08	87.7	12.3	0	25	32	4	0	4	65
5757771	G	A	8.85E-08	97.2	2.8	45	25	0	0	0	2	72
1725740	TGCC	CGCT	8.93E-08	89.3	10.7	0	25	0	0	0	3	28

1882558	A	CTT	8.93E-08	89.3	10.7	0	25	0	0	0	3	28
2234550	C	T	8.93E-08	89.3	10.7	0	25	0	0	0	3	28
2825873	T	C	8.93E-08	89.3	10.7	0	25	0	0	0	3	28
3079180	C	T	8.93E-08	89.3	10.7	0	25	0	0	0	3	28
5882912	G	A	8.93E-08	89.3	10.7	0	25	0	0	0	3	28
6134671	G	A	8.93E-08	89.3	10.7	0	25	0	0	0	3	28
6206115	C	T	8.93E-08	89.3	10.7	0	25	0	0	0	3	28
2517203	C	T	9.26E-08	97.2	2.8	45	25	0	0	0	2	72
3653004	G	A	9.40E-08	94.6	5.4	45	25	0	0	0	4	74
5006295	C	T	9.61E-08	92.1	7.9	45	25	0	0	0	6	76
2720154	A	G	9.88E-08	90.9	9.1	45	25	0	0	0	7	77
4985858	A	G	9.88E-08	94.6	5.4	45	25	0	0	0	4	74
4985916	C	G	9.88E-08	94.6	5.4	45	25	0	0	0	4	74
2154646	C	T	9.89E-08	93.4	6.6	0	25	32	0	0	4	61
5183580	A	G	1.00E-07	46.4	53.6	45	25	0	0	31	50	151
1817400	C	T	1.00E-07	23.1	76.9	0	24	0	0	31	49	104
5202856	A	C	1.05E-07	22.1	77.9	0	25	0	10	31	47	113
5571591	G	A	1.07E-07	97.2	2.8	45	25	0	0	0	2	72
3433819	A	G	1.10E-07	85.6	14.4	45	0	32	9	0	4	90
5768470	T	G	1.11E-07	74.4	25.6	0	0	32	10	0	1	43
4683064	C	A	1.11E-07	93.3	6.7	45	25	0	0	0	5	75
4350352	C	T	1.12E-07	95.9	4.1	45	25	0	0	0	3	73
5850194	A	C	1.13E-07	21.9	78.1	0	25	0	10	31	48	114
938	C	T	1.16E-07	89.5	10.5	45	0	32	0	0	9	86
2133061	G	A	1.16E-07	90.9	9.1	45	25	0	0	0	7	77
5106244	G	A	1.21E-07	46.9	53.1	45	0	0	0	0	51	96
5719481	C	G	1.21E-07	94.6	5.4	45	25	0	0	0	4	74
189887	T	C	1.22E-07	47.4	52.6	45	0	0	0	0	50	95

4895377	T	C	1.22E-07	94.6	5.4	45	25	0	0	0	4	74
1950748	T	G	1.26E-07	46.7	53.3	45	25	0	0	31	49	150
1960411	A	G	1.28E-07	26.9	73.1	0	0	32	10	31	46	119
4021529	C	T	1.29E-07	72.7	27.3	0	0	32	10	0	2	44
4487732	C	T	1.29E-07	72.7	27.3	0	0	32	10	0	2	44
4591753	A	G	1.33E-07	93.3	6.7	45	25	0	0	0	5	75
1406339	AG	GA	1.38E-07	46.1	53.9	45	25	0	0	31	51	152
2003327	G	A	1.38E-07	46.1	53.9	45	25	0	0	31	51	152
989907	C	T	1.38E-07	74.4	25.6	0	0	32	10	0	1	43
1157581	C	G	1.43E-07	74.4	25.6	0	0	32	10	0	1	43
1374214	C	A	1.43E-07	88.6	11.4	45	25	0	0	0	9	79
740175	G	A	1.45E-07	92.6	7.4	0	25	0	0	0	2	27
740445	C	T	1.45E-07	92.6	7.4	0	25	0	0	0	2	27
741001	C	T	1.45E-07	92.6	7.4	0	25	0	0	0	2	27
1749094	C	T	1.45E-07	92.6	7.4	0	25	0	0	0	2	27
3241064	C	A	1.45E-07	92.6	7.4	0	25	0	0	0	2	27
3339117	T	C	1.45E-07	92.6	7.4	0	25	0	0	0	2	27
4627946	C	T	1.45E-07	92.6	7.4	0	25	0	0	0	2	27
5096196	C	T	1.45E-07	92.6	7.4	0	25	0	0	0	2	27
3725404	A	C	1.47E-07	90.5	9.5	0	25	32	0	0	6	63
5942095	G	A	1.50E-07	93.3	6.7	45	25	0	0	0	5	75
5942326	C	T	1.50E-07	93.3	6.7	45	25	0	0	0	5	75
3444754	T	C	1.50E-07	95.1	4.9	45	0	32	0	0	4	81
6205992	G	A	1.50E-07	96.3	3.8	45	0	32	0	0	3	80
6234389	A	G	1.51E-07	36.3	63.7	45	0	0	0	31	48	124
2142335	C	T	1.54E-07	92.1	7.9	45	25	0	0	0	6	76
553496	C	T	1.56E-07	93.3	6.7	45	25	0	0	0	5	75
1786531	C	T	1.56E-07	94.6	5.4	45	25	0	0	0	4	74

4210188	T	C	1.70E-07	72.7	27.3	0	0	32	10	0	2	44
3291522	G	C	1.71E-07	90.9	9.1	45	25	0	0	0	7	77
1778026	G	C	1.72E-07	76.0	24.0	0	25	32	10	0	8	75
1157221	C	T	1.77E-07	74.4	25.6	0	0	32	10	0	1	43
5749544	A	G	1.77E-07	74.4	25.6	0	0	32	10	0	1	43
1767598	C	T	1.79E-07	86.4	13.6	45	25	0	0	0	11	81
3710037	G	A	1.79E-07	92.1	7.9	45	25	0	0	0	6	76
3121900	C	G	1.84E-07	90.9	9.1	45	25	0	0	0	7	77
2025696	G	A	1.87E-07	94.1	5.9	0	0	32	0	0	2	34
2869150	G	A	1.87E-07	94.1	5.9	0	0	32	0	0	2	34
3232758	G	A	1.87E-07	94.1	5.9	0	0	32	0	0	2	34
6029062	T	C	1.89E-07	22.9	77.1	0	25	0	10	31	43	109
4988933	GC	G	1.92E-07	94.6	5.4	45	25	0	0	0	4	74
1391862	T	C	1.93E-07	23.8	76.2	0	25	0	0	31	49	105
1396342	G	A	1.93E-07	72.2	27.8	0	25	32	10	0	12	79
5809645	G	A	1.95E-07	94.6	5.4	45	25	0	0	0	4	74
5333666	T	C	2.04E-07	79.2	20.8	0	25	32	10	0	5	72
853844	C	T	2.04E-07	87.5	12.5	45	25	0	0	0	10	80
1858569	C	T	2.05E-07	46.1	53.9	45	25	0	0	31	51	152
260926	C	T	2.08E-07	94.6	5.4	45	25	0	0	0	4	74
1613687	G	C	2.10E-07	94.6	5.4	45	25	0	0	0	4	74
1639629	T	C	2.11E-07	89.3	10.7	0	25	0	0	0	3	28
1640235	T	G	2.11E-07	89.3	10.7	0	25	0	0	0	3	28
1640262	A	C	2.11E-07	89.3	10.7	0	25	0	0	0	3	28
1640941	C	G	2.11E-07	89.3	10.7	0	25	0	0	0	3	28
1640946	C	T	2.11E-07	89.3	10.7	0	25	0	0	0	3	28
2885187	G	A	2.11E-07	89.3	10.7	0	25	0	0	0	3	28
4202888	G	A	2.11E-07	89.3	10.7	0	25	0	0	0	3	28

5019310	C	A	2.11E-07	89.3	10.7	0	25	0	0	0	3	28
5113472	G	A	2.11E-07	89.3	10.7	0	25	0	0	0	3	28
5162249	G	A	2.11E-07	89.3	10.7	0	25	0	0	0	3	28
3419031	C	T	2.11E-07	97.2	2.8	45	25	0	0	0	2	72
6028489	T	G	2.12E-07	23.1	76.9	0	25	0	10	31	42	108
6237341	G	A	2.12E-07	90.9	9.1	45	25	0	0	0	7	77
3118819	G	A	2.13E-07	95.9	4.1	45	25	0	0	0	3	73
565636	C	T	2.14E-07	92.6	7.4	0	25	0	0	0	2	27
2791936	G	A	2.14E-07	92.6	7.4	0	25	0	0	0	2	27
3186450	TGCCAGCG	CTAAAGGA	2.14E-07	92.6	7.4	0	25	0	0	0	2	27
3751632	G	A	2.14E-07	92.6	7.4	0	25	0	0	0	2	27
3752031	C	T	2.14E-07	92.6	7.4	0	25	0	0	0	2	27
5662956	ACCTC	GCCTG	2.14E-07	92.6	7.4	0	25	0	0	0	2	27
5882786	A	C	2.15E-07	22.1	77.9	0	25	0	10	31	47	113
5353634	G	A	2.22E-07	93.3	6.7	45	25	0	0	0	5	75
2017750	GACA	AACG	2.27E-07	46.7	53.3	45	25	0	0	31	49	150
2033645	T	C	2.27E-07	46.7	53.3	45	25	0	0	31	49	150
1722485	C	T	2.30E-07	88.6	11.4	45	25	0	0	0	9	79
4591718	C	T	2.31E-07	95.9	4.1	45	25	0	0	0	3	73
4186763	C	T	2.41E-07	95.9	4.1	45	25	0	2	0	1	73
3585379	G	A	2.48E-07	94.6	5.4	45	25	0	0	0	4	74
4386856	ACAA	GCAG	2.64E-07	24.3	75.7	0	25	0	0	31	47	103
1857038	T	G	2.65E-07	46.4	53.6	45	25	0	0	31	50	151
3591684	G	A	2.65E-07	72.7	27.3	0	0	32	10	0	2	44
1622660	T	C	2.71E-07	45.5	54.5	45	25	0	1	31	52	154
645152	G	A	2.71E-07	78.0	22.0	0	0	32	9	0	0	41
1870062	G	C	2.71E-07	78.0	22.0	0	0	32	9	0	0	41
346765	A	G	2.78E-07	92.6	7.4	0	25	0	0	0	2	27

369635	G	A	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
677537	C	G	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
678062	T	C	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
742356	G	A	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
742878	G	A	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
1505507	G	A	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
4333618	ACGTG	GCGTA	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
4629132	G	A	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
4737582	ACG	GCA	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
5070843	C	T	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
5175015	CC	TT	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
5435316	A	G	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
5983852	C	A	2.78E-07	92.6	7.4	0	25	0	0	0	2	27
3303390	GCGC	ACGT	2.79E-07	93.3	6.7	45	25	0	0	0	5	75
3578999	CAGG	TAGA	2.79E-07	93.3	6.7	45	25	0	0	0	5	75
3581769	G	A	2.79E-07	93.3	6.7	45	25	0	0	0	5	75
3684901	T	C	2.79E-07	93.3	6.7	45	25	0	0	0	5	75
1696061	T	C	2.80E-07	94.6	5.4	45	25	0	0	0	4	74
5119778	G	A	2.84E-07	46.4	53.6	45	25	0	0	31	50	151
5967972	G	A	2.93E-07	94.6	5.4	45	25	0	0	0	4	74
1715898	C	T	2.96E-07	93.3	6.7	45	25	0	0	0	5	75
1768488	G	A	2.99E-07	46.4	53.6	45	25	0	0	31	50	151
368729	T	C	2.99E-07	72.7	27.3	0	0	32	10	0	2	44
630243	GT	G	3.00E-07	95.1	4.9	45	1	32	0	0	4	82
1133830	C	T	3.08E-07	85.4	14.6	45	25	0	0	0	12	82
2197504	C	T	3.08E-07	89.3	10.7	0	25	0	0	0	3	28
2220723	C	T	3.08E-07	89.3	10.7	0	25	0	0	0	3	28
3416418	G	A	3.08E-07	89.3	10.7	0	25	0	0	0	3	28

4185738	CGCA	TGCG	3.08E-07	89.3	10.7	0	25	0	0	0	3	28
5216898	GCCG	ACCA	3.08E-07	89.3	10.7	0	25	0	0	0	3	28
5663326	G	A	3.08E-07	89.3	10.7	0	25	0	0	0	3	28
5571693	C	T	3.13E-07	90.9	9.1	45	25	0	0	0	7	77
5048698	A	G	3.23E-07	46.1	53.9	45	25	0	0	31	51	152
2975232	C	T	3.23E-07	74.4	25.6	0	0	32	10	0	1	43
1128907	G	A	3.23E-07	90.9	9.1	45	25	0	0	0	7	77
1129286	G	A	3.23E-07	90.9	9.1	45	25	0	0	0	7	77
2509558	A	G	3.23E-07	93.3	6.7	45	25	0	0	0	5	75
1261352	C	T	3.26E-07	88.6	11.4	45	25	0	0	0	9	79
5965752	C	T	3.28E-07	93.3	6.7	45	25	0	0	0	5	75
6051207	T	A	3.28E-07	93.3	6.7	45	25	0	0	0	5	75
943089	G	C	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073413	T	A	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073695	C	T	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073738	A	G	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073743	T	A	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073757	ATAC	GGGT	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073780	AAT	CAA	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073792	GTC	CTT	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073830	C	A	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073861	A	G	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073881	G	C	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073938	T	C	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073950	C	T	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1073957	A	G	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1074180	T	C	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1074196	C	A	3.29E-07	94.6	5.4	45	25	0	0	0	4	74

1074430	C	T	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1074640	A	C	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1074707	A	G	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1074745	G	T	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1074811	TTCG	CTCA	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1075200	C	A	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
1075302	T	C	3.29E-07	94.6	5.4	45	25	0	0	0	4	74
701	G	C	3.33E-07	86.4	13.6	45	25	0	0	0	11	81
3831477	G	A	3.38E-07	90.9	9.1	45	25	0	0	0	7	77
3111797	T	C	3.40E-07	94.6	5.4	45	25	0	0	0	4	74
5948116	T	C	3.41E-07	92.1	7.9	45	25	0	0	0	6	76
5835634	C	T	3.43E-07	94.6	5.4	45	25	0	0	0	4	74
4678910	AAT	TAC	3.47E-07	94.6	5.4	45	25	0	0	0	4	74
5606855	T	G	3.53E-07	46.1	53.9	45	25	0	0	31	51	152
5192048	A	G	3.53E-07	74.4	25.6	0	0	32	10	0	1	43
5192276	G	A	3.53E-07	74.4	25.6	0	0	32	10	0	1	43
6028865	C	T	3.54E-07	25.3	74.7	0	25	0	0	31	43	99
6029038	C	T	3.54E-07	25.3	74.7	0	25	0	0	31	43	99
4819664	G	A	3.56E-07	87.5	12.5	45	25	0	0	0	10	80
1295015	G	A	3.56E-07	92.6	7.4	0	25	0	0	0	2	27
2877319	C	T	3.56E-07	92.6	7.4	0	25	0	0	0	2	27
2891331	G	A	3.56E-07	92.6	7.4	0	25	0	0	0	2	27
3824511	A	G	3.56E-07	92.6	7.4	0	25	0	0	0	2	27
4261859	G	A	3.56E-07	92.6	7.4	0	25	0	0	0	2	27
4261907	G	A	3.56E-07	92.6	7.4	0	25	0	0	0	2	27
5666096	G	A	3.56E-07	92.6	7.4	0	25	0	0	0	2	27
5674281	G	A	3.56E-07	92.6	7.4	0	25	0	0	0	2	27
5046202	T	C	3.60E-07	22.1	77.9	0	25	0	9	31	48	113

2928227	G	A	3.60E-07	90.9	9.1	45	25	0	0	0	7	77
1081939	C	T	3.64E-07	88.6	11.4	45	25	0	0	0	9	79
1082925	C	T	3.64E-07	88.6	11.4	45	25	0	0	0	9	79
4621360	A	G	3.71E-07	69.4	30.6	0	25	0	10	0	1	36
6016491	C	T	3.71E-07	69.4	30.6	0	25	0	10	0	1	36
2563851	A	C	3.73E-07	89.7	10.3	45	25	0	0	0	8	78
549971	A	C	3.77E-07	97.2	2.8	44	25	0	0	0	2	71
4834911	A	T	3.84E-07	92.1	7.9	45	25	0	0	0	6	76
5068589	G	A	3.84E-07	96.3	3.8	45	0	32	2	0	1	80
3729320	TTCCTGCT	CTCTTGCC	3.88E-07	90.9	9.1	45	25	0	0	0	7	77
3729335	T	C	3.88E-07	90.9	9.1	45	25	0	0	0	7	77
3026622	A	C	3.94E-07	93.3	6.7	45	25	0	0	0	5	75
1037868	T	C	4.03E-07	78.0	22.0	0	0	32	9	0	0	41
1918319	C	T	4.08E-07	92.1	7.9	45	25	0	0	0	6	76
5492800	C	T	4.11E-07	90.9	9.1	45	25	0	0	0	7	77
5398784	A	G	4.20E-07	45.8	54.2	45	0	32	10	31	50	168
1820564	C	T	4.20E-07	92.6	7.4	0	25	0	0	0	2	27
2475227	G	C	4.20E-07	92.6	7.4	0	25	0	0	0	2	27
2771873	G	A	4.20E-07	92.6	7.4	0	25	0	0	0	2	27
4249731	C	A	4.20E-07	92.6	7.4	0	25	0	0	0	2	27
4377796	C	T	4.20E-07	92.6	7.4	0	25	0	0	0	2	27
4525652	C	G	4.20E-07	92.6	7.4	0	25	0	0	0	2	27
5398784	ACCG	GCCA	4.20E-07	92.6	7.4	0	25	0	0	0	2	27
6023601	C	T	4.20E-07	92.6	7.4	0	25	0	0	0	2	27
2478666	C	T	4.26E-07	88.6	11.4	45	25	0	0	0	9	79
3649903	G	A	4.27E-07	89.7	10.3	45	25	0	0	0	8	78
5857839	G	T	4.34E-07	93.3	6.7	45	25	0	0	0	5	75
6108130	T	C	4.36E-07	26.4	73.6	0	0	32	10	31	48	121

3666587	T	C	4.45E-07	43.3	56.7	45	0	0	10	0	49	104
4204023	C	A	4.51E-07	93.3	6.7	45	25	0	0	0	5	75
151259	GCCG	ACCT	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
614528	G	A	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
614642	C	T	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
955376	G	T	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
1136728	G	A	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
1258815	T	C	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
1291963	C	T	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
1444733	G	C	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
1444821	C	T	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
1445712	C	T	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
2490387	C	T	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
2931290	C	T	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
2937206	C	T	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
3031405	C	T	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
3184511	ACAC	GCAT	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
3200829	G	A	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
3202484	GGAA	AGAG	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
3291486	G	A	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
3326449	T	C	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
3778895	C	G	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
4121396	C	G	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
4741191	C	A	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
5415085	G	C	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
5712101	G	A	4.57E-07	89.3	10.7	0	25	0	0	0	3	28
559781	G	A	4.63E-07	93.3	6.7	45	25	0	0	0	5	75
2802555	A	G	4.66E-07	44.6	55.4	45	25	0	10	31	46	157

1116476	C	G	4.66E-07	84.2	15.8	0	0	32	0	0	6	38
1518133	G	T	4.66E-07	84.2	15.8	0	0	32	0	0	6	38
1925545	G	T	4.66E-07	84.2	15.8	0	0	32	0	0	6	38
3332200	A	C	4.66E-07	84.2	15.8	0	0	32	0	0	6	38
3382793	C	T	4.66E-07	84.2	15.8	0	0	32	0	0	6	38
3383243	C	T	4.66E-07	84.2	15.8	0	0	32	0	0	6	38
4265459	G	A	4.66E-07	84.2	15.8	0	0	32	0	0	6	38
4289467	C	T	4.66E-07	84.2	15.8	0	0	32	0	0	6	38
4398775	C	T	4.66E-07	84.2	15.8	0	0	32	0	0	6	38
4271878	G	A	4.66E-07	93.3	6.7	45	25	0	0	0	5	75
1791310	C	T	4.71E-07	90.9	9.1	45	25	0	0	0	7	77
1517168	A	T	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
1605414	C	T	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
1704170	G	A	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
3084743	T	C	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
3113865	G	A	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
4835407	A	G	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
4989979	G	A	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
5403889	C	T	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
5661965	G	A	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
5663149	C	T	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
6127125	C	A	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
6166491	G	A	4.72E-07	92.6	7.4	0	25	0	0	0	2	27
3585815	G	A	4.78E-07	69.4	30.6	0	25	0	10	0	1	36
1128449	C	T	4.82E-07	93.3	6.7	45	25	0	0	0	5	75
172567	C	T	4.86E-07	94.6	5.4	45	25	0	0	0	4	74
3261259	G	A	4.96E-07	88.6	11.4	45	25	0	0	0	9	79
6238868	C	T	4.97E-07	85.4	14.6	45	25	0	0	0	12	82

2800757	G	A	4.97E-07	86.4	13.6	45	25	0	0	0	11	81
5760744	A	G	5.01E-07	89.7	10.3	45	25	0	0	0	8	78
626857	G	A	5.15E-07	22.3	77.7	0	25	0	8	31	48	112
538847	G	A	5.16E-07	89.7	10.3	45	25	0	0	0	8	78
216128	C	T	5.17E-07	91.4	8.6	0	0	32	0	0	3	35
3145180	G	A	5.18E-07	90.9	9.1	45	25	0	0	0	7	77
3186075	C	T	5.29E-07	37.5	62.5	45	0	0	0	31	44	120
3204308	A	G	5.41E-07	22.3	77.7	0	25	0	8	31	48	112
5457793	T	G	5.48E-07	21.9	78.1	0	25	0	10	31	48	114
3362509	G	A	5.50E-07	90.9	9.1	45	25	0	0	0	7	77
5385257	T	C	5.94E-07	85.1	14.9	0	25	32	0	0	10	67
5890940	G	A	6.06E-07	94.6	5.4	45	25	0	0	0	4	74
5143907	C	A	6.10E-07	88.6	11.4	45	25	0	0	0	9	79
1881878	C	T	6.10E-07	92.1	7.9	45	25	0	0	0	6	76
3717585	G	A	6.13E-07	93.3	6.7	45	25	0	4	0	1	75
2180562	G	A	6.18E-07	95.9	4.1	45	25	0	0	0	3	73
5134146	A	G	6.32E-07	90.9	9.1	45	25	0	0	0	7	77
5144650	G	A	6.33E-07	89.7	10.3	45	25	0	0	0	8	78
6108534	T	A	6.35E-07	91.9	8.1	0	25	32	0	0	5	62
5140142	G	A	6.45E-07	92.1	7.9	45	25	0	0	0	6	76
3306303	G	A	6.63E-07	88.6	11.4	45	25	0	0	0	9	79
1711922	C	T	6.67E-07	86.4	13.6	45	25	0	0	0	11	81
5423521	C	T	6.71E-07	26.4	73.6	0	0	32	10	31	48	121
4879991	C	G	6.73E-07	94.6	5.4	45	25	0	0	0	4	74
1849615	G	A	6.89E-07	94.6	5.4	45	25	0	0	0	4	74
5009336	A	G	6.98E-07	64.0	36.0	0	25	32	0	31	1	89
1049085	C	T	7.14E-07	88.6	11.4	45	25	0	0	0	9	79
1578874	C	G	7.14E-07	88.6	11.4	45	25	0	0	0	9	79

365559	G	A	7.18E-07	92.1	7.9	45	25	0	0	0	6	76
1967496	A	G	7.20E-07	67.6	32.4	0	25	0	10	0	2	37
3351893	G	A	7.28E-07	74.4	25.6	0	0	32	10	0	1	43
2499346	C	T	7.33E-07	94.6	5.4	45	25	0	0	0	4	74
614725	A	C	7.40E-07	90.9	9.1	45	25	0	0	0	7	77
3780351	TACAGCGTC GCTC	T	7.46E-07	95.9	4.1	45	25	0	0	0	3	73
4321300	C	T	7.59E-07	94.6	5.4	45	25	0	0	0	4	74
551788	G	C	7.68E-07	93.3	6.7	45	25	0	0	0	5	75
4225780	C	A	7.74E-07	97.5	2.5	45	1	32	0	0	2	80
1294806	T	C	7.83E-07	93.3	6.7	45	25	0	0	0	5	75
2078472	G	A	8.05E-07	87.5	12.5	45	25	0	0	0	10	80
5420066	C	T	8.15E-07	69.4	30.6	0	25	0	10	0	1	36
4835000	A	G	8.20E-07	81.4	18.6	45	25	0	10	0	6	86
1842446	T	C	8.23E-07	63.3	36.7	0	25	32	0	31	2	90
491392	T	C	8.42E-07	76.0	24.0	0	25	32	10	0	8	75
4335588	G	A	8.44E-07	92.1	7.9	45	25	0	0	0	6	76
5223206	C	G	8.49E-07	97.2	2.8	45	25	0	0	0	2	72
5942867	AA	GG	8.49E-07	97.2	2.8	45	25	0	0	0	2	72
5067305	T	A	8.52E-07	93.3	6.7	45	25	0	0	0	5	75
3905671	C	A	8.55E-07	88.6	11.4	45	25	0	0	0	9	79
5772765	GCTGTCT	ACTATCC	8.57E-07	92.1	7.9	45	25	0	0	0	6	76
1122802	C	T	8.68E-07	93.3	6.7	45	25	0	0	0	5	75
1979300	C	T	8.69E-07	86.4	13.6	45	25	0	0	0	11	81
967263	T	C	8.74E-07	21.7	78.3	0	25	0	10	31	49	115
5372333	G	C	8.82E-07	82.8	17.2	45	0	32	10	0	6	93
1830413	A	G	8.89E-07	78.7	21.3	45	25	0	10	0	9	89
3713760	CAA	GAG	8.91E-07	89.7	10.3	45	25	0	0	0	8	78
4268632	G	A	9.05E-07	87.5	12.5	45	25	0	8	0	2	80

1249502	G	T	9.12E-07	90.9	9.1	45	25	0	0	0	7	77
4549195	TGCGT	GGCGC	9.23E-07	92.8	7.2	45	0	32	0	0	6	83
5661389	C	T	9.35E-07	67.6	32.4	0	25	0	10	0	2	37
3736361	GGCA	AGCG	9.38E-07	93.3	6.7	45	25	0	0	0	5	75
4186820	G	A	9.39E-07	93.3	6.7	45	25	0	0	0	5	75
4041432	G	A	9.47E-07	93.3	6.7	45	25	0	0	0	5	75
4952131	C	T	9.63E-07	88.6	11.4	45	25	0	0	0	9	79
5355162	G	C	9.63E-07	94.0	6.0	45	1	32	0	0	5	83
4517448	T	C	9.72E-07	42.9	57.1	45	0	0	10	0	50	105
204112	C	T	9.73E-07	95.9	4.1	45	25	0	0	0	3	73
2942388	G	A	1.00E-06	93.3	6.7	45	25	0	0	0	5	75
2944082	AG	CA	1.00E-06	93.3	6.7	45	25	0	0	0	5	75
4628973	G	A	1.00E-06	93.3	6.7	45	25	0	0	0	5	75
5620694	G	A	1.00E-06	93.3	6.7	45	25	0	0	0	5	75

Appendix - Table 11: Median and interquartile range of metrics used to analyse growth curves of strains which have evolved mutations in the MexEF-OprN operon.

	Strain	Media	Antibiotic	AUC experimental		Relative Fitness*	
				Mdn	IQR	Mdn	IQR
A	Parent	BHI	None	17.18	0.542	1.01	0.16
A1	Mutant			11.224	0.26	1.08	0.37
A1.1	Revertant			23.116	2.374	3.92	0.26
A1.2	Revertant			23.03	2.439	3.72	0.32
A2	Mutant			10.106	0.674	1.10	0.30
A2.1	Revertant			10.969	0.824	1.04	0.21
A2.2	Revertant			14.572	0.295	1.34	0.26
B	Parent			21.98	1.846	1.03	0.08
B3	Mutant			19.063	0.589	1.08	0.04
B3.1	Revertant			19.327	5.26	1.19	0.39
A	Parent	BHI	CHL	6.058	0.299	0.98	0.19
A1	Mutant			10.986	0.87	1.04	0.20
A1.1	Revertant			8.916	0.977	1.61	0.29
A1.2	Revertant			8.802	2.344	1.67	0.40
A2	Mutant			10.147	0.884	1.04	0.24
A2.1	Revertant			6.11	0.198	1.26	0.26
A2.2	Revertant			6.084	0.367	1.06	0.12
B	Parent			8.191	1.838	1.02	0.03
B3	Mutant			18.723	1.264	1.25	0.06
B3.1	Revertant			6.759	1.042	0.93	0.07
A	Parent	SSM9PR	None	16.78	0.397	1.00	0.05
A1	Mutant			12.925	7.866	1.02	0.36
A1.1	Revertant			22.216	0.878	2.54	0.16
A1.2	Revertant			23.222	0.775	2.61	0.10
A2	Mutant			14.779	1.398	1.32	0.08
A2.1	Revertant			11.619	0.224	0.97	0.04
A2.2	Revertant			17.599	0.351	1.28	0.09
B	Parent			31.915	2.163	1.01	0.10
B3	Mutant			26.642	0.393	0.94	0.10
B3.1	Revertant			31.984	1.572	1.07	0.04
A	Parent	SSM9PR	CHL	10.602	0.175	1.00	0.04
A1	Mutant			11.865	8.302	1.07	0.53
A1.1	Revertant			14.672	1.629	2.57	0.23
A1.2	Revertant			15.417	1.599	2.48	0.18
A2	Mutant			15.053	0.534	1.29	0.12
A2.1	Revertant			8.923	0.612	0.95	0.09
A2.2	Revertant			11.734	0.235	1.16	0.08
B	Parent			19.063	5.103	1.00	0.20
B3	Mutant			26.255	0.653	1.78	0.15
B3.1	Revertant			16.494	3.269	1.02	0.10

** Relative fitness is reported relative to the mean average growth rate of the ancestral parental strain in the same growth condition*

Appendix - Table 12: Mann-Whitney U test on relative fitness of strains grown in **BHI** with evolved mutations in mexS and mexT. P-values are adjusted using the Benjamini-Hochberg correction.*

Revertant		group1	group2	U	p.adj
A1.1	none	A1	A	59	5.21×10^{-1}
		A1.1	A	100	2.74×10^{-4}
		A1	A1.1	0	2.74×10^{-4}
	CHL	A1 + CHL	A + CHL	55	7.34×10^{-1}
		A1.1 + CHL	A + CHL	100	2.74×10^{-4}
		A1 + CHL	A1.1 + CHL	0	2.74×10^{-4}
A1.2	none	A1	A	59	5.21×10^{-1}
		A1.2	A	100	2.74×10^{-4}
		A1	A1.2	0	2.74×10^{-4}
	CHL	A1 + CHL	A + CHL	55	7.34×10^{-1}
		A1.2 + CHL	A + CHL	100	2.74×10^{-1}
		A1 + CHL	A1.2 + CHL	0	2.74×10^{-1}
A2.1	none	A2	A	67	2.54×10^{-1}
		A2.1	A	44	6.78×10^{-1}
		A2	A2.1	68	2.54×10^{-1}
	CHL	A2 + CHL	A + CHL	57	7.48×10^{-1}
		A2.1 + CHL	A + CHL	88	1.40×10^{-2}
		A2 + CHL	A2.1 + CHL	18	3.50×10^{-2}
A2.2	none	A2	A	67	2.54×10^{-1}
		A2.2	A	99	7.38×10^{-4}
		A2	A2.2	17	2.80×10^{-2}
	CHL	A2 + CHL	A + CHL	57	7.48×10^{-1}
		A2.2 + CHL	A + CHL	62	5.78×10^{-1}
		A2 + CHL	A2.2 + CHL	49	9.70×10^{-1}
B3.1	none	B	B3	12	1.40×10^{-2}
		B	B3.1	30	2.10×10^{-1}
		B3	B3.1	46	7.91×10^{-1}
	CHL	B + CHL	B3 + CHL	0	2.74×10^{-4}
		B + CHL	B3.1 + CHL	86	7.00×10^{-3}
		B3 + CHL	B3.1 + CHL	100	2.74×10^{-4}

** Relative fitness is calculated with respect to the average growth rate of the ancestral parent strain*

Appendix - Table 13: Mann-Whitney U test on relative fitness of strains grown in **SSM9PR** with evolved mutations in mexS and mexT. P-values are adjusted using the Benjamini-Hochberg correction.*

Revertant		group1	group2	U	p.adj
A1.1	none	A1	A	57	6.23×10^{-1}
		A1.1	A	100	2.74×10^{-4}
		A1	A1.1	0	2.74×10^{-4}
	CHL	A1 + CHL	A + CHL	58	5.71×10^{-1}
		A1.1 + CHL	A + CHL	100	2.74×10^{-4}
		A1 + CHL	A1.1 + CHL	0	2.74×10^{-4}
A1.2	none	A1	A	57	6.23×10^{-1}
		A1.2	A	100	2.74×10^{-4}
		A1	A1.2	0	2.74×10^{-4}
	CHL	A1 + CHL	A + CHL	58	5.71×10^{-1}
		A1.2 + CHL	A + CHL	100	2.74×10^{-4}
		A1 + CHL	A1.2 + CHL	0	2.74×10^{-4}
A2.1	none	A2	A	100	2.74×10^{-4}
		A2.1	A	33	2.12×10^{-1}
		A2	A2.1	100	2.74×10^{-4}
	CHL	A2 + CHL	A + CHL	100	5.49×10^{-4}
		A2.1 + CHL	A + CHL	32	1.86×10^{-1}
		A2 + CHL	A2.1 + CHL	92	3.00×10^{-3}
A2.2	none	A2	A	100	2.74×10^{-4}
		A2.2	A	100	2.74×10^{-4}
		A2	A2.2	68	2.12×10^{-1}
	CHL	A2 + CHL	A + CHL	100	5.49×10^{-4}
		A2.2 + CHL	A + CHL	100	5.49×10^{-4}
		A2 + CHL	A2.2 + CHL	91	3.00×10^{-3}
B3.1	none	B	B3	80	3.80×10^{-2}
		B	B3.1	22	3.80×10^{-2}
		B3	B3.1	11	1.10×10^{-2}
	CHL	B + CHL	B3 + CHL	0	2.74×10^{-4}
		B + CHL	B3.1 + CHL	44	6.78×10^{-1}
		B3 + CHL	B3.1 + CHL	100	2.74×10^{-4}

** Relative fitness is calculated with respect to the average growth rate of the ancestral parent strain*

*Appendix - Table 14: Mann-Whitney U test on the area under the curve of strains grown in **BHI** with evolved mutations in mexS and mexT. P-values are adjusted using the Benjamini-Hochberg correction.*

		group1	group2	U	p.adj
A1.1	none	A1	A	0	2.20×10^{-4}
		A1.1	A	100	2.20×10^{-4}
		A1	A1.1	0	2.20×10^{-4}
	CHL	A1 + CHL	A + CHL	100	2.74×10^{-4}
		A1.1 + CHL	A + CHL	100	2.74×10^{-4}
		A1 + CHL	A1.1 + CHL	100	2.74×10^{-4}
A1.2	none	A1	A	0	2.20×10^{-4}
		A1.2	A	100	2.20×10^{-4}
		A1	A1.2	0	2.20×10^{-4}
	CHL	A1 + CHL	A + CHL	100	2.74×10^{-4}
		A1.2 + CHL	A + CHL	100	2.74×10^{-4}
		A1 + CHL	A1.2 + CHL	95	9.23×10^{-4}
A2.1	none	A2	A	0	2.20×10^{-4}
		A2.1	A	0	2.20×10^{-4}
		A2	A2.1	8	2.00×10^{-3}
	CHL	A2 + CHL	A + CHL	100	3.66×10^{-4}
		A2.1 + CHL	A + CHL	61	5.12×10^{-1}
		A2 + CHL	A2.1 + CHL	100	3.66×10^{-4}
A2.2	none	A2	A	0	2.20×10^{-4}
		A2.2	A	0	2.20×10^{-4}
		A2	A2.2	0	2.20×10^{-4}
	CHL	A2 + CHL	A + CHL	100	3.66×10^{-4}
		A2.2 + CHL	A + CHL	62	5.12×10^{-1}
		A2 + CHL	A2.2 + CHL	100	3.66×10^{-4}
B3.1	none	B	B3	100	5.49×10^{-4}
		B	B3.1	75	9.60×10^{-2}
		B3	B3.1	50	1.00×10^{0}
	CHL	B + CHL	B3 + CHL	0	2.74×10^{-4}
		B + CHL	B3.1 + CHL	88	5.00×10^{-3}
		B3 + CHL	B3.1 + CHL	100	2.74×10^{-4}

*Appendix - Table 15: Mann-Whitney U test on the area under the curve of strains grown in **SSM9PR** with evolved mutations in mexS and mexT. P-values are adjusted using the Benjamini-Hochberg correction.*

Revertant		group1	group2	U	p.adj
A1.1	none	A1	A	16	1.10×10^{-2}
		A1.1	A	100	2.74×10^{-4}
		A1	A1.1	0	2.74×10^{-4}
	CHL	A1 + CHL	A + CHL	50	1.00
		A1.1 + CHL	A + CHL	100	5.49×10^{-4}
		A1 + CHL	A1.1 + CHL	44	8.14×10^{-1}
A1.2	none	A1	A	16	1.10×10^{-2}
		A1.2	A	100	2.74×10^{-4}
		A1	A1.2	0	2.74×10^{-4}
	CHL	A1 + CHL	A + CHL	50	1.00
		A1.2 + CHL	A + CHL	100	5.49×10^{-4}
		A1 + CHL	A1.2 + CHL	39	6.40×10^{-1}
A2.1	none	A2	A	0	2.20×10^{-4}
		A2.1	A	0	2.20×10^{-4}
		A2	A2.1	100	2.20×10^{-4}
	CHL	A2 + CHL	A + CHL	100	5.49×10^{-4}
		A2.1 + CHL	A + CHL	32	1.86×10^{-1}
		A2 + CHL	A2.1 + CHL	92	3.00×10^{-3}
A2.2	none	A2	A	0	2.20×10^{-4}
		A2.2	A	93	1.00×10^{-3}
		A2	A2.2	0	2.20×10^{-4}
	CHL	A2 + CHL	A + CHL	100	5.49×10^{-4}
		A2.2 + CHL	A + CHL	100	5.49×10^{-4}
		A2 + CHL	A2.2 + CHL	91	3.00×10^{-3}
B3.1	none	B	B3	99	3.69×10^{-4}
		B	B3.1	46	7.91×10^{-1}
		B3	B3.1	0	3.69×10^{-4}
	CHL	B + CHL	B3 + CHL	0	2.74×10^{-4}
		B + CHL	B3.1 + CHL	75	6.40×10^{-2}
		B3 + CHL	B3.1 + CHL	100	2.74×10^{-4}

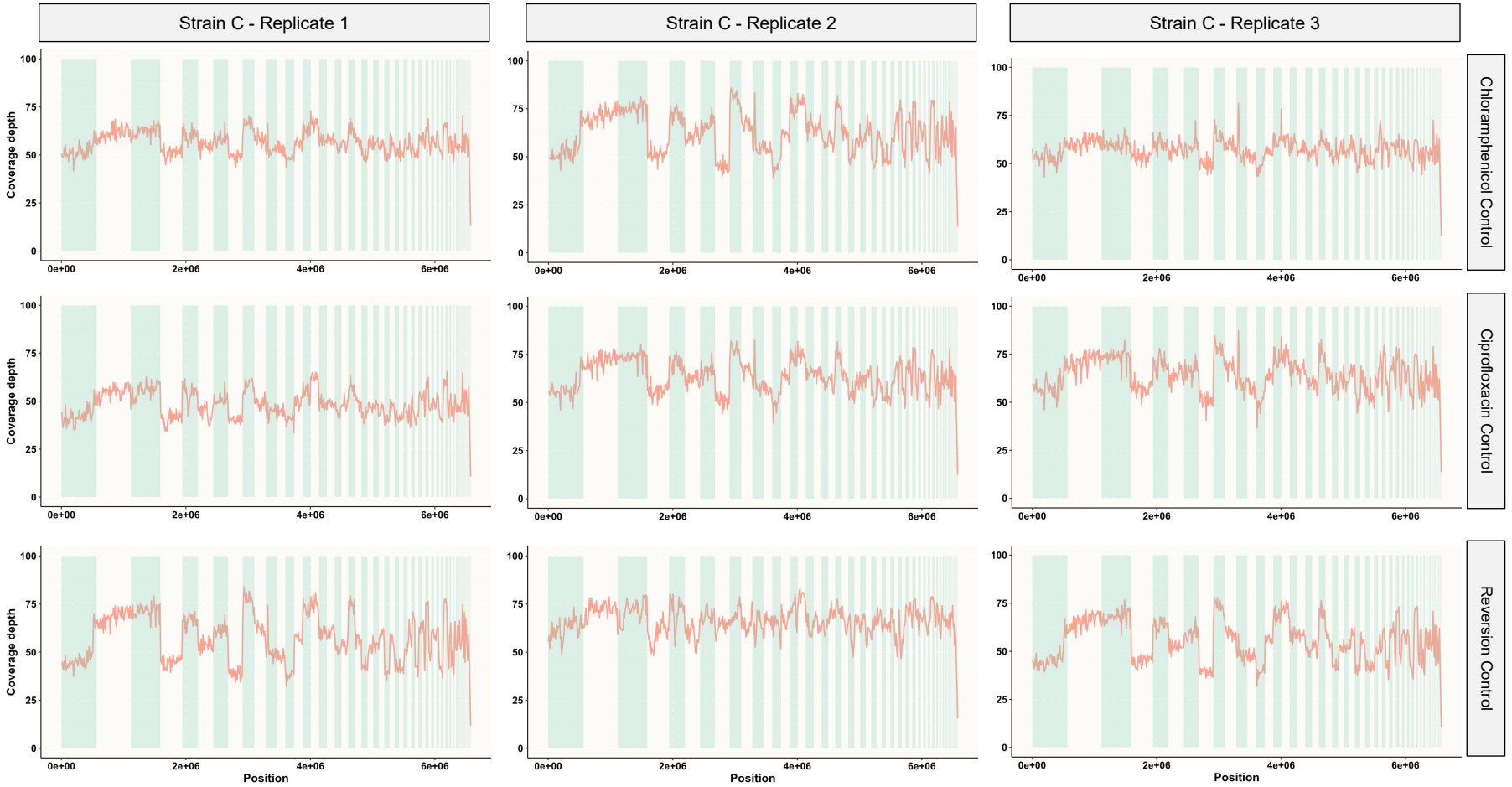
Appendix - Table 16: Mean and Standard Deviation of the area under the curve for three environmental strains grown in various plasma concentrations.

