**Towards engineering insect-free cereals**

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A cluster of three rice lectin receptor kinases confers resistance to planthopper insects.

Insect pests reduce yields of crops worldwide through direct damage and because they spread devastating viral diseases. In Asia, the brown planthopper (BPH) decimates rice (*Oryza sativa*) crops, causing losses of billions of dollars annually**1**. In this issue, Liu *et al*. 2 report the cloning of a rice genetic locus that confers broad-spectrum resistance to BPH and at least one other planthopper species (white-back planthopper). Introducing this locus into plant genomes is likely to provide an effective means of combating insect pests of rice and of other cereals such as maize**.**

In modern rice agriculture, BPH damage is controlled through breeding and application of vast amounts of chemical pesticides1. Pesticides are not a sustainable approach, however, owing to high costs, harmful environmental effects and rapid development of resistant insects. Breeding programs have identified in cultivated or wild rice species more than 20 genetic loci that confer BPH resistance1. But these *Bph* loci are usually effective only against specific BPH biotypes, and newly evolved BPH populations have rapidly overcome several *Bph* resistance loci when deployed in the field1.

Of the >20 identified *Bph* loci, only *Bph14* and *Bph26* have been cloned. Both of these loci encode coiled-coil, nucleotide-binding and leucine-rich repeat proteins3,4, the main class of plant intracellular immune receptors5. *Bph3* is a resistance locus that was first identified genetically in the Sri Lankan rice *indica* cultivar Rathu Heenati. Importantly, unlike most other *Bph* loci, including *Bph14* and *Bph26*, *Bph3* confers broad-spectrum resistance to many BPH biotypes as well as to the white-back planthopper1,2. The success of *Bph3* as a resistance locus might be linked to the fact that it acts against BPH at an early stage of the feeding cycle, before the insect can deploy its virulence arsenal, which could circumvents plant defences.

Despite the huge potential of *Bph3* for rice agriculture, its molecular identity has been unknown. Liu *et al*.2  have now identified *Bph3* through map-based cloning in a cross between the resistant *indica* cultivar Rathu Heenati and the susceptible *japonica* cultivar 02428. *Bph3* maps to a 79-kb genomic region that contains a cluster of three lectin receptor kinases, OsLecRK1–3 2. The authors find that single nucleotide polymorphisms in these genes are associated with BPH resistance in different cultivated rice accessions**.** They also show that ectopic expression of the *OsLecRK1–3* gene cluster in the susceptible *japonica* Kitaake cultivar confers BPH resistance.

Intriguingly, concomitant expression of the three *OsLecRK* genes has a larger effect on BPH resistance than expression of each gene alone, confirming the need for a gene cluster. RNA interference experiments to silence the *OsLecRK1–3* cluster in a near-isogenic line carrying the Rathu Heenati *Bph3* locus in the background of the susceptible *japonica* cultivar 02428 further showed that these genes are important for BPH resistance. Finally, examination of multiple different recombinant lines harboring breakpoints in the *OsLecRK1–3* clusterconfirms that all three genes are required for robust resistance to BPH.

The identification of *Bph3* as a cluster of lectin receptor kinases provides important clues as to its potential mode of action. Lectin receptor kinases have been linked to various functions in plant immunity, as receptors or receptor-associated proteins, although the underlying mechanisms are not always clearly defined 6. In recent years it has become clear that plants can detect insect-derived elicitors, or that insect feeding leads to the release of plant-derived elicitors, known as herbivore-associated molecular patterns or damage-associated molecular patterns, that induce plant immune responses7. Several plasma membrane-localized lectin receptor kinases have been shown or proposed to function as pattern recognition receptors (PRRs) for these elicitors. For example, the *Arabidopsis thaliana* LecRK-I.9/DORN1 protein recognizes extracellular ATP, which acts as a damage-associated molecular pattern6. Furthermore, the *Nicotiana attenuata* LecRK1 protein is involved in the plant’s response to feeding by *Manduca sexta* 6, and LecRK-I.8 in *Arabidopsis thaliana* plays a role in the induction of immune response triggered by egg extracts from *Pieris brassicae* 8, although no ligand for these latter lectin receptor kinases has been found. In this context, it is plausible that OsLecRK proteinsfunction as PRRs (Figure 1).

Given that *Bph3* confers resistance to all BPH biotypes tested and to the white back planthopper, any OsLecRK1–3 ligand would have to be conserved across these insect species or universally produced by rice plants in response to infection by these pests. OsLecRK1–3 may also recognize distinct ligands.

Another possibility is that OsLecRK1–3 are not PRRs at all but rather signaling molecules associated with PRRs (Figure 1). Indeed, certain lectin receptor kinases, such as the *Arabidopsis thaliana* LecRK-VI.2**,** are known to associate with well-defined PRRs to positively or negatively regulate immune signaling 6. Defining the roles of OsLecRK1–3 will require identification of rice proteins associated with them and of the plant- or insect-derived ligands that induce *Bph3*-dependent resistance.

*Bph3* has conferred durable resistance to BPH in the Philippines for the past 30 years in rice varieties carrying this locus. But introgression of genes through breeding often results in ‘linkage drag’, which can negatively affect agronomical performance through the transfer of agronomically-poor alleles of neighbouring genes or the creation of novel interfering allele pairs. Cloning of the *Bph3* locus is a crucial step toward the development of high-performance resistant rice varieties because it enables precise marker-assisted selection for *Bph3* in breeding programs. Thus, the work of Liu *et al*. 2 opens up exciting biotechnological opportunities to engineer broad-spectrum insect resistance in rice and potentially in other cereals.

Recent studies have revealed that PRRs or associated proteins (including lectin receptor kinases) can be transferred across plant families and even plant classes 9,10. It is tempting to propose that introduction of *OsLecRK1–3* by transgenesis could confer broad-spectrum resistance to planthoppers, and potentially other insects in other agronomically important cereals, including maize or wheat, that suffer huge losses from insect pests. The wide applicability of *Bph3* will depend on the conservation of the ligands recognised directly or indirectly by OsLecRK1-3.

The main problem facing breeders and biotechnologists who are developing pest-resistant crops is the evolution of new populations of pests and pathogens that escape the resistance mechanisms5. Although *Bph3* has already provided resistance over decades, the duration of resistance could be increased even more by combining it with other loci encoding either intracellular (*eg.* coiled-coil, nucleotide-binding and leucine-rich repeat proteins) or transmembrane (*eg.* PRRs) immune receptors. This combinatorial strategy, known as ‘pyramiding’, may reduce the likelihood that resistance will emerge because the insect would have to simultaneously evolve multiple suppressive or evasive mechanisms 5,11

In conclusion, Wan and colleagues have greatly advanced our understanding of mechanisms involved in plant resistance to insect pests and demonstrate that this knowledge unfolds new strategies to protect crops from damaging insects in a sustainable manner.

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**Figure legend**

The rice brown planthopper (BPH) does not cause damage in rice containing the *Bph3* locus (middle panel). The *Bph3* locus encodes three lectin receptor kinases (OsLecRK1- OsLecRK3), which act collectively to trigger immune signalling and resistance to BPH upon recognition of BPH-derived herbivore-associated molecular pattern molecules (HAMPs) and/or plant-derived damage-associated molecular pattern molecules (DAMPs) released upon BPH feeding. In the absence of the *Bph3* locus (right panel), this immune signalling is not triggered and the insects are able to colonise rice plants and cause damage. OsLecRK1-OsLecRK3 may be transferred to other cereals (left panel), such as maize cultivars that are susceptible to the corn planthopper (*Peregrinus maidis*), thereby conferring resistance to this insect pest.