Plasma Concentration (%)	Strain C		Strain D		Strain E	
	M	SD	M	SD	M	SD
0	13.968	2.647	13.764	3.052	13.973	2.825
5	15.423	2.993	10.231	1.777	12.009	0.827
10	10.22	0.601	8.168	1.28	10.126	0.754
20	5.208	0.901	0.631	0.511	5.544	0.742
30	4.577	0.627	0.112	0.131	5.262	0.7
40	3.242	0.378	0.515	0.652	3.866	0.348
50	2.297	0.504	0.404	0.151	2.605	0.48
60	1.6	0.244	0.076	0.152	1.709	0.373
70	1.641	0.341	0.095	0.111	1.086	0.335
80	1.421	0.268	0.668	0.199	0.971	0.153
90	1.021	0.313	0.534	0.18	0.661	0.148
100	0.799	0.329	0.453	0.527	0.612	0.244

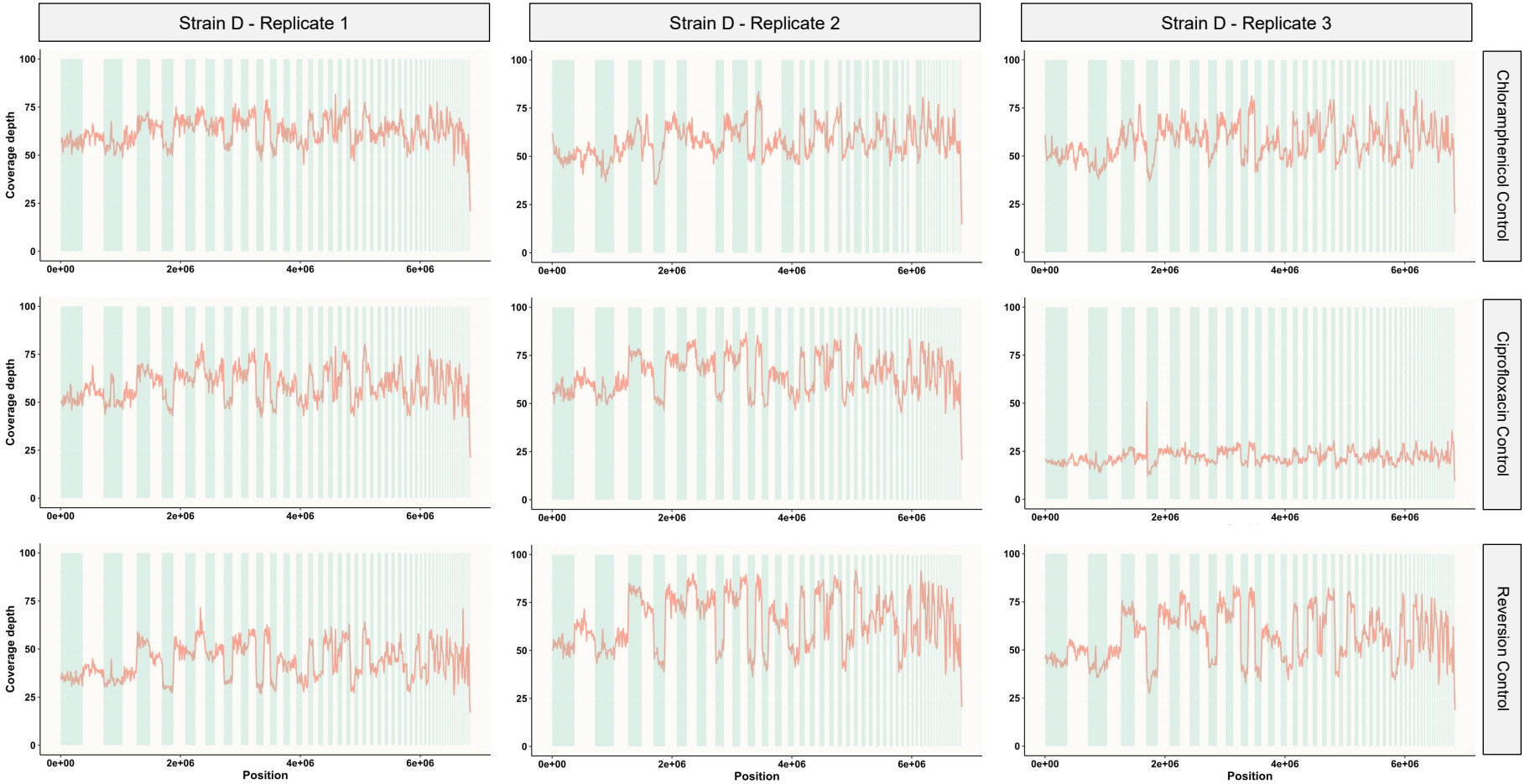
Appendix - Table 17: Comparison of plasma concentrations of bacterial growth. P-*values were determined with a pairwise students t-test.*

Strain	Plasma Concentration (%)	5	10	20	30	40	50	60	70	80	90	100
	0	7.89×10^{-06}	0.282	0.000279	1.68×10^{-05}	4.05×10^{-08}	3.61×10^{-10}	3.11×10^{-12}	5.74×10^{-12}	3.07×10^{-13}	1.58×10^{-13}	5.91×10^{-13}
	5		0.000227	6.06×10^{-11}	5.26×10^{-12}	5.25×10^{-14}	1.96×10^{-15}	6.37×10^{-17}	8.9×10^{-17}	1.85×10^{-17}	1.85×10^{-17}	2.27×10^{-17}
	10			9.52×10^{-06}	5.26×10^{-07}	1.52×10^{-09}	1.61×10^{-11}	2.22×10^{-13}	3.8×10^{-13}	3.1×10^{-14}	1.62×10^{-14}	5.25×10^{-14}
	20				0.367	0.00562	5.22×10^{-05}	2.28×10^{-07}	5.22×10^{-07}	1.33×10^{-08}	5.05×10^{-09}	3.34×10^{-08}
	30					0.057	0.000846	4.05×10^{-06}	9.11×10^{-06}	2.16×10^{-07}	7.93×10^{-08}	5.26×10^{-07}
C	40						0.123	0.00154	0.00329	9.05×10^{-05}	3.36×10^{-05}	0.000227
	50							0.0885	0.146	0.00903	0.00381	0.0199
	60								0.779	0.358	0.218	0.530
	70									0.237	0.136	0.368
	80										0.756	0.759
	90											0.533
	0	0.0174	0.00382	4.88×10^{-17}	3.14×10^{-17}	3.48×10^{-17}	3.51×10^{-17}	3.14×10^{-17}	3.14×10^{-17}	3.29×10^{-17}	3.14×10^{-17}	7.71×10^{-17}
	5		0.931	7.47×10^{-15}	3.28×10^{-15}	5.1×10^{-15}	5.76×10^{-15}	3.28×10^{-15}	3.28×10^{-15}	4.16×10^{-15}	3.28×10^{-15}	1.27×10^{-14}
	10			2.31×10^{-14}	7.47×10^{-15}	1.25×10^{-14}	1.39×10^{-14}	7.47×10^{-15}	7.47×10^{-15}	9.84×10^{-15}	7.47×10^{-15}	4.4×10^{-14}
	20				0.931	1.00	1.00	0.931	0.931	1.00	0.931	1.00
	30					1.00	1.00	1.00	1.00	1.00	1.00	0.78
D	40						1.00	1.00	1.00	1.00	1.00	0.931
	50							1.00	1.00	1.00	1.00	0.972
	60								1.00	1.00	1.00	0.78
	70									1.00	1.00	0.78
	80										1.00	0.914
	90											0.78
	0	0.798	0.536	2.94×10^{-06}	4.77×10^{-07}	3.29×10^{-08}	1.49×10^{-10}	4.85×10^{-13}	7.12×10^{-14}	2.73×10^{-14}	2.44×10^{-14}	3.49×10^{-14}
	5		0.383	1.38×10^{-06}	2.24×10^{-07}	1.6×10^{-08}	7.48×10^{-11}	2.85×10^{-13}	4.42×10^{-14}	2.46×10^{-14}	2.44×10^{-14}	2.73×10^{-14}
	10			2.33×10^{-05}	3.49×10^{-06}	2.24×10^{-07}	1.05×10^{-09}	2.73×10^{-12}	2.85×10^{-13}	7.12×10^{-14}	3.49×10^{-14}	1.14×10^{-13}
	20				0.552	0.137	0.00136	1.96×10^{-06}	1.39×10^{-07}	2.17×10^{-08}	6.17×10^{-09}	3.86×10^{-08}
	30					0.383	0.00765	1.31×10^{-05}	8.24×10^{-07}	1.29×10^{-07}	3.5×10^{-08}	2.29×10^{-07}
E	40						0.0742	0.000234	1.37×10^{-05}	1.93×10^{-06}	5.15×10^{-07}	3.6×10^{-06}
	50							0.0396	0.0037	0.000571	0.000154	0.00111
	60								0.389	0.136	0.055	0.203
	70									0.536	0.310	0.675
	80										0.675	0.813
	90											0.536

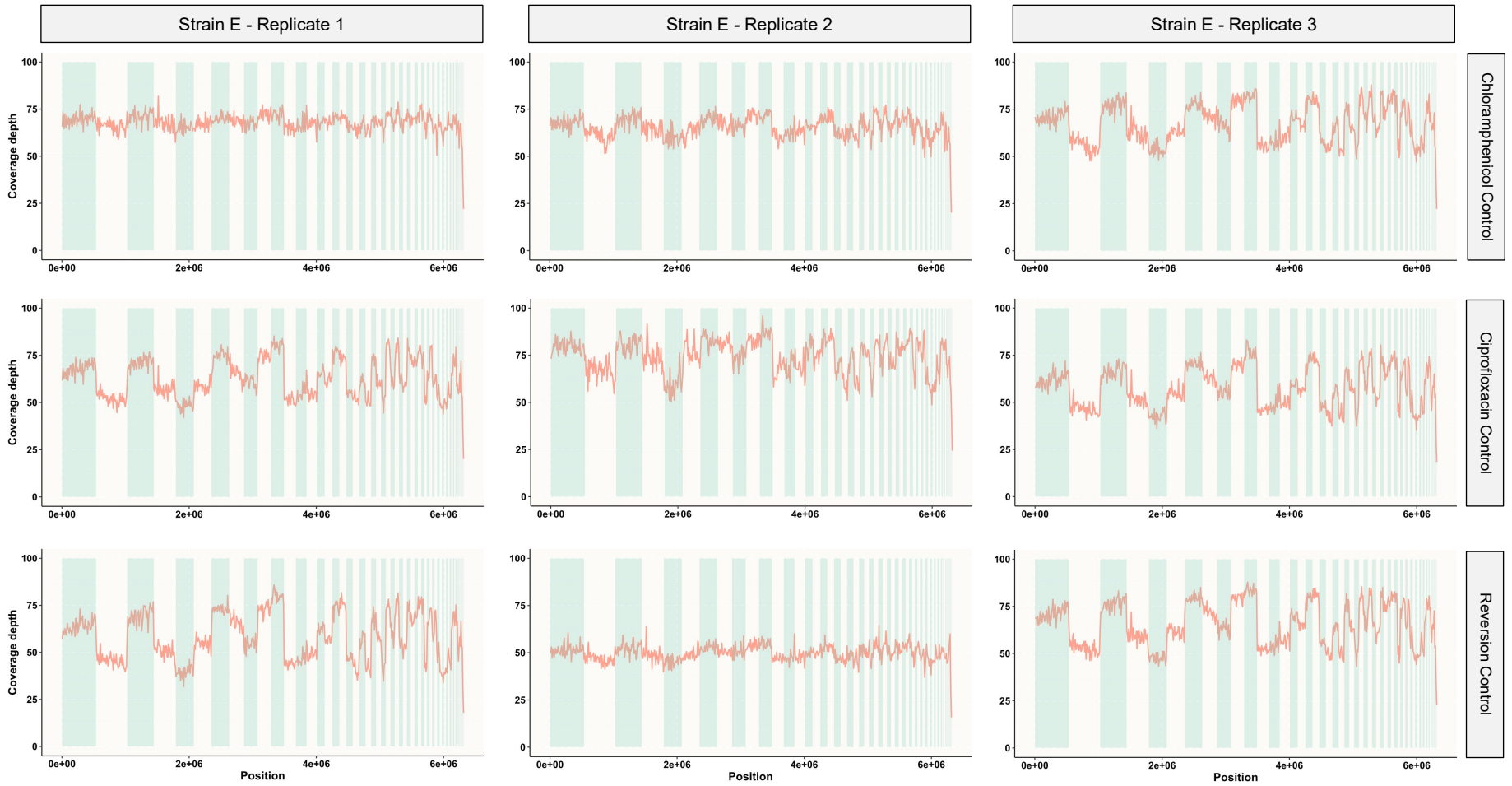
** Highlighted in red are the adjusted P-values where P ≤0.05*



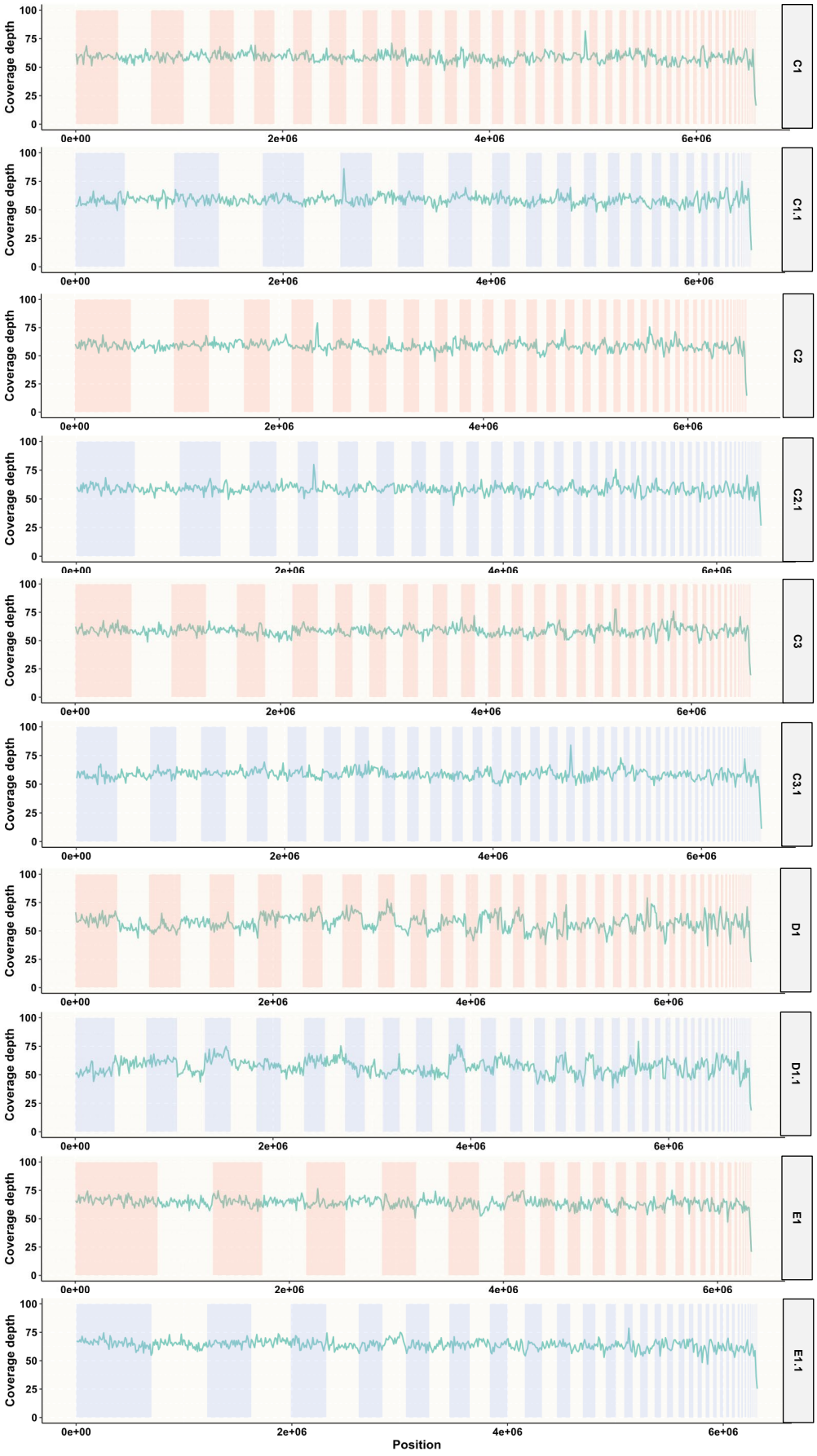
Appendix - Figure 3: Coverage depth of sequencing reads generated from control strains. Reads are mapped to the genome assembly of the respective parental strain with and plotted as the average coverage over 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.



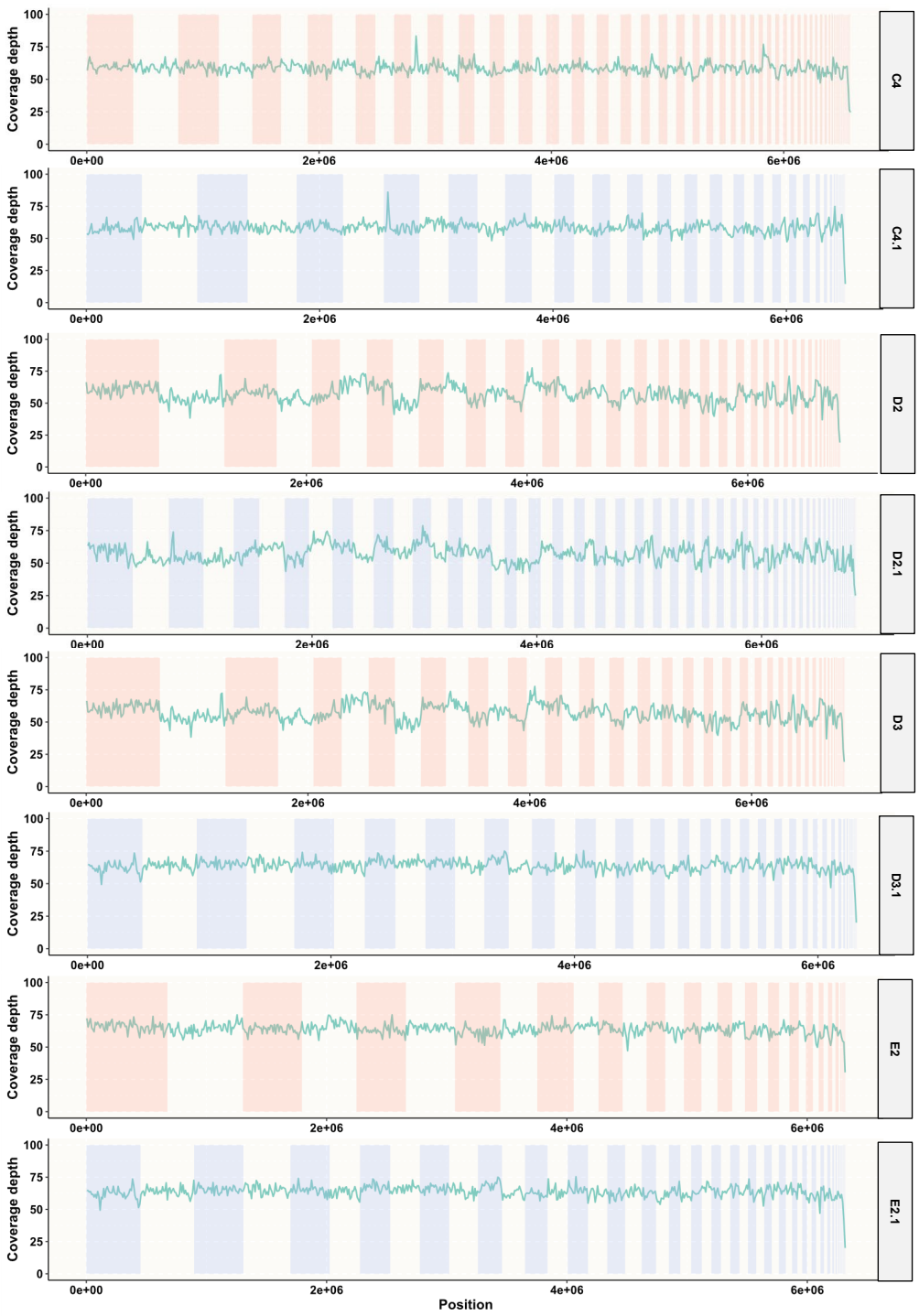
Appendix - Figure 4: Coverage depth of sequencing reads generated from control strains. Reads are mapped to the genome assembly of the respective parental strain with and plotted as the average coverage over 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.



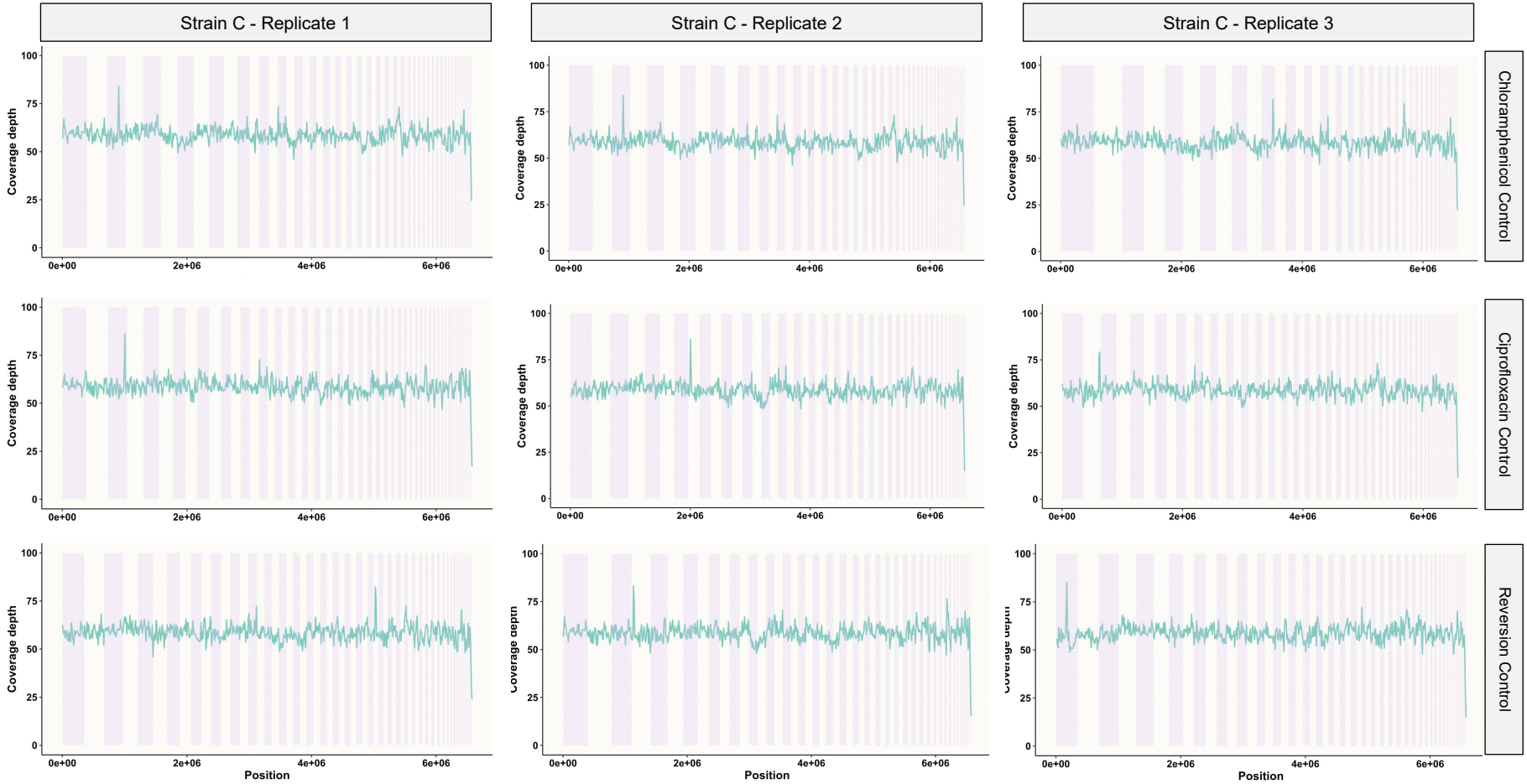
Appendix - Figure 5: Coverage depth of sequencing reads generated from control strains. Reads are mapped to the genome assembly of the respective parental strain with and plotted as the average coverage over 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.



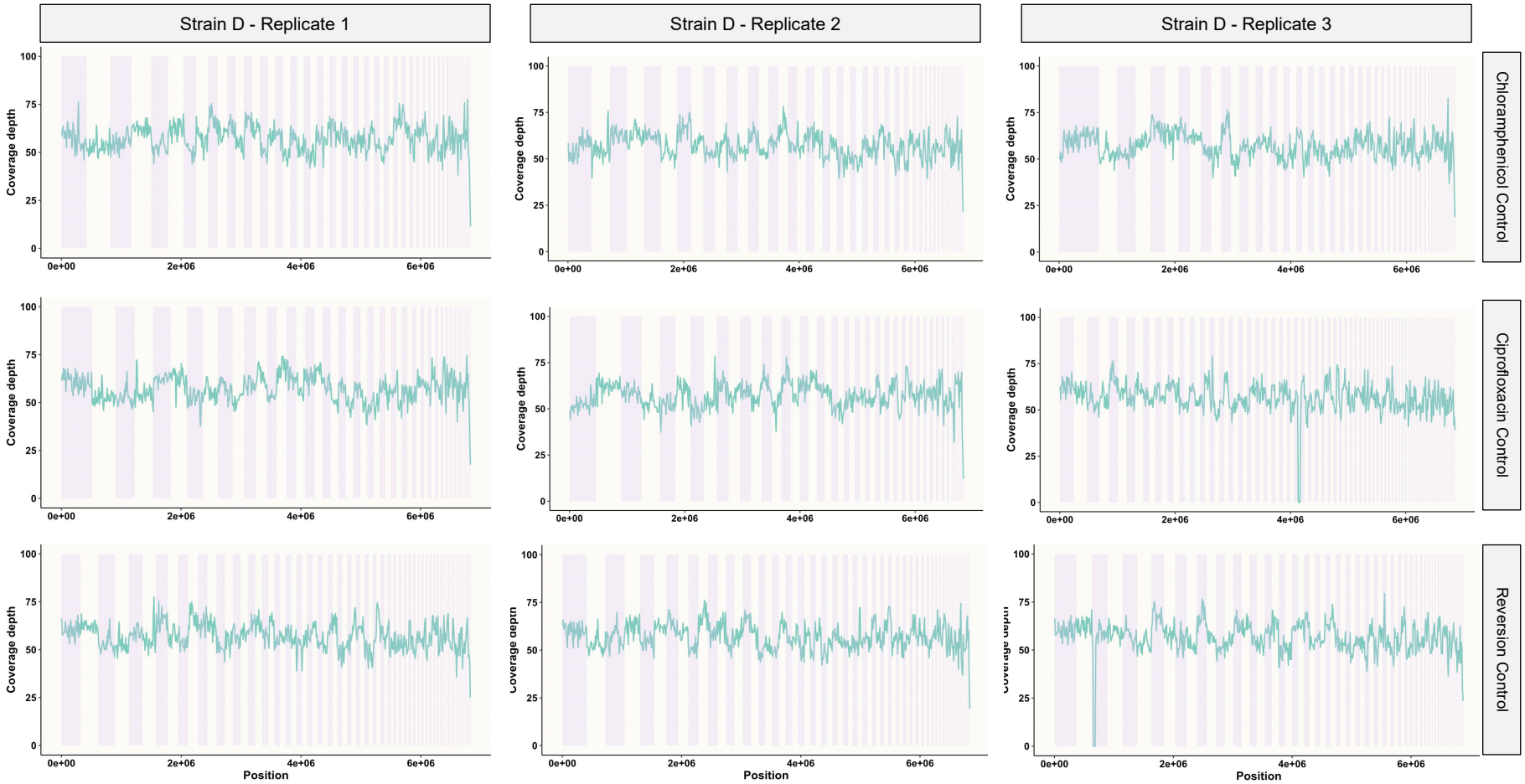
Appendix - Figure 6: Coverage depth of parental sequencing reads mapped to mutant and revertant strains evolved in chloramphenicol. Reads are mapped to the de novo *genome assembly and plotted as the average coverage over 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.*



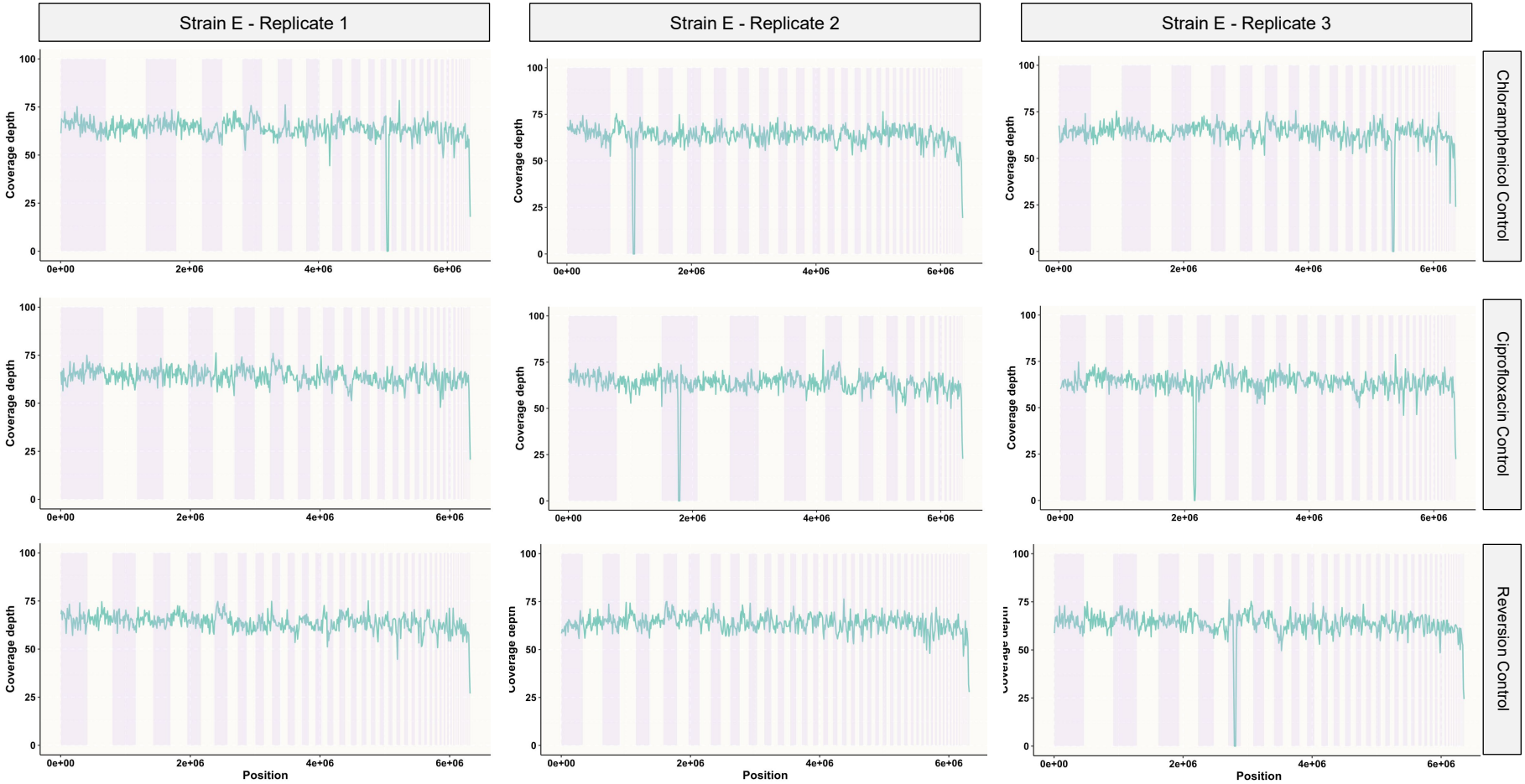
Appendix - Figure 7: Coverage depth of parental sequencing reads mapped to mutant and revertant strains evolved in ciprofloxacin. Reads are mapped to the de novo *genome assembly and plotted as the average coverage over 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.*



Appendix - Figure 8: Coverage depth of sequencing reads generated from parental strain C. Reads are mapped to the de novo *genome assembly of the respective control strains with and plotted as the average coverage over 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.*

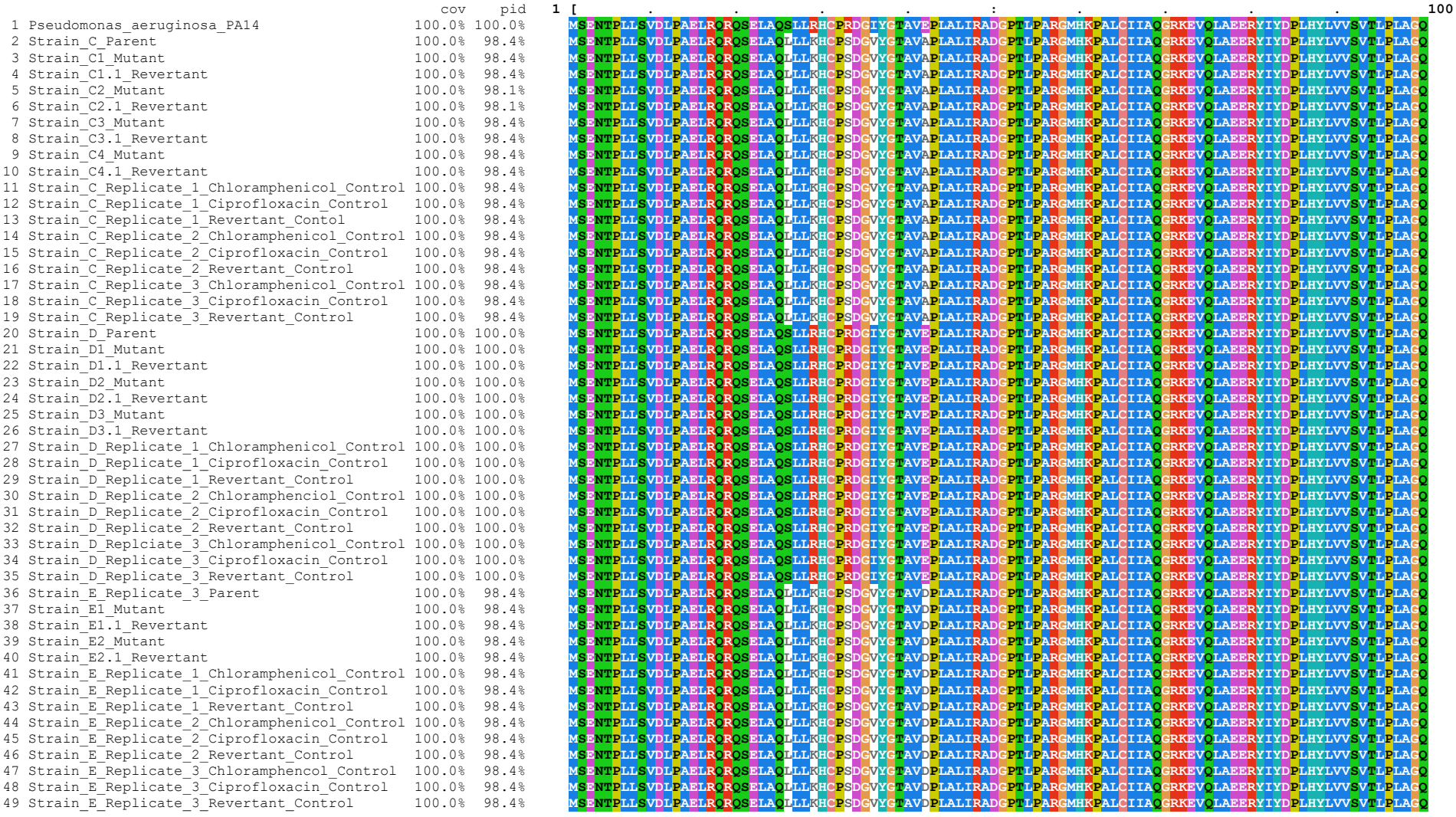


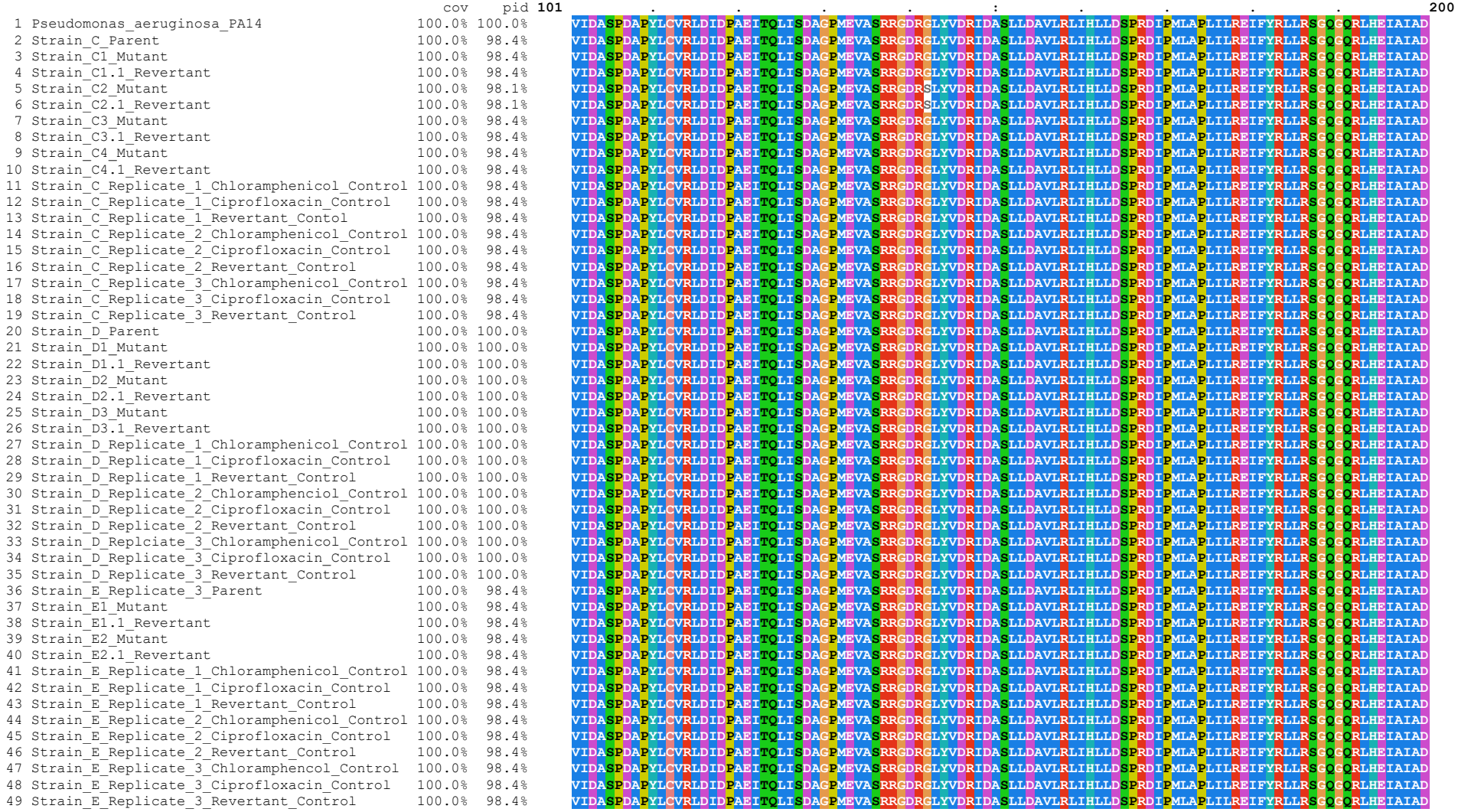
Appendix - Figure 9: Coverage depth of sequencing reads generated from parental strain D. Reads are mapped to the de novo *genome assembly of the respective control strains with and plotted as the average coverage over 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.*



Appendix - Figure 10: Coverage depth of sequencing reads generated from parental strain E. Reads are mapped to the de novo *genome assembly of the respective control strains with and plotted as the average coverage over 10,000 base pairs. Background highlighting marks the contigs in the parental assembly.*

Appendix - Alignment 3: Protein alignment of CmrA in strains evolved under clinical conditions. Amino acids are coloured according to amino acid physiochemical property.

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3 Strain_C1_Mutant 100.0% 98.4%
4 Strain_C1.1_Revertant 100.0% 98.4%
5 Strain_C2_Mutant 100.0% 98.1%
6 Strain_C2.1_Revertant 100.0% 98.1%
7 Strain_C3_Mutant 100.0% 98.4%
8 Strain_C3.1_Revertant 100.0% 98.4%
9 Strain_C4_Mutant 100.0% 98.4%
10 Strain_C4.1_Revertant 100.0% 98.4%
11 Strain_C_Replicate_1_Chloramphenicol_Control 100.0% 98.4%
12 Strain_C_Replicate_1_Ciprofloxacin_Control 100.0% 98.4%
13 Strain_C_Replicate_1_Revertant_Contol 100.0% 98.4%
14 Strain_C_Replicate_2_Chloramphenicol_Control 100.0% 98.4%
15 Strain_C_Replicate_2_Ciprofloxacin_Control 100.0% 98.4%
16 Strain_C_Replicate_2_Revertant_Control 100.0% 98.4%
17 Strain_C_Replicate_3_Chloramphenicol_Control 100.0% 98.4%
18 Strain_C_Replicate_3_Ciprofloxacin_Control 100.0% 98.4%
19 Strain_C_Replicate_3_Revertant_Control 100.0% 98.4%
20 Strain_D_Parent 100.0% 100.0%
21 Strain_D1_Mutant 100.0% 100.0%
22 Strain_D1.1_Revertant 100.0% 100.0%
23 Strain_D2_Mutant 100.0% 100.0%
24 Strain_D2.1_Revertant 100.0% 100.0%
25 Strain_D3_Mutant 100.0% 100.0%
26 Strain_D3.1_Revertant 100.0% 100.0%
27 Strain_D_Replicate_1_Chloramphenicol_Control 100.0% 100.0%
28 Strain_D_Replicate_1_Ciprofloxacin_Control 100.0% 100.0%
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30 Strain_D_Replicate_2_Chloramphenciol_Control 100.0% 100.0%
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37 Strain_E1_Mutant 100.0% 98.4%
38 Strain_E1.1_Revertant 100.0% 98.4%
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41 Strain_E_Replicate_1_Chloramphenicol_Control 100.0% 98.4%
42 Strain_E_Replicate_1_Ciprofloxacin_Control 100.0% 98.4%
43 Strain_E_Replicate_1_Revertant_Control 100.0% 98.4%
44 Strain_E_Replicate_2_Chloramphenicol_Control 100.0% 98.4%
45 Strain_E_Replicate_2_Ciprofloxacin_Control 100.0% 98.4%
46 Strain_E_Replicate_2_Revertant_Control 100.0% 98.4%
47 Strain_E_Replicate_3_Chloramphencol_Control 100.0% 98.4%
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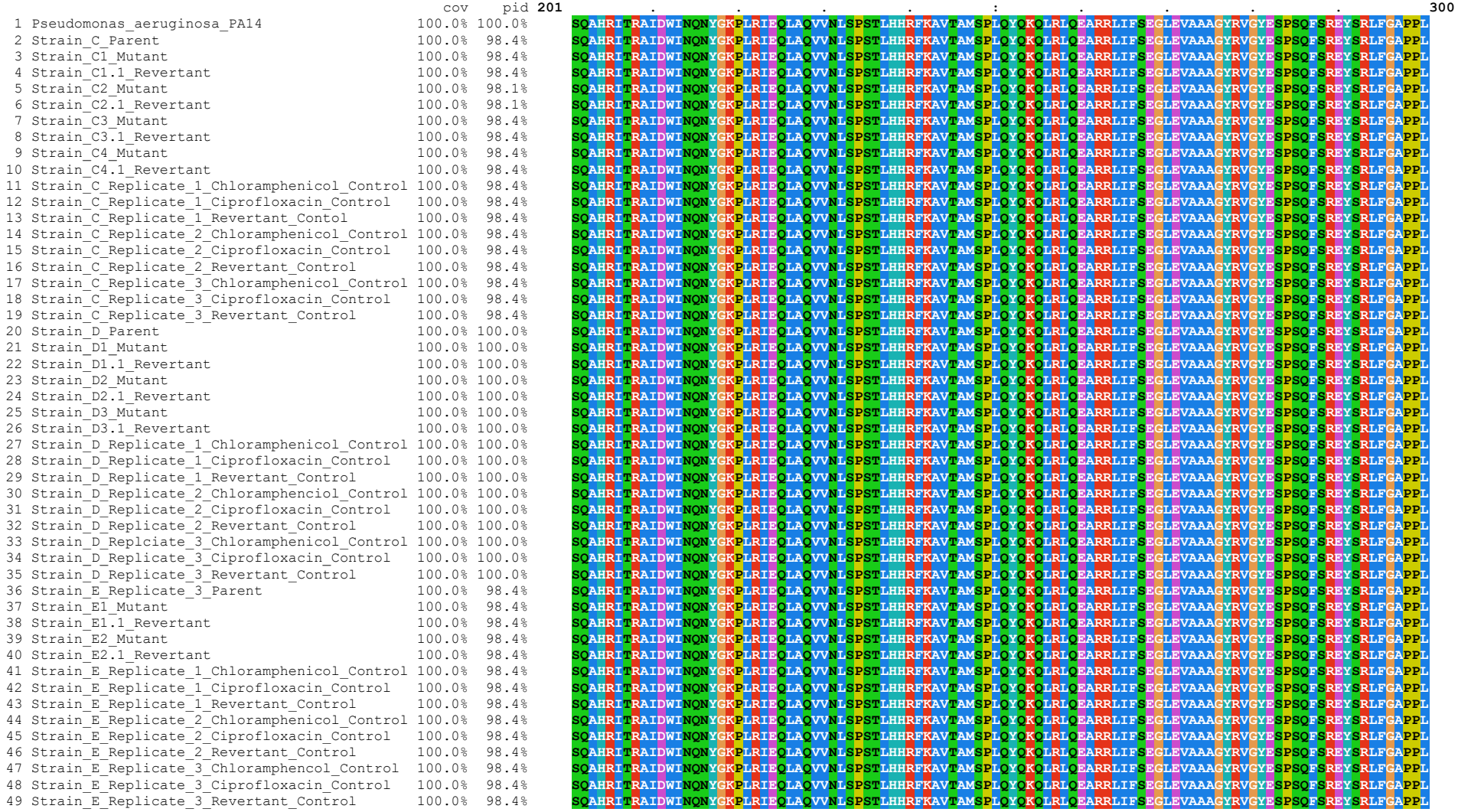
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5 Strain_C2_Mutant 100.0% 98.1%
6 Strain_C2.1_Revertant 100.0% 98.1%
7 Strain_C3_Mutant 100.0% 98.4%
8 Strain_C3.1_Revertant 100.0% 98.4%
9 Strain_C4_Mutant 100.0% 98.4%
10 Strain_C4.1_Revertant 100.0% 98.4%
11 Strain_C_Replicate_1_Chloramphenicol_Control 100.0% 98.4%
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37 Strain_E1_Mutant 100.0% 98.4%
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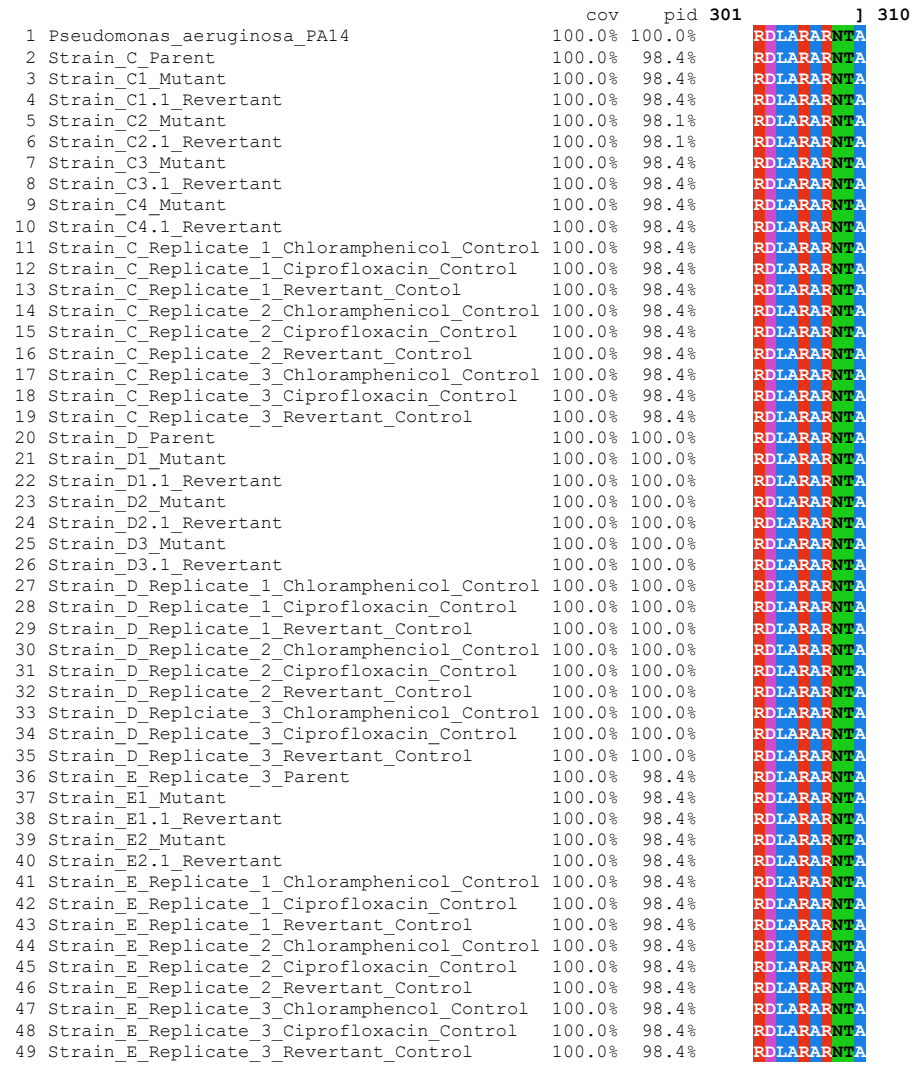
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43 Strain_E_Replicate_1_Revertant_Control 100.0% 98.4% RDLARARNTA
44 Strain_E_Replicate_2_Chloramphenicol_Control 100.0% 98.4% RDLARARNTA
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46 Strain_E_Replicate_2_Revertant_Control 100.0% 98.4% RDLARARNTA
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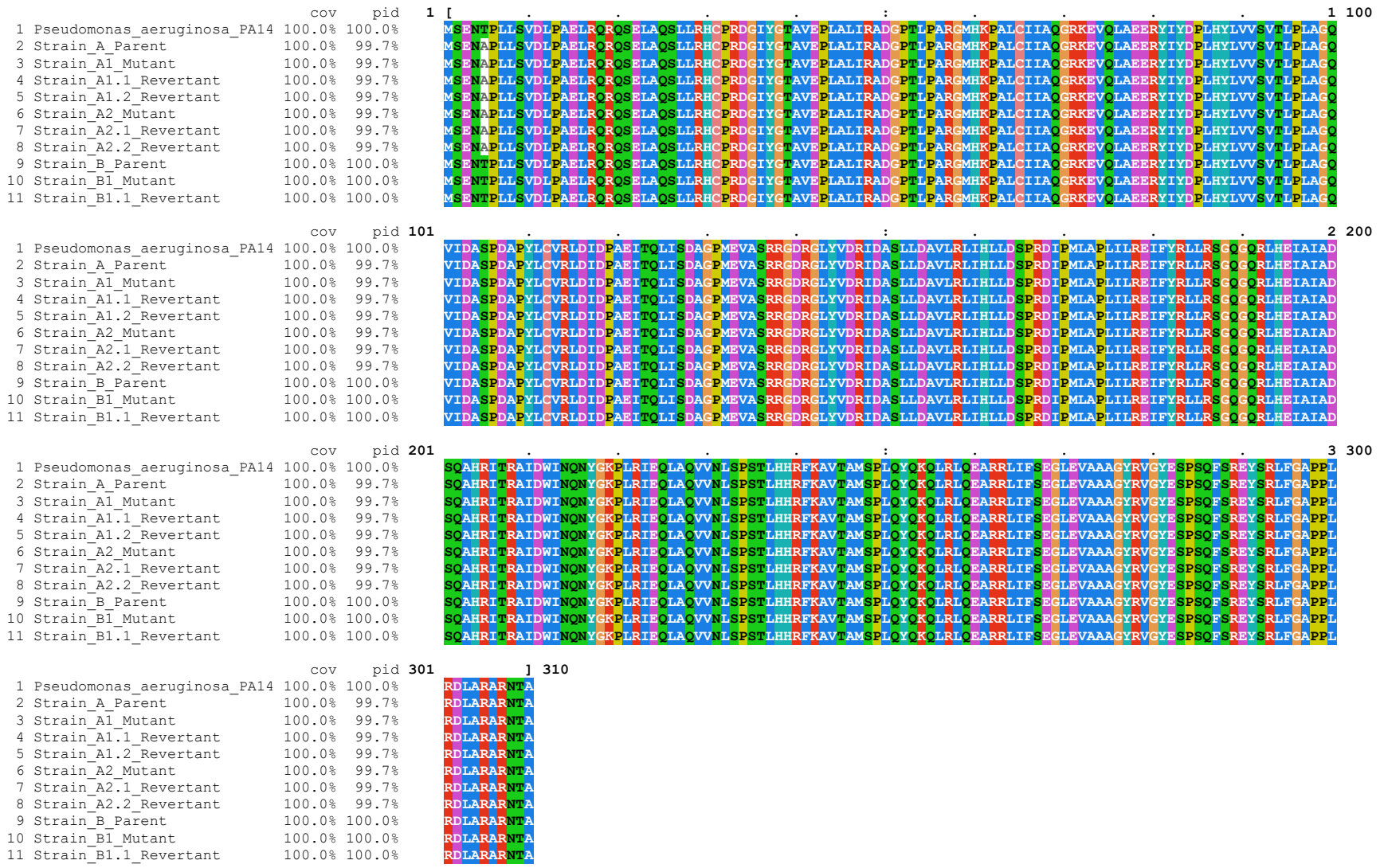
48 Strain_E_Replicate_3_Ciprofloxacin_Control 100.0% 98.4% RDLARARNTA
49 Strain_E_Replicate_3_Revertant_Control 100.0% 98.4% RDLARARNTA

Appendix - Alignment 4: Protein alignment of CmrA genes from chloramphenicol evolved strains. Amino acids are coloured according to amino acid physiochemical property



Appendix - Table 18: Median and interquartile range of the area under the curve and relative fitness of strains evolved in chloramphenicol and MHB + 10% plasma.

Strain		Antibiotic	AUC experimental		Relative Fitness*	
			Mdn	IQR	Mdn	IQR
C	Parent	None	11.81	0.38	0.97	0.09
C1	Mutant	None	6.34	1.39	1.85	0.10
C1.1	Revertant	None	7.78	0.56	1.77	0.73
C2	Mutant	None	16.09	0.63	2.59	0.06
C2.1	Revertant	None	18.12	0.79	2.47	0.14
C3	Mutant	None	16.95	0.80	2.57	0.10
C3.1	Revertant	None	7.59	0.53	1.66	0.20
C	Parent	CHL	4.14	1.00	0.97	0.04
C1	Mutant	CHL	6.01	1.44	1.31	0.19
C1.1	Revertant	CHL	2.28	0.34	1.19	0.12
C2	Mutant	CHL	14.64	0.36	1.72	0.21
C2.1	Revertant	CHL	4.41	1.13	1.40	0.11
C3	Mutant	CHL	15.41	0.36	1.68	0.04
C3.1	Revertant	CHL	3.22	0.45	1.35	0.12
D	Parent	None	3.00	0.64	1.04	0.17
D1	Mutant	None	3.14	1.62	1.05	0.23
D1.1	Revertant	None	4.25	2.25	0.92	0.44
D	Parent	CHL	1.00	0.54	1.06	0.34
D1	Mutant	CHL	2.19	2.48	1.15	0.38
D1.1	Revertant	CHL	0.41	0.45	0.59	0.27
E	Parent	None	9.61	2.65	9.61	2.65
E1	Mutant	None	8.52	3.45	8.52	3.45
E1.1	Revertant	None	13.69	3.13	13.69	3.13
E	Parent	CHL	3.10	0.25	3.10	0.25
E1	Mutant	CHL	6.78	4.10	6.78	4.10
E1.1	Revertant	CHL	2.48	2.31	2.48	2.31

** Relative fitness is calculated with respect to the average growth rate of the ancestral parent strain*

Appendix - Table 19: Full list of mutations identified in chloramphenicol evolved strains. Highlighted in yellow are the genes also found in the control strains.

Strain		Gene	Mutation	Ancestor	Strain	Type	Effect	Product
C1	Mutant	*wspA* ←	Asp419Gly	T	C	sub	Missense	Methyl-accepting chemotaxis protein
		mexS ←	Ser60phe	G	A	sub	Missense	Oxidoreductase MexS
		C_02551 ←	Pro146Pro	G	C	sub	Synonymous	Hypothetical protein
		tssI →	Val241Met	G	A	sub	Missense	Type VI secretion system tip protein TssI/VgrG
		C_05965 ←	Pro225Ala	G	C	sub	Missense	Erythronate-4-phosphate dehydrogenase
		11-2-day0_03924 ←	Thr60Ile	G	A	sub	Missense	Hypothetical protein
		C_00095 → / → *nuoK*		G	C	sub	Intergenic	NADH-quinone oxidoreductase subunit J/NADH-quinone oxidoreductase subunit NuoK
		C_00471 → / ← *C_00472*		C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
		C_03413 → / ← *C_03414*		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03413 → / ← *C_03414*		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		ompR → / → *C_03691*		G	C	sub	Intergenic	two-component system response regulator OmpR/two-component sensor histidine kinase
		C_01796 ← / ← *lpdA_2*		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
C1.1	Revertant	*wspA* ←	Asp419Gly	T	C	sub	Missense	Methyl-accepting chemotaxis protein
		mexS ←	Ser60phe	G	A	sub	Missense	Oxidoreductase MexS
		mexT →	Trp277*	G	A	sub	Stop gain	Multidrug efflux system transcriptional regulator MexT
		clp →	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
		C_05965 ←	Pro225Ala	G	C	sub	Missense	Erythronate-4-phosphate dehydrogenase
		tssI →	Val241Met	G	A	sub	Missense	Type VI secretion system tip protein TssI/VgrG
		C_00471 → / ← *C_00472*	C→G	C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
		C_03056 → / ← *C_03057*	G→A	G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
		C_03413 → / ← *C_03414*	C→G	C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03413 → / ← *C_03414*	T→C	T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_04411 → / → *C_04412*	G→C	G	C	sub	Intergenic	ammonium transporter/YjbQ family protein

C2	Mutant	*C_01253 → / ← C_01254*	G→C	G	C	sub	Intergenic	acyltransferase/hypothetical protein
		C_01796 ← / ← lpdA_2	C→A	C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
		cmrA ←	Gly142Ser	C	T	sub	Missense	AraC family transcriptional regulator CmrA
		mnmG →	Ala99Thr	G	A	sub	Missense	tRNA uridine-5-carboxymethylaminomethyl(34) synthesis enzyme MnmG
		mexS ←	Arg332Cys	G	A	sub	Missense	Oxidoreductase MexS
		hisF ←	Gly256Arg	C	G	sub	Missense	Imidazole glycerol phosphate synthase subunit HisF
		dipA →	Ile816Phe	A	T	sub	Missense	Phosphodiesterase DipA
		tssI →	Val241Met	G	A	sub	Missense	Type VI secretion system tip protein TssI/VgrG
		C_00343 → / ← C_00344	C→A	C	A	sub	Intergenic	lipase chaperone/DoxX family protein
		C_00471 → / ← C_00472	C→G	C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
		C_03056 → / ← C_03057	G→A	G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
		C_03413 → / ← C_03414	C→G	C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03413 → / ← C_03414	T→C	T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03472 ← / → C_03473	C→A	C	A	sub	Intergenic	hypothetical protein/response regulator transcription factor
		C_03472 ← / → C_03473	C→A	C	A	sub	Intergenic	hypothetical protein/response regulator transcription factor
		C_01253 → / ← C_01254	G→C	G	C	sub	Intergenic	acyltransferase/hypothetical protein
		C_01796 ← / ← lpdA_2	C→A	C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
		C_01796 ← / ← lpdA_2	C→A	C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
		ccoP_1 → / → ccoN_2	C→G	C	G	sub	Intergenic	cytochrome-c oxidase%2C cbb3-type subunit III/cytochrome-c oxidase%2C cbb3-type subunit I
		C_02651 → / ← C_02652	G→C	G	C	sub	Intergenic	LysR family transcriptional regulator/hypothetical protein
C2.1	Revertant	*hmpA ←*	Gln48His	C	G	sub	Missense	NO-inducible flavohemoprotein
		cmrA ←	Gly142Ser	C	T	sub	Missense	AraC family transcriptional regulator CmrA
		mnmG →	Ala99Thr	G	A	sub	Missense	tRNA uridine-5-carboxymethylaminomethyl(34) synthesis enzyme MnmG
		pilR	Leu42_Glu46del	GCTCGCGGGCCAGCAA	G	del	Deletion	Two-component system response regulator PilR
		11-2-day0_04529–11-2-day0_04569	Δ43,475 bp	wildtype		del	Deletion	40 genes
		11-2-day0_4927–11-2-day0_4959	Δ40,131 bp	wildtype		del	Deletion	32 genes

	C_05093–C_05152	Δ70,601 bp	wildtype		del	Deletion	60 genes
	dipA →	Ile816Phe	A	T	sub	Missense	Phosphodiesterase DipA
	11-2-day0_02551	Pro146Pro	G	C	sub	Synonymous	Hypothetical protein
	tssI →	Val241Met	G	A	sub	Missense	Type VI secretion system tip protein TssI/VgrG
	C_00095 → / → nuoK		G	C	sub	Intergenic	NADH-quinone oxidoreductase subunit J/NADH-quinone oxidoreductase subunit NuoK
	C_00471 → / ← C_00472		C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
	C_03056 → / ← C_03057		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
	C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_01253 → / ← C_01254		G	C	sub	Intergenic	acyltransferase/hypothetical protein
	C_01796 ← / ← lpdA_2		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
	– / → C_06063		G	A	sub	Intergenic	–/hypothetical protein
C3 Mutant	*mexS ←*	Leu281Arg	A	C	sub	Missense	Oxidoreductase MexS
	hisF ←	Gly256Arg	C	G	sub	Missense	Imidazole glycerol phosphate synthase subunit HisF
	11-2-day0_00129 →	Pro22Gln	C	A	sub	Missense	Quinone oxidoreductase
	clp →	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
	C_05965 ←	Pro225Ala	G	C	sub	Missense	erythronate-4-phosphate dehydrogenase
	dipA →	Ile816Phe	A	T	sub	Missense	Phosphodiesterase DipA
	tssI →	Val241Met	G	A	sub	Missense	Type VI secretion system tip protein TssI/VgrG
	C_00095 → / → nuoK		G	C	sub	Intergenic	NADH-quinone oxidoreductase subunit J/NADH-quinone oxidoreductase subunit NuoK
	C_03056 → / ← C_03057		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
	C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03472 ← / → C_03473		C	A	sub	Intergenic	hypothetical protein/response regulator transcription factor
	C_03472 ← / → C_03473		C	A	sub	Intergenic	hypothetical protein/response regulator transcription factor

		ompR → / → C_03691		G	C	sub	Intergenic	two-component system response regulator OmpR/two-component sensor histidine kinase
		C_01253 → / ← C_01254		G	C	sub	Intergenic	acyltransferase/hypothetical protein
		C_01796 ← / ← lpdA_2		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
C3.1	Revertant	*fleQ ←*	Val383Gly	A	C	sub	Missense	Transcriptional regulator FleQ
		mexS ←	Leu281Arg	A	C	sub	Missense	Oxidoreductase MexS
		mexT →	Gly113Asp	G	A	sub	Missense	Multidrug efflux system transcriptional regulator MexT
		tssI →	Val241Met	G	A	sub	Missense	Type VI secretion system tip protein TssI/VgrG
		clp →	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
		dipA →	Ile816Phe	A	T	sub	Missense	Phosphodiesterase DipA
		C_00471 → / ← C_00472		C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
		C_03056 → / ← C_03057		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
		C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_04423 → / ← C_04424		C	G	sub	Intergenic	nucleoside diphosphate kinase regulator/hypothetical protein
		C_02029 ← / ← C_02030		G	C	sub	Intergenic	MFS transporter/cupin domain-containing protein
D1	Mutant	*mexS ←*	Leu186Phe	G	A	sub	Missense	Oxidoreductase MexS
		phzC	Δ343 bp	wildtype		sub	Deletion	phenazine biosynthesis protein PhzC
		mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC
		D_06299 ←	Pro238His	T	C	sub	Missense	hemolysin D
		rbbA ←	Ala590Glu	G	T	sub	Missense	Ribosome-associated ATPase/putative transporter RbbA
		D_00712 ← / ← D_00713		G	C	sub	Intergenic	amino acid permease/exotoxin
		D_03694 → / ← D_03695		G	T	sub	Intergenic	transcriptional regulator/heme-binding protein
		D_03769 ← / ← D_03770		G	C	sub	Intergenic	cation-transporting P-type ATPase/acetyltransferase
		cmrA ← / → D_04509		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
		D_04739 ← / ← D_04740		G	C	sub	Intergenic	MFS transporter/HAD-IB family hydrolase
		D_01449 → / ← D_01450		C	G	sub	Intergenic	TonB-dependent siderophore receptor/protein phosphatase 2C domain-containing protein

		asnB_2 ← / ← *D_05555*		G	C	sub	Intergenic	asparagine synthase (glutamine-hydrolyzing)/hypothetical protein
		D_05635 → / → *D_05636*		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
		pncB_1 ← / ← *D_01663*		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
		– / → *fabG_2*		G	T	sub	Intergenic	–/3-ketoacyl-ACP reductase
		D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
D1.1	Revertant	*mexS* ←	Leu186Phe	G	A	sub	Missense	Oxidoreductase MexS
		mexT →	Thr19Pro	A	C	sub	Missense	Multidrug efflux system transcriptional regulator MexT
		D_04695 ←	Gly165Gly	C	G	sub	Synonymous	threonylcarbamoyl-AMP synthase
		D_03769 ← / ← *D_03770*		G	c	sub	Intergenic	cation-transporting P-type ATPase/acetyltransferase
		D_04062 ← / ← *D_04063*		G	C	sub	Intergenic	CPBP family intramembrane metalloprotease/2,3-bisphosphoglycerate-independent phosphoglycerate mutase
		cmrA ← / → *D_04509*		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
		cmrA ← / → *D_04509*		G	T	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
		D_04664 → / ← *D_04665*		A	G	sub	Intergenic	transcriptional regulator/hypothetical protein
		D_01252 ← / –		G	C	sub	Intergenic	cell division protein/–
		D_01252 ← / –		G	T	sub	Intergenic	cell division protein/–
		D_01449 → / ← *D_01450*		C	G	sub	Intergenic	TonB-dependent siderophore receptor/protein phosphatase 2C domain-containing protein
		D_05635 → / → *D_05636*		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
		pncB_1 ← / ← *D_01663*		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
		D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
E1	Mutant	*dipA* →	Asp825Asn	G	A	sub	Missense	Phosphodiesterase DipA
		mexS ←	Δ91 bp	wildtype		del	Deletion	Oxidoreductase MexS
		E_02751 ←	ArgAsp65LeuAsp	GCGCTG	GAGCTA	sub	Missense	Hypothetical protein
		29-1-day0_03854 →	ProPro817ArgThr	CGC	GGA	sub	Missense	Hypothetical protein

	ptcC	Lys428Lys	T	C	sub	Synonymous	Methyl-accepting chemotaxis protein PctC
	mexY →	Phe110Leu	TTT	CTG	sub	Missense	Multidrug efflux RND transporter permease subunit MexY
	mexY →	Ser112Ile	G	T	sub	Missense	Multidrug efflux RND transporter permease subunit MexY
	E_04243 ← / ← *E_04244*	C→G	C	G	sub	Intergenic	hypothetical protein/pyridoxal phosphate-dependent aminotransferase
	E_00789 → / ← *E_00790*	G→A	G	A	sub	Intergenic	3-hydroxyacyl-CoA dehydrogenase/transcriptional regulator
	E_04472 ← / → *E_04473*	G→T	G	T	sub	Intergenic	tRNA-Cys/hypothetical protein
	E_04568 → / ← *E_04569*	C→G	C	G	sub	Intergenic	hypothetical protein/DoxX family protein
	ahpF ← / ← *ahpC*	C→G	C	G	sub	Intergenic	alkyl hydroperoxide reductase subunit F/peroxiredoxin
	E_05349 → / → *asnB_3*	+G	GC	GGC	ins	Intergenic	hypothetical protein/asparagine synthase (glutamine-hydrolyzing)
	E_05456 → / ← *E_05457*	C→G	C	G	sub	Intergenic	aldehyde dehydrogenase (NADP(+))/Ldh family oxidoreductase
	E_00022 → / ← *E_00023*	Undefined				Undefined	LuxR family transcriptional regulator/50S ribosomal protein L36
	E_00306 → / → *E_00307*	Undefined				Undefined	hypothetical protein/valine--tRNA ligase
E1.1 Revertant	*dipA* →	Asp825Asn	G	A	sub	Missense	Phosphodiesterase DipA
	mexS ←	Δ91 bp	wildtype		del	Deletion	Oxidoreductase MexS
	mexT →	Arg48Cys	C	T	sub	Missense	Multidrug efflux system transcriptional regulator MexT
	E_04710 ←	Gln291Glu	G	C	sub	Missense	NAD(P)(+) transhydrogenase (Re/Si-specific) subunit beta
	rpoA →	Val286Leu	G	C	sub	Missense	DNA-directed RNA polymerase subunit alpha
	29-1-day0_03854	Pro818Thr	C	A	sub	Missense	Hypothetical protein
	ptcC	Lys428Lys	T	C	sub	Synonymous	Methyl-accepting chemotaxis protein PctC
	mexY →	Phe110Leu	TTT	CTG	sub	Missense	Multidrug efflux RND transporter permease subunit MexY
	mexY →	Ser112Ile	G	T	sub	Missense	Multidrug efflux RND transporter permease subunit MexY
	E_04243 ← / ← *E_04244*		C	G	sub	Intergenic	hypothetical protein/pyridoxal phosphate-dependent aminotransferase
	E_00789 → / ← *E_00790*		G	A	sub	Intergenic	3-hydroxyacyl-CoA dehydrogenase/transcriptional regulator
	E_04472 ← / → *E_04473*		G	T	sub	Intergenic	tRNA-Cys/hypothetical protein
	E_04568 → / ← *E_04569*		C	G	sub	Intergenic	hypothetical protein/DoxX family protein
	E_00022 → / ← *E_00023*	Undefined				Undefined	LuxR family transcriptional regulator/50S ribosomal protein L36

	E_00306 → / → E_00307	Undefined	Undefined	hypothetical protein/valine--tRNA ligase

Appendix - Table 20: Full list of mutations identified in ciprofloxacin evolved strains. Highlighted in yellow are the genes also found in the control strains.

Strain		Gene	Mutation	Ancestor	Strain	Type	Effect	Product
C4	Mutant	*parC* ←	Arg518Cys	G	A	sub	Missense	DNA topoisomerase 4 subunit A
		chpA ←	Gln1137*	G	A	sub	Stop gain	Chemotaxis signal transduction system protein ChpA
		C_01688 ←	Thr287fs	G	GTC	ins	Frameshift	LTA synthase family protein
		fliG ←	Leu160fs	ACGATATCCAGG	A	del	Frameshift	Flagellar motor switch protein FliG
		gyrB ←	Ser466Tyr	G	T	sub	Missense	DNA gyrase subunit B
		hexR →	Ser275_Arg277del	AGCGCAGCCT	A	del	Deletion	Transcriptional regulator HexR
		gyrA →	Thr83Ala	A	G	sub	Missense	DNA gyrase subunit A
		rplC ←	His68Tyr	G	A	sub	Missense	50S ribosomal protein L3
		C_00129 →	Pro22Gln	C	A	sub	Missense	Quinone oxidoreductase
		clp →	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
		nfxB ←	Δ741 bp	wildtype	Δ741 bp	sub	Deletion	Efflux pump transcriptional repressor NfxB
		phzF	Δ464 bp	wildtype	Δ464 bp	sub	Deletion	Phenazine biosynthesis protein PhzF
		C_05880 →	Ala402Ala	C	G	sub	Synonymous	MFS transporter
		C_05965 ←	Pro225Ala	C	G	sub	Missense	Erythronate-4-phosphate dehydrogenase
		tssI →	Val241Met	G	A	sub	Missense	Type VI secretion system tip protein TssI/VgrG
		C_00343 → / ← *C_00344*		C	A	sub	Intergenic	lipase chaperone/DoxX family protein
		C_00471 → / ← *C_00472*		C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
		C_03056 → / ← *C_03057*		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
		C_03413 → / ← *C_03414*		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03413 → / ← *C_03414*		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_01521 → / → *C_01522*		G	T	sub	Intergenic	hypothetical protein/secretion protein

	C_01796 ← / ← lpdA_2		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
	C_01796 ← / ← lpdA_2		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
	C_06133 → / –		C	A	sub	Intergenic	hypothetical protein/–
C4.1 Revertant	*parC ←*	Arg518Cys	G	A	sub	Missense	DNA topoisomerase 4 subunit A
	hisF ←	Gly256Arg	C	G	sub	Missense	Imidazole glycerol phosphate synthase subunit HisF
	chpA ←	Gln1137*	G	A	sub	Stop gain	Chemotaxis signal transduction system protein ChpA
	C_01688 ←	Thr287fs	G	GTC	ins	Frameshift	LTA synthase family protein
	fliG ←	Leu160fs	ACGATATCCAGG	A	del	Frameshift	Flagellar motor switch protein FliG
	gyrB ←	Ser466Tyr	G	T	sub	Missense	DNA gyrase subunit B
	hexR →	Ser275_Arg277del	AGCGCAGCCT	A	sub	Deletion	Transcriptional regulator HexR
	nfxB ←	Δ741 bp	wildtype	Δ741 bp	sub	Deletion	Efflux pump transcriptional repressor NfxB
	mexC →	Tyr217*	C	A	sub	Stop gain	Multidrug efflux RND transporter periplasmic adaptor subunit MexC
	gyrA →	Thr83Ala	A	G	sub	Missense	DNA gyrase subunit A
	rplC ←	His68Tyr	G	A	sub	Missense	50S ribosomal protein L3
	C_06081–C_06089	Δ8,095 bp	wildtype		sub	Deletion	*C_06081, C_06082, C_06083, C_06084, C_06085, C_06086, C_06087, C_06088, C_06089*
	C_06121–C_06123	Δ3,225 bp	wildtype		sub	Deletion	C_06121, C_06122, C_06123
	nirB →	Gly475Gly	G	C	sub	Synonymous	Nitrite reductase large subunit NirB
	pdxB ←	Pro225Ala	C	G	sub	Missense	4-phosphoerythronate dehydrogenase PdxB"
	11-2-day0_02734-11-2-day0_02777	Δ48,799 bp	wildtype		del	Deletion	43 genes
	clp →	Arg214Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
	tssI →	Val241Met	G	A	sub	Missense	Type VI secretion system tip protein TssI/VgrG
	C_03056 → / ← C_03057		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
	C_03407 → / ← C_03408		G	C	sub	Intergenic	2-hydroxyacid dehydrogenase/hypothetical protein

	C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	ompR → / → C_03691		G	C	sub	Intergenic	two-component system response regulator OmpR/two-component sensor histidine kinase
	hrpA → / ← C_04796		G	T	sub	Intergenic	ATP-dependent RNA helicase HrpA/alkaline phosphatase
	C_01253 → / ← C_01254		G	C	sub	Intergenic	acyltransferase/hypothetical protein
	C_01796 ← / ← lpdA_2		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
	C_05671 ← / ← narI		C	G	sub	Intergenic	peptidyl-prolyl cis-trans isomerase/respiratory nitrate reductase subunit gamma
	C_01882 → / ← C_01883		G	C	sub	Intergenic	isopenicillin N synthase family oxygenase/monooxygenase
	C_02029 ← / ← C_02030		G	C	sub	Intergenic	MFS transporter/cupin domain-containing protein
	– / → C_02105		C	G	sub	Intergenic	–/amino acid permease
	– / → C_02105		C	G	sub	Intergenic	–/amino acid permease
D2 Mutant	*D_00441 →*	Glu225fs	A	AGC	ins	Frameshift	ABC transporter substrate-binding protein
	relA →	His442Tyr	C	T	sub	Missense	GTP diphosphokinase
	spoT ←	His472fs	TTGAGCGCATG	T	del	Frameshift	bifunctional GTP diphosphokinase/guanosine-3'%2C5'-bis pyrophosphate 3'-pyrophosphohydrolase
	nfxB ←	Arg23fs	GTCGCTCGC	G	del	Frameshift	Efflux pump transcriptional repressor NfxB
	mexC →	Arg36fs	TGC	T	del	Frameshift	Multidrug efflux RND transporter periplasmic adaptor subunit MexC
	arnC →	Ala263_Asn267 del	CCGCCTGGGC CGGCAA	C	sub	Deletion	Undecaprenyl-phosphate 4-deoxy-4-formamido-L-arabinose transferase
	D_04260 ←	Met460fs	C	CA	ins	Frameshift	bifunctional prephenate dehydrogenase/3-phosphoshikimate 1-carboxyvinyltransferase
	D_04260 ←	Arg457fs	C	CGG	ins	Frameshift	bifunctional prephenate dehydrogenase/3-phosphoshikimate 1-carboxyvinyltransferase
	gyrA ←	Asp87Asn	C	T	sub	Missense	DNA gyrase subunit A
	D_04443 →	Thr59_Ala61dup	A	ATCGCC ACCG	sub	Insertion	Acyl-CoA thioesterase
	rbbA ←	Ala590Glu	G	T	sub	Missense	Ribosome-associated ATPase/putative transporter RbbA

	D_04062 ← / ← D_04063		G	C	sub	Intergenic	CPBP family intramembrane metalloprotease/2,3-bisphosphoglycerate-independent phosphoglycerate mutase
	D_04205 → / → D_04206		C	A	sub	Intergenic	sulfite exporter TauE/SafE family protein/M48 family peptidase
	cmrA ← / → D_04509		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
	cmrA ← / → D_04509		G	T	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
	D_01449 → / ← D_01450		C	G	sub	Intergenic	TonB-dependent siderophore receptor/protein phosphatase 2C domain-containing protein
	asnB_2 ← / ← D_05555		G	C	sub	Intergenic	asparagine synthase (glutamine-hydrolyzing)/hypothetical protein
	D_05635 → / → D_05636		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
	pncB_1 ← / ← D_01663		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
	– / → fabG_2		G	T	sub	Intergenic	–/3-ketoacyl-ACP reductase
	D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
D2.1 Revertant	*D_00441 →*	Glu225fs	A	AGC	ins	Frameshift	ABC transporter substrate-binding protein
	relA →	His442Tyr	C	T	sub	Missense	GTP diphosphokinase
	spoT ←	His472fs	TTGAGCGCATG	T	del	Frameshift	Bifunctional GTP diphosphokinase/guanosine-3'%2C5'-bis pyrophosphate 3'-pyrophosphohydrolase
	nfxB ←	Arg23fs	GTCGCTCGC	G	del	Frameshift	Efflux pump transcriptional repressor NfxB
	mexC →	Arg36fs	TGC	T	del	Frameshift	Multidrug efflux RND transporter periplasmic adaptor subunit MexC
	arnC →	Ala263_Asn267 del	CCGCCTGGGC CGGCAA	C	del	Deletion	Undecaprenyl-phosphate 4-deoxy-4-formamido-L-arabinose transferase
	D_04260 ←	Met460fs	C	CA	ins	Frameshift	Bifunctional prephenate dehydrogenase/3-phosphoshikimate 1-carboxyvinyltransferase
	D_04260 ←	Arg457fs	C	CGG	ins	Frameshift	Bifunctional prephenate dehydrogenase/3-phosphoshikimate 1-carboxyvinyltransferase
	gyrA ←	Asp87Asn	C	T	sub	Missense	DNA gyrase subunit A
	D_04443 →	Thr59_Ala61dup	A	ATCGCC ACCG	sub	Insertion	Acyl-CoA thioesterase
	rbbA ←	Ala590glu	G	T	sub	Missense	Ribosome-associated ATPase/putative transporter RbbA
	D_03551 →	Ala18Asp	C	A	sub	Missense	4-deoxy-4-formamido-L-arabinose-phospho-UDP deformylase

		mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC
		D_03404 → / –		C	A	sub	Intergenic	LysE family translocator/–
		D_04062 ← / ← *D_04063*		G	C	sub	Intergenic	CPBP family intramembrane metalloprotease/2,3-bisphosphoglycerate-independent phosphoglycerate mutase
		D_01449 → / ← *D_01450*		C	G	sub	Intergenic	TonB-dependent siderophore receptor/protein phosphatase 2C domain-containing protein
		pncB_1 ← / ← *D_01663*		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
		urtA ← / ← *D_01971*		C	A	sub	Intergenic	urea ABC transporter substrate-binding protein/MarC family protein
		D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
D3	Mutant	*D_00441* →	Ala227fs	C	CGAGCT	ins	Frameshift	ABC transporter substrate-binding protein
		D_02366 →	Ala176_Arg177insArgAla	G	GGCCCGC	sub	Insertion	Histidine-tRNA ligase
		nfxB ←	Arg163Gln	C	T	sub	Missense	Efflux pump transcriptional repressor NfxB
		gyrB ←	Ser466Phe	G	A	sub	Missense	DNA gyrase subunit B
		edd →	Ile530fs	CCATCGCCGGCG	C	del	Frameshift	Phosphogluconate dehydratase
		D_06299 ←	Pro238His	C	A	sub	Missense	hemolysin D
		mreC →	Leu29Pro	T	C	sub	Missense	Rod shape determining protein MreC
		rbbA ←	Ala590Glu	G	T	sub	Missense	Ribosome-associated ATPase/putative transporter RbbA
		cmrA ← / → *D_04509*		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
		cmrA ← / → *D_04509*		G	T	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
		D_01252 ← / –		G	T	sub	Intergenic	cell division protein/–
		D_05221 → / → *tsaB*		C	G	sub	Intergenic	adenylate kinase/tRNA (adenosine(37)-N6)-threonylcarbamoyltransferase complex dimerization subunit type 1 TsaB
		D_01449 → / ← *D_01450*		C	G	sub	Intergenic	TonB-dependent siderophore receptor/protein phosphatase 2C domain-containing protein
		D_05635 → / → *D_05636*		G	C	sub	Intergenic	hypothetical protein/hypothetical protein

		pncB_1 ← / ← *D_01663*		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
		– / → *fabG_2*		G	T	sub	Intergenic	–/3-ketoacyl-ACP reductase
		D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
D3.1	Revertant	*parS* →	Arg385His	G	A	sub	Missense	Histidine kinase
		nfxB ←	Arg163Gln	C	T	sub	Missense	Efflux pump transcriptional repressor NfxB
		gyrB ←	Ser466Phe	G	A	sub	Missense	DNA gyrase subunit B
		rbbA ←	Ala590Glu	G	T	sub	Missense	Ribosome-associated ATPase/putative transporter RbbA
		D_05635 → / → *D_05636*		G	C	sub	Intergenic	Hypothetical protein/Hypothetical protein
		pncB_1 ← / ← *D_01663*		G	C	sub	Intergenic	Nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
		D_05949 ← / → *D_05950*		G	A	sub	Intergenic	Hypothetical protein/Hypothetical protein
		D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
E2	Mutant	*nfxB* ←	His109fs	C	CGGGT	ins	Frameshift	Efflux pump transcriptional repressor NfxB
		pilV ←	Cys164fs	GGCGTTGACGCA	G	del	Frameshift	Type 4a pilus minor pilin PilV
		gyrB ←	Ser466Tyr	G	T	sub	Missense	DNA gyrase subunit B
		E_04760 ←	Ala30Glu	C	A	sub	Missense	BMP family ABC transporter substrate-binding protein
		E_05464 ←	Pro25Ala	C	A	sub	Missense	Hypothetical protein
		E_02751 ←	ArgAsp65LeuAsp	GTCGC	ATCGA	sub	Missense	Hypothetical protein
		E_03854 →	ProPro817ArgThr	CGC	GGA	sub	Missense	Hypothetical protein
		ptcC ←	Lys428Lys	T	C	sub	Synonymous	Methyl-accepting chemotaxis protein PctC
		mexY →	Phe110Leu	TTT	CTG	sub	Missense	Multidrug efflux RND transporter permease subunit MexY
		mexY →	Ser112Ile	G	T	sub	Missense	Multidrug efflux RND transporter permease subunit MexY
		E_00309 → / → *E_00310*		G	C	sub	Intergenic	ABC transporter substrate-binding protein/ABC transporter permease
		E_03460 ← / → *E_03461*		A	G	sub	Intergenic	hydrolase/amidohydrolase

	E_04243 ← / ← E_04244		C	G	sub	Intergenic	hypothetical protein/pyridoxal phosphate-dependent aminotransferase
	E_04568 → / ← E_04569		C	G	sub	Intergenic	hypothetical protein/DoxX family protein
	ahpF ← / ← ahpC		C	G	sub	Intergenic	alkyl hydroperoxide reductase subunit F/peroxiredoxin
	E_05349 → / → asnB_3		GC	GGC	ins	Intergenic	hypothetical protein/asparagine synthase (glutamine-hydrolyzing)
	E_05456 → / ← E_05457		A	G	sub	Intergenic	aldehyde dehydrogenase (NADP(+))/Ldh family oxidoreductase
	E_05464 ← / → E_05465		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
	E_00022 → / ← E_00023	Undefined				Undefined	LuxR family transcriptional regulator/50S ribosomal protein L36
	E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase
	E_01907 → / → E_01908	Undefined				Undefined	sodium:alanine symporter family protein/asparaginase
E2.1 Revertant	*nfxB ←*	His109fs	C	CGGGT	ins	Frameshift	Efflux pump transcriptional repressor NfxB
	mexC →	Arg36fs	TGC	T	del	Frameshift	Multidrug efflux RND transporter periplasmic adaptor subunit MexC
	pilV ←	Cys164fs	GGCGTTGACGCA	G	del	Frameshift	Type 4a pilus minor pilin PilV
	gyrB ←	Ser466Tyr	G	T	sub	Missense	DNA gyrase subunit B
	E_03887 →	Ala163Glu	C	A	sub	Missense	TetR family transcriptional regulator
	E_04760 ←	Ala30Glu	C	A	sub	Missense	BMP family ABC transporter substrate-binding protein
	E_02751 ←	ArgAsp65LeuAsp	GTCGC	ATCGA	sub	Missense	Hypothetical protein
	ptcC	Lys428Lys	T	C	sub	Synonymous	Methyl-accepting chemotaxis protein PctC
	mexY →	Phe110Leu	TTT	CTG	sub	Missense	Multidrug efflux RND transporter permease subunit MexY
	mexY →	Ser112Ile	G	T	sub	Missense	Multidrug efflux RND transporter permease subunit MexY
	E_00309 → / → E_00310		G	C	sub	Intergenic	ABC transporter substrate-binding protein/ABC transporter permease
	E_02979 → / → gloA_1		CC	GG	sub	Intergenic	autotransporter domain-containing protein/lactoylglutathione lyase
	E_03460 ← / → E_03461		A	G	sub	Intergenic	hydrolase/amidohydrolase

E_04243 ← / ← E_04244		C	G	sub	Intergenic	hypothetical protein/pyridoxal phosphate-dependent aminotransferase
E_04472 ← / → E_04473		G	T	sub	Intergenic	tRNA-Cys/hypothetical protein
ahpF ← / ← ahpC		C	G	sub	Intergenic	alkyl hydroperoxide reductase subunit F/peroxiredoxin
E_04981 → / → E_04982		C	G	sub	Intergenic	hydrolase/OsmC family peroxiredoxin
E_05464 ← / → E_05465		A	C	sub	Intergenic	hypothetical protein/hypothetical protein
E_00022 → / ← E_00023	Undefined				Undefined	LuxR family transcriptional regulator/50S ribosomal protein L36
E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase

Appendix - Table 21: : Mutations identified in control strains. The mutations shown are those found only in the control strains.

Strain	Gene	Mutation	Ancestor	Strain	Type	Effect	Product
Strain C - Replicate 1 Chloramphenicol Control	C_00129 →	Pro22Gln	C	A	sub	Missense	quinone oxidoreductase
	C_00175 →	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
	C_03056 → / ← C_03057		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
	C_03174 →		GGC	GC	del	Frameshift	peptidoglycan-binding protein LysM
	C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03924 ←	Asn129Asn	A	G	sub	Synonymous	hypothetical protein
	C_01253 → / ← C_01254		G	C	sub	Intergenic	acyltransferase/hypothetical protein
	C_01796 ← / ← lpdA_2		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
	C_01796 ← / ← lpdA_2		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
	C_02029 ← / ← C_02030		G	C	sub	Intergenic	MFS transporter/cupin domain-containing protein
	C_05965 ←	Pro225Ala	G	C	sub	Missense	erythronate-4-phosphate dehydrogenase
	C_06112 →	Val241Met	G	A	sub	Missense	hypothetical protein
	C_02375 ←	Gly275Ser	C	T	sub	Missense	chemotaxis response regulator protein-glutamate methylesterase
Strain C - Replicate 2 Chloramphenicol	C_00095 → / → nuoK		G	C	sub	Intergenic	NADH-quinone oxidoreductase subunit J/NADH-quinone oxidoreductase subunit NuoK
	C_00129 →	Pro22Gln	C	A	sub	Missense	quinone oxidoreductase
	C_00471 → / ← C_00472		C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
	C_03022 ←	Cys87*	G	T	sub	Missense	type 4 fimbrial biogenesis protein PilX
	C_03056 → / ← C_03057		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase

	C_03356 ←	Ala231Val	G	A	sub	Missense	LuxR family transcriptional regulator
	C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_00897 →	Ile816Phe	A	T	sub	Missense	EAL domain-containing protein
	C_01253 → / ← C_01254		G	C	sub	Intergenic	acyltransferase/hypothetical protein
	C_01796 ← / ← lpdA_2		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
	C_01796 ← / ← lpdA_2		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
	C_02029 ← / ← C_02030		G	C	sub	Intergenic	MFS transporter/cupin domain-containing protein
	C_06112 →	Val241Met	G	A	sub	Missense	hypothetical protein
Strain C - Replicate 3 Chloramphenicol Control	*C_00175 →*	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
	C_03056 → / ← C_03057		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
	C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03593 ←	Ala866Ala	C	G	sub	Missense	Fe/S-dependent 2-methylisocitrate dehydratase AcnD
	C_05965 ←	Pro225Ala	G	C	sub	Missense	erythronate-4-phosphate dehydrogenase
	C_02134 →	Gly173Asp	G	A	sub	Missense	diguanylate cyclase
	C_06112 →	Val241Met	G	A	sub	Missense	hypothetical protein
	C_02551 ←	Pro146Pro	G	C	sub	Missense	hypothetical protein
Strain C - Replicate Ciprofloxacin	*C_00175 →*	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
	C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	hrpA → / ← C_04796		G	T	sub	Intergenic	ATP-dependent RNA helicase HrpA/alkaline phosphatase

	C_05965 ←	Pro225Ala	G	C	sub	Missense	erythronate-4-phosphate dehydrogenase
	C_06112 →	Val241Met	G	A	sub	Missense	hypothetical protein
Strain C - Replicate 2 Ciprofloxacin Control	*C_00471* → / ← *C_00472*		C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
	pilB ←	Asp388Ala	T	G	sub	Missense	type IV-A pilus assembly ATPase PilB
	C_03056 → / ← *C_03057*		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
	C_03356 ←	Ala231Val	G	A	sub	Missense	LuxR family transcriptional regulator
	C_03413 → / ← *C_03414*		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03413 → / ← *C_03414*		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
	C_03472 ← / → *C_03473*		C	G	sub	Intergenic	hypothetical protein/response regulator transcription factor
	C_03472 ← / → *C_03473*		C	A	sub	Intergenic	hypothetical protein/response regulator transcription factor
	C_03472 ← / → *C_03473*		C	A	sub	Intergenic	hypothetical protein/response regulator transcription factor
	C_03472 ← / → *C_03473*		C	A	sub	Intergenic	hypothetical protein/response regulator transcription factor
	ompR → / → *C_03691*		G	C	sub	Intergenic	two-component system response regulator OmpR/two-component sensor histidine kinase
	C_04051 →	Glu297Lys	G	A	sub	Missense	bifunctional diguanylate cyclase/phosphodiesterase
	C_00897 →	Ile816Phe	A	T	sub	Missense	EAL domain-containing protein
	sdiA →	Asp81Glu	T	A	sub	Missense	transcriptional regulator SdiA
	C_01253 → / ← *C_01254*		G	C	sub	Intergenic	acyltransferase/hypothetical protein
	C_06112 →	Val241Met	G	A	sub	Missense	hypothetical protein
Strain C - [illegible] Ciprofloxacin	*C_00095* → / → *nuoK*		G	C	sub	Intergenic	NADH-quinone oxidoreductase subunit J/NADH-quinone oxidoreductase subunit NuoK
	C_00129 →	Pro22Gln	C	A	sub	Missense	quinone oxidoreductase
	C_00175 →	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
	C_03056 → / ← *C_03057*		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase

		C_03356 ←	Arg231Val	G	A	sub	Missense	LuxR family transcriptional regulator
		C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		ompR → / → C_03691		G	C	sub	Intergenic	two-component system response regulator OmpR/two-component sensor histidine kinase
		C_04051 →	Thr143Pro	A	C	sub	Missense	bifunctional diguanylate cyclase/phosphodiesterase
		C_00897 →	Ile816Phe	A	T	sub	Missense	EAL domain-containing protein
		sdiA →	Ile188Ser	T	G	sub	Missense	transcriptional regulator SdiA
		C_01253 → / ← C_01254		G	C	sub	Intergenic	acyltransferase/hypothetical protein
		C_06019 →	Gly91Gly	C	G	sub	Missense	phosphonate metabolism protein PhnP
		C_06112 →	Val241Met	G	A	sub	Missense	hypothetical protein
Strain C - Replicate 1	Reversion Control	*C_00095 → / → nuoK*		G	C	sub	Intergenic	NADH-quinone oxidoreductase subunit J/NADH-quinone oxidoreductase subunit NuoK
		C_00129 →	Pro22Gln	C	A	sub	Missense	quinone oxidoreductase
		C_00175 →	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
		C_00471 → / ← C_00472		C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
		pilB ←	Gly395Asp	C	T	sub	Intergenic	type IV-A pilus assembly ATPase PilB
		C_03056 → / ← C_03057		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
		C_03356 ←	Ala231Val	G	A	sub	Missense	LuxR family transcriptional regulator
		C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_04051 →	Asp578Asn	G	A	sub	Intergenic	bifunctional diguanylate cyclase/phosphodiesterase
		C_00897 →	Ile816Phe	A	T	sub	Intergenic	EAL domain-containing protein
		sdiA →	Ala120Glu	C	A	sub	Intergenic	transcriptional regulator SdiA
		C_01253 → / ← C_01254		G	C	sub	Intergenic	acyltransferase/hypothetical protein

		C_01430 ←	Ala209Gly	G	C	sub	Missense	LysR family transcriptional regulator
		C_05196 ←		C	CCACCGCTTCGGT	ins	Insertion	LysR family transcriptional regulator
		C_01595 →	Gly475Gly	G	C	sub	Synonymous	NAD(P)/FAD-dependent oxidoreductase
		C_02029 ← / ← *C_02030*		G	C	sub	Intergenic	MFS transporter/cupin domain-containing protein
		C_05965 ←	Pro225Ala	G	C	sub	Intergenic	erythronate-4-phosphate dehydrogenase
		C_06112 →	Val241Met	G	A	sub	Intergenic	hypothetical protein
Strain C - Replicate 2	Reversion Control	*C_00129* →	Pro22Gln	C	A	sub	Missense	quinone oxidoreductase
		C_00175 →	Arg219Leu	G	T	sub	Missense	ATP-dependent Clp protease ATP-binding subunit
		pilB ←	Thr278Pro	T	G	sub	Missense	type IV-A pilus assembly ATPase PilB
		C_03056 → / ← *C_03057*		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
		C_03356 ←	Ala231Val	G	A	sub	Missense	LuxR family transcriptional regulator
		C_03413 → / ← *C_03414*		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03413 → / ← *C_03414*		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03472 ← / → *C_03473*		C	G	sub	Intergenic	hypothetical protein/response regulator transcription factor
		C_03472 ← / → *C_03473*		C	A	sub	Intergenic	hypothetical protein/response regulator transcription factor
		C_00897 →	Ile816Phe	A	T	sub	Missense	EAL domain-containing protein
		sdiA →	Glu110Val	A	T	sub	Missense	transcriptional regulator SdiA
		C_04411 → / → *C_04412*		G	C	sub	Intergenic	ammonium transporter/YjbQ family protein
		C_01253 → / ← *C_01254*		G	C	sub	Intergenic	acyltransferase/hypothetical protein
		C_01521 → / → *C_01522*		G	T	sub	Intergenic	hypothetical protein/secretion protein
		C_01796 ← / ← *lpdA_2*		C	A	sub	Intergenic	ADP-forming succinate--CoA ligase subunit beta/dihydrolipoyl dehydrogenase
		C_05814 → / → *C_05815*		C	A	sub	Intergenic	YheV family putative metal-binding protein/radical SAM protein

		C_05965 ←	Pro225Ala	G	C	sub	Missense	erythronate-4-phosphate dehydrogenase
		C_02159 ←	Arg157Gln	C	T	sub	Missense	sigma-54-dependent Fis family transcriptional regulator
		C_06112 →	Val241Met	G	A	sub	Missense	hypothetical protein
Strain C - Replicate 3	Reversion Control	*C_00471 → / ← C_00472*		C	G	sub	Intergenic	glycerophosphodiester phosphodiesterase/Si-specific NAD(P)(+) transhydrogenase
		pilB ←	Thr514Pro	T	G	sub	Missense	type IV-A pilus assembly ATPase PilB
		C_03056 → / ← C_03057		G	A	sub	Intergenic	tRNA-Thr/carboxylating nicotinate-nucleotide diphosphorylase
		C_03356 ←	Ala231Val	G	A	sub	Missense	LuxR family transcriptional regulator
		C_03413 → / ← C_03414		C	G	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03413 → / ← C_03414		T	C	sub	Intergenic	cupin domain-containing protein/GntR family transcriptional regulator
		C_03850 →	Δ6 bp	wildtype		del	Deletion	FHA domain-containing protein
		C_04051 →	Phe254Leu	C	A	sub	Missense	bifunctional diguanylate cyclase/phosphodiesterase
		C_00897 →	Ile816Phe	A	T	sub	Missense	EAL domain-containing protein
		hisF ←	Gly256Arg	C	G	sub	Missense	imidazole glycerol phosphate synthase subunit HisF
		sdiA →	Ile188Ser	T	G	sub	Missense	transcriptional regulator SdiA
		C_01253 → / ← C_01254		G	C	sub	Intergenic	acyltransferase/hypothetical protein
		C_01281 → / → C_01282		C	A	sub	Intergenic	adenosylhomocysteinase/bifunctional (p)ppGpp synthetase/guanosine-3',5'-bis(diphosphate) 3'-pyrophosphohydrolase
		C_06112 →	Val241Met	G	A	sub	Missense	hypothetical protein
Strain D - Replicate 1	Chloramphenicol Control	*D_03310 ← / ← D_03311*		G	A	sub	Intergenic	HAMP domain-containing protein/chemotaxis response regulator protein-glutamate methylesterase
		D_03404 → / –		G	T	sub	Intergenic	LysE family translocator/–
		D_03694 → / ← D_03695		G	T	sub	Intergenic	transcriptional regulator/heme-binding protein
		D_03769 ← / ← D_03770		G	C	sub	Intergenic	cation-transporting P-type ATPase/acetyltransferase
		D_04062 ← / ← D_04063		G	C	sub	Intergenic	CPBP family intramembrane metalloprotease/2,3-bisphosphoglycerate-independent phosphoglycerate mutase

	D_04205 → / → D_04206		C	A	sub	Intergenic	sulfite exporter TauE/SafE family protein/M48 family peptidase
	cmrA ← / → D_04509		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
	cmrA ← / → D_04509		G	T	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
	D_01252 ← / –		G	C	sub	Intergenic	cell division protein/–
	D_01252 ← / –		G	T	sub	Intergenic	cell division protein/–
	D_01449 → / ← D_01450		C	G	sub	Intergenic	TonB-dependent siderophore receptor/protein phosphatase 2C domain-containing protein
	D_05635 → / → D_05636		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
	mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC
	pncB_1 ← / ← D_01663		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
	D_05743 ←	Val292Ala	A	G	sub	Missense	NAD(P)(+) transhydrogenase (Re/Si-specific) subunit beta
	D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
Strain D - Replicate 2 Chloramphenicol Control	*D_02836 ←*	Ala590Glu	G	T	sub	Missense	ABC transporter ATP-binding protein/permease
	D_03352 →	Pro198Pro	C	A	sub	Synonymous	DotU family type IV/VI secretion system protein
	D_03404 → / –		G	T	sub	Intergenic	LysE family translocator/–
	D_00712 ← / ← D_00713		G	C	sub	Intergenic	amino acid permease/exotoxin
	D_03694 → / ← D_03695		G	T	sub	Intergenic	transcriptional regulator/heme-binding protein
	D_03694 → / ← D_03695		G	T	sub	Intergenic	transcriptional regulator/heme-binding protein
	D_03890 →	Δ54 bp	wildtype		del	Deletion	bifunctional diguanylate cyclase/phosphodiesterase
	D_04062 ← / ← D_04063		G	C	sub	Intergenic	CPBP family intramembrane metalloprotease/2,3-bisphosphoglycerate-independent phosphoglycerate mutase
	D_04215 ← / ← asd		C	G	sub	Intergenic	aspartate-semialdehyde dehydrogenase/aspartate-semialdehyde dehydrogenase
	cmrA ← / → D_04509		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase

	D_01252 ← / –		G	C	sub	Intergenic	cell division protein/–
	D_01252 ← / –		G	T	sub	Intergenic	cell division protein/–
	asnB_2 ← / ← D_05555		G	C	sub	Intergenic	asparagine synthase (glutamine-hydrolyzing)/hypothetical protein
	D_05635 → / → D_05636		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
	mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC
	pncB_1 ← / ← D_01663		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
	– / → D_05959		T	C	sub	Intergenic	–/hypothetical protein
	– / → fabG_2		G	T	sub	Intergenic	–/3-ketoacyl-ACP reductase
	– / → D_06289		C	G	sub	Intergenic	–/hypothetical protein
	D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
Strain D - Replicate 3	Chloramphenicol Control	*D_06319 ← / –*		C	G	sub	Intergenic	hypothetical protein/–
		D_06319 ← / –		G	T	sub	Intergenic	hypothetical protein/–
		D_02836 ←	Ala590Glu	G	T	sub	Missense	ABC transporter ATP-binding protein/permease
		D_03551 →	Ala18Asp	C	A	sub	Missense	4-deoxy-4-formamido-L-arabinose-phospho-UDP deformylase
		D_03769 ← / ← D_03770		G	C	sub	Intergenic	cation-transporting P-type ATPase/acetyltransferase
		D_03890 →	Gln132*	C	T	sub	Stop Gain	bifunctional diguanylate cyclase/phosphodiesterase
		D_04134 → / –		C	G	sub	Intergenic	poly(3-hydroxyalkanoate) granule-associated protein PhaI/–
		D_04205 → / → D_04206		C	A	sub	Intergenic	sulfite exporter TauE/SafE family protein/M48 family peptidase
		cmrA ← / → D_04509		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
		cmrA ← / → D_04509		G	T	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
		D_01252 ← / –		G	T	sub	Intergenic	cell division protein/–
		D_05635 → / → D_05636		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
		mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC

		pncB_1 ← / ← D_01663		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
		D_05743 ←	Val292Ala	A	G	sub	Missense	NAD(P)(+) transhydrogenase (Re/Si-specific) subunit beta
		– / → fabG_2		G	T	sub	Intergenic	–/3-ketoacyl-ACP reductase
		D_02024 ← / –		G	C	sub	Intergenic	hypothetical protein/–
		D_06299 ←	Pro238His	G	T	sub	Missense	hemolysin D
		D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
Strain D - Replicate 1	Ciprofloxacin Control	*D_06319 ← / –*		C	G	sub	Intergenic	hypothetical protein/–
		D_02836 ←	Ala590Glu	G	T	sub	Missense	ABC transporter ATP-binding protein/permease
		D_03352 →	Pro198Pro	C	A	sub	Missense	DotU family type IV/VI secretion system protein
		D_03404 → / –		G	T	sub	Intergenic	LysE family translocator/–
		D_03551 →	Ala18Asp	C	A	sub	Missense	4-deoxy-4-formamido-L-arabinose-phospho-UDP deformylase
		cmrA ← / → D_04509		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
		cmrA ← / → D_04509		G	T	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
		D_04810 → / ← D_04811		A	G	sub	Intergenic	ATP-dependent Clp protease proteolytic subunit/metal-dependent hydrolase
		asnB_2 ← / ← D_05555		G	C	sub	Intergenic	asparagine synthase (glutamine-hydrolyzing)/hypothetical protein
		D_05635 → / → D_05636		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
		mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC
		pncB_1 ← / ← D_01663		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
		– / → fabG_2		G	T	sub	Intergenic	–/3-ketoacyl-ACP reductase
		D_06299 ←	Pro238His	G	T	sub	Missense	hemolysin D
		D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
Strain [illegible]	Ciprofl[illegible]	*D_02836 ←*	Ala590Glu	G	T	sub	Missense	ABC transporter ATP-binding protein/permease
		– / → D_02990		A	G	sub	Intergenic	–/TAXI family TRAP transporter solute-binding subunit

D_03309 ←	Δ12 bp	wildtype		del	Deletion	hypothetical protein
D_03352 →	Pro198Pro	C	A	sub	Missense	DotU family type IV/VI secretion system protein
D_03404 → / –		G	T	sub	Intergenic	LysE family translocator/–
D_00561 ←	Ile21Thr	A	G	sub	Missense	LysR family transcriptional regulator
D_00712 ← / ← D_00713		G	C	sub	Intergenic	amino acid permease/exotoxin
D_03694 → / ← D_03695		T	T	sub	Intergenic	transcriptional regulator/heme-binding protein
D_04134 → / –		A	G	sub	Intergenic	poly(3-hydroxyalkanoate) granule-associated protein PhaI/–
cmrA ← / → D_04509		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
cmrA ← / → D_04509		G	T	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
D_01252 ← / –		G	C	sub	Intergenic	cell division protein/–
D_01252 ← / –		G	T	sub	Intergenic	cell division protein/–
crp →		ACA	A	del	Fremshift	cAMP-activated global transcriptional regulator CRP
D_01449 → / ← D_01450		C	G	sub	Intergenic	TonB-dependent siderophore receptor/protein phosphatase 2C domain-containing protein
D_05635 → / → D_05636		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC
pncB_1 ← / ← D_01663		G	G	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
D_05743 ←	Val292Ala	A	G	sub	Missense	NAD(P)(+) transhydrogenase (Re/Si-specific) subunit beta
– / → D_05959		T	C	sub	Intergenic	–/hypothetical protein
– / → fabG_2		G	T	sub	Intergenic	–/3-ketoacyl-ACP reductase
– / → D_06289		C	G	sub	Intergenic	–/hypothetical protein
D_06299 ←	Pro238His	G	T	sub	Intergenic	hemolysin D
D_05705 →	Undefined				Undefined	MFS transporter
D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase

Strain D - Replicate 3	Ciprofloxacin Control	*D_06319 ← / –*		C	G	sub	Intergenic	hypothetical protein/–
		D_06319 ← / –		G	T	sub	Intergenic	hypothetical protein/–
		D_02836 ←	Ala590Glu	G	T	sub	Missense	ABC transporter ATP-binding protein/permease
		D_03352 →	Pro198Pro	C	A	sub	Synonymous	DotU family type IV/VI secretion system protein
		D_03404 → / –		G	T	sub	Intergenic	LysE family translocator/–
		D_03890 →		T	A	sub	Intergenic	bifunctional diguanylate cyclase/phosphodiesterase
		D_05705 →	Ala10Ala	G	T	sub	Synonymous	MFS transporter
		– / → fabG_2		G	T	sub	Intergenic	–/3-ketoacyl-ACP reductase
		D_02024 ← / –		G	C	sub	Intergenic	hypothetical protein/–
		sdiA ←	Thr211Met	G	A	sub	Missense	transcriptional regulator SdiA
		D_02065 ← / ← D_02066		G	C	sub	Intergenic	sel1 repeat family protein/glutamate-1-semialdehyde 2%2C1-aminomutase
		D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
Strain D - Replicate 1	Reversion Control	*D_03310 ← / ← D_03311*		G	A		Intergenic	HAMP domain-containing protein/chemotaxis response regulator protein-glutamate methylesterase
		D_00561 ←	Δ12 bp	wildtype		del	Deletion	LysR family transcriptional regulator
		D_03694 → / ← D_03695		G	T	sub	Intergenic	transcriptional regulator/heme-binding protein
		D_04062 ← / ← D_04063		G	C	sub	Intergenic	CPBP family intramembrane metalloprotease/2,3-bisphosphoglycerate-independent phosphoglycerate mutase
		D_04205 → / → D_04206		C	A	sub	Intergenic	sulfite exporter TauE/SafE family protein/M48 family peptidase
		D_05635 → / → D_05636		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
		D_01536 ← / ← D_01537		A	T	sub	Intergenic	ABC transporter substrate-binding protein/cupin domain-containing protein
		mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC
		pncB_1 ← / ← D_01663		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
		D_05743 ←	Val292Ala	A	G	sub	Missense	NAD(P)(+) transhydrogenase (Re/Si-specific) subunit beta

	urtA ← / ← D_01971		C	A	sub	Intergenic	urea ABC transporter substrate-binding protein/MarC family protein
	D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
Strain D - Replicate 2 Reversion Control	*D_03404 → / –*		G	T	sub	Intergenic	LysE family translocator/–
	D_03404 → / –		C	A	sub	Intergenic	LysE family translocator/–
	D_00561 ←	Asp45Asn	C	T	sub	Missense	LysR family transcriptional regulator
	D_03890 →	Δ2 bp	TGGA	TA	del	Frameshift	bifunctional diguanylate cyclase/phosphodiesterase
	D_01449 → / ← D_01450		C	G	sub	Intergenic	TonB-dependent siderophore receptor/protein phosphatase 2C domain-containing protein
	asnB_2 ← / ← D_05555		G	C	sub	Intergenic	asparagine synthase (glutamine-hydrolyzing)/hypothetical protein
	D_05635 → / → D_05636		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
	pncB_1 ← / ← D_01663		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
	– / → D_05959		T	C	sub	Intergenic	–/hypothetical protein
	urtA ← / ← D_01971		C	A	sub	Intergenic	urea ABC transporter substrate-binding protein/MarC family protein
	D_06299 ←	Pro238His	G	T	sub	Intergenic	hemolysin D
	D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
Strain D - Replicate 3 Reversion Control	*– / ← D_02874*		C	A	sub	Intergenic	–/hypothetical protein
	D_03404 → / –		G	T	sub	Intergenic	LysE family translocator/–
	D_03551 →	Ala18Asp	C	A	sub	Missense	4-deoxy-4-formamido-L-arabinose-phospho-UDP deformylase
	D_03890 →	Leu890Gln	T	A	sub	Missense	bifunctional diguanylate cyclase/phosphodiesterase
	cmrA ← / → D_04509		G	C	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
	cmrA ← / → D_04509		G	T	sub	Intergenic	AraC family transcriptional regulator CmrA/antibiotic biosynthesis monooxygenase
	D_04810 → / ← D_04811		A	G	sub	Intergenic	ATP-dependent Clp protease proteolytic subunit/metal-dependent hydrolase
	D_01252 ← / –		G	C	sub	Intergenic	cell division protein/–

		D_01252 ← / –		G	T	sub	Intergenic	cell division protein/–
		D_01449 → / ← D_01450		C	G	sub	Intergenic	TonB-dependent siderophore receptor/protein phosphatase 2C domain-containing protein
		D_05635 → / → D_05636		G	C	sub	Intergenic	hypothetical protein/hypothetical protein
		mreC →	Leu291Pro	T	C	sub	Missense	rod shape-determining protein MreC
		pncB_1 ← / ← D_01663		G	C	sub	Intergenic	nicotinate phosphoribosyltransferase/MexW/MexI family multidrug efflux RND transporter permease subunit
		D_05743 ←	Val292Ala	A	G	sub	Missense	NAD(P)(+) transhydrogenase (Re/Si-specific) subunit beta
		– / → D_06289		C	G	sub	Intergenic	–/hypothetical protein
		D_03994 →	Undefined				Undefined	gamma-glutamyltranspeptidase
Strain E- Replicate 1	Chloramphenicol Control	*E_04243 ← / ← E_04244*		C	G	sub	Intergenic	hypothetical protein/pyridoxal phosphate-dependent aminotransferase
		E_04472 ← / → E_04473		G	T	sub	Intergenic	tRNA-Cys/hypothetical protein
		E_04568 → / ← E_04569		C	G	sub	Intergenic	hypothetical protein/DoxX family protein
		E_04760 ←	Ala30Glu	G	T	sub	Missense	BMP family ABC transporter substrate-binding protein
		E_05637 →	Phe110Met	TTT	CTG	sub	Missense	multidrug transporter
		E_05637 →	Ser112Ile	G	T	sub	Missense	multidrug transporter
		E_02135 ←	Ala184Pro	C	G	sub	Missense	YfiR family protein
		E_00022 → / ← E_00023		G	C	sub	Intergenic	LuxR family transcriptional regulator/50S ribosomal protein L36
		E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase
Strain E - Replicate 2	Chloramphenicol Control	*E_00131 ←*	Gln286Leu	T	A	sub	Missense	chemotaxis transducer
		E_00309 → / → E_00310		G	C	sub	Intergenic	ABC transporter substrate-binding protein/ABC transporter permease
		E_02979 → / → glo A_1		CC	GG	sub	Intergenic	autotransporter domain-containing protein/lactoylglutathione lyase
		E_05801	Δ282 bp	wildtype		del	Deletion	29-1-day0_05801
		E_04243 ← / ← E_04244		C	G	sub	Intergenic	hypothetical protein/pyridoxal phosphate-dependent aminotransferase

	E_05349 → / → asnB_3		GC	GGC	ins	Intergenic	hypothetical protein/asparagine synthase (glutamine-hydrolyzing)
	E_05637 →	Phe110Met	TTT	CTG	sub	Missense	multidrug transporter
	E_05637 →	Ser112Ile	G	T	sub	Missense	multidrug transporter
	E_02161 ← / ← E_02162		G	T	sub	Intergenic	amino acid permease/exotoxin
	E_00022 → / ← E_00023	Undefined				Undefined	LuxR family transcriptional regulator/50S ribosomal protein L36
	E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase
Strain E - Replcate 3 Chloramphenicol Control	*E_02979 → / → glo A_1*		C	G	sub	Intergenic	autotransporter domain-containing protein/lactoylglutathione lyase
	E_04472 ← / → E_04473		G	T	sub	Intergenic	tRNA-Cys/hypothetical protein
	E_04710 ←	Gln291Glu	G	C	sub	Intergenic	NAD(P)(+) transhydrogenase (Re/Si-specific) subunit beta
	E_05637 →	Phe110Met	TTT	CTG	sub	Intergenic	multidrug transporter
	E_05637 →	Ser112Ile	T	G	sub	Intergenic	multidrug transporter
	E_02531 ←	Arg1162Ser	G	T	sub	Intergenic	EAL domain-containing protein
	E_00022 → / ← E_00023	Undefined				Undefined	LuxR family transcriptional regulator/50S ribosomal protein L36
	E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase
Strain E - Replciate 1 Ciprofloxacin Control	*E_00309 → / → E_00310*		G	C	sub	Intergenic	ABC transporter substrate-binding protein/ABC transporter permease
	E_02979 → / → glo A_1		C	G	sub	Intergenic	autotransporter domain-containing protein/lactoylglutathione lyase
	E_05801	Δ282 bp	wildtype		del	Deletion	29-1-day0_05801
	E_03854 →	Pro809Pro	C	G	sub	Missense	hypothetical protein
	E_04243 ← / ← E_04244		C	G	sub	Intergenic	hypothetical protein/pyridoxal phosphate-dependent aminotransferase
	E_04472 ← / → E_04473		G	T	sub	Intergenic	tRNA-Cys/hypothetical protein
	E_04568 → / ← E_04569		C	G	sub	Intergenic	hypothetical protein/DoxX family protein
	E_05028 →	Ala193Asp	C	A	sub	Missense	shikimate dehydrogenase

		E_05349 → / → asnB_3		GC	GGC	ins	Intergenic	hypothetical protein/asparagine synthase (glutamine-hydrolyzing)
		E_05637 →	Phe110Met	TTT	CTG	sub	Missense	multidrug transporter
		E_05637 →	Ser112Ile	T	G	sub	Missense	multidrug transporter
		E_02161 ← / ← E_02162		G	G	sub	Intergenic	amino acid permease/exotoxin
		E_02751 ←	Asp66Asp	G	G	sub	Synonymous	hypothetical protein
		E_02751 ←	Arg65Leu	C	C	sub	Missense	hypothetical protein
		E_00022 → / ← E_00023		G	C	sub	Intergenic	LuxR family transcriptional regulator/50S ribosomal protein L36
		E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase
Strain E - Replicate 2	Ciprofloxacin Control	*tsaB ← / ← E_00109*		C	G	sub	Intergenic	tRNA (adenosine(37)-N6)-threonylcarbamoyltransferase complex dimerization subunit type 1 TsaB/adenylate kinase
		E_03666 ←	Gly235Val	C	A	sub	Missense	LuxR family transcriptional regulator
		E_03819 ← / ← E_03820		C	G	sub	Intergenic	mechanosensitive ion channel family protein/YajQ family cyclic di-GMP-binding protein
		E_04017 ← / ← E_04018		G	C	sub	Intergenic	DNA-binding protein/fumarylacetoacetate hydrolase family protein
		sbrR →	Ala47Asp	C	A	sub	Missense	anti-sigma factor SbrR
		E_04243 ← / ← E_04244		C	G	sub	Intergenic	hypothetical protein/pyridoxal phosphate-dependent aminotransferase
		E_00789 → / ← E_00790		G	A	sub	Intergenic	3-hydroxyacyl-CoA dehydrogenase/transcriptional regulator
		E_04472 ← / → E_04473		G	T	sub	Intergenic	tRNA-Cys/hypothetical protein
		E_04568 → / ← E_04569		C	G	sub	Intergenic	hypothetical protein/DoxX family protein
		E_04731 →	Cys24Phe	G	T	sub	Missense	methyl-accepting chemotaxis protein
		E_04760 ←	Ala30Glu	G	T	sub	Missense	BMP family ABC transporter substrate-binding protein
		ahpF ← / ← ahpC		C	G	sub	Intergenic	alkyl hydroperoxide reductase subunit F/peroxiredoxin
		E_01314 →	Δ6 bp	wildtype		del	Intergenic	EAL domain-containing protein
		E_05149 → / ← E_05150		G	C	sub	Intergenic	isopenicillin N synthase family oxygenase/monooxygenase

	E_05529 →	Arg354Leu	G	T	sub	Missense	hypothetical protein
	E_05637 →	Phe110Met	TTT	CTG	sub	Missense	multidrug transporter
	E_05637 →	Ser112Ile	T	G	sub	Missense	multidrug transporter
	E_01665 → / ← E_01666		G	C	sub	Intergenic	pseudouridine synthase/hypothetical protein
	E_00022 → / ← E_00023		G	C	sub	Intergenic	LuxR family transcriptional regulator/50S ribosomal protein L36
	E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase
Strain E- Replicate 3 Ciprofloxacin Control	*E_03666 ←*	Gly235Val	C	A	sub	Intergenic	LuxR family transcriptional regulator
	– / → sbrR		G	C	sub	Intergenic	–/anti-sigma factor SbrR
	sbrR →	Ala47Asp	C	A	sub	Intergenic	anti-sigma factor SbrR
	E_04472 ← / → E_04473		G	T	sub	Intergenic	tRNA-Cys/hypothetical protein
	E_04568 → / ← E_04569		C	G	sub	Intergenic	hypothetical protein/DoxX family protein
	ahpF ← / ← ahpC		C	G	sub	Intergenic	alkyl hydroperoxide reductase subunit F/peroxiredoxin
	E_04981 → / → E_04982		C	G	sub	Intergenic	hydrolase/OsmC family peroxiredoxin
	E_05637 →	Phe110Met	TTT	CTG	sub	Missense	multidrug transporter
	E_05637 →	Ser112Ile	T	G	sub	Missense	multidrug transporter
	E_02161 ← / ← E_02162		G	C	sub	Intergenic	amino acid permease/exotoxin
	E_02161 ← / ← E_02162		G	T	sub	Intergenic	amino acid permease/exotoxin
	E_00022 → / ← E_00023		G	C	sub	Intergenic	LuxR family transcriptional regulator/50S ribosomal protein L36
	E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase
Strain E - Reversion Control	*E_03666 ←*	Val76Ala	A	G	sub	Missense	LuxR family transcriptional regulator
	E_03791 →	Ile142Ser	T	G	sub	Missense	bifunctional diguanylate cyclase/phosphodiesterase
	E_04243 ← / ← E_04244		C	G	sub	Intergenic	hypothetical protein/pyridoxal phosphate-dependent aminotransferase
	E_04472 ← / → E_04473		G	T	sub	Intergenic	tRNA-Cys/hypothetical protein

	E_04568 → / ← E_04569		C	G	sub	Intergenic	hypothetical protein/DoxX family protein
	E_01314 →	Phe642Leu	T	C	sub	Missense	EAL domain-containing protein
	E_04981 → / → E_04982		C	G	sub	Intergenic	hydrolase/OsmC family peroxiredoxin
	E_05349 → / → asnB_3		GC	GGC	ins	Intergenic	hypothetical protein/asparagine synthase (glutamine-hydrolyzing)
	E_05637 →	Phe110Met	TTT	CTG	sub	Missense	multidrug transporter
	E_05637 →	Ser112Ile	T	G	sub	Missense	multidrug transporter
	E_02428 ←	Δ24 bp	wildtype		del	Deletion	response regulator
	E_00022 → / ← E_00023	Undefined				Undefined	LuxR family transcriptional regulator/50S ribosomal protein L36
	E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase
Strain E- Replicate 2 Reversion Control	*E_00323 ←*		G	A	sub	Intergenic	hypothetical protein
	E_04472 ← / → E_04473		G	T	sub	Intergenic	tRNA-Cys/hypothetical protein
	E_04981 → / → E_04982		C	G	sub	Intergenic	hydrolase/OsmC family peroxiredoxin
	E_05464 ← / → E_05465		A	C	sub	Intergenic	hypothetical protein/hypothetical protein
	E_05637 →	Phe110Met	TTT	CTG	sub	Missense	multidrug transporter
	E_05637 →	Ser112Ile	T	G	sub	Missense	multidrug transporter
	E_02505 ←	Leu118Leu	C	T	sub	Intergenic	glycerate dehydrogenase
	E_02751 ←	Asp66Asp	G	A	sub	Intergenic	hypothetical protein
	E_00022 → / ← E_00023		G	C	sub	Intergenic	LuxR family transcriptional regulator/50S ribosomal protein L36
	E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase

Strain E - Replicate 3	Reversion Control	*E_02979 → / → gloA_1*		CC	GG	sub	Intergenic	autotransporter domain-containing protein/lactoylglutathione lyase
		E_03666 ←	Gly235Val	C	A	sub	Missense	LuxR family transcriptional regulator
		E_03819 ← / ← E_03820		G	C	sub	Intergenic	mechanosensitive ion channel family protein/YajQ family cyclic di-GMP-binding protein
		E_03854 →	ProPro817ArgThr	CCGCCG	CGCACG	sub	Missense	hypothetical protein
		sdiA →	Δ4 bp	wildtype		del	Intergenic	transcriptional regulator SdiA
		E_04568 → / ← E_04569		C	G	sub	Intergenic	hypothetical protein/DoxX family protein
		E_04710 ←	Gln291Glu	G	C	sub	Missense	NAD(P)(+) transhydrogenase (Re/Si-specific) subunit beta
		ahpF ← / ← ahpC		C	G	sub	Intergenic	alkyl hydroperoxide reductase subunit F/peroxiredoxin
		E_04906 ← / ← E_04907		C	G	sub	Intergenic	hybrid sensor histidine kinase/response regulator/peptidase M42
		E_01314 →	Gly673Asp	G	A	sub	Missense	EAL domain-containing protein
		E_05456 → / ← E_05457		C	G	sub	Intergenic	aldehyde dehydrogenase (NADP(+))/Ldh family oxidoreductase
		E_05637 →	Phe110Met	TTT	CTG	sub	Missense	multidrug transporter
		E_05637 →	Ser112Ile	T	G	sub	Missense	multidrug transporter
		E_01907 → / → E_01908		G	C	sub	Intergenic	sodium:alanine symporter family protein/asparaginase
		E_02751 ←	Asp66Asp	G	A	sub	Missense	hypothetical protein
		E_02751 ←	Arg65Leu	C	A	sub	Missense	hypothetical protein
		E_00022 → / ← E_00023	Undefined				Undefined	LuxR family transcriptional regulator/50S ribosomal protein L36
		E_00306 → / → E_00307	Undefined				Undefined	hypothetical protein/valine--tRNA ligase

Appendix - Table 22: Median and interquartile range of the area under the curve and relative fitness of strains evolved in ciprofloxacin and MHB + 10% plasma.

Strain		Antibiotic	AUC experimental		Relative Fitness*	
			Mdn	IQR	Mdn	IQR
C	Parent	None	14.71	2.26	0.99	0.74
C4	Mutant	None	2.63	0.48	0.96	0.31
C4.1	Revertant	None	2.44	0.59	0.71	0.08
C	Parent	CIP	13.34	1.23	1.00	0.78
C4	Mutant	CIP	2.40	0.45	0.85	0.10
C4.1	Revertant	CIP	3.05	0.31	0.80	0.32
D	Parent	None	1.31	1.64	0.94	0.19
D2	Mutant	None	2.04	1.77	0.82	0.16
D2.1	Revertant	None	2.20	1.74	0.82	0.14
D3	Mutant	None	0.27	0.11	0.39	0.25
D3.1	Revertant	None	4.12	1.02	0.75	0.07
D	Parent	CIP	1.97	1.28	0.98	0.14
D2	Mutant	CIP	2.34	1.75	0.93	0.12
D2.1	Revertant	CIP	3.21	3.10	0.99	0.15
D3	Mutant	CIP	0.30	0.38	0.36	0.31
D3.1	Revertant	CIP	4.44	0.50	0.78	0.07
E	Parent	None	11.30	3.69	0.96	0.33
E1	Mutant	None	11.62	4.63	1.31	0.33
E1.1	Revertant	None	15.31	2.92	1.64	0.18
E	Parent	CIP	10.05	2.55	0.97	0.35
E1	Mutant	CIP	11.49	3.63	1.41	0.43
E1.1	Revertant	CIP	15.67	3.13	1.58	0.17

** Relative fitness is calculated with respect to the average growth rate of the ancestral parent strain*

Appendix - Table 23: Mann-Whitney U test comparing relative fitness of environmental strains evolved to clinical conditions. P-values are adjusted using the Benjamini-Hochberg correction.*

Revertant		group1	group2	U	p.adj
C1.1	none	C	C1	0	2.74×10^{-4}
		C	C1.1	1	3.44×10^{-4}
		C1	C1.1	61	4.48×10^{-1}
	CHL	C + CHL	C1 + CHL	0	3.49×10^{-4}
		C + CHL	C1.1 + CHL	8	3.00×10^{-3}
		C1 + CHL	C1.1 + CHL	85	1.30×10^{-2}
C2.1	none	C	C2	0	1.83×10^{-1}
		C	C2.1	0	1.83×10^{-1}
		C2	C2.1	90	4.00×10^{-3}
	CHL	C + CHL	C2 + CHL	0	3.49×10^{-4}
		C + CHL	C2.1 + CHL	3	7.11×10^{-4}
		C2 + CHL	C2.1 + CHL	100	3.49×10^{-4}
C3.1	none	C	C3	0	2.74×10^{-4}
		C	C3.1	0	2.74×10^{-4}
		C3	C3.1	100	2.74×10^{-4}
	CHL	C + CHL	C3 + CHL	0	3.49×10^{-4}
		C + CHL	C3.1 + CHL	2	5.78×10^{-4}
		C3 + CHL	C3.1 + CHL	100	3.49×10^{-4}
D1.1	none	D	D1	37	5.17×10^{-1}
		D	D1.1	58	5.71×10^{-1}
		D1	D1.1	65	5.17×10^{-1}
	CHL	D + CHL	D1 + CHL	38	3.85×10^{-1}
		D + CHL	D1.1 + CHL	90	4.00×10^{-3}
		D1 + CHL	D1.1 + CHL	100	5.49×10^{-4}
E1.1	none	E	E1	27	8.90×10^{-2}
		E	E1.1	0	4.95×10^{-4}
		E1	E1.1	2	4.95×10^{-4}
	CHL	E + CHL	E1 + CHL	83	4.20×10^{-2}
		E + CHL	E1.1 + CHL	57	6.23×10^{-1}
		E1 + CHL	E1.1 + CHL	26	1.14×10^{-1}
C4.1	none	C	C4	50	1.00
		C	C4.1	60	7.10×10^{-1}
		C4	C4.1	82	5.20×10^{-2}
	CIP	C + CIP	C4 + CHL	50	1.00
		C + CHL	C4.1 + CHL	65	5.78×10^{-1}
		C4 + CHL	C4.1 + CHL	62	5.78×10^{-1}
D2.1	none	D	D2	68	2.07×10^{-1}
		D	D2.1	70	1.75×10^{-1}
		D2	D2.1	51	9.70×10^{-1}
	CIP	D + CHL	D2 + CHL	68	2.32×10^{-1}
		D + CHL	D2.1 + CHL	53	8.50×10^{-1}
		D2 + CIP	D2.1 + CIP	63	3.83×10^{-1}
D3.1	none	D	D3	99	8.20×10^{-4}
		D	D3.1	84	2.30×10^{-2}
		D3	D3.1	2	8.25×10^{-4}
	CIP	D + CIP	D3 + CIP	99	6.15×10^{-4}
		D + CIP	D3.1 + CIP	90	4.00×10^{-3}
		D3 + CIP	D3.1 + CIP	100	6.10×10^{-4}
E2.1	none	E	E2	14	7.00×10^{-3}
		E	E2.1	0	5.49×10^{-4}
		E2	E2.1	12	7.00×10^{-3}
	CIP	E + CIP	E2 + CIP	14	1.10×10^{-2}
		E + CIP	E2.1 + CIP	0	5.49×10^{-4}
		E2 + CIP	E2.1 + CIP	32	1.86×10^{-1}

** Relative fitness is calculated with respect to the average growth rate of the ancestral parent strain*

Appendix - Table 24: Mann-Whitney U test comparing area under the curve of environmental strains evolved to clinical conditions. P-values are adjusted using the Benjamini-Hochberg correction.

Revertant		group1	group2	U	p.adj
C1.1	none	C	C1	100	1.83×10^{-4}
		C	C1.1	100	1.83×10^{-4}
		C1	C1.1	0	1.83×10^{-4}
	CHL	C + CHL	C1 + CHL	2	3.30×10^{-4}
		C + CHL	C1.1 + CHL	100	1.83×10^{-4}
		C1 + CHL	C1.1 + CHL	100	1.83×10^{-4}
C2.1	none	C	C2	0	1.83×10^{-4}
		C	C2.1	0	1.83×10^{-4}
		C2	C2.1	0	1.83×10^{-4}
	CHL	C + CHL	C2 + CHL	0	1.83×10^{-4}
		C + CHL	C2.1 + CHL	52	9.10×10^{-1}
		C2 + CHL	C2.1 + CHL	100	2.96×10^{-4}
C3.1	none	C	C3	0	1.83×10^{-4}
		C	C3.1	100	1.83×10^{-4}
		C3	C3.1	100	1.83×10^{-4}
	CHL	C + CHL	C3 + CHL	0	1.83×10^{-4}
		C + CHL	C3.1 + CHL	87	7.00×10^{-3}
		C3 + CHL	C3.1 + CHL	100	1.83×10^{-4}
D1.1	none	D	D1	45	7.34×10^{-1}
		D	D1.1	29	2.79×10^{-1}
		D1	D1.1	32	2.79×10^{-1}
	CHL	D + CHL	D1 + CHL	13	6.00×10^{-3}
		D + CHL	D1.1 + CHL	87	6.00×10^{-3}
		D1 + CHL	D1.1 + CHL	100	5.49×10^{-4}
E1.1	none	E	E1	72	1.04×10^{-1}
		E	E1.1	0	2.74×10^{-4}
		E1	E1.1	0	2.74×10^{-4}
	CHL	E + CHL	E1 + CHL	0	2.74×10^{-4}
		E + CHL	E1.1 + CHL	53	8.50×10^{-1}
		E1 + CHL	E1.1 + CHL	100	2.74×10^{-4}
C4.1	none	C	C4	100	2.74×10^{-4}
		C	C4.1	100	2.74×10^{-4}
		C4	C4.1	64	3.07×10^{-1}
	CIP	C + CIP	C4 + CIP	100	2.74×10^{-4}
		C + CIP	C4.1 + CIP	100	2.74×10^{-4}
		C4 + CIP	C4.1 + CIP	90	3.00×10^{-3}
D2.1	none	D	D2	31	1.80×10^{-1}
		D	D2.1	28	1.30×10^{-1}
		D2	D2.1	49	9.70×10^{-1}
	CIP	D + CIP	D2 + CIP	41	5.79×10^{-1}
		D + CIP	D2.1 + CIP	34	3.01×10^{-1}
		D2 + CIP	D2.1 + CIP	54	7.91×10^{-1}
D3.1	none	D	D3	100	4.59×10^{-4}
		D	D3.1	9	4.00×10^{-3}
		D3	D3.1	0	4.58×10^{-4}
	CIP	D + CIP	D3 + CIP	95	2.00×10^{-3}
		D + CIP	D3.1 + CIP	8	3.00×10^{-3}
		D3 + CIP	D3.1 + CIP	100	9.15×10^{-4}
E2.1	none	E	E2	44	6.78×10^{-1}
		E	E2.1	8	5.00×10^{-3}
		E2	E2.1	18	2.60×10^{-2}
	CIP	E + CIP	E2 + CIP	31	1.62×10^{-1}
		E + CIP	E2.1 + CIP	3	1.00×10^{-3}
		E2 + CIP	E2.1 + CIP	9	3.00×10^{-3}

Appendix II - Raw data for heatmaps

Appendix - Table 25: Raw data displaying the gene flow as F_{ST} *between core groups of* Pseudomonas aeruginosa *with the PA7-like strains included.*

	Core1	*Core2*	*Core3*	*Core4*	*Core5*	*Core6*	*Core7*	*Core8*	*Core9*	*Core10*	*Core11*	*Core12*	*Core13*	*Core14*	*Core15*	*Core16*	*Core17*	*Core18*	*Core19*
Core1	0.000	0.987	0.986	0.981	0.952	0.925	0.862	0.991	0.986	0.970	0.966	0.975	0.985	0.967	0.891	0.936	0.852	0.731	0.458
Core2	0.987	0.000	0.988	0.984	0.952	0.926	0.861	0.993	0.988	0.971	0.966	0.976	0.986	0.968	0.890	0.939	0.850	0.724	0.466
Core3	0.986	0.988	0.000	0.981	0.952	0.926	0.861	0.991	0.985	0.969	0.965	0.973	0.983	0.966	0.885	0.934	0.849	0.724	0.510
Core4	0.981	0.984	0.981	0.000	0.951	0.924	0.858	0.987	0.984	0.968	0.964	0.973	0.983	0.966	0.889	0.934	0.850	0.726	0.442
Core5	0.952	0.952	0.952	0.951	0.000	0.925	0.920	0.952	0.952	0.949	0.949	0.950	0.951	0.948	0.936	0.945	0.933	0.917	0.903
Core6	0.925	0.926	0.926	0.924	0.925	0.000	0.858	0.927	0.923	0.916	0.916	0.919	0.922	0.917	0.887	0.906	0.877	0.834	0.805
Core7	0.862	0.861	0.861	0.858	0.920	0.858	0.000	0.864	0.854	0.845	0.842	0.848	0.852	0.848	0.803	0.825	0.779	0.709	0.672
Core8	0.991	0.993	0.991	0.987	0.952	0.927	0.864	0.000	0.990	0.974	0.970	0.978	0.988	0.971	0.895	0.942	0.857	0.737	0.479
Core9	0.986	0.988	0.985	0.984	0.952	0.923	0.854	0.990	0.000	0.933	0.927	0.941	0.961	0.935	0.799	0.878	0.708	0.487	0.639
Core10	0.970	0.971	0.969	0.968	0.949	0.916	0.845	0.974	0.933	0.000	0.893	0.897	0.924	0.904	0.751	0.846	0.639	0.419	0.636
Core11	0.966	0.966	0.965	0.964	0.949	0.916	0.842	0.970	0.927	0.893	0.000	0.899	0.917	0.904	0.764	0.842	0.659	0.443	0.628
Core12	0.975	0.976	0.973	0.973	0.950	0.919	0.848	0.978	0.941	0.897	0.899	0.000	0.936	0.914	0.769	0.858	0.666	0.451	0.642
Core13	0.985	0.986	0.983	0.983	0.951	0.922	0.852	0.988	0.961	0.924	0.917	0.936	0.000	0.928	0.778	0.865	0.678	0.450	0.644
Core14	0.967	0.968	0.966	0.966	0.948	0.917	0.848	0.971	0.935	0.904	0.904	0.914	0.928	0.000	0.788	0.862	0.714	0.519	0.652
Core15	0.891	0.890	0.885	0.889	0.936	0.887	0.803	0.895	0.799	0.751	0.764	0.769	0.778	0.788	0.000	0.722	0.550	0.374	0.580
Core16	0.936	0.939	0.934	0.934	0.945	0.906	0.825	0.942	0.878	0.846	0.842	0.858	0.865	0.862	0.722	0.000	0.623	0.413	0.586
Core17	0.852	0.850	0.849	0.850	0.933	0.877	0.779	0.857	0.708	0.639	0.659	0.666	0.678	0.714	0.550	0.623	0.000	0.209	0.524
Core18	0.731	0.724	0.724	0.726	0.917	0.834	0.709	0.737	0.487	0.419	0.443	0.451	0.450	0.519	0.374	0.413	0.209	0.000	0.402
Core19	0.458	0.466	0.510	0.442	0.903	0.805	0.672	0.479	0.639	0.636	0.628	0.642	0.644	0.652	0.580	0.586	0.524	0.402	0.000

Appendix - Table 26: Raw data displaying the nucleotide divergence as D_{xy} *between core groups of* Pseudomonas aeruginosa *with the PA7-like strains included.*

	Core1	***Core2***	***Core3***	***Core4***	***Core5***	***Core6***	***Core7***	***Core8***	***Core9***	***Core10***	***Core11***	***Core12***	***Core13***	***Core14***	***Core15***	***Core16***	***Core17***	***Core18***	***Core19***
Core1	0.00	628.42	701.25	588.38	7375.51	2961.61	1852.04	644.81	996.00	1029.60	1012.99	1041.63	1024.71	1092.83	1101.85	958.93	1022.82	1012.52	692.56
Core2	628.42	0.00	695.85	588.61	7351.76	2963.40	1827.02	627.29	966.16	999.54	972.79	1018.27	973.53	1065.92	1078.51	969.68	996.84	979.77	699.61
Core3	701.25	695.85	0.00	627.81	7382.71	2984.26	1846.73	688.42	971.29	1023.03	1013.73	1018.60	976.26	1072.61	1056.11	937.88	1007.41	987.53	767.60
Core4	588.38	588.61	627.81	0.00	7340.71	2934.60	1813.29	577.33	970.28	1024.81	1009.55	1033.75	999.55	1081.68	1099.32	953.08	1019.10	998.41	674.60
Core5	7375.51	7351.76	7382.71	7340.71	0.00	7547.14	7481.50	7362.39	7423.37	7407.64	7420.48	7429.38	7399.61	7334.26	7326.66	7406.62	7419.67	7406.98	7409.80
Core6	2961.61	2963.40	2984.26	2934.60	7547.14	0.00	3291.88	2965.78	2915.11	2900.50	2914.82	2932.69	2905.55	2971.53	2944.35	2909.69	2941.51	2918.70	3008.49
Core7	1852.04	1827.02	1846.73	1813.29	7481.50	3291.88	0.00	1845.08	1773.92	1786.54	1775.11	1794.81	1761.05	1853.57	1854.62	1748.84	1795.69	1776.85	1892.72
Core8	644.81	627.29	688.42	577.33	7362.39	2965.78	1845.08	0.00	989.00	1047.93	1023.68	1052.29	1010.37	1096.31	1106.10	985.66	1035.56	1019.65	713.39
Core9	996.00	966.16	971.29	970.28	7423.37	2915.11	1773.92	989.00	0.00	521.79	527.38	519.85	501.05	605.93	620.00	531.74	533.22	537.90	1050.91
Core10	1029.60	999.54	1023.03	1024.81	7407.64	2900.50	1786.54	1047.93	521.79	0.00	522.53	465.80	490.98	596.65	569.69	537.25	479.59	505.23	1088.50
Core11	1012.99	972.79	1013.73	1009.55	7420.48	2914.82	1775.11	1023.68	527.38	522.53	0.00	511.01	490.91	628.30	616.83	542.54	517.70	533.38	1074.62
Core12	1041.63	1018.27	1018.60	1033.75	7429.38	2932.69	1794.81	1052.29	519.85	465.80	511.01	0.00	514.09	610.58	593.90	548.03	504.62	526.41	1096.76
Core13	1024.71	973.53	976.26	999.55	7399.61	2905.55	1761.05	1010.37	501.05	490.98	490.91	514.09	0.00	582.24	570.85	498.79	490.14	506.34	1069.82
Core14	1092.83	1065.92	1072.61	1081.68	7334.26	2971.53	1853.57	1096.31	605.93	596.65	628.30	610.58	582.24	0.00	691.93	632.71	620.55	620.28	1153.01
Core15	1101.85	1078.51	1056.11	1099.32	7326.66	2944.35	1854.62	1106.10	620.00	569.69	616.83	593.90	570.85	691.93	0.00	618.81	583.56	611.71	1157.08
Core16	958.93	969.68	937.88	953.08	7406.62	2909.69	1748.84	985.66	531.74	537.25	542.54	548.03	498.79	632.71	618.81	0.00	538.67	550.89	1030.33
Core17	1022.82	996.84	1007.41	1019.10	7419.67	2941.51	1795.69	1035.56	533.22	479.59	517.70	504.62	490.14	620.55	583.56	538.67	0.00	523.77	1086.75
Core18	1012.52	979.77	987.53	998.41	7406.98	2918.70	1776.85	1019.65	537.90	505.23	533.38	526.41	506.34	620.28	611.71	550.89	523.77	0.00	1067.15
Core19	692.56	699.61	767.60	674.60	7409.80	3008.49	1892.72	713.39	1050.91	1088.50	1074.62	1096.76	1069.82	1153.01	1157.08	1030.33	1086.75	1067.15	0.00

Appendix - Table 27: Raw data displaying the average nucleotide identities between Pseudomonas species. Due to its size, the table is continued on page 558.

	P. aeruginosa DSM50071.1	*P. aeruginosa DSM50071.2*	*P. aeruginosa LESB58*	*P. aeruginosa PA14*	*P. aeruginosa PA7*	*P. aeruginosa PAK*	*P. alcaligenes*	*P. campi*	*P. chlororaphis*	*P. citronellolis*	*P. composti*	*P. delhiensis*	*P. fluorescens*	*P. furukawaii*	*P. humi*	*P. indoloxydans*	*P. jinjuensis*	*P. knackmussii*	*P. lactis*	*P. lalkuanensis*	*P. mucoides*	*P. nicosulfuronedens*	*P. nitritireducens*	*P. nitroreducens*	*P. nosocomialis*	*P. otitidis*	*P. panipatensis*
P. aeruginosa DSM50071.1	100	99.98	99.32	98.64	94.10	99.30	82.35	81.68	80.87	84.64	81.07	84.91	78.89	82.23	84.81	81.27	84.72	83.88	79.19	82.22	79.08	83.40	83.62	83.55	81.08	82.51	83.82
P. aeruginosa DSM50071.2	100	100	99.29	98.65	94.06	99.30	82.29	81.69	80.92	84.62	81.02	84.81	78.94	82.26	84.74	81.28	84.75	83.78	79.14	82.24	79.13	83.35	83.59	83.54	81.16	82.46	83.86
P. aeruginosa LESB58	99.34	99.35	100	98.61	94.01	99.22	82.37	81.76	80.98	84.57	80.95	84.77	78.97	82.28	84.70	81.40	84.69	84.00	79.70	82.27	79.13	83.36	83.66	83.55	81.01	82.44	83.90
P. aeruginosa PA14	98.74	98.69	98.64	100	93.95	98.68	82.51	81.84	80.98	84.64	80.94	84.85	79.06	82.26	84.83	81.28	84.68	83.95	79.25	82.38	79.18	83.51	83.66	83.54	81.15	82.63	84.00
P. aeruginosa PA7	94.01	94.02	93.95	93.95	100	94.02	82.73	81.91	81.06	84.95	81.00	84.95	79.09	82.36	85.03	81.47	85.02	84.20	79.29	82.35	79.20	83.51	83.75	83.63	81.28	82.69	84.04
P. aeruginosa PAK	99.28	99.27	99.20	98.70	94.05	100	82.44	81.71	80.88	84.68	81.08	84.74	79.03	82.33	84.79	81.36	84.72	84.02	79.34	82.32	79.12	83.34	83.60	83.55	81.05	82.58	83.87
P. alcaligenes	82.17	82.21	82.21	82.26	82.59	82.36	100	86.16	81.19	83.59	82.84	83.69	79.46	83.12	83.55	83.27	83.36	83.10	79.81	83.28	79.44	82.42	82.67	82.60	81.78	83.73	82.63
P. campi	81.57	81.79	81.73	81.75	82.02	81.84	86.08	100	81.21	82.55	82.57	82.46	79.97	82.08	82.54	82.78	82.64	82.21	80.11	82.59	79.86	81.68	82.06	82.09	81.22	82.55	82.02
P. chlororaphis	80.89	80.99	80.86	80.77	80.95	81.00	81.17	81.19	100	81.02	80.58	81.21	83.65	80.79	81.10	80.46	81.04	80.89	83.62	80.91	84.39	80.51	80.74	80.68	80.14	81.04	80.72
P. citronellolis	84.66	84.66	84.58	84.64	84.92	84.58	83.69	82.60	81.08	100	81.74	95.12	79.39	83.19	97.17	82.08	87.03	88.84	79.50	83.35	79.29	86.26	86.60	86.61	81.72	83.96	87.78
P. composti	80.86	80.99	80.87	80.97	81.08	81.05	82.95	82.57	80.56	81.53	100	81.72	79.51	81.43	81.68	89.44	81.56	81.68	79.62	81.54	79.40	81.21	81.34	81.30	80.93	81.82	81.39
P. delhiensis	84.79	84.80	84.69	84.82	85.15	84.79	83.81	82.49	81.04	95.07	82.00	100	79.26	83.40	95.13	82.16	87.19	88.89	79.65	83.47	79.07	86.22	86.51	86.67	81.65	84.10	87.82
P. fluorescens	78.97	78.93	79.06	79.10	78.97	79.05	79.47	79.88	83.67	79.29	79.50	79.39	100	79.26	79.51	79.37	79.36	79.50	87.51	79.41	83.48	79.16	79.42	79.39	79.10	79.34	79.15
P. furukawaii	82.16	82.20	82.13	82.17	82.28	82.18	82.98	82.23	80.68	83.29	81.48	83.49	79.36	100	83.21	82.14	82.96	82.68	79.51	86.79	79.18	82.31	82.40	82.39	81.23	85.39	82.38
P. humi	84.74	84.66	84.56	84.69	84.91	84.66	83.81	82.68	81.12	97.14	81.71	95.07	79.49	83.24	100	82.10	87.13	88.63	79.50	83.32	79.31	86.21	86.44	86.44	81.74	84.06	87.71
P. indoloxydans	81.04	81.30	81.27	81.33	81.40	81.27	83.46	82.83	80.58	81.75	89.34	81.93	79.48	82.22	81.86	100	82.09	81.75	80.07	81.74	79.45	81.46	81.53	81.44	81.24	82.30	81.39
P. jinjuensis	84.60	84.57	84.64	84.58	84.96	84.58	83.36	82.74	80.99	86.87	81.59	87.10	79.38	82.91	87.01	81.93	100	86.04	79.70	83.09	79.39	85.45	85.56	85.63	81.68	83.28	85.74

P. knackmussii	83.81	83.74	83.77	83.82	84.10	83.84	82.93	82.24	80.98	88.69	81.63	88.89	79.52	82.63	88.61	81.91	86.05	100	79.68	82.93	79.27	85.68	85.97	85.94	81.12	83.08	87.14
P. lactis	79.13	79.20	79.69	79.24	79.18	79.41	79.82	80.12	83.66	79.34	79.78	79.43	87.52	79.50	79.39	80.08	79.72	79.69	100	79.62	83.21	79.43	79.41	79.43	79.08	79.73	79.32
P. lalkuanensis	82.32	82.31	82.37	82.29	82.38	82.35	83.21	82.45	80.79	83.37	81.61	83.35	79.45	86.91	83.29	81.59	83.08	82.84	79.61	100	79.31	82.58	82.64	82.68	81.26	84.73	82.47
P. mucoides	79.04	79.14	79.04	79.18	79.18	79.20	79.57	79.80	84.38	79.22	79.38	79.16	83.38	79.11	79.29	79.42	79.36	79.38	83.34	79.44	100	79.15	79.40	79.33	79.02	79.21	79.17
P. nicosulfuronedens	83.33	83.27	83.27	83.46	83.45	83.31	82.43	81.76	80.55	86.24	81.20	86.31	79.34	82.20	86.25	81.37	85.45	85.71	79.44	82.59	79.20	100	92.00	91.71	80.84	82.74	84.95
P. nitritireducens	83.58	83.66	83.73	83.69	83.74	83.49	82.79	82.04	80.74	86.66	81.32	86.59	79.43	82.45	86.59	81.50	85.67	85.98	79.62	82.74	79.42	92.04	100	98.96	81.18	82.90	85.27
P. nitroreducens	83.59	83.58	83.70	83.68	83.82	83.52	82.70	81.95	80.63	86.56	81.33	86.65	79.34	82.43	86.57	81.50	85.79	85.93	79.51	82.71	79.41	91.74	98.96	100	80.99	82.89	85.26
P. nosocomialis	80.99	81.00	80.99	81.13	81.32	81.05	81.97	81.32	79.96	81.77	80.90	81.56	78.82	81.16	81.67	81.15	81.67	81.28	78.97	81.09	78.91	80.81	81.15	81.18	100	81.38	80.83
P. otitidis	82.55	82.53	82.43	82.48	82.78	82.59	83.87	82.67	81.14	83.91	82.02	84.12	79.32	85.51	84.00	82.18	83.44	83.10	79.77	84.84	79.22	82.60	82.92	82.90	81.40	100	82.80
P. panipatensis	83.82	83.79	83.80	83.90	84.03	83.81	82.72	82.06	80.76	87.48	81.43	87.77	79.16	82.32	87.57	81.32	85.78	86.96	79.33	82.55	79.29	84.94	85.11	85.07	80.90	82.60	100
P. peli	79.79	79.72	79.73	79.68	79.80	79.71	81.32	82.17	80.17	80.08	81.50	80.19	79.79	80.10	80.17	81.45	80.10	80.14	79.86	80.22	79.67	79.90	80.02	80.08	79.60	80.45	80.07
P. pseudoalcaligenes	81.07	81.24	81.63	81.21	81.32	81.37	83.33	82.64	80.62	81.92	89.47	81.90	79.46	81.79	81.94	96.15	81.93	81.91	79.92	81.76	79.49	81.30	81.54	81.50	81.15	82.24	81.38
P. putida	80.04	80.11	80.18	80.16	80.34	80.13	81.02	80.96	81.97	80.96	80.38	81.06	80.74	80.65	81.22	80.52	80.95	80.85	81.11	80.81	80.54	80.34	80.72	80.61	79.96	80.87	80.49
P. sediminis	80.77	80.82	80.88	80.98	80.85	80.78	82.79	82.51	80.50	81.46	90.71	81.57	79.48	81.38	81.61	90.89	81.58	81.48	79.42	81.58	79.51	81.04	81.10	81.31	81.00	81.71	81.15
P. stutzeri	80.72	80.78	80.69	80.74	80.91	80.72	81.69	81.27	79.93	81.24	80.95	81.20	78.72	81.20	81.34	81.67	81.33	81.05	78.92	81.16	78.69	80.66	80.76	80.72	82.69	80.99	81.00
P. synxantha	79.38	79.36	79.31	79.32	79.33	79.43	79.89	80.03	83.67	79.58	79.52	79.60	87.43	79.39	79.66	79.52	79.56	79.63	89.80	79.43	82.99	79.57	79.59	79.59	79.14	79.71	79.37
P. syringae	78.78	78.75	78.86	78.86	78.97	78.73	79.15	79.37	81.07	78.80	79.20	78.82	80.41	78.85	78.89	79.17	78.87	79.16	80.28	79.34	80.80	78.91	78.99	78.96	78.77	78.89	78.81
P. tohonis	82.84	82.84	82.76	82.87	83.13	82.89	84.32	83.18	81.20	83.95	82.18	84.23	79.61	85.33	84.03	82.50	83.62	83.23	79.75	85.19	79.70	82.93	83.14	83.25	81.93	88.29	83.11
P. toyotomiensis	80.97	81.08	81.00	81.02	81.18	80.93	83.28	82.72	80.41	81.77	90.04	81.71	79.51	81.61	81.75	92.56	81.80	81.62	79.45	81.67	79.41	81.18	81.45	81.39	81.17	81.90	81.33
PA1129	93.76	93.81	93.71	93.74	98.89	93.75	82.64	81.88	80.92	84.95	81.04	84.92	79.05	82.34	84.99	81.65	84.97	84.32	79.59	82.35	79.23	83.54	83.82	83.59	81.21	82.60	84.12
PA1130	93.81	93.84	93.68	93.71	98.88	93.72	82.62	81.85	81.02	84.99	81.02	84.94	79.01	82.34	84.95	81.63	85.05	84.23	79.58	82.33	79.15	83.55	83.81	83.68	81.20	82.68	84.09
PA1145	93.79	93.82	93.74	93.75	98.98	93.85	82.74	81.91	81.10	84.97	81.01	85.12	79.12	82.35	85.09	81.38	85.04	84.24	79.32	82.39	79.21	83.56	83.76	83.70	81.28	82.63	84.17
PA1646	93.81	93.85	93.73	93.78	98.83	93.77	82.63	81.88	80.96	84.91	80.95	85.01	79.02	82.29	85.10	81.40	85.03	84.15	79.25	82.36	79.21	83.47	83.76	83.71	81.31	82.68	84.20
PA1780	93.79	93.83	93.76	93.76	98.80	93.74	82.69	81.85	80.91	84.92	80.97	84.98	79.03	82.19	84.98	81.32	84.97	84.05	79.25	82.32	79.20	83.43	83.76	83.74	81.28	82.63	84.03
PA1794	93.96	94.02	93.87	93.89	99.34	93.92	82.90	81.86	81.01	85.00	81.17	85.04	79.01	82.34	85.00	81.91	85.08	84.19	79.47	82.25	79.17	83.48	83.85	83.73	81.29	82.82	83.97

PA1802	93.96	94.03	93.86	93.87	99.35	93.97	82.90	81.81	81.03	84.96	81.16	84.95	79.00	82.31	85.00	81.95	85.04	84.15	79.46	82.20	79.23	83.52	83.84	83.70	81.31	82.79	84.02
PA2078	93.99	94.01	93.92	93.93	99.87	93.96	82.61	81.75	81.09	84.94	81.07	85.11	79.02	82.30	85.03	81.26	85.08	84.14	79.25	82.33	79.23	83.46	83.84	83.72	81.33	82.66	84.03
PA2506	93.35	93.31	93.26	93.24	98.51	93.22	82.54	81.85	80.83	84.82	80.99	84.83	79.10	82.17	84.76	81.75	84.84	83.91	79.53	82.07	79.20	83.44	83.66	83.55	81.41	82.75	83.87
PA2541	93.82	93.93	93.75	93.77	98.84	93.86	82.65	81.77	80.98	84.87	80.94	84.99	79.07	82.17	84.90	81.38	84.90	84.14	79.32	82.34	79.18	83.49	83.76	83.71	81.36	82.60	84.10
PA2548	93.83	93.79	93.71	93.77	98.86	93.79	82.68	81.78	81.05	84.98	81.04	85.00	79.03	82.25	85.10	81.34	85.04	84.19	79.30	82.31	79.21	83.48	83.77	83.72	81.24	82.72	84.12
PA259	94.02	94.02	93.88	93.89	99.43	94.02	82.58	81.91	81.05	84.87	81.02	84.97	79.09	82.31	85.01	81.27	85.07	84.14	79.28	82.29	79.19	83.54	83.76	83.77	81.33	82.64	84.11
PA580	93.85	93.88	93.77	93.79	98.90	93.72	82.59	81.83	80.94	84.90	81.01	85.00	79.06	82.24	84.92	81.44	85.03	84.25	79.38	82.35	79.24	83.49	83.70	83.71	81.35	82.68	84.05
PA628	93.85	93.89	93.78	93.81	98.94	93.83	82.65	82.00	81.05	84.91	81.05	85.06	79.07	82.23	85.03	81.37	84.96	84.18	79.29	82.38	79.20	83.47	83.75	83.63	81.46	82.66	84.17
PA828	93.77	93.82	93.72	93.64	98.75	93.68	82.71	81.86	80.96	84.90	81.01	85.06	79.06	82.42	84.99	81.67	84.91	84.30	79.46	82.40	79.17	83.44	83.84	83.72	81.36	82.73	83.95
PA868	94.00	94.06	93.77	93.85	99.29	93.90	82.65	81.86	81.03	84.93	81.23	85.00	78.98	82.33	84.91	81.92	85.01	84.19	79.44	82.21	79.27	83.44	83.78	83.67	81.22	82.86	84.04
PA964	93.78	93.86	93.72	93.69	98.87	93.71	82.57	81.83	81.01	84.89	80.96	85.02	79.03	82.22	85.01	81.75	85.02	84.10	79.42	82.34	79.22	83.42	83.83	83.67	81.32	82.65	84.07

Continuation of Appendix - Table 27

	P. peli	*P. pseudoalcaligenes*	*P. putida*	*P. sediminis*	*P. stutzeri*	*P. synxantha*	*P. syringae*	*P. tohonis*	*P. toyotomiensis*	*PA1129*	*PA1130*	*PA1145*	*PA1646*	*PA1780*	*PA1794*	*PA1802*	*PA2078*	*PA2506*	*PA2541*	*PA2548*	*PA259*	*PA580*	*PA628*	*PA828*	*PA868*	*PA964*
P. aeruginosa DSM50071.1	79.72	81.24	80.13	80.75	80.83	79.40	78.74	82.74	81.12	93.85	93.88	93.86	93.81	93.75	94.05	94.02	94.04	93.56	93.88	93.88	94.01	93.90	93.82	93.86	94.04	93.77
P. aeruginosa DSM50071.2	79.70	81.27	80.14	80.78	80.92	79.49	78.74	82.76	81.05	93.89	93.87	93.87	93.82	93.76	94.01	94.01	94.05	93.56	93.89	93.90	94.02	93.94	93.81	93.91	94.05	93.83
P. aeruginosa LESB58	79.75	81.55	80.22	80.82	80.94	79.45	78.84	82.69	81.08	93.69	93.69	93.80	93.67	93.73	93.93	93.91	93.88	93.35	93.77	93.71	93.89	93.86	93.72	93.67	93.76	93.77
P. aeruginosa PA14	79.73	81.13	80.32	80.80	80.98	79.43	78.88	82.85	81.05	93.70	93.69	93.84	93.77	93.74	93.90	93.93	93.99	93.44	93.69	93.78	93.90	93.87	93.79	93.79	93.89	93.74
P. aeruginosa PA7	79.84	81.32	80.26	80.90	80.98	79.42	78.86	82.95	81.16	98.89	98.89	99.01	98.86	98.87	99.30	99.30	99.94	98.67	98.84	98.89	99.43	98.85	98.94	98.82	99.30	98.85
P. aeruginosa PAK	79.71	81.39	80.23	80.77	80.97	79.50	78.80	82.70	81.07	93.65	93.65	93.88	93.69	93.73	93.91	93.88	93.93	93.44	93.78	93.82	93.98	93.77	93.75	93.72	93.86	93.64
P. alcaligenes	81.18	83.21	81.00	82.80	81.74	79.86	79.22	84.13	83.22	82.53	82.42	82.50	82.42	82.54	82.78	82.72	82.62	82.38	82.43	82.57	82.49	82.58	82.54	82.79	82.48	82.67
P. campi	82.12	82.80	80.95	82.58	81.17	79.91	79.49	83.19	82.84	81.97	81.93	82.15	81.90	81.79	81.93	81.91	82.01	81.68	81.79	82.03	81.86	81.94	81.98	81.96	81.90	82.01
P. chlororaphis	80.23	80.77	81.82	80.43	79.91	83.74	81.22	81.28	80.57	80.96	80.99	80.94	81.00	80.86	80.94	80.88	80.85	80.71	80.93	80.92	80.92	80.98	80.97	81.00	81.00	80.96
P. citronellolis	80.17	81.96	81.11	81.70	81.25	79.74	78.91	83.94	81.95	84.93	85.04	85.15	84.96	84.91	84.99	84.96	85.02	84.83	85.00	85.00	84.97	85.00	85.10	84.97	84.95	85.07
P. composti	81.50	89.64	80.33	90.78	80.99	79.45	79.17	82.20	89.97	80.99	81.08	80.96	81.03	80.94	80.91	80.85	80.98	80.89	80.93	80.97	80.97	81.09	80.98	81.03	81.15	80.97
P. delhiensis	80.01	82.01	81.01	81.70	81.24	79.73	78.85	84.19	82.04	85.12	85.09	85.27	85.09	85.05	85.09	84.99	85.11	84.89	85.10	85.14	85.10	85.16	85.15	85.12	85.10	85.12
P. fluorescens	79.61	79.54	80.78	79.40	78.75	87.40	80.53	79.70	79.42	79.14	79.04	79.16	79.15	79.00	79.08	79.06	79.07	79.11	79.02	79.06	79.13	79.02	79.14	79.14	79.00	79.03
P. furukawaii	80.12	81.79	80.72	81.39	81.15	79.48	78.79	85.15	81.76	82.43	82.35	82.29	82.26	82.24	82.30	82.33	82.30	82.20	82.21	82.28	82.32	82.24	82.39	82.38	82.36	82.24
P. humi	80.12	82.03	81.17	81.73	81.33	79.71	78.98	84.10	82.02	85.00	85.02	85.09	84.98	84.92	84.83	84.83	85.04	84.63	84.95	85.09	85.00	85.03	85.08	85.04	84.84	85.04
P. indoloxydans	81.53	96.31	80.30	90.76	81.70	79.62	79.30	82.38	92.53	81.57	81.57	81.27	81.17	81.35	81.77	81.81	81.28	81.73	81.22	81.29	81.32	81.41	81.21	81.61	81.90	81.65
P. jinjuensis	80.17	81.87	80.84	81.33	81.32	79.64	79.04	83.53	81.81	84.75	84.93	84.83	84.85	84.74	84.93	84.91	84.95	84.61	84.87	84.97	84.85	84.99	84.94	84.99	84.81	84.98
P. knackmussii	80.19	81.80	80.83	81.52	80.96	79.69	79.29	83.16	81.62	84.06	84.18	84.11	84.01	84.06	84.03	84.02	84.17	83.68	84.05	83.90	83.99	84.19	84.04	84.17	84.00	84.04
P. lactis	79.85	80.02	81.27	79.39	78.96	89.77	80.45	79.77	79.55	79.57	79.51	79.31	79.31	79.24	79.34	79.48	79.28	79.42	79.19	79.34	79.24	79.42	79.29	79.49	79.52	79.47
P. lalkuanensis	80.30	81.81	80.78	81.45	81.02	79.65	79.15	85.07	81.86	82.28	82.25	82.43	82.22	82.25	82.29	82.34	82.26	82.06	82.29	82.30	82.30	82.34	82.38	82.39	82.28	82.32

P. mucoides	79.65	79.44	80.52	79.50	78.96	83.13	80.70	79.61	79.33	79.27	79.13	79.16	79.14	79.14	79.29	79.28	79.21	79.18	79.17	79.08	79.25	79.13	79.24	79.14	79.22	79.13
P. nicosulfuronedens	79.95	81.34	80.47	81.21	80.96	79.55	78.87	82.94	81.25	83.57	83.53	83.50	83.47	83.47	83.42	83.38	83.42	83.39	83.47	83.53	83.51	83.53	83.52	83.52	83.44	83.52
P. nitritireducens	80.11	81.70	80.72	81.39	80.88	79.66	79.07	83.21	81.54	83.75	83.84	83.83	83.73	83.76	83.72	83.76	83.74	83.66	83.68	83.77	83.73	83.78	83.75	83.78	83.67	83.72
P. nitroreducens	80.09	81.60	80.69	81.35	80.89	79.65	78.90	83.26	81.48	83.89	83.88	83.88	83.70	83.90	83.72	83.76	83.81	83.64	83.72	83.88	83.82	83.77	83.80	83.81	83.67	83.86
P. nosocomialis	79.72	81.18	79.88	81.00	82.76	79.18	78.73	81.89	81.08	81.36	81.22	81.22	81.28	81.29	81.35	81.37	81.39	81.32	81.35	81.32	81.30	81.27	81.38	81.42	81.29	81.34
P. otitidis	80.41	82.43	80.83	81.63	81.01	79.53	78.74	88.20	82.04	82.82	82.84	82.72	82.66	82.69	82.74	82.84	82.83	82.63	82.59	82.70	82.76	82.79	82.66	82.82	82.81	82.77
P. panipatensis	79.88	81.41	80.54	81.13	80.98	79.44	78.83	82.87	81.43	84.04	84.23	84.12	84.12	84.14	84.12	84.02	84.02	83.81	84.23	84.12	84.16	84.15	84.16	84.15	84.04	84.21
P. peli	100	81.38	79.86	81.56	79.88	79.67	79.24	80.70	81.51	80.00	79.89	79.76	79.73	79.85	79.89	80.07	79.79	79.84	79.82	79.84	79.95	79.90	79.86	79.96	79.89	79.81
P. pseudoalcaligenes	81.52	100	80.44	91.20	81.37	79.57	79.31	82.42	92.41	81.58	81.53	81.30	81.34	81.42	81.77	81.78	81.25	81.66	81.33	81.49	81.44	81.58	81.39	81.43	81.77	81.78
P. putida	79.92	80.55	100	80.37	79.82	80.85	80.07	81.00	80.52	80.35	80.31	80.36	80.25	80.24	80.18	80.21	80.27	80.21	80.26	80.28	80.25	80.35	80.36	80.32	80.23	80.27
P. sediminis	81.33	91.31	80.26	100	80.97	79.54	79.06	81.98	91.27	80.89	80.94	80.92	80.93	80.96	80.87	80.92	80.99	80.70	80.83	80.95	80.92	80.82	80.92	80.99	80.89	80.92
P. stutzeri	79.91	81.35	79.88	81.00	100	78.75	78.69	81.39	81.24	81.09	80.85	80.91	80.76	80.85	80.89	80.91	80.72	80.72	80.82	80.87	80.86	80.79	80.99	80.97	80.89	80.94
P. synxantha	79.67	79.57	80.92	79.50	78.87	100	80.67	79.75	79.50	79.40	79.41	79.39	79.34	79.38	79.40	79.32	79.38	79.36	79.25	79.36	79.29	79.41	79.46	79.42	79.31	79.24
P. syringae	79.13	79.42	80.16	79.02	78.66	80.66	100	79.13	79.21	79.03	78.80	78.93	78.73	78.81	78.97	78.88	78.95	78.88	78.74	78.81	78.88	78.95	78.87	79.00	78.88	78.91
P. tohonis	80.65	82.50	80.91	81.94	81.43	79.81	79.16	100	82.59	83.06	82.89	83.10	82.86	83.01	83.05	83.06	83.03	82.87	82.94	82.81	83.00	83.04	82.97	83.04	83.04	83.02
P. toyotomiensis	81.39	92.57	80.42	91.25	81.46	79.49	79.13	82.31	100	81.23	81.30	81.08	81.16	81.14	81.41	81.33	81.14	81.32	81.15	81.13	81.15	81.07	81.13	81.27	81.41	81.33
PA1129	79.84	81.49	80.26	80.90	80.97	79.33	78.83	82.86	81.26	100	99.97	99.42	99.15	99.39	98.78	98.75	98.95	98.02	99.34	99.16	98.95	99.22	99.39	99.10	98.75	99.20
PA1130	79.86	81.52	80.24	80.99	80.84	79.32	78.75	82.83	81.28	99.95	100	99.44	99.12	99.37	98.81	98.79	98.93	97.98	99.33	99.19	98.95	99.19	99.42	99.07	98.74	99.18
PA1145	79.84	81.37	80.34	81.00	81.04	79.39	78.85	82.91	81.26	99.43	99.46	100	99.39	99.43	99.02	99.00	98.98	98.28	99.39	99.42	99.00	99.41	99.78	99.42	98.99	99.43
PA1646	79.90	81.28	80.33	80.96	80.89	79.41	78.74	82.86	81.24	99.14	99.17	99.36	100	99.32	98.91	98.92	98.93	98.12	99.29	99.94	98.88	99.25	99.30	99.17	98.85	99.29
PA1780	79.85	81.27	80.31	80.84	80.92	79.32	78.85	82.85	81.15	99.31	99.34	99.42	99.27	100	98.80	98.81	98.96	98.14	99.89	99.28	98.93	99.26	99.36	99.26	98.81	99.28
PA1794	79.86	81.73	80.18	80.93	80.93	79.41	78.69	83.02	81.47	98.79	98.75	99.02	98.86	98.86	100	99.99	99.44	99.36	98.86	98.91	99.32	98.92	98.95	98.83	99.52	98.89
PA1802	79.86	81.69	80.15	80.89	80.92	79.38	78.68	83.00	81.44	98.80	98.76	99.01	98.84	98.86	100	100	99.45	99.33	98.86	98.90	99.32	98.89	98.95	98.83	99.52	98.88
PA2078	79.85	81.30	80.23	80.95	80.94	79.35	78.76	82.90	81.23	98.88	98.89	98.97	98.85	98.94	99.37	99.35	100	98.78	98.91	98.91	99.42	98.85	98.91	98.92	99.36	98.94
PA2506	79.83	81.65	80.22	80.86	80.86	79.45	78.75	82.83	81.28	97.90	97.83	98.10	98.01	97.93	99.09	99.11	98.63	100	98.01	98.04	98.47	98.12	98.07	97.99	98.58	98.02

PA2541	79.86	81.20	80.27	80.93	80.91	79.31	78.76	82.76	81.18	99.33	99.37	99.42	99.29	99.96	98.85	98.84	98.99	98.16	100	99.30	98.90	99.30	99.37	99.33	98.81	99.31
PA2548	79.88	81.32	80.31	80.91	80.91	79.39	78.75	82.79	81.23	99.17	99.20	99.41	99.95	99.36	98.94	98.94	98.98	98.16	99.32	100	98.92	99.32	99.36	99.19	98.88	99.34
PA259	79.85	81.39	80.21	80.88	80.86	79.31	78.85	82.86	81.18	98.92	98.93	98.98	98.86	98.94	99.33	99.32	99.44	98.65	98.91	98.93	100	98.97	98.87	98.92	99.34	98.94
PA580	79.87	81.60	80.21	80.99	80.84	79.37	78.75	82.87	81.25	99.22	99.19	99.37	99.29	99.35	98.94	98.95	98.97	98.22	99.32	99.29	98.93	100	99.30	99.26	98.82	99.28
PA628	79.89	81.44	80.27	80.95	81.20	79.37	78.78	82.84	81.33	99.40	99.43	99.82	99.29	99.41	98.92	98.93	98.98	98.31	99.42	99.35	98.88	99.28	100	99.39	98.91	99.36
PA828	79.90	81.47	80.25	80.94	80.93	79.34	78.76	82.93	81.30	99.06	99.03	99.37	99.10	99.24	98.79	98.81	98.91	98.19	99.26	99.13	98.88	99.20	99.28	100	98.74	99.18
PA868	79.85	81.69	80.14	80.90	80.90	79.41	78.74	82.95	81.54	98.75	98.78	99.03	98.79	98.87	99.46	99.45	99.42	98.81	98.79	98.82	99.32	98.81	98.90	98.77	100	98.71
PA964	79.87	81.85	80.22	80.90	80.84	79.32	78.83	82.87	81.37	99.18	99.17	99.37	99.27	99.32	98.86	98.86	98.99	98.19	99.31	99.32	98.94	99.21	99.31	99.16	98.79	100

Appendix - Table 28: Raw data comparing the Jaccard similarity index of genomic sketches of Pseudomonas species based on a k-mer length of 31. The table is continued on page 563.

	A.agilis	*PA1129*	*PA1130*	*PA1145*	*PA1646*	*PA1780*	*PA1794*	*PA1802*	*PA2045*	*PA2078*	*PA2506*	*PA2541*	*PA2548*	*PA259*	*PA580*	*PA628*	*PA828*	*PA868*	*PA964*	*P. aeruginosa DSM50071.1*	*P. aeruginosa DSM50071.2*	*P. aeruginosa LESB58*	*P. aeruginosa PA14*	*P. aeruginosa PA7*	*P. aeruginosa PAK*	*P. aeruginosa PAO1*	*P. alcaligenes*	*P. campi*
A.agilis	1.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
PA1129	0.000	1.000	0.986	0.723	0.672	0.684	0.533	0.533	0.572	0.585	0.460	0.678	0.682	0.583	0.677	0.689	0.656	0.562	0.671	0.124	0.124	0.117	0.124	0.572	0.117	0.125	0.005	0.002
PA1130	0.000	0.986	1.000	0.723	0.677	0.684	0.535	0.535	0.574	0.589	0.463	0.678	0.686	0.583	0.677	0.689	0.658	0.564	0.673	0.125	0.124	0.117	0.123	0.574	0.118	0.126	0.005	0.002
PA1145	0.000	0.723	0.723	1.000	0.708	0.740	0.555	0.555	0.583	0.610	0.486	0.733	0.718	0.607	0.712	0.828	0.685	0.582	0.689	0.139	0.140	0.131	0.136	0.583	0.129	0.142	0.005	0.002
PA1646	0.000	0.672	0.677	0.708	1.000	0.690	0.550	0.550	0.567	0.595	0.466	0.682	0.983	0.579	0.676	0.701	0.664	0.560	0.681	0.131	0.131	0.122	0.133	0.567	0.121	0.130	0.005	0.002
PA1780	0.000	0.684	0.684	0.740	0.690	1.000	0.542	0.542	0.568	0.599	0.479	0.965	0.693	0.589	0.683	0.714	0.684	0.571	0.674	0.129	0.130	0.121	0.130	0.568	0.120	0.129	0.005	0.002
PA1794	0.000	0.533	0.535	0.555	0.550	0.542	1.000	1.000	0.682	0.713	0.732	0.540	0.554	0.681	0.557	0.558	0.516	0.785	0.533	0.129	0.129	0.133	0.132	0.682	0.125	0.135	0.009	0.002
PA1802	0.000	0.533	0.535	0.555	0.550	0.542	1.000	1.000	0.682	0.713	0.732	0.540	0.554	0.681	0.557	0.558	0.516	0.785	0.533	0.129	0.129	0.133	0.132	0.682	0.125	0.135	0.009	0.002
PA2045	0.000	0.572	0.574	0.583	0.567	0.568	0.682	0.682	1.000	0.926	0.589	0.561	0.577	0.738	0.575	0.566	0.532	0.692	0.558	0.135	0.135	0.130	0.139	1.000	0.129	0.139	0.007	0.002
PA2078	0.000	0.585	0.589	0.610	0.595	0.599	0.713	0.713	0.926	1.000	0.603	0.594	0.601	0.777	0.607	0.591	0.560	0.725	0.584	0.139	0.139	0.134	0.141	0.926	0.133	0.143	0.005	0.002
PA2506	0.000	0.460	0.463	0.486	0.466	0.479	0.732	0.732	0.589	0.603	1.000	0.475	0.471	0.579	0.496	0.483	0.476	0.646	0.481	0.117	0.117	0.122	0.121	0.589	0.113	0.122	0.007	0.002
PA2541	0.000	0.678	0.678	0.733	0.682	0.965	0.540	0.540	0.561	0.594	0.475	1.000	0.684	0.586	0.682	0.716	0.678	0.565	0.667	0.128	0.129	0.121	0.129	0.561	0.119	0.128	0.004	0.002
PA2548	0.000	0.682	0.686	0.718	0.983	0.693	0.554	0.554	0.577	0.601	0.471	0.684	1.000	0.585	0.681	0.707	0.666	0.565	0.685	0.131	0.131	0.123	0.131	0.577	0.122	0.130	0.005	0.002
PA259	0.000	0.583	0.583	0.607	0.579	0.589	0.681	0.681	0.738	0.777	0.579	0.586	0.585	1.000	0.596	0.587	0.561	0.717	0.578	0.140	0.140	0.130	0.134	0.738	0.129	0.141	0.005	0.002
PA580	0.000	0.677	0.677	0.712	0.676	0.683	0.557	0.557	0.575	0.607	0.496	0.682	0.681	0.596	1.000	0.675	0.683	0.569	0.689	0.129	0.130	0.132	0.137	0.575	0.124	0.133	0.005	0.002
PA628	0.000	0.689	0.689	0.828	0.701	0.714	0.558	0.558	0.566	0.591	0.483	0.716	0.707	0.587	0.675	1.000	0.665	0.573	0.664	0.130	0.130	0.125	0.134	0.566	0.122	0.133	0.004	0.002
PA828	0.000	0.656	0.658	0.685	0.664	0.684	0.516	0.516	0.532	0.560	0.476	0.678	0.666	0.561	0.683	0.665	1.000	0.530	0.703	0.121	0.121	0.119	0.124	0.532	0.115	0.124	0.005	0.002
PA868	0.000	0.562	0.564	0.582	0.560	0.571	0.785	0.785	0.692	0.725	0.646	0.565	0.565	0.717	0.569	0.573	0.530	1.000	0.549	0.133	0.133	0.130	0.135	0.692	0.128	0.139	0.005	0.002
PA964	0.000	0.671	0.673	0.689	0.681	0.674	0.533	0.533	0.558	0.584	0.481	0.667	0.685	0.578	0.689	0.664	0.703	0.549	1.000	0.125	0.125	0.119	0.123	0.558	0.115	0.123	0.004	0.002
P. aeruginosa DSM50071.1	0.000	0.124	0.125	0.139	0.131	0.129	0.129	0.129	0.135	0.139	0.117	0.128	0.131	0.140	0.129	0.130	0.121	0.133	0.125	1.000	0.997	0.688	0.525	0.135	0.744	0.724	0.003	0.002
P. aeruginosa DSM50071.2	0.000	0.124	0.124	0.140	0.131	0.130	0.129	0.129	0.135	0.139	0.117	0.129	0.131	0.140	0.130	0.130	0.121	0.133	0.125	0.997	1.000	0.689	0.524	0.135	0.742	0.725	0.003	0.002
P. aeruginosa LESB58	0.000	0.117	0.117	0.131	0.122	0.121	0.133	0.133	0.130	0.134	0.122	0.121	0.123	0.130	0.132	0.125	0.119	0.130	0.119	0.688	0.689	1.000	0.503	0.130	0.696	0.697	0.003	0.002
P. aeruginosa PA14	0.000	0.124	0.123	0.136	0.133	0.130	0.132	0.132	0.139	0.141	0.121	0.129	0.131	0.134	0.137	0.134	0.124	0.135	0.123	0.525	0.524	0.503	1.000	0.139	0.517	0.549	0.004	0.003
P. aeruginosa PA7	0.000	0.572	0.574	0.583	0.567	0.568	0.682	0.682	1.000	0.926	0.589	0.561	0.577	0.738	0.575	0.566	0.532	0.692	0.558	0.135	0.135	0.130	0.139	1.000	0.129	0.139	0.007	0.002

P. aeruginosa PAK	0.000	0.117	0.118	0.129	0.121	0.120	0.125	0.125	0.129	0.133	0.113	0.119	0.122	0.129	0.124	0.122	0.115	0.128	0.115	0.744	0.742	0.696	0.517	0.129	1.000	0.728	0.004	0.002
P. aeruginosa PAO1	0.000	0.125	0.126	0.142	0.130	0.129	0.135	0.135	0.139	0.143	0.122	0.128	0.130	0.141	0.133	0.133	0.124	0.139	0.123	0.724	0.725	0.697	0.549	0.139	0.728	1.000	0.003	0.002
P. alcaligenes	0.000	0.005	0.005	0.005	0.005	0.005	0.009	0.009	0.007	0.005	0.007	0.004	0.005	0.005	0.005	0.004	0.005	0.005	0.004	0.003	0.003	0.003	0.004	0.007	0.004	0.003	1.000	0.020
P. campi	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.003	0.002	0.002	0.002	0.020	1.000
P. chlororaphis	0.000	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.003	0.000	0.000	0.000	0.001	0.004	0.000	0.000	0.005	0.003
P. citronellolis	0.000	0.014	0.013	0.015	0.015	0.015	0.015	0.015	0.014	0.014	0.015	0.015	0.015	0.014	0.014	0.016	0.012	0.013	0.015	0.016	0.016	0.014	0.014	0.014	0.015	0.015	0.007	0.003
P. composti	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.003	0.001	0.002	0.002	0.006	0.007
P. delhiensis	0.000	0.014	0.013	0.015	0.015	0.014	0.012	0.012	0.013	0.013	0.012	0.014	0.015	0.013	0.013	0.014	0.012	0.013	0.014	0.015	0.015	0.015	0.013	0.013	0.015	0.014	0.010	0.003
P. fluorescens	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.002	0.002
P. furukawaii	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.002	0.004	0.004	0.004	0.005	0.002	0.005	0.005	0.005	0.006
P. humi	0.000	0.015	0.014	0.014	0.015	0.015	0.015	0.015	0.015	0.016	0.015	0.015	0.015	0.016	0.014	0.015	0.013	0.014	0.015	0.014	0.014	0.013	0.012	0.015	0.013	0.013	0.006	0.004
P. indoloxydans	0.000	0.001	0.001	0.000	0.000	0.000	0.004	0.004	0.004	0.000	0.005	0.000	0.000	0.000	0.001	0.000	0.001	0.004	0.001	0.004	0.004	0.004	0.007	0.004	0.005	0.004	0.009	0.005
P. jinjuensis	0.000	0.015	0.015	0.015	0.015	0.015	0.013	0.013	0.014	0.014	0.013	0.015	0.015	0.014	0.013	0.015	0.014	0.014	0.014	0.016	0.016	0.013	0.014	0.014	0.013	0.014	0.006	0.004
P. knackmussii	0.000	0.012	0.012	0.012	0.012	0.011	0.011	0.011	0.011	0.011	0.011	0.011	0.012	0.011	0.011	0.012	0.009	0.011	0.011	0.012	0.012	0.011	0.014	0.011	0.012	0.013	0.007	0.005
P. lactis	0.000	0.002	0.002	0.001	0.001	0.001	0.002	0.002	0.001	0.001	0.002	0.001	0.001	0.001	0.002	0.001	0.001	0.002	0.002	0.000	0.000	0.002	0.000	0.001	0.002	0.000	0.000	0.002
P. lalkuanensis	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.003	0.003	0.003	0.002	0.002	0.003	0.003	0.005	0.005
P. mucoides	0.000	0.004	0.004	0.003	0.004	0.002	0.004	0.004	0.004	0.003	0.002	0.002	0.004	0.003	0.003	0.003	0.003	0.003	0.003	0.000	0.000	0.000	0.000	0.004	0.000	0.000	0.004	0.003
P. nicosulfuronedens	0.000	0.009	0.008	0.009	0.010	0.010	0.009	0.009	0.010	0.011	0.008	0.010	0.010	0.010	0.008	0.009	0.008	0.009	0.009	0.011	0.011	0.010	0.010	0.010	0.010	0.011	0.006	0.002
P. nitritireducens	0.000	0.010	0.010	0.011	0.011	0.010	0.010	0.010	0.011	0.011	0.010	0.010	0.011	0.011	0.010	0.011	0.009	0.010	0.009	0.012	0.012	0.011	0.011	0.011	0.011	0.011	0.009	0.004
P. nitroreducens	0.000	0.011	0.011	0.012	0.012	0.011	0.011	0.011	0.012	0.012	0.011	0.011	0.012	0.012	0.011	0.012	0.010	0.011	0.010	0.013	0.013	0.012	0.012	0.012	0.012	0.012	0.010	0.004
P. nosocomialis	0.000	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.002	0.001	0.006	0.001	0.001	0.001	0.001	0.002	0.001	0.002	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.005	0.003
P. otitidis	0.000	0.005	0.005	0.005	0.005	0.005	0.006	0.006	0.008	0.006	0.008	0.005	0.005	0.005	0.005	0.005	0.006	0.007	0.005	0.005	0.005	0.005	0.008	0.008	0.006	0.005	0.015	0.007
P. panipatensis	0.000	0.013	0.013	0.014	0.014	0.013	0.013	0.013	0.015	0.015	0.013	0.013	0.014	0.014	0.012	0.014	0.013	0.014	0.013	0.016	0.016	0.016	0.018	0.015	0.015	0.016	0.010	0.005
P. peli	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.002	0.002	0.002	0.004	0.001	0.002	0.002	0.007	0.006
P. pseudoalcaligenes	0.000	0.002	0.002	0.001	0.001	0.001	0.003	0.003	0.002	0.001	0.004	0.001	0.001	0.001	0.002	0.001	0.001	0.002	0.003	0.003	0.003	0.004	0.005	0.002	0.003	0.003	0.004	0.005
P. putida	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.003	0.003	0.003	0.003	0.001	0.003	0.003	0.004	0.003
P. sediminis	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.002	0.002	0.001	0.001	0.002	0.004	0.004	0.004	0.004	0.001	0.004	0.004	0.007	0.008
P. stutzeri	0.000	0.004	0.004	0.002	0.003	0.002	0.003	0.003	0.005	0.002	0.005	0.002	0.003	0.002	0.002	0.003	0.002	0.003	0.002	0.003	0.003	0.003	0.006	0.005	0.003	0.003	0.008	0.005
P. synxantha	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.001	0.002	0.002	0.001	0.001	0.002	0.002
P. syringae	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.002
P. tohonis	0.000	0.010	0.009	0.010	0.010	0.010	0.010	0.010	0.011	0.010	0.010	0.009	0.010	0.009	0.009	0.009	0.010	0.010	0.009	0.007	0.007	0.007	0.009	0.011	0.009	0.008	0.018	0.008
P. toyotomiensis	0.000	0.000	0.000	0.000	0.000	0.000	0.002	0.002	0.002	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.004	0.004	0.004	0.004	0.002	0.004	0.004	0.011	0.006

Continuation of Appendix - Table 28

	P. chlororaphis	*P. citronellolis*	*P. composti*	*P. delhiensis*	*P. fluorescens*	*P. furukawaii*	*P. humi*	*P. indoloxydans*	*P. jinjuensis*	*P. knackmussii*	*P. lactis*	*P. lalkuanensis*	*P. mucoides*	*P. nicosulfuronedens*	*P. nitritireducens*	*P. nitroreducens*	*P. nosocomialis*	*P. otitidis*	*P. panipatensis*	*P. peli*	*P. pseudoalcaligenes*	*P. putida*	*P. sediminis*	*P. stutzeri*	*P. synxantha*	*P. syringae*	*P. tohonis*	*P. toyotomiensis*
A.agilis	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
PA1129	0.004	0.014	0.002	0.014	0.002	0.002	0.015	0.001	0.015	0.012	0.002	0.002	0.004	0.009	0.010	0.011	0.001	0.005	0.013	0.001	0.002	0.001	0.002	0.004	0.002	0.001	0.010	0.000
PA1130	0.004	0.013	0.002	0.013	0.002	0.002	0.014	0.001	0.015	0.012	0.002	0.002	0.004	0.008	0.010	0.011	0.001	0.005	0.013	0.001	0.002	0.001	0.002	0.004	0.002	0.001	0.009	0.000
PA1145	0.004	0.015	0.002	0.015	0.002	0.002	0.014	0.000	0.015	0.012	0.001	0.002	0.003	0.009	0.011	0.012	0.001	0.005	0.014	0.001	0.001	0.001	0.002	0.002	0.002	0.001	0.010	0.000
PA1646	0.004	0.015	0.002	0.015	0.002	0.002	0.015	0.000	0.015	0.012	0.001	0.002	0.004	0.010	0.011	0.012	0.001	0.005	0.014	0.001	0.001	0.001	0.002	0.003	0.002	0.001	0.010	0.000
PA1780	0.004	0.015	0.002	0.014	0.002	0.002	0.015	0.000	0.015	0.011	0.001	0.002	0.002	0.010	0.010	0.011	0.002	0.005	0.013	0.001	0.001	0.001	0.002	0.002	0.002	0.001	0.010	0.000
PA1794	0.004	0.015	0.001	0.012	0.001	0.002	0.015	0.004	0.013	0.011	0.002	0.002	0.004	0.009	0.010	0.011	0.001	0.006	0.013	0.001	0.003	0.001	0.001	0.003	0.002	0.001	0.010	0.002
PA1802	0.004	0.015	0.001	0.012	0.001	0.002	0.015	0.004	0.013	0.011	0.002	0.002	0.004	0.009	0.010	0.011	0.001	0.006	0.013	0.001	0.003	0.001	0.001	0.003	0.002	0.001	0.010	0.002
PA2045	0.004	0.014	0.001	0.013	0.002	0.002	0.015	0.004	0.014	0.011	0.001	0.002	0.004	0.010	0.011	0.012	0.002	0.008	0.015	0.001	0.002	0.001	0.001	0.005	0.002	0.001	0.011	0.002
PA2078	0.004	0.014	0.001	0.013	0.002	0.002	0.016	0.000	0.014	0.011	0.001	0.002	0.003	0.011	0.011	0.012	0.001	0.006	0.015	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.010	0.001
PA2506	0.004	0.015	0.001	0.012	0.002	0.002	0.015	0.005	0.013	0.011	0.002	0.002	0.002	0.008	0.010	0.011	0.006	0.008	0.013	0.002	0.004	0.001	0.001	0.005	0.002	0.001	0.010	0.001
PA2541	0.004	0.015	0.002	0.014	0.002	0.002	0.015	0.000	0.015	0.011	0.001	0.002	0.002	0.010	0.010	0.011	0.001	0.005	0.013	0.001	0.001	0.001	0.002	0.002	0.002	0.001	0.009	0.001
PA2548	0.004	0.015	0.002	0.015	0.002	0.002	0.015	0.000	0.015	0.012	0.001	0.002	0.004	0.010	0.011	0.012	0.001	0.005	0.014	0.001	0.001	0.001	0.002	0.003	0.002	0.001	0.010	0.000
PA259	0.004	0.014	0.001	0.013	0.002	0.002	0.016	0.000	0.014	0.011	0.001	0.002	0.003	0.010	0.011	0.012	0.001	0.005	0.014	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.009	0.000
PA580	0.004	0.014	0.002	0.013	0.002	0.001	0.014	0.001	0.013	0.011	0.002	0.002	0.003	0.008	0.010	0.011	0.001	0.005	0.012	0.001	0.002	0.001	0.002	0.002	0.002	0.001	0.009	0.000
PA628	0.004	0.016	0.002	0.014	0.002	0.002	0.015	0.000	0.015	0.012	0.001	0.002	0.003	0.009	0.011	0.012	0.002	0.005	0.014	0.001	0.001	0.001	0.002	0.003	0.002	0.001	0.009	0.000
PA828	0.004	0.012	0.002	0.012	0.001	0.002	0.013	0.001	0.014	0.009	0.001	0.002	0.003	0.008	0.009	0.010	0.001	0.006	0.013	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.010	0.000
PA868	0.004	0.013	0.002	0.013	0.001	0.002	0.014	0.004	0.014	0.011	0.002	0.002	0.003	0.009	0.010	0.011	0.002	0.007	0.014	0.001	0.002	0.001	0.001	0.003	0.002	0.001	0.010	0.002
PA964	0.003	0.015	0.002	0.014	0.002	0.002	0.015	0.001	0.014	0.011	0.002	0.002	0.003	0.009	0.009	0.010	0.002	0.005	0.013	0.000	0.003	0.001	0.002	0.002	0.002	0.001	0.009	0.000
P. aeruginosa DSM50071.1	0.000	0.016	0.002	0.015	0.001	0.004	0.014	0.004	0.016	0.012	0.000	0.003	0.000	0.011	0.012	0.013	0.001	0.005	0.016	0.002	0.003	0.003	0.004	0.003	0.001	0.000	0.007	0.004
P. aeruginosa DSM50071.2	0.000	0.016	0.002	0.015	0.001	0.004	0.014	0.004	0.016	0.012	0.000	0.003	0.000	0.011	0.012	0.013	0.001	0.005	0.016	0.002	0.003	0.003	0.004	0.003	0.001	0.000	0.007	0.004
P. aeruginosa LESB58	0.000	0.014	0.002	0.015	0.001	0.004	0.013	0.004	0.013	0.011	0.002	0.003	0.000	0.010	0.011	0.012	0.001	0.005	0.016	0.002	0.004	0.003	0.004	0.003	0.001	0.000	0.007	0.004
P. aeruginosa PA14	0.001	0.014	0.003	0.013	0.001	0.005	0.012	0.007	0.014	0.014	0.000	0.002	0.000	0.010	0.011	0.012	0.001	0.008	0.018	0.004	0.005	0.003	0.004	0.006	0.002	0.000	0.009	0.004
P. aeruginosa PA7	0.004	0.014	0.001	0.013	0.002	0.002	0.015	0.004	0.014	0.011	0.001	0.002	0.004	0.010	0.011	0.012	0.002	0.008	0.015	0.001	0.002	0.001	0.001	0.005	0.002	0.001	0.011	0.002
P. aeruginosa PAK	0.000	0.015	0.002	0.015	0.001	0.005	0.013	0.005	0.013	0.012	0.002	0.003	0.000	0.010	0.011	0.012	0.001	0.006	0.015	0.002	0.003	0.003	0.004	0.003	0.001	0.000	0.009	0.004

P. aeruginosa PAO1	0.000	0.015	0.002	0.014	0.001	0.005	0.013	0.004	0.014	0.013	0.000	0.003	0.000	0.011	0.011	0.012	0.001	0.005	0.016	0.002	0.003	0.003	0.004	0.003	0.001	0.000	0.008	0.004
P. alcaligenes	0.005	0.007	0.006	0.010	0.002	0.005	0.006	0.009	0.006	0.007	0.000	0.005	0.004	0.006	0.009	0.010	0.005	0.015	0.010	0.007	0.004	0.004	0.007	0.008	0.002	0.002	0.018	0.011
P. campi	0.003	0.003	0.007	0.003	0.002	0.006	0.004	0.005	0.004	0.005	0.002	0.005	0.003	0.002	0.004	0.004	0.003	0.007	0.005	0.006	0.005	0.003	0.008	0.005	0.002	0.002	0.008	0.006
P. chlororaphis	1.000	0.003	0.001	0.002	0.004	0.002	0.002	0.002	0.002	0.002	0.010	0.002	0.011	0.003	0.004	0.004	0.001	0.003	0.004	0.002	0.003	0.004	0.001	0.002	0.007	0.007	0.002	0.002
P. citronellolis	0.003	1.000	0.004	0.157	0.001	0.005	0.300	0.005	0.022	0.030	0.001	0.004	0.002	0.025	0.030	0.029	0.002	0.009	0.026	0.003	0.005	0.003	0.003	0.006	0.001	0.000	0.010	0.003
P. composti	0.001	0.004	1.000	0.004	0.002	0.002	0.005	0.029	0.003	0.002	0.001	0.004	0.002	0.003	0.004	0.003	0.002	0.003	0.006	0.006	0.032	0.002	0.061	0.002	0.000	0.001	0.004	0.039
P. delhiensis	0.002	0.157	0.004	1.000	0.002	0.006	0.172	0.005	0.024	0.032	0.001	0.004	0.001	0.029	0.033	0.032	0.002	0.009	0.028	0.003	0.004	0.005	0.004	0.005	0.002	0.000	0.010	0.004
P. fluorescens	0.004	0.001	0.002	0.002	1.000	0.000	0.000	0.002	0.004	0.001	0.027	0.001	0.012	0.002	0.003	0.003	0.000	0.000	0.002	0.003	0.002	0.006	0.002	0.003	0.030	0.006	0.002	0.001
P. furukawaii	0.002	0.005	0.002	0.006	0.000	1.000	0.005	0.007	0.002	0.004	0.001	0.017	0.001	0.004	0.005	0.004	0.002	0.017	0.006	0.001	0.003	0.001	0.003	0.006	0.001	0.001	0.013	0.005
P. humi	0.002	0.300	0.005	0.172	0.000	0.005	1.000	0.004	0.024	0.034	0.001	0.004	0.001	0.021	0.026	0.025	0.003	0.010	0.024	0.003	0.004	0.002	0.004	0.005	0.001	0.000	0.009	0.003
P. indoloxydans	0.002	0.005	0.029	0.005	0.002	0.007	0.004	1.000	0.005	0.003	0.006	0.005	0.002	0.003	0.005	0.005	0.003	0.009	0.007	0.004	0.299	0.002	0.051	0.008	0.002	0.003	0.006	0.083
P. jinjuensis	0.002	0.022	0.003	0.024	0.004	0.002	0.024	0.005	1.000	0.018	0.002	0.006	0.001	0.017	0.019	0.018	0.002	0.007	0.020	0.002	0.004	0.004	0.004	0.004	0.002	0.001	0.006	0.004
P. knackmussii	0.002	0.030	0.002	0.032	0.001	0.004	0.034	0.003	0.018	1.000	0.002	0.008	0.000	0.021	0.028	0.029	0.002	0.007	0.031	0.003	0.005	0.003	0.002	0.007	0.001	0.001	0.014	0.001
P. lactis	0.010	0.001	0.001	0.001	0.027	0.001	0.001	0.006	0.002	0.002	1.000	0.001	0.009	0.002	0.002	0.002	0.000	0.002	0.002	0.004	0.003	0.006	0.001	0.002	0.038	0.007	0.002	0.001
P. lalkuanensis	0.002	0.004	0.004	0.004	0.001	0.017	0.004	0.005	0.006	0.008	0.001	1.000	0.001	0.003	0.007	0.007	0.002	0.007	0.007	0.001	0.004	0.002	0.002	0.004	0.000	0.002	0.010	0.004
P. mucoides	0.011	0.002	0.002	0.001	0.012	0.001	0.001	0.002	0.001	0.000	0.009	0.001	1.000	0.003	0.002	0.002	0.000	0.001	0.002	0.002	0.004	0.001	0.000	0.003	0.004	0.004	0.001	0.000
P. nicosulfuronedens	0.003	0.025	0.003	0.029	0.002	0.004	0.021	0.003	0.017	0.021	0.002	0.003	0.003	1.000	0.102	0.073	0.001	0.005	0.020	0.003	0.004	0.004	0.002	0.004	0.002	0.001	0.009	0.002
P. nitritireducens	0.004	0.030	0.004	0.033	0.003	0.005	0.026	0.005	0.019	0.028	0.002	0.007	0.002	0.102	1.000	0.604	0.001	0.005	0.022	0.004	0.004	0.003	0.002	0.006	0.003	0.001	0.011	0.004
P. nitroreducens	0.004	0.029	0.003	0.032	0.003	0.004	0.025	0.005	0.018	0.029	0.002	0.007	0.002	0.073	0.604	1.000	0.001	0.006	0.024	0.004	0.003	0.003	0.003	0.006	0.003	0.001	0.010	0.004
P. nosocomialis	0.001	0.002	0.002	0.002	0.000	0.002	0.003	0.003	0.002	0.002	0.000	0.002	0.000	0.001	0.001	0.001	1.000	0.003	0.002	0.000	0.005	0.002	0.002	0.008	0.000	0.000	0.003	0.004
P. otitidis	0.003	0.009	0.003	0.009	0.000	0.017	0.010	0.009	0.007	0.007	0.002	0.007	0.001	0.005	0.005	0.006	0.003	1.000	0.007	0.002	0.005	0.005	0.002	0.008	0.002	0.001	0.058	0.007
P. panipatensis	0.004	0.026	0.006	0.028	0.002	0.006	0.024	0.007	0.020	0.031	0.002	0.007	0.002	0.020	0.022	0.024	0.002	0.007	1.000	0.005	0.008	0.004	0.004	0.006	0.002	0.001	0.008	0.006
P. peli	0.002	0.003	0.006	0.003	0.003	0.001	0.003	0.004	0.002	0.003	0.004	0.001	0.002	0.003	0.004	0.004	0.000	0.002	0.005	1.000	0.005	0.004	0.002	0.003	0.004	0.001	0.002	0.003
P. pseudoalcaligenes	0.003	0.005	0.032	0.004	0.002	0.003	0.004	0.299	0.004	0.005	0.003	0.004	0.004	0.004	0.004	0.003	0.005	0.005	0.008	0.005	1.000	0.001	0.055	0.002	0.001	0.001	0.003	0.089
P. putida	0.004	0.003	0.002	0.005	0.006	0.001	0.002	0.002	0.004	0.003	0.006	0.002	0.001	0.004	0.003	0.003	0.002	0.005	0.004	0.004	0.001	1.000	0.003	0.004	0.004	0.002	0.006	0.003
P. sediminis	0.001	0.003	0.061	0.004	0.002	0.003	0.004	0.051	0.004	0.002	0.001	0.002	0.000	0.002	0.002	0.003	0.002	0.002	0.004	0.002	0.055	0.003	1.000	0.002	0.000	0.002	0.004	0.068
P. stutzeri	0.002	0.006	0.002	0.005	0.003	0.006	0.005	0.008	0.004	0.007	0.002	0.004	0.003	0.004	0.006	0.006	0.008	0.008	0.006	0.003	0.002	0.004	0.002	1.000	0.001	0.004	0.007	0.005
P. synxantha	0.007	0.001	0.000	0.002	0.030	0.001	0.001	0.002	0.002	0.001	0.038	0.000	0.004	0.002	0.003	0.003	0.000	0.002	0.002	0.004	0.001	0.004	0.000	0.001	1.000	0.004	0.004	0.001
P. syringae	0.007	0.000	0.001	0.000	0.006	0.001	0.000	0.003	0.001	0.001	0.007	0.002	0.004	0.001	0.001	0.001	0.000	0.001	0.001	0.001	0.001	0.002	0.002	0.004	0.004	1.000	0.002	0.001
P. tohonis	0.002	0.010	0.004	0.010	0.002	0.013	0.009	0.006	0.006	0.014	0.002	0.010	0.001	0.009	0.011	0.010	0.003	0.058	0.008	0.002	0.003	0.006	0.004	0.007	0.004	0.002	1.000	0.008
P. toyotomiensis	0.002	0.003	0.039	0.004	0.001	0.005	0.003	0.083	0.004	0.001	0.001	0.004	0.000	0.002	0.004	0.004	0.004	0.007	0.006	0.003	0.089	0.003	0.068	0.005	0.001	0.001	0.008	1.000

Appendix - Table 29: Raw data comparing the Jaccard similarity index of genomic sketches of Pseudomonas *species based on a k-mer length of 51. The table is continued on page 567.*

	A.agilis	*PA1129*	*PA1130*	*PA1145*	*PA1646*	*PA1780*	*PA1794*	*PA1802*	*PA2045*	*PA2078*	*PA2506*	*PA2541*	*PA2548*	*PA259*	*PA580*	*PA628*	*PA828*	*PA868*	*PA964*	*P.aeruginosaDSM50071.1*	*P.aeruginosaDSM50071.2*	*P.aeruginosaLESB58*	*P.aeruginosaPA14*	*P.aeruginosaPA7*	*P.aeruginosaPAK*	*P.aeruginosaPAO1*	*P.alcaligenes*	*P.campi*
A.agilis	1.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
PA1129	0.000	1.000	0.974	0.657	0.596	0.615	0.456	0.456	0.503	0.506	0.399	0.611	0.599	0.486	0.624	0.619	0.561	0.488	0.611	0.069	0.070	0.062	0.067	0.503	0.066	0.066	0.002	0.002
PA1130	0.000	0.974	1.000	0.649	0.591	0.605	0.449	0.449	0.493	0.498	0.391	0.601	0.595	0.477	0.612	0.611	0.553	0.483	0.600	0.069	0.068	0.061	0.067	0.493	0.065	0.065	0.002	0.002
PA1145	0.000	0.657	0.649	1.000	0.625	0.660	0.469	0.469	0.515	0.526	0.407	0.656	0.628	0.505	0.643	0.836	0.563	0.490	0.634	0.074	0.074	0.066	0.071	0.515	0.070	0.072	0.002	0.002
PA1646	0.000	0.596	0.591	0.625	1.000	0.600	0.451	0.451	0.493	0.499	0.384	0.598	0.988	0.475	0.604	0.607	0.553	0.466	0.617	0.070	0.069	0.064	0.072	0.493	0.066	0.067	0.002	0.002
PA1780	0.000	0.615	0.605	0.660	0.600	1.000	0.457	0.457	0.504	0.519	0.402	0.976	0.603	0.482	0.621	0.633	0.579	0.483	0.611	0.072	0.074	0.065	0.068	0.504	0.068	0.068	0.001	0.003
PA1794	0.000	0.456	0.449	0.469	0.451	0.457	1.000	1.000	0.602	0.617	0.715	0.456	0.452	0.587	0.473	0.454	0.430	0.747	0.455	0.070	0.071	0.064	0.070	0.602	0.067	0.069	0.004	0.002
PA1802	0.000	0.456	0.449	0.469	0.451	0.457	1.000	1.000	0.602	0.617	0.715	0.456	0.452	0.587	0.473	0.454	0.430	0.747	0.455	0.070	0.071	0.064	0.070	0.602	0.067	0.069	0.004	0.002
PA2045	0.000	0.503	0.493	0.515	0.493	0.504	0.602	0.602	1.000	0.948	0.520	0.501	0.494	0.669	0.505	0.489	0.455	0.626	0.497	0.080	0.080	0.073	0.078	1.000	0.077	0.079	0.004	0.002
PA2078	0.000	0.506	0.498	0.526	0.499	0.519	0.617	0.617	0.948	1.000	0.535	0.516	0.501	0.679	0.517	0.502	0.470	0.640	0.507	0.081	0.081	0.075	0.078	0.948	0.078	0.081	0.002	0.002
PA2506	0.000	0.399	0.391	0.407	0.384	0.402	0.715	0.715	0.520	0.535	1.000	0.400	0.385	0.496	0.403	0.397	0.399	0.625	0.414	0.066	0.067	0.061	0.064	0.520	0.063	0.062	0.005	0.002
PA2541	0.000	0.611	0.601	0.656	0.598	0.976	0.456	0.456	0.501	0.516	0.400	1.000	0.601	0.481	0.619	0.635	0.577	0.480	0.607	0.071	0.073	0.064	0.068	0.501	0.068	0.067	0.001	0.003
PA2548	0.000	0.599	0.595	0.628	0.988	0.603	0.452	0.452	0.494	0.501	0.385	0.601	1.000	0.474	0.606	0.611	0.556	0.467	0.622	0.070	0.069	0.064	0.071	0.494	0.066	0.067	0.002	0.002
PA259	0.000	0.486	0.477	0.505	0.475	0.482	0.587	0.587	0.669	0.679	0.496	0.481	0.474	1.000	0.499	0.497	0.449	0.621	0.487	0.079	0.078	0.071	0.074	0.669	0.076	0.078	0.002	0.002
PA580	0.000	0.624	0.612	0.643	0.604	0.621	0.473	0.473	0.505	0.517	0.403	0.619	0.606	0.499	1.000	0.610	0.566	0.490	0.626	0.071	0.071	0.067	0.067	0.505	0.069	0.065	0.002	0.002
PA628	0.000	0.619	0.611	0.836	0.607	0.633	0.454	0.454	0.489	0.502	0.397	0.635	0.611	0.497	0.610	1.000	0.543	0.475	0.607	0.070	0.071	0.064	0.072	0.489	0.066	0.067	0.002	0.002
PA828	0.000	0.561	0.553	0.563	0.553	0.579	0.430	0.430	0.455	0.470	0.399	0.577	0.556	0.449	0.566	0.543	1.000	0.441	0.587	0.070	0.070	0.063	0.068	0.455	0.066	0.066	0.002	0.002
PA868	0.000	0.488	0.483	0.490	0.466	0.483	0.747	0.747	0.626	0.640	0.625	0.480	0.467	0.621	0.490	0.475	0.441	1.000	0.475	0.071	0.072	0.064	0.070	0.626	0.068	0.069	0.002	0.002
PA964	0.000	0.611	0.600	0.634	0.617	0.611	0.455	0.455	0.497	0.507	0.414	0.607	0.622	0.487	0.626	0.607	0.587	0.475	1.000	0.070	0.070	0.065	0.068	0.497	0.066	0.066	0.002	0.002
P.aeruginosaDSM50071.1	0.000	0.069	0.069	0.074	0.070	0.072	0.070	0.070	0.080	0.081	0.066	0.071	0.070	0.079	0.071	0.070	0.070	0.071	0.070	1.000	0.993	0.651	0.450	0.080	0.655	0.645	0.004	0.001
P.aeruginosaDSM50071.2	0.000	0.070	0.068	0.074	0.069	0.074	0.071	0.071	0.080	0.081	0.067	0.073	0.069	0.078	0.071	0.071	0.070	0.072	0.070	0.993	1.000	0.651	0.447	0.080	0.653	0.645	0.004	0.001
P.aeruginosaLESB58	0.000	0.062	0.061	0.066	0.064	0.065	0.064	0.064	0.073	0.075	0.061	0.064	0.064	0.071	0.067	0.064	0.063	0.064	0.065	0.651	0.651	1.000	0.419	0.073	0.623	0.639	0.004	0.001
P.aeruginosaPA14	0.000	0.067	0.067	0.071	0.072	0.068	0.070	0.070	0.078	0.078	0.064	0.068	0.071	0.074	0.067	0.072	0.068	0.070	0.068	0.450	0.447	0.419	1.000	0.078	0.443	0.437	0.004	0.001

P.aeruginosaPA7	0.000	0.503	0.493	0.515	0.493	0.504	0.602	0.602	1.000	0.948	0.520	0.501	0.494	0.669	0.505	0.489	0.455	0.626	0.497	0.080	0.080	0.073	0.078	1.000	0.077	0.079	0.004	0.002
P.aeruginosaPAK	0.000	0.066	0.065	0.070	0.066	0.068	0.067	0.067	0.077	0.078	0.063	0.068	0.066	0.076	0.069	0.066	0.066	0.068	0.066	0.655	0.653	0.623	0.443	0.077	1.000	0.642	0.004	0.001
P.aeruginosaPAO1	0.000	0.066	0.065	0.072	0.067	0.068	0.069	0.069	0.079	0.081	0.062	0.067	0.067	0.078	0.065	0.067	0.066	0.069	0.066	0.645	0.645	0.639	0.437	0.079	0.642	1.000	0.004	0.001
P.alcaligenes	0.000	0.002	0.002	0.002	0.002	0.001	0.004	0.004	0.004	0.002	0.005	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.004	0.004	0.004	0.004	0.004	0.004	0.004	1.000	0.003
P.campi	0.000	0.002	0.002	0.002	0.002	0.003	0.002	0.002	0.002	0.002	0.002	0.003	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.003	1.000
P.chlororaphis	0.000	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
P.citronellolis	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.003	0.003	0.003	0.003	0.002	0.003	0.003	0.003	0.001
P.composti	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.003	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002
P.delhiensis	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.004	0.002
P.fluorescens	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.001
P.furukawaii	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.004	0.001
P.humi	0.000	0.003	0.003	0.004	0.003	0.003	0.003	0.003	0.003	0.003	0.002	0.003	0.003	0.004	0.003	0.004	0.003	0.003	0.003	0.004	0.004	0.004	0.004	0.003	0.004	0.004	0.004	0.002
P.indoloxydans	0.000	0.002	0.002	0.002	0.002	0.002	0.005	0.005	0.002	0.002	0.003	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.003	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.005	0.005
P.jinjuensis	0.000	0.004	0.004	0.005	0.004	0.003	0.004	0.004	0.004	0.004	0.004	0.003	0.004	0.003	0.004	0.005	0.003	0.004	0.003	0.004	0.004	0.005	0.005	0.004	0.004	0.005	0.006	0.000
P.knackmussii	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.002	0.002	0.003	0.003	0.002	0.002	0.003	0.002	0.002
P.lactis	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.004	0.001	0.001	0.001	0.001	0.001	0.001
P.lalkuanensis	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001
P.mucoides	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
P.nicosulfuronedens	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002
P.nitritireducens	0.000	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.001	0.003
P.nitroreducens	0.000	0.002	0.002	0.002	0.001	0.002	0.001	0.001	0.001	0.002	0.002	0.002	0.001	0.002	0.002	0.001	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.001	0.002	0.001	0.001	0.003
P.nosocomialis	0.000	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.003	0.003	0.005	0.001	0.001	0.002	0.001	0.003	0.001	0.002	0.001	0.004	0.004	0.003	0.002	0.003	0.004	0.003	0.004	0.001
P.otitidis	0.000	0.002	0.002	0.002	0.004	0.002	0.002	0.002	0.002	0.002	0.003	0.002	0.004	0.002	0.002	0.002	0.002	0.001	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.006	0.001
P.panipatensis	0.000	0.002	0.002	0.003	0.003	0.003	0.003	0.003	0.003	0.003	0.003	0.003	0.003	0.003	0.002	0.003	0.003	0.003	0.002	0.005	0.005	0.005	0.005	0.003	0.005	0.005	0.004	0.003
P.peli	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.003
P.pseudoalcaligenes	0.000	0.002	0.002	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.003	0.006	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.003	0.006
P.putida	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
P.sediminis	0.000	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.002
P.stutzeri	0.000	0.003	0.003	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.003	0.002	0.003	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.001
P.synxantha	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002
P.syringae	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001
P.tohonis	0.000	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.002	0.001	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.008	0.002
P.toyotomiensis	0.000	0.001	0.001	0.001	0.001	0.001	0.003	0.003	0.002	0.002	0.003	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.002	0.002

Continuation of Appendix - Table 29

	P.chlororaphis	*P.citronellolis*	*P.composti*	*P.delhiensis*	*P.fluorescens*	*P.furukawaii*	*P.humi*	*P.indoloxydans*	*P.jinjuensis*	*P.knackmussii*	*P.lactis*	*P.lalkuanensis*	*P.mucoides*	*P.nicosulfuronedens*	*P.nitritireducens*	*P.nitroreducens*	*P.nosocomialis*	*P.otitidis*	*P.panipatensis*	*P.peli*	*P.pseudoalcaligenes*	*P.putida*	*P.sediminis*	*P.stutzeri*	*P.synxantha*	*P.syringae*	*P.tohonis*	*P.toyotomiensis*
A.agilis	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
PA1129	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.002	0.001	0.002	0.000	0.001	0.003	0.001	0.001	0.001	0.001
PA1130	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.002	0.001	0.002	0.000	0.001	0.003	0.001	0.001	0.001	0.001
PA1145	0.002	0.002	0.001	0.002	0.001	0.002	0.004	0.002	0.005	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.002	0.001
PA1646	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.001	0.001	0.001	0.004	0.003	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.001	0.001
PA1780	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.002	0.003	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.001	0.001
PA1794	0.001	0.002	0.001	0.001	0.001	0.001	0.003	0.005	0.004	0.001	0.001	0.002	0.001	0.002	0.002	0.001	0.002	0.002	0.003	0.001	0.001	0.000	0.002	0.002	0.001	0.001	0.001	0.003
PA1802	0.001	0.002	0.001	0.001	0.001	0.001	0.003	0.005	0.004	0.001	0.001	0.002	0.001	0.002	0.002	0.001	0.002	0.002	0.003	0.001	0.001	0.000	0.002	0.002	0.001	0.001	0.001	0.003
PA2045	0.001	0.002	0.001	0.002	0.002	0.002	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.001	0.001	0.003	0.002	0.003	0.001	0.002	0.000	0.002	0.002	0.001	0.001	0.001	0.002
PA2078	0.001	0.002	0.001	0.002	0.002	0.002	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.002	0.003	0.001	0.001	0.000	0.002	0.002	0.001	0.001	0.001	0.002
PA2506	0.001	0.001	0.001	0.002	0.002	0.002	0.002	0.003	0.004	0.002	0.001	0.002	0.001	0.002	0.002	0.002	0.005	0.003	0.003	0.001	0.002	0.000	0.002	0.002	0.001	0.001	0.001	0.003
PA2541	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.002	0.003	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.001	0.001
PA2548	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.001	0.001	0.001	0.004	0.003	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.001	0.001
PA259	0.001	0.002	0.001	0.002	0.001	0.002	0.004	0.002	0.003	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.002	0.002	0.003	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.001	0.001
PA580	0.002	0.002	0.001	0.002	0.001	0.002	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.002	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.002	0.001
PA628	0.001	0.002	0.001	0.002	0.001	0.002	0.004	0.002	0.005	0.002	0.001	0.002	0.001	0.002	0.001	0.001	0.003	0.002	0.003	0.001	0.001	0.000	0.001	0.003	0.001	0.001	0.001	0.001
PA828	0.001	0.002	0.001	0.001	0.001	0.002	0.003	0.002	0.003	0.001	0.001	0.002	0.001	0.002	0.001	0.001	0.001	0.002	0.003	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.001	0.002
PA868	0.001	0.002	0.003	0.001	0.001	0.001	0.003	0.002	0.004	0.001	0.001	0.002	0.001	0.002	0.001	0.001	0.002	0.001	0.003	0.001	0.003	0.000	0.002	0.003	0.001	0.001	0.002	0.002
PA964	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.003	0.003	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.001	0.002	0.002	0.001	0.006	0.000	0.001	0.002	0.001	0.001	0.001	0.002
P.aeruginosaDSM50071.1	0.001	0.003	0.001	0.002	0.001	0.001	0.004	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.002	0.002	0.004	0.001	0.005	0.001	0.001	0.000	0.001	0.001	0.001	0.001	0.002	0.001
P.aeruginosaDSM50071.2	0.001	0.003	0.001	0.002	0.001	0.001	0.004	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.002	0.002	0.004	0.001	0.005	0.001	0.001	0.000	0.001	0.001	0.001	0.001	0.002	0.001
P.aeruginosaLESB58	0.001	0.003	0.001	0.002	0.001	0.001	0.004	0.002	0.005	0.003	0.004	0.002	0.001	0.002	0.002	0.002	0.003	0.001	0.005	0.001	0.001	0.000	0.001	0.001	0.001	0.001	0.002	0.001
P.aeruginosaPA14	0.001	0.003	0.001	0.002	0.001	0.001	0.004	0.002	0.005	0.003	0.001	0.002	0.001	0.002	0.002	0.002	0.002	0.001	0.005	0.001	0.001	0.000	0.001	0.001	0.001	0.001	0.002	0.001
P.aeruginosaPA7	0.001	0.002	0.001	0.002	0.002	0.002	0.003	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.001	0.001	0.003	0.002	0.003	0.001	0.002	0.000	0.002	0.002	0.001	0.001	0.001	0.002
P.aeruginosaPAK	0.001	0.003	0.001	0.002	0.001	0.001	0.004	0.002	0.004	0.002	0.001	0.002	0.001	0.002	0.002	0.002	0.004	0.001	0.005	0.001	0.001	0.000	0.001	0.001	0.001	0.001	0.002	0.001

P.aeruginosaPAO1	0.001	0.003	0.001	0.002	0.001	0.001	0.004	0.002	0.005	0.003	0.001	0.002	0.001	0.001	0.002	0.001	0.003	0.001	0.005	0.001	0.001	0.000	0.001	0.001	0.001	0.001	0.002	0.001
P.alcaligenes	0.001	0.003	0.001	0.004	0.001	0.004	0.004	0.005	0.006	0.002	0.001	0.002	0.001	0.001	0.001	0.001	0.004	0.006	0.004	0.001	0.003	0.000	0.001	0.001	0.001	0.001	0.008	0.002
P.campi	0.001	0.001	0.002	0.002	0.001	0.001	0.002	0.005	0.000	0.002	0.001	0.001	0.001	0.002	0.003	0.003	0.001	0.001	0.003	0.003	0.006	0.000	0.002	0.001	0.002	0.001	0.002	0.002
P.chlororaphis	1.000	0.001	0.002	0.001	0.003	0.001	0.001	0.002	0.001	0.001	0.003	0.001	0.004	0.001	0.001	0.001	0.001	0.002	0.001	0.002	0.002	0.000	0.002	0.001	0.004	0.004	0.001	0.002
P.citronellolis	0.001	1.000	0.001	0.098	0.000	0.001	0.239	0.000	0.009	0.013	0.000	0.003	0.000	0.006	0.005	0.004	0.002	0.004	0.009	0.000	0.000	0.000	0.001	0.001	0.000	0.000	0.005	0.001
P.composti	0.002	0.001	1.000	0.001	0.001	0.001	0.002	0.009	0.001	0.002	0.001	0.002	0.002	0.001	0.002	0.002	0.001	0.002	0.001	0.003	0.012	0.000	0.020	0.001	0.001	0.001	0.004	0.022
P.delhiensis	0.001	0.098	0.001	1.000	0.001	0.004	0.109	0.002	0.010	0.011	0.001	0.005	0.001	0.012	0.008	0.009	0.002	0.005	0.010	0.001	0.001	0.000	0.002	0.002	0.001	0.001	0.005	0.002
P.fluorescens	0.003	0.000	0.001	0.001	1.000	0.001	0.001	0.001	0.000	0.001	0.010	0.001	0.004	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.002	0.001	0.012	0.002	0.001	0.002
P.furukawaii	0.001	0.001	0.001	0.004	0.001	1.000	0.002	0.006	0.001	0.002	0.001	0.007	0.001	0.002	0.001	0.001	0.002	0.007	0.002	0.001	0.002	0.000	0.002	0.005	0.001	0.001	0.005	0.003
P.humi	0.001	0.239	0.002	0.109	0.001	0.002	1.000	0.001	0.008	0.015	0.001	0.005	0.001	0.008	0.007	0.006	0.003	0.005	0.010	0.001	0.001	0.000	0.002	0.002	0.001	0.001	0.007	0.002
P.indoloxydans	0.002	0.000	0.009	0.002	0.001	0.006	0.001	1.000	0.000	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.005	0.001	0.004	0.209	0.000	0.033	0.003	0.001	0.001	0.003	0.035
P.jinjuensis	0.001	0.009	0.001	0.010	0.000	0.001	0.008	0.000	1.000	0.010	0.000	0.003	0.000	0.004	0.003	0.004	0.002	0.002	0.008	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.002	0.000
P.knackmussii	0.001	0.013	0.002	0.011	0.001	0.002	0.015	0.001	0.010	1.000	0.001	0.002	0.001	0.005	0.006	0.006	0.002	0.003	0.009	0.001	0.001	0.000	0.001	0.001	0.001	0.001	0.003	0.001
P.lactis	0.003	0.000	0.001	0.001	0.010	0.001	0.001	0.001	0.000	0.001	1.000	0.001	0.004	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.002	0.022	0.002	0.001	0.001
P.lalkuanensis	0.001	0.003	0.002	0.005	0.001	0.007	0.005	0.001	0.003	0.002	0.001	1.000	0.001	0.002	0.001	0.001	0.003	0.007	0.003	0.001	0.002	0.000	0.004	0.001	0.001	0.001	0.005	0.003
P.mucoides	0.004	0.000	0.002	0.001	0.004	0.001	0.001	0.001	0.000	0.001	0.004	0.001	1.000	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.000	0.001	0.001	0.003	0.001	0.001	0.001
P.nicosulfuronedens	0.001	0.006	0.001	0.012	0.001	0.002	0.008	0.001	0.004	0.005	0.001	0.002	0.001	1.000	0.048	0.027	0.001	0.002	0.006	0.001	0.001	0.000	0.002	0.001	0.001	0.001	0.003	0.002
P.nitritireducens	0.001	0.005	0.002	0.008	0.001	0.001	0.007	0.002	0.003	0.006	0.001	0.001	0.001	0.048	1.000	0.507	0.002	0.002	0.005	0.001	0.002	0.000	0.001	0.001	0.001	0.001	0.004	0.001
P.nitroreducens	0.001	0.004	0.002	0.009	0.001	0.001	0.006	0.002	0.004	0.006	0.001	0.001	0.001	0.027	0.507	1.000	0.001	0.002	0.006	0.001	0.002	0.000	0.001	0.001	0.001	0.001	0.003	0.001
P.nosocomialis	0.001	0.002	0.001	0.002	0.001	0.002	0.003	0.001	0.002	0.002	0.002	0.003	0.002	0.001	0.002	0.001	1.000	0.004	0.002	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.003	0.001
P.otitidis	0.002	0.004	0.002	0.005	0.001	0.007	0.005	0.005	0.002	0.003	0.001	0.007	0.001	0.002	0.002	0.002	0.004	1.000	0.003	0.001	0.005	0.000	0.003	0.001	0.001	0.001	0.023	0.003
P.panipatensis	0.001	0.009	0.001	0.010	0.001	0.002	0.010	0.001	0.008	0.009	0.001	0.003	0.001	0.006	0.005	0.006	0.002	0.003	1.000	0.001	0.001	0.000	0.002	0.001	0.001	0.001	0.003	0.002
P.peli	0.002	0.000	0.003	0.001	0.001	0.001	0.001	0.004	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	1.000	0.003	0.000	0.005	0.001	0.001	0.001	0.002	0.003
P.pseudoalcaligenes	0.002	0.000	0.012	0.001	0.001	0.002	0.001	0.209	0.001	0.001	0.001	0.002	0.001	0.001	0.002	0.002	0.001	0.005	0.001	0.003	1.000	0.000	0.030	0.002	0.001	0.001	0.003	0.038
P.putida	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	1.000	0.000	0.000	0.000	0.000	0.000	0.000
P.sediminis	0.002	0.001	0.020	0.002	0.002	0.002	0.002	0.033	0.000	0.001	0.001	0.004	0.001	0.002	0.001	0.001	0.001	0.003	0.002	0.005	0.030	0.000	1.000	0.001	0.001	0.001	0.003	0.030
P.stutzeri	0.001	0.001	0.001	0.002	0.001	0.005	0.002	0.003	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.002	0.000	0.001	1.000	0.001	0.001	0.002	0.001
P.synxantha	0.004	0.000	0.001	0.001	0.012	0.001	0.001	0.001	0.000	0.001	0.022	0.001	0.003	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.001	0.001	1.000	0.002	0.001	0.001
P.syringae	0.004	0.000	0.001	0.001	0.002	0.001	0.001	0.001	0.000	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.001	0.001	0.002	1.000	0.002	0.001
P.tohonis	0.001	0.005	0.004	0.005	0.001	0.005	0.007	0.003	0.002	0.003	0.001	0.005	0.001	0.003	0.004	0.003	0.003	0.023	0.003	0.002	0.003	0.000	0.003	0.002	0.001	0.002	1.000	0.005
P.toyotomiensis	0.002	0.001	0.022	0.002	0.002	0.003	0.002	0.035	0.000	0.001	0.001	0.003	0.001	0.002	0.001	0.001	0.001	0.003	0.002	0.003	0.038	0.000	0.030	0.001	0.001	0.001	0.005	1.000

Appendix - Table 30: Raw data comparing the Jaccard similarity index of genomic sketches of Pseudomonas *species based on a k-mer length of 71. The table is continued on page 571.*

	A.agilis	*PA1129*	*PA1130*	*PA1145*	*PA1646*	*PA1780*	*PA1794*	*PA1802*	*PA2045*	*PA2078*	*PA2506*	*PA2541*	*PA2548*	*PA259*	*PA580*	*PA628*	*PA828*	*PA868*	*PA964*	*P.aeruginosaDSM50071.1*	*P.aeruginosaDSM50071.2*	*P.aeruginosaLESB58*	*P.aeruginosaPA14*	*P.aeruginosaPA7*	*P.aeruginosaPAK*	*P.aeruginosaPAO1*	*P.alcaligenes*	*P.campi*
A.agilis	1.000	0.001	0.001	0.001	0.001	0.000	0.001	0.001	0.000	0.000	0.001	0.000	0.001	0.001	0.001	0.001	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.001	0.001	0.000	0.000
PA1129	0.001	1.000	0.979	0.604	0.566	0.576	0.379	0.379	0.413	0.418	0.327	0.577	0.574	0.426	0.560	0.581	0.521	0.394	0.557	0.050	0.050	0.049	0.049	0.413	0.054	0.050	0.001	0.001
PA1130	0.001	0.979	1.000	0.601	0.563	0.571	0.378	0.378	0.411	0.416	0.326	0.572	0.571	0.425	0.556	0.578	0.516	0.394	0.554	0.051	0.050	0.049	0.050	0.411	0.055	0.051	0.001	0.001
PA1145	0.001	0.604	0.601	1.000	0.565	0.559	0.377	0.377	0.399	0.410	0.326	0.560	0.575	0.425	0.581	0.795	0.530	0.397	0.568	0.052	0.053	0.055	0.053	0.399	0.059	0.052	0.001	0.001
PA1646	0.001	0.566	0.563	0.565	1.000	0.560	0.382	0.382	0.407	0.416	0.326	0.559	0.976	0.419	0.535	0.563	0.497	0.395	0.540	0.049	0.049	0.046	0.050	0.407	0.053	0.049	0.001	0.001
PA1780	0.000	0.576	0.571	0.559	0.560	1.000	0.382	0.382	0.414	0.428	0.323	0.964	0.568	0.426	0.549	0.553	0.533	0.401	0.545	0.049	0.049	0.048	0.048	0.414	0.055	0.049	0.002	0.001
PA1794	0.001	0.379	0.378	0.377	0.382	0.382	1.000	1.000	0.546	0.566	0.692	0.382	0.387	0.542	0.406	0.378	0.367	0.730	0.394	0.050	0.050	0.060	0.052	0.546	0.055	0.048	0.004	0.001
PA1802	0.001	0.379	0.378	0.377	0.382	0.382	1.000	1.000	0.546	0.566	0.692	0.382	0.387	0.542	0.406	0.378	0.367	0.730	0.394	0.050	0.050	0.060	0.052	0.546	0.055	0.048	0.004	0.001
PA2045	0.000	0.413	0.411	0.399	0.407	0.414	0.546	0.546	1.000	0.932	0.461	0.409	0.412	0.586	0.410	0.401	0.383	0.583	0.402	0.053	0.054	0.053	0.057	1.000	0.057	0.055	0.002	0.001
PA2078	0.000	0.418	0.416	0.410	0.416	0.428	0.566	0.566	0.932	1.000	0.472	0.425	0.421	0.601	0.425	0.414	0.394	0.595	0.414	0.055	0.055	0.053	0.056	0.932	0.058	0.056	0.001	0.001
PA2506	0.001	0.327	0.326	0.326	0.326	0.323	0.692	0.692	0.461	0.472	1.000	0.319	0.328	0.455	0.345	0.319	0.346	0.588	0.360	0.047	0.047	0.056	0.052	0.461	0.051	0.047	0.004	0.001
PA2541	0.000	0.577	0.572	0.560	0.559	0.964	0.382	0.382	0.409	0.425	0.319	1.000	0.567	0.423	0.549	0.564	0.530	0.396	0.539	0.048	0.048	0.049	0.047	0.409	0.054	0.049	0.001	0.001
PA2548	0.001	0.574	0.571	0.575	0.976	0.568	0.387	0.387	0.412	0.421	0.328	0.567	1.000	0.423	0.546	0.571	0.502	0.399	0.549	0.050	0.050	0.046	0.047	0.412	0.053	0.049	0.001	0.001
PA259	0.001	0.426	0.425	0.425	0.419	0.426	0.542	0.542	0.586	0.601	0.455	0.423	0.423	1.000	0.431	0.418	0.414	0.576	0.427	0.062	0.063	0.057	0.058	0.586	0.064	0.061	0.001	0.001
PA580	0.001	0.560	0.556	0.581	0.535	0.549	0.406	0.406	0.410	0.425	0.345	0.549	0.546	0.431	1.000	0.556	0.523	0.410	0.543	0.058	0.059	0.066	0.052	0.410	0.062	0.057	0.001	0.001
PA628	0.001	0.581	0.578	0.795	0.563	0.553	0.378	0.378	0.401	0.414	0.319	0.564	0.571	0.418	0.556	1.000	0.530	0.390	0.563	0.049	0.049	0.051	0.051	0.401	0.055	0.049	0.001	0.001
PA828	0.000	0.521	0.516	0.530	0.497	0.533	0.367	0.367	0.383	0.394	0.346	0.530	0.502	0.414	0.523	0.530	1.000	0.377	0.545	0.049	0.049	0.054	0.049	0.383	0.056	0.048	0.001	0.001
PA868	0.001	0.394	0.394	0.397	0.395	0.401	0.730	0.730	0.583	0.595	0.588	0.396	0.399	0.576	0.410	0.390	0.377	1.000	0.400	0.054	0.054	0.051	0.058	0.583	0.059	0.053	0.002	0.001
PA964	0.001	0.557	0.554	0.568	0.540	0.545	0.394	0.394	0.402	0.414	0.360	0.539	0.549	0.427	0.543	0.563	0.545	0.400	1.000	0.051	0.051	0.054	0.051	0.402	0.055	0.049	0.002	0.001
P.aeruginosaDSM50071.1	0.001	0.050	0.051	0.052	0.049	0.049	0.050	0.050	0.053	0.055	0.047	0.048	0.050	0.062	0.058	0.049	0.049	0.054	0.051	1.000	0.990	0.540	0.354	0.053	0.569	0.551	0.001	0.001
P.aeruginosaDSM50071.2	0.001	0.050	0.050	0.053	0.049	0.049	0.050	0.050	0.054	0.055	0.047	0.048	0.050	0.063	0.059	0.049	0.049	0.054	0.051	0.990	1.000	0.539	0.353	0.054	0.566	0.550	0.001	0.001
P.aeruginosaLESB58	0.001	0.049	0.049	0.055	0.046	0.048	0.060	0.060	0.053	0.053	0.056	0.049	0.046	0.057	0.066	0.051	0.054	0.051	0.054	0.540	0.539	1.000	0.351	0.053	0.552	0.548	0.001	0.001
P.aeruginosaPA14	0.001	0.049	0.050	0.053	0.050	0.048	0.052	0.052	0.057	0.056	0.052	0.047	0.047	0.058	0.052	0.051	0.049	0.058	0.051	0.354	0.353	0.351	1.000	0.057	0.365	0.365	0.001	0.001
P.aeruginosaPA7	0.000	0.413	0.411	0.399	0.407	0.414	0.546	0.546	1.000	0.932	0.461	0.409	0.412	0.586	0.410	0.401	0.383	0.583	0.402	0.053	0.054	0.053	0.057	1.000	0.057	0.055	0.002	0.001
P.aeruginosaPAK	0.001	0.054	0.055	0.059	0.053	0.055	0.055	0.055	0.057	0.058	0.051	0.054	0.053	0.064	0.062	0.055	0.056	0.059	0.055	0.569	0.566	0.552	0.365	0.057	1.000	0.569	0.001	0.001

P.aeruginosaPAO1	0.001	0.050	0.051	0.052	0.049	0.049	0.048	0.048	0.055	0.056	0.047	0.049	0.049	0.061	0.057	0.049	0.048	0.053	0.049	0.551	0.550	0.548	0.365	0.055	0.569	1.000	0.001	0.001
P.alcaligenes	0.000	0.001	0.001	0.001	0.001	0.002	0.004	0.004	0.002	0.001	0.004	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	1.000	0.001
P.campi	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	1.000
P.chlororaphis	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.001	0.001	0.001	0.001	0.001	0.000	0.000
P.citronellolis	0.000	0.001	0.002	0.001	0.001	0.002	0.001	0.001	0.001	0.002	0.002	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.001	0.001	0.001	0.002	0.002	0.001
P.composti	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
P.delhiensis	0.000	0.002	0.002	0.002	0.001	0.002	0.001	0.001	0.001	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.001	0.001	0.001	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.001
P.fluorescens	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
P.furukawaii	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001
P.humi	0.000	0.002	0.002	0.002	0.003	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.003	0.002	0.002	0.003	0.003	0.001	0.003	0.003	0.003	0.003	0.003	0.001	0.003	0.003	0.002	0.001
P.indoloxydans	0.000	0.002	0.002	0.000	0.000	0.000	0.001	0.001	0.001	0.000	0.003	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.001	0.001	0.000	0.000	0.002	0.000
P.jinjuensis	0.000	0.003	0.003	0.003	0.002	0.003	0.002	0.002	0.002	0.003	0.003	0.002	0.002	0.003	0.003	0.002	0.002	0.002	0.002	0.003	0.003	0.002	0.002	0.002	0.003	0.003	0.002	0.001
P.knackmussii	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.001	0.000
P.lactis	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.003	0.000	0.000	0.000	0.000	0.000	0.000
P.lalkuanensis	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001
P.mucoides	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000
P.nicosulfuronedens	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.001	0.001
P.nitritireducens	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000
P.nitroreducens	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000
P.nosocomialis	0.000	0.002	0.002	0.001	0.001	0.002	0.002	0.002	0.002	0.001	0.005	0.001	0.001	0.001	0.001	0.002	0.001	0.002	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.002	0.001
P.otitidis	0.000	0.002	0.002	0.001	0.001	0.002	0.001	0.001	0.002	0.001	0.004	0.001	0.001	0.001	0.001	0.001	0.001	0.003	0.002	0.001	0.001	0.001	0.001	0.002	0.001	0.001	0.006	0.001
P.panipatensis	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.001	0.001
P.peli	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
P.pseudoalcaligenes	0.000	0.000	0.000	0.000	0.000	0.000	0.002	0.002	0.001	0.000	0.002	0.000	0.000	0.000	0.002	0.000	0.000	0.002	0.003	0.000	0.000	0.002	0.000	0.001	0.000	0.000	0.002	0.000
P.putida	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001
P.sediminis	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.001
P.stutzeri	0.000	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.001	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.002	0.002	0.001	0.001	0.002	0.001
P.synxantha	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
P.syringae	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
P.tohonis	0.000	0.002	0.002	0.002	0.002	0.002	0.001	0.001	0.002	0.001	0.002	0.002	0.002	0.001	0.002	0.002	0.001	0.002	0.002	0.002	0.002	0.002	0.001	0.002	0.002	0.002	0.009	0.002
P.toyotomiensis	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.001

Continuation of Appendix - Table 30

	P.chlororaphis	*P.citronellolis*	*P.composti*	*P.delhiensis*	*P.fluorescens*	*P.furukawaii*	*P.humi*	*P.indoloxydans*	*P.jinjuensis*	*P.knackmussii*	*P.lactis*	*P.lalkuanensis*	*P.mucoides*	*P.nicosulfuronedens*	*P.nitritireducens*	*P.nitroreducens*	*P.nosocomialis*	*P.otitidis*	*P.panipatensis*	*P.peli*	*P.pseudoalcaligenes*	*P.putida*	*P.sediminis*	*P.stutzeri*	*P.synxantha*	*P.syringae*	*P.tohonis*	*P.toyotomiensis*
A.agilis	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
PA1129	0.001	0.001	0.000	0.002	0.000	0.001	0.002	0.002	0.003	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
PA1130	0.001	0.002	0.000	0.002	0.000	0.001	0.002	0.002	0.003	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
PA1145	0.001	0.001	0.000	0.002	0.000	0.001	0.002	0.000	0.003	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
PA1646	0.001	0.001	0.000	0.001	0.000	0.001	0.003	0.000	0.002	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
PA1780	0.001	0.002	0.000	0.002	0.000	0.001	0.002	0.000	0.003	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
PA1794	0.001	0.001	0.000	0.001	0.000	0.001	0.002	0.001	0.002	0.001	0.000	0.001	0.001	0.002	0.001	0.001	0.002	0.001	0.001	0.000	0.002	0.000	0.000	0.001	0.000	0.000	0.001	0.000
PA1802	0.001	0.001	0.000	0.001	0.000	0.001	0.002	0.001	0.002	0.001	0.000	0.001	0.001	0.002	0.001	0.001	0.002	0.001	0.001	0.000	0.002	0.000	0.000	0.001	0.000	0.000	0.001	0.000
PA2045	0.001	0.001	0.000	0.001	0.000	0.001	0.001	0.001	0.002	0.001	0.000	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.001	0.000	0.001	0.000	0.001	0.002	0.000	0.000	0.002	0.000
PA2078	0.001	0.002	0.000	0.002	0.000	0.001	0.002	0.000	0.003	0.001	0.000	0.001	0.001	0.002	0.002	0.002	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.000
PA2506	0.001	0.002	0.000	0.002	0.000	0.001	0.002	0.003	0.003	0.001	0.000	0.001	0.001	0.002	0.002	0.002	0.005	0.004	0.001	0.000	0.002	0.000	0.000	0.002	0.000	0.000	0.002	0.000
PA2541	0.001	0.001	0.000	0.002	0.000	0.001	0.002	0.000	0.002	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
PA2548	0.001	0.001	0.000	0.001	0.000	0.001	0.003	0.000	0.002	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
PA259	0.001	0.001	0.000	0.002	0.000	0.001	0.002	0.000	0.003	0.001	0.000	0.001	0.000	0.002	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.000
PA580	0.001	0.002	0.000	0.002	0.000	0.001	0.002	0.000	0.003	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.002	0.000	0.000	0.001	0.000	0.000	0.002	0.000
PA628	0.001	0.001	0.000	0.002	0.000	0.001	0.003	0.000	0.002	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.002	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
PA828	0.001	0.001	0.000	0.001	0.000	0.001	0.003	0.000	0.002	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.000
PA868	0.001	0.001	0.002	0.001	0.000	0.002	0.001	0.001	0.002	0.001	0.000	0.001	0.000	0.002	0.001	0.002	0.002	0.003	0.001	0.000	0.002	0.000	0.000	0.001	0.000	0.000	0.002	0.002
PA964	0.001	0.001	0.000	0.001	0.000	0.001	0.003	0.000	0.002	0.001	0.000	0.001	0.000	0.002	0.002	0.002	0.002	0.002	0.002	0.000	0.003	0.000	0.000	0.001	0.000	0.000	0.002	0.000
P.aeruginosaDSM50071.1	0.000	0.002	0.000	0.002	0.000	0.001	0.003	0.000	0.003	0.002	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
P.aeruginosaDSM50071.2	0.000	0.002	0.000	0.002	0.000	0.001	0.003	0.000	0.003	0.002	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
P.aeruginosaLESB58	0.001	0.001	0.000	0.002	0.000	0.001	0.003	0.000	0.002	0.002	0.003	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.002	0.000	0.000	0.001	0.000	0.000	0.002	0.000
P.aeruginosaPA14	0.001	0.001	0.000	0.002	0.000	0.001	0.003	0.001	0.002	0.002	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.002	0.000	0.000	0.001	0.000
P.aeruginosaPA7	0.001	0.001	0.000	0.001	0.000	0.001	0.001	0.001	0.002	0.001	0.000	0.001	0.001	0.002	0.002	0.002	0.002	0.002	0.001	0.000	0.001	0.000	0.001	0.002	0.000	0.000	0.002	0.000
P.aeruginosaPAK	0.001	0.001	0.000	0.002	0.000	0.001	0.003	0.000	0.003	0.002	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
P.aeruginosaPAO1	0.001	0.002	0.000	0.002	0.000	0.001	0.003	0.000	0.003	0.002	0.000	0.001	0.000	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000

P.alcaligenes	0.000	0.002	0.000	0.002	0.000	0.002	0.002	0.002	0.002	0.001	0.000	0.002	0.000	0.001	0.000	0.000	0.002	0.006	0.001	0.000	0.002	0.000	0.001	0.002	0.000	0.000	0.009	0.001
P.campi	0.000	0.001	0.000	0.001	0.000	0.001	0.001	0.000	0.001	0.000	0.000	0.001	0.000	0.001	0.000	0.000	0.001	0.001	0.001	0.000	0.000	0.001	0.001	0.001	0.000	0.000	0.002	0.001
P.chlororaphis	1.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
P.citronellolis	0.000	1.000	0.000	0.065	0.000	0.001	0.160	0.000	0.002	0.003	0.000	0.002	0.001	0.002	0.002	0.002	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.000
P.composti	0.000	0.000	1.000	0.000	0.000	0.001	0.000	0.005	0.000	0.000	0.000	0.000	0.000	0.001	0.001	0.001	0.000	0.000	0.001	0.000	0.009	0.000	0.012	0.000	0.000	0.001	0.001	0.009
P.delhiensis	0.000	0.065	0.000	1.000	0.000	0.001	0.065	0.000	0.005	0.002	0.000	0.002	0.001	0.003	0.002	0.003	0.001	0.001	0.002	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.000
P.fluorescens	0.001	0.000	0.000	0.000	1.000	0.000	0.000	0.000	0.000	0.000	0.008	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.001	0.000	0.000	0.007	0.000	0.000	0.000
P.furukawaii	0.000	0.001	0.001	0.001	0.000	1.000	0.001	0.003	0.002	0.001	0.000	0.004	0.000	0.002	0.000	0.000	0.001	0.004	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.004	0.001
P.humi	0.000	0.160	0.000	0.065	0.000	0.001	1.000	0.000	0.004	0.004	0.000	0.002	0.001	0.003	0.003	0.003	0.001	0.001	0.003	0.000	0.000	0.000	0.000	0.002	0.000	0.001	0.002	0.000
P.indoloxydans	0.000	0.000	0.005	0.000	0.000	0.003	0.000	1.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.003	0.000	0.000	0.200	0.000	0.010	0.002	0.000	0.000	0.001	0.019
P.jinjuensis	0.000	0.002	0.000	0.005	0.000	0.002	0.004	0.000	1.000	0.003	0.000	0.002	0.001	0.002	0.002	0.002	0.002	0.001	0.003	0.000	0.000	0.000	0.000	0.002	0.000	0.001	0.002	0.000
P.knackmussii	0.000	0.003	0.000	0.002	0.000	0.001	0.004	0.000	0.003	1.000	0.000	0.003	0.000	0.002	0.004	0.002	0.000	0.000	0.001	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.000
P.lactis	0.001	0.000	0.000	0.000	0.008	0.000	0.000	0.001	0.000	0.000	1.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.002	0.000	0.000	0.009	0.000	0.000	0.000
P.lalkuanensis	0.000	0.002	0.000	0.002	0.000	0.004	0.002	0.000	0.002	0.003	0.000	1.000	0.000	0.002	0.001	0.001	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.002	0.000
P.mucoides	0.002	0.001	0.000	0.001	0.000	0.000	0.001	0.000	0.001	0.000	0.000	0.000	1.000	0.000	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.001	0.000
P.nicosulfuronedens	0.000	0.002	0.001	0.003	0.000	0.002	0.003	0.000	0.002	0.002	0.000	0.002	0.000	1.000	0.044	0.020	0.001	0.001	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001	0.000
P.nitritireducens	0.000	0.002	0.001	0.002	0.000	0.000	0.003	0.000	0.002	0.004	0.000	0.001	0.001	0.044	1.000	0.472	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000
P.nitroreducens	0.000	0.002	0.001	0.003	0.000	0.000	0.003	0.000	0.002	0.002	0.000	0.001	0.001	0.020	0.472	1.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000
P.nosocomialis	0.000	0.001	0.000	0.001	0.000	0.001	0.001	0.000	0.002	0.000	0.000	0.001	0.001	0.001	0.000	0.000	1.000	0.002	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.003	0.000
P.otitidis	0.000	0.001	0.000	0.001	0.000	0.004	0.001	0.003	0.001	0.000	0.000	0.001	0.000	0.001	0.001	0.001	0.002	1.000	0.001	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.015	0.002
P.panipatensis	0.000	0.002	0.001	0.002	0.000	0.001	0.003	0.000	0.003	0.001	0.000	0.001	0.000	0.001	0.000	0.000	0.001	0.001	1.000	0.000	0.000	0.000	0.000	0.002	0.000	0.002	0.002	0.000
P.peli	0.001	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	1.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.001
P.pseudoalcaligenes	0.000	0.000	0.009	0.000	0.000	0.000	0.000	0.200	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	1.000	0.000	0.013	0.002	0.000	0.000	0.002	0.020
P.putida	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	1.000	0.001	0.000	0.000	0.000	0.000	0.001
P.sediminis	0.000	0.000	0.012	0.000	0.000	0.000	0.000	0.010	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.013	0.001	1.000	0.000	0.000	0.000	0.000	0.013
P.stutzeri	0.000	0.001	0.000	0.001	0.000	0.001	0.002	0.002	0.002	0.000	0.000	0.001	0.000	0.001	0.000	0.000	0.001	0.001	0.002	0.000	0.002	0.000	0.000	1.000	0.000	0.001	0.002	0.000
P.synxantha	0.000	0.000	0.000	0.000	0.007	0.000	0.000	0.000	0.000	0.000	0.009	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.001	0.000	0.000	0.000	0.000	1.000	0.000	0.000	0.000
P.syringae	0.000	0.000	0.001	0.000	0.000	0.000	0.001	0.000	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.000	0.000	0.000	0.001	0.000	1.000	0.000	0.000
P.tohonis	0.000	0.001	0.001	0.001	0.000	0.004	0.002	0.001	0.002	0.000	0.000	0.002	0.001	0.001	0.001	0.001	0.003	0.015	0.002	0.000	0.002	0.000	0.000	0.002	0.000	0.000	1.000	0.001
P.toyotomiensis	0.000	0.000	0.009	0.000	0.000	0.001	0.000	0.019	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.002	0.000	0.001	0.020	0.001	0.013	0.000	0.000	0.000	0.001	1.000

Appendix - Table 31: Raw data of pairwise digital DNA-DNA hybridisation (dDDH) of Pseudomonas strains.

	PA259	PA580	PA628	PA828	PA868	PA964	PA1129	PA1130	PA1145	PA1646	PA1780	PA1794	PA1802	PA2078	PA2506	PA2541	PA2548	P. aeruginosaLESB58	P. aeruginosaPA7	P. aeruginosaPAK	P. aeruginosaPA14	P. citronellolis	P. delhiensis	P. humi	P. indoloxydans	P. nitritireducens	P. nitroreducens	P. pseudoalcaligenes
PA259	100	91.6	90.7	91.6	95.2	91.9	91.6	91.7	92	90.9	91.9	95.2	95.2	96	93.4	91.6	91.1	52.2	95.8	52.3	52.4	25.5	25.6	25.6	22.2	24	24	22.1
PA580	91.6	100	94.7	94.5	90.4	94.6	93.9	94.1	95.7	94.7	95.1	91.6	91.6	91.7	89.8	95	95	52.1	91.1	51.7	52.1	25.6	25.6	25.6	22.4	24	24	22.5
PA628	90.7	94.7	100	95.1	91.1	95.1	96	96.1	99	94.7	95.8	91.4	91.4	91.6	89.6	95.4	94.9	51.4	91.6	51.7	51.8	25.6	25.7	25.7	22.2	24	24	22.2
PA828	91.6	94.5	95.1	100	90	94.1	93	93.1	95.8	93.7	94.7	90.3	90.3	91.6	89	94.6	94	51.7	90.8	51.3	51.6	25.6	25.8	25.7	23	24.1	24.1	22.4
PA868	95.2	90.4	91.1	90	100	90.4	90.4	90.4	92.2	90.9	92	96.5	96.5	95.8	95.1	91.3	91.2	52	95.5	52.2	52.4	25.5	25.6	25.6	23.5	24	24	22.8
PA964	91.9	94.6	95.1	94.1	90.4	100	94.2	94.2	95.8	95	95.6	91.1	91.1	92.1	89.6	95.5	95.3	51.9	91.8	51.4	51.8	25.6	25.7	25.7	22.9	24.1	24	23
PA1129	91.6	93.9	96	93	90.4	94.2	100	99.7	96.1	93.8	95.6	90.3	90.3	91.9	88.7	95.4	93.9	51.3	91.3	51.2	51.6	25.5	25.6	25.7	22.9	24.1	24	22.5
PA1130	91.7	94.1	96.1	93.1	90.4	94.2	99.7	100	96.2	93.8	95.7	90.4	90.4	92	88.7	95.5	94	51.4	91.4	51.2	51.6	25.5	25.6	25.6	22.8	24.1	24.1	22.4
PA1145	92	95.7	99	95.8	92.2	95.8	96.1	96.2	100	95.6	96.3	92.3	92.2	92.3	90.6	96.2	95.8	51.7	92.2	51.9	51.8	25.6	25.7	25.7	22.3	24.1	24.1	22.2
PA1646	90.9	94.7	94.7	93.7	90.9	95	93.8	93.8	95.6	100	94.8	90.9	90.9	91.6	89	94.6	99.7	51.6	90.9	51.7	51.8	25.6	25.7	25.7	22.2	24	24	22.2
PA1780	91.9	95.1	95.8	94.7	92	95.6	95.6	95.7	96.3	94.8	100	91.9	91.9	92.3	90.2	99.7	95.1	51.8	91.3	51.8	51.7	25.5	25.6	25.6	22.2	24.1	24.1	22.1
PA1794	95.2	91.6	91.4	90.3	96.5	91.1	90.3	90.4	92.3	90.9	91.9	100	100	95.9	97.9	91.6	91.2	52.5	95.8	52.3	52.4	25.5	25.6	23.7	24	24	24	22.7
PA1802	95.2	91.6	91.4	90.3	96.5	91.1	90.3	90.4	92.2	90.9	91.9	100	100	95.9	97.9	91.6	91.2	52.4	91.1	51.7	52.1	25.6	25.6	25.6	23.7	24	24	22.7
PA2078	96	91.7	91.6	91.6	95.8	92.1	91.9	92	92.3	91.6	92.3	95.9	95.9	100	94.3	92.1	91.9	52.5	99.7	52.5	52.6	25.7	25.8	25.7	22.4	24.1	24.1	22.3
PA2506	93.4	89.8	89.6	89	95.1	89.6	88.7	88.7	90.6	89	90.2	97.9	97.9	94.3	100	89.8	89.3	52.9	94	52.4	52.9	26.3	26.4	26.4	23.7	24.8	24.7	23.3
PA2541	91.6	95	95.4	94.6	91.3	95.5	95.4	95.5	96.2	94.6	99.7	91.6	91.6	92.1	89.8	100	94.8	51.7	90.9	51.7	51.6	25.5	25.6	25.6	22.3	24	24	22.1
PA2548	91.1	95	94.9	94	91.2	95.3	93.9	94	95.8	99.7	95.1	91.2	91.2	91.9	89.3	94.8	100	51.6	91.3	51.7	51.6	25.6	25.7	25.7	22.2	24.1	24	22.2
***P. aeruginosa* DSM50071**	52.8	52.4	52.1	52.2	52.8	52.2	52.1	52.1	52.3	52.1	52.2	52.7	52.8	53	53.1	52.2	52.1	95.6	53	95.1	90.3	25.2	25.3	25.4	22	23.7	23.9	22.1
***P. aeruginosa* LESB58**	52.2	52.1	51.4	51.7	52	51.9	51.3	51.4	51.7	51.6	51.8	52.5	52.4	52.5	52.9	51.7	51.6	95.6	52.6	94	90	25.2	25.3	25.4	22	23.7	23.9	22.4

P. aeruginosa PA7	95.8	91.1	91.6	90.8	95.5	91.8	91.3	91.4	92.2	90.9	91.3	95.8	91.1	99.7	94	90.9	91.3	52.6	100	52.6	52.5	25.5	25.6	25.6	22.6	24	24	22.4
P. aeruginosa PAK	52.3	51.7	51.7	51.3	52.2	51.4	51.2	51.2	51.9	51.7	51.8	52.3	51.7	52.5	52.4	51.7	51.7	94	52.6	100	90.5	25.2	25.3	25.3	22.2	23.8	23.9	22.1
P. aeruginosa PA14	52.4	52.1	51.8	51.6	52.4	51.8	51.6	51.6	51.8	51.8	51.7	52.4	52.1	52.6	52.9	51.6	51.6	90	52.5	90.5	100	25.3	25.4	25.4	22.2	23.7	23.9	22.1
P. citronellolis	25.5	25.5	25.6	25.6	25.5	25.6	25.6	25.7	26.3	25.5	25.6	25.5	25.6	25.6	25.6	25.5	25.6	25.2	25.5	25.2	25.3	100	57.4	72.8	22.6	27.4	27.3	22.6
P. delhiensis	25.6	25.6	25.7	25.8	25.6	25.7	25.6	25.6	25.7	25.7	25.6	25.6	25.6	25.8	26.4	25.6	25.7	25.3	25.6	25.3	25.4	57.4	100	57.2	22.5	27.4	27.4	22.6
P. humi	25.6	25.6	25.7	25.7	25.6	25.7	25.7	25.6	25.7	25.7	25.6	23.7	25.6	25.7	26.4	25.6	25.7	25.4	25.6	25.3	25.4	72.8	57.2	100	22.6	27.6	27.7	22.6
P. indoloxydans	22.2	22.4	22.2	23	23.5	22.9	22.9	22.8	22.3	22.2	22.2	24	23.7	22.4	23.7	22.3	22.2	22	22.6	22.2	22.2	22.6	22.5	22.6	100	22.2	22.2	64.5
P. nitritireducens	24	24	24	24.1	24	24.1	24.1	24.1	24.1	24	24.1	24	24	24.1	24.8	24	24.1	23.7	24	23.8	23.7	27.4	27.4	27.6	22.2	100	90.5	22.1
P. nitroreducens	24	24	24	24.1	24	24	24	24.1	24.1	24	24.1	24	24	24.1	24.7	24	24	23.9	24	23.9	23.9	27.3	27.4	27.7	22.2	90.5	100	22.2
P. pseudoalcaligenes	22.1	22.5	22.2	22.4	22.8	23	22.5	22.4	22.2	22.2	22.1	22.7	22.7	22.3	23.3	22.1	22.2	22.4	22.4	22.1	22.1	22.6	22.6	22.6	64.5	22.1	22.2	100
P. alcaligenes	22.7	22.7	22.7	22.9	22.8	22.8	22.8	22.8	22.7	22.8	22.7	23.1	23.1	22.7	23.6	22.7	22.8	22.6	23	22.7	22.6	23.4	23.5	23.5	24.6	22.7	22.7	24.2
P. alcaliphila	21.8	21.8	21.7	21.9	21.8	21.8	21.8	21.8	21.8	21.7	21.7	21.8	21.8	21.8	22.4	21.7	21.7	21.8	21.8	21.7	21.7	22.3	22.2	22.4	41.7	21.6	21.6	41.6
P. boanensis	22.2	22.2	22.2	22.5	22.3	22.3	22.6	22.6	22.3	22.3	22.3	22.2	22.2	22.3	22.7	22.2	22.3	22.4	22.3	22.3	22.4	22.7	22.8	22.7	22.2	22.1	22	22.2
P. chengduensis	22	22	22.1	22.2	22.5	22.2	22.2	22.1	22.1	22.1	22	22.3	22.3	22.1	22.8	22	22.1	21.9	22.3	21.9	22	22.2	22.3	22.3	51.5	21.7	21.7	51.6
P. composti	21.4	21.6	21.6	21.6	21.7	21.6	21.7	21.7	21.6	21.6	21.6	21.6	21.6	21.6	22.1	21.6	21.6	21.5	21.5	21.5	21.5	22.1	22.2	22.2	37.5	21.6	21.6	37.5
P. defluvii	21	21.4	21	22	25.4	21.7	22.5	22.4	21.1	21	21.1	27.9	27.9	21.2	22.7	21.1	21	21.3	21.6	21.1	21	21.2	21.2	21.4	23.4	20.8	20.8	22.3
P. furukawaii	23	23	23.1	23.4	23.2	23.1	23.2	23.2	23.1	23.1	23.1	23.1	23.1	23	23.8	23	23.1	23	23	23	23	23.7	23.9	24	23.8	22.7	22.5	23
P. guguanensis	22.4	22.4	22.5	22.5	22.6	22.4	22.5	22.4	22.5	22.5	22.4	22.5	22.5	22.5	23.1	22.4	22.5	22.2	22.4	22.2	22.2	22.9	22.8	22.9	36.9	22.3	22.3	36.6
P. jinjuensis	26	25.9	25.8	25.9	25.9	25.9	25.9	25.9	25.9	25.9	25.8	25.9	25.9	26	26.6	25.8	25.9	25.6	25.9	25.5	25.6	28.3	28.5	28.6	22.7	26.8	27	22.7
P. khazarica	22.3	22.2	22.3	22.3	22.2	22.3	22.3	22.3	22.3	22.3	22.3	22.2	22.2	22.4	22.7	22.3	22.3	22	22.3	22.1	22.1	22.8	22.9	22.9	31.8	22.1	22	32
P. knackmussii	24.4	24.5	24.4	24.6	24.5	24.5	24.5	24.5	24.5	24.4	24.4	24.5	24.5	24.5	25.1	24.4	24.4	24.5	24.4	24.4	24.3	33	32.9	32.9	22.7	26.2	26.1	22.6
P. lalkuanensis	22.8	22.8	22.8	22.9	22.8	22.9	22.9	22.8	23	22.9	22.9	22.8	22.8	22.8	23.4	22.8	22.9	22.8	22.9	22.8	22.9	23.3	23.5	23.6	22.7	22.7	22.8	22.7
P. mendocina	21.6	21.5	21.6	21.7	21.5	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.6	21.7	22.3	21.6	21.6	21.5	21.6	21.5	21.6	22.1	22.2	22.1	36.1	21.6	21.6	36.2
P. nicosulfuronedens	23.8	23.8	23.8	23.9	23.8	23.8	23.8	23.8	23.8	23.8	23.9	23.8	23.8	23.9	24.5	23.8	23.8	23.8	23.8	23.8	23.8	26.9	27.1	27.2	22.1	43.7	42.6	22.2
P. nosocomialis	21.7	21.8	21.8	21.9	21.8	21.8	21.8	21.8	21.8	21.8	21.9	21.9	21.9	21.9	22.8	21.8	21.8	21.8	21.9	21.8	21.8	22	22.1	22.1	22.5	21.3	21.3	22.3

P. otitidis	22.8	22.7	22.8	23	23.1	22.8	22.9	22.9	22.8	22.8	22.8	22.9	22.9	22.9	23.8	22.7	22.8	22.7	22.9	22.7	22.7	23.8	23.8	23.9	23.4	22.6	22.5	23.2
P. panipatensis	24.6	24.7	24.7	24.7	24.6	24.7	24.7	24.7	24.7	24.6	24.7	24.6	24.6	24.7	25.2	24.7	24.7	24.5	24.6	24.4	24.5	30.8	31	31.1	22.1	25.8	25.8	22.2
P. peli	20.4	20.4	20.3	20.5	20.4	20.4	20.5	20.4	20.4	20.4	20.4	20.4	20.4	20.4	21	20.4	20.4	20.5	20.5	20.5	20.5	21	21.1	21	22.7	20.8	20.8	22.7
P. schmalbachii	25.4	25.4	25.5	25.5	25.4	25.4	25.4	25.4	25.5	25.5	25.4	25.4	25.4	25.6	26.1	25.4	25.5	25.3	25.5	25.4	25.3	27.8	28	28	22.5	26.6	26.6	22.5
P. sediminis	21.6	21.7	21.6	21.7	21.7	21.7	21.8	21.7	21.7	21.6	21.7	21.7	21.7	21.7	22.2	21.7	21.6	21.6	21.7	21.6	21.6	22.1	22.1	22.2	41.7	21.5	21.6	42.1
P. sihuiensis	22	22.1	22.1	22.7	22.4	22.3	22.4	22.4	22.1	22.1	22.2	22.3	22.3	22.1	22.9	22.3	22.1	21.9	22.2	21.9	22	22.5	22.5	22.6	51	21.9	21.9	51.6
P. songnenensis	21.5	21.5	21.8	21.6	21.4	21.5	21.6	21.5	21.5	21.5	21.6	21.4	21.4	21.6	21.9	21.5	21.5	21.4	21.6	21.4	21.4	21.7	21.8	22	22.1	21.3	21.3	22.1
P. tohonis	23	23.1	23.1	23.2	23.3	23.1	23.1	23.1	23.1	23	23.1	23.2	23.2	23.2	23.8	23	23	23	23.2	22.9	23	24	24.1	24	23.2	22.8	22.8	23.4
P. toyotomiensis	21.8	21.8	21.8	22.1	22.2	22	21.9	21.9	21.8	21.8	21.8	22.1	22.1	21.9	22.7	21.8	21.8	21.6	21.8	21.6	21.7	22.2	22.1	22.1	48	21.6	21.6	46.9
P. wenzhouensis	22.3	22.2	22.4	22.3	22.4	22.4	22.4	22.3	22.3	22.3	22.1	22.4	22.4	22.3	22.7	22.1	22.3	22.1	22.4	22.2	22.2	22.5	22.7	22.6	41	22.1	22.1	41.1
P. yangonensis	22	22	22	22.1	22.7	22.2	22.3	22.2	22.1	22	22.2	22.4	22.4	22.2	23.1	22.1	22	22.1	22.3	22.1	22.1	22.5	22.5	22.6	36.2	21.9	21.9	36.1

Appendix - Table 32: Raw data of nucleotides divergence measured as D_{xy} *between core groups of* Pseudomonas aeruginosa.

	Core1	Core2	Core3	Core4	Core5	Core6	Core7	Core8	Core9	Core10	Core11	Core12	Core13	Core14	Core15	Core16	Core17	Core18	Core19	Core20	Core21	Core22	Core23
Core1	0.00	1054.37	999.36	1153.90	1060.32	1031.25	2740.20	990.60	4273.73	1543.09	1510.83	1558.59	1543.01	1565.53	1557.41	1642.05	1479.89	1184.35	1533.36	1487.20	1064.58	1530.71	1671.50
Core2	1054.37	0.00	785.27	935.94	855.00	874.26	2548.15	788.32	4088.11	1378.52	1330.30	1372.69	1342.05	1374.62	1347.77	1459.79	1286.09	1165.46	1362.27	1308.72	843.08	1357.30	1482.32
Core3	999.36	785.27	0.00	836.47	779.55	766.83	2505.97	771.26	4049.11	1332.02	1279.36	1353.30	1323.37	1357.40	1328.08	1426.80	1271.02	1114.39	1326.86	1269.47	806.36	1326.93	1456.92
Core4	1153.90	935.94	836.47	0.00	932.54	891.64	2533.95	894.20	4115.46	1306.40	1280.08	1339.63	1354.08	1343.91	1311.79	1417.40	1236.72	1215.67	1317.24	1266.40	925.83	1315.14	1409.33
Core5	1060.32	855.00	779.55	932.54	0.00	828.78	2525.49	795.91	4087.33	1308.03	1275.23	1325.69	1306.20	1352.02	1316.17	1419.15	1289.88	1172.44	1317.22	1268.53	850.02	1325.93	1440.93
Core6	1031.25	874.26	766.83	891.64	828.78	0.00	2537.25	773.18	4087.96	1333.40	1304.64	1361.55	1340.34	1362.30	1348.19	1434.05	1295.94	1166.98	1343.54	1278.27	852.85	1345.10	1459.37
Core7	2740.20	2548.15	2505.97	2533.95	2525.49	2537.25	0.00	2525.93	4579.61	2414.12	2411.65	2421.59	2433.49	2430.08	2450.79	2506.00	2378.57	2647.91	2425.03	2446.29	2555.62	2405.78	2519.42
Core8	990.60	788.32	771.26	894.20	795.91	773.18	2525.93	0.00	4064.91	1382.31	1300.02	1391.65	1339.59	1394.40	1376.82	1471.92	1293.54	1163.60	1361.65	1300.79	815.70	1354.62	1478.13
Core9	4273.73	4088.11	4049.11	4115.46	4087.33	4087.96	4579.61	4064.91	0.00	4003.94	4007.91	3982.02	4024.51	4019.72	4049.92	4072.21	3988.59	4187.63	4015.26	4030.61	4097.59	4008.69	4052.23
Core10	1543.09	1378.52	1332.02	1306.40	1308.03	1333.40	2414.12	1382.31	4003.94	0.00	661.66	650.07	656.34	661.72	671.57	747.83	640.97	1559.97	665.12	788.01	1353.72	663.34	767.57
Core11	1510.83	1330.30	1279.36	1280.08	1275.23	1304.64	2411.65	1300.02	4007.91	661.66	0.00	657.60	682.05	672.30	713.93	781.29	675.67	1531.14	699.98	808.09	1312.22	655.95	798.67
Core12	1558.59	1372.69	1353.30	1339.63	1325.69	1361.55	2421.59	1391.65	3982.02	650.07	657.60	0.00	665.58	584.23	635.19	740.34	661.94	1553.04	642.61	758.31	1366.15	626.61	737.89
Core13	1543.01	1342.05	1323.37	1354.08	1306.20	1340.34	2433.49	1339.59	4024.51	656.34	682.05	665.58	0.00	665.54	702.09	806.69	692.56	1527.65	701.64	813.86	1349.64	669.98	817.44
Core14	1565.53	1374.62	1357.40	1343.91	1352.02	1362.30	2430.08	1394.40	4019.72	661.72	672.30	584.23	665.54	0.00	678.35	751.81	663.16	1575.86	666.44	770.47	1374.40	639.22	764.93
Core15	1557.41	1347.77	1328.08	1311.79	1316.17	1348.19	2450.79	1376.82	4049.92	671.57	713.93	635.19	702.09	678.35	0.00	806.05	696.91	1556.54	689.72	804.87	1354.27	671.55	767.46
Core16	1642.05	1459.79	1426.80	1417.40	1419.15	1434.05	2506.00	1471.92	4072.21	747.83	781.29	740.34	806.69	751.81	806.05	0.00	768.04	1643.96	786.46	883.32	1454.75	724.22	876.11
Core17	1479.89	1286.09	1271.02	1236.72	1289.88	1295.94	2378.57	1293.54	3988.59	640.97	675.67	661.94	692.56	663.16	696.91	768.04	0.00	1503.50	687.25	745.66	1297.93	615.91	769.19
Core18	1184.35	1165.46	1114.39	1215.67	1172.44	1166.98	2647.91	1163.60	4187.63	1559.97	1531.14	1553.04	1527.65	1575.86	1556.54	1643.96	1503.50	0.00	1545.50	1503.38	1183.00	1546.84	1666.83
Core19	1533.36	1362.27	1326.86	1317.24	1317.22	1343.54	2425.03	1361.65	4015.26	665.12	699.98	642.61	701.64	666.44	689.72	786.46	687.25	1545.50	0.00	801.47	1354.68	667.80	789.02
Core20	1487.20	1308.72	1269.47	1266.40	1268.53	1278.27	2446.29	1300.79	4030.61	788.01	808.09	758.31	813.86	770.47	804.87	883.32	745.66	1503.38	801.47	0.00	1297.07	779.84	913.80
Core21	1064.58	843.08	806.36	925.83	850.02	852.85	2555.62	815.70	4097.59	1353.72	1312.22	1366.15	1349.64	1374.40	1354.27	1454.75	1297.93	1183.00	1354.68	1297.07	0.00	1353.19	1471.99
Core22	1530.71	1357.30	1326.93	1315.14	1325.93	1345.10	2405.78	1354.62	4008.69	663.34	655.95	626.61	669.98	639.22	671.55	724.22	615.91	1546.84	667.80	779.84	1353.19	0.00	759.68
Core23	1671.50	1482.32	1456.92	1409.33	1440.93	1459.37	2519.42	1478.13	4052.23	767.57	798.67	737.89	817.44	764.93	767.46	876.11	769.19	1666.83	789.02	913.80	1471.99	759.68	0.00

Appendix - Table 33: Raw data of gene flow measured as F_{ST} between core groups of Pseudomonas aeruginosa.

	Core1	Core2	Core3	Core4	Core5	Core6	Core7	Core8	Core9	Core10	Core11	Core12	Core13	Core14	Core15	Core16	Core17	Core18	Core19	Core20	Core21	Core22	Core23
Core1	1.000	0.955	0.950	0.958	0.955	0.958	0.865	0.949	0.926	0.965	0.965	0.950	0.941	0.958	0.922	0.954	0.946	0.520	0.748	0.729	0.579	0.818	0.885
Core2	0.955	1.000	0.983	0.987	0.987	0.992	0.869	0.982	0.931	0.987	0.987	0.969	0.959	0.978	0.936	0.973	0.966	0.543	0.743	0.720	0.511	0.821	0.895
Core3	0.950	0.983	1.000	0.983	0.983	0.989	0.866	0.978	0.930	0.985	0.985	0.967	0.957	0.976	0.934	0.970	0.963	0.521	0.735	0.710	0.486	0.815	0.891
Core4	0.958	0.987	0.983	1.000	0.987	0.992	0.868	0.983	0.931	0.986	0.986	0.968	0.959	0.977	0.934	0.971	0.964	0.562	0.734	0.710	0.554	0.815	0.889
Core5	0.955	0.987	0.983	0.987	1.000	0.992	0.868	0.982	0.931	0.987	0.986	0.968	0.958	0.978	0.935	0.972	0.966	0.546	0.734	0.711	0.515	0.817	0.892
Core6	0.958	0.992	0.989	0.992	0.992	1.000	0.870	0.987	0.932	0.990	0.990	0.972	0.963	0.981	0.940	0.975	0.969	0.548	0.743	0.717	0.522	0.823	0.896
Core7	0.865	0.869	0.866	0.868	0.868	0.870	1.000	0.867	0.868	0.859	0.859	0.850	0.845	0.855	0.834	0.856	0.846	0.677	0.723	0.719	0.713	0.765	0.810
Core8	0.949	0.982	0.978	0.983	0.982	0.987	0.867	1.000	0.930	0.985	0.984	0.967	0.957	0.976	0.935	0.971	0.963	0.540	0.740	0.716	0.490	0.818	0.892
Core9	0.926	0.931	0.930	0.931	0.931	0.932	0.868	0.930	1.000	0.928	0.928	0.921	0.919	0.925	0.912	0.924	0.921	0.808	0.845	0.842	0.833	0.872	0.895
Core10	0.965	0.987	0.985	0.986	0.987	0.990	0.859	0.985	0.928	1.000	0.964	0.925	0.907	0.945	0.863	0.938	0.921	0.655	0.464	0.527	0.691	0.624	0.788
Core11	0.965	0.987	0.985	0.986	0.986	0.990	0.859	0.984	0.928	0.964	1.000	0.927	0.911	0.946	0.871	0.941	0.925	0.648	0.491	0.539	0.681	0.620	0.797
Core12	0.950	0.969	0.967	0.968	0.968	0.972	0.850	0.967	0.921	0.925	0.927	1.000	0.872	0.896	0.816	0.904	0.886	0.637	0.407	0.476	0.675	0.563	0.747
Core13	0.941	0.959	0.957	0.959	0.958	0.963	0.845	0.957	0.919	0.907	0.911	0.872	1.000	0.890	0.816	0.897	0.874	0.623	0.439	0.496	0.662	0.573	0.756
Core14	0.958	0.978	0.976	0.977	0.978	0.981	0.855	0.976	0.925	0.945	0.946	0.896	0.890	1.000	0.846	0.922	0.905	0.650	0.447	0.500	0.686	0.591	0.772
Core15	0.922	0.936	0.934	0.934	0.935	0.940	0.834	0.935	0.912	0.863	0.871	0.816	0.816	0.846	1.000	0.858	0.829	0.610	0.384	0.452	0.640	0.527	0.699
Core16	0.954	0.973	0.970	0.971	0.972	0.975	0.856	0.971	0.924	0.938	0.941	0.904	0.897	0.922	0.858	1.000	0.905	0.659	0.518	0.552	0.697	0.625	0.789
Core17	0.946	0.966	0.963	0.964	0.966	0.969	0.846	0.963	0.921	0.921	0.925	0.886	0.874	0.905	0.829	0.905	1.000	0.624	0.442	0.464	0.657	0.552	0.754
Core18	0.520	0.543	0.521	0.562	0.546	0.548	0.677	0.540	0.808	0.655	0.648	0.637	0.623	0.650	0.610	0.659	0.624	1.000	0.436	0.410	0.211	0.506	0.594
Core19	0.748	0.743	0.735	0.734	0.734	0.743	0.723	0.740	0.845	0.464	0.491	0.407	0.439	0.447	0.384	0.518	0.442	0.436	1.000	0.120	0.445	0.129	0.373
Core20	0.729	0.720	0.710	0.710	0.711	0.717	0.719	0.716	0.842	0.527	0.539	0.476	0.496	0.500	0.452	0.552	0.464	0.410	0.120	1.000	0.408	0.233	0.440
Core21	0.579	0.511	0.486	0.554	0.515	0.522	0.713	0.490	0.833	0.691	0.681	0.675	0.662	0.686	0.640	0.697	0.657	0.211	0.445	0.408	1.000	0.524	0.621
Core22	0.818	0.821	0.815	0.815	0.817	0.823	0.765	0.818	0.872	0.624	0.620	0.563	0.573	0.591	0.527	0.625	0.552	0.506	0.129	0.233	0.524	1.000	0.490
Core23	0.885	0.895	0.891	0.889	0.892	0.896	0.810	0.892	0.895	0.788	0.797	0.747	0.756	0.772	0.699	0.789	0.754	0.594	0.373	0.440	0.621	0.490	1.000

Appendix III - Python scripts used in bioinformatic analysis

Identification of clonally linked strains

File name: remove_duplicates.py

```
import pandas as pd

#open file containing snp distances data for sequences <30 snps apart
snp_file = open("core_gene_snp_dist.csv", 'r', encoding='utf-8-sig')

#create files to save output lists
output_keep = "keep_table.csv"
output_dup = "duplicates_table.txt"

#create empty lists to insert variables into
duplicate_df = []
done = []
keep_df = []
dup_list = []

#create dictionaries for the source and project ID from metadata
source_dict = pd.read_csv('source_dict.csv', header=None, index_col=0,
squeeze=True).to_dict()
project_dict = pd.read_csv('project_dict.csv', header=None, index_col=0,
squeeze=True).to_dict()

#read each line of the snp_file to check for project ID duplicates and then for
sources duplicates in order to keep strains which don't have the same project ID
and to keep strains that have both the same project ID but a difference source
for line in snp_file:
    line = line.rstrip()
    list = line.split(',')
    list_name = str(list[0])
    list = list[1:]
    for item in list:
        list_project = str(project_dict[list_name])
        list_source = str(source_dict[list_name])
        item_project = str(project_dict[item])
        item_source = str(source_dict[item])
        if item != list_name and item not in dup_list and list_name not in
dup_list:
            if list_project == item_project:
                if list_source == item_source:
                    dup_list.append(item)
                    duplicate = []
                    duplicate.append(list_name)
                    duplicate.append(list_source)
                    duplicate.append(list_project)
                    duplicate.append(item)
                    duplicate.append(item_source)
                    duplicate.append(item_project)
                    duplicate_df.append(duplicate)
                else:
                    keep = []
                    keep.append(list_name)
```

```
                    keep.append(list_source)
                    keep.append(list_project)
                    keep.append(item)
                    keep.append(item_source)
                    keep.append(item_project)
                    keep_df.append(keep)
            else:
                keep = []
                keep.append(list_name)
                keep.append(list_source)
                keep.append(list_project)
                keep.append(item)
                keep.append(item_source)
                keep.append(item_project)
                keep_df.append(keep)


#write table containing sequences to be kept in the alignment along with metadata
df = pd.DataFrame(keep_df, columns = ["List_name", "List_source", "List_project",
"item", "item_source", "item_project"])
df.to_csv(output_keep)

#write table containing metadata on sequences marked as a duplicate
df = pd.DataFrame(duplicate_df, columns = ["List_name", "List_source",
"List_project", "item", "item_source", "item_project"])
df.to_csv(output_dup)

#write list to file
with open(output_list, "w") as f:
    for d in duplicates_list:
        f.write(f"{d}\n")
```

Removal of clonally linked strains from the core SNP alignment

File name: remove_duplicates_from_aln.py

```
from Bio import SeqIO

#create variable to hold the filtered alignment
filtered_aln = []

#open file containing list of sequences that are duplicates to convert into a
list for python
with open("remove_duplicates_list.txt", "r") as file:
     list = [line.rstrip("\n") for line in file.readlines()]

#read through the duplicates list removing any seqeunces it contains and copying
the sequences it does not to the filtered alignment variable
for record in SeqIO.parse("core_gene_alignment_snps.aln", "fasta"):
    id = record.id
    if id in list:
        print(record.id, " removed from aln")
    else:
        filtered_aln.append(record)

#write the filtered alignment variable to file
SeqIO.write(filtered_aln, "core_gene_snp_aln_nodupe.fasta", "fasta")
```