PLANT IMMUNITY

Buy one, get two

Dual recognition specificity of an MLA immune receptor in barley demonstrates that the deployment of mildew-resistant cultivars by plant breeders has unintentionally affected nonhost resistance to wheat stripe rust.

Isabel M. L. Saur, Aaron W. Lawson and Paul Schulze-Lefert

Most plants are immune to most microorganisms with pathogenic potential, and the likelihood that a pathogen can infect two plant species in a natural environment decreases with phylogenetic distance between the plants[1]. Species outside of the host range of a particular pathogen show nonhost resistance to the, in this case, non-adapted pathogen. The genetic architecture and molecular basis of nonhost resistance has sparked interest not only from an academic viewpoint, but also for plant breeding as nonhost resistance in crops is typically more durable compared to disease resistance against host-adapted pathogens.

In a study recently published in *Nature Communications*, Bettgenhaueser et al.[2] demonstrate that resistance of a domesticated variety of barley to *Puccinia striiformis* forma specialis *tritici* (*Pst*) (a basidiomycete fungus that is the causal agent of stripe rust on wheat) is under the control of three quantitative trait loci, designated *Rps6*, *Rps7* and *Rps8*. A single gene explains *Rps7* variation, and is identical to the *Mla8* allele of *mildew locus a* (*Mla*) resistance gene that is known to confer strain-specific immunity to the host-adapted ascomycete *Blumeria graminis* forma specialis *hordei* (*Bgh*), the causal agent of barley powdery mildew. Thus, *Mla8* confers resistance to isolates of adapted *Bgh* and non-adapted *Pst* in cultivated barley (Fig. 1). A co-evolutionary arms race with *Bgh* has driven functional diversification of the barley *Mla* resistance locus. The resulting allelic *Mla* resistance specificities in barley populations (termed *Mla1*, *Mla2*, *Mla3* and so on) each confer immunity to different strains of the *Bgh* population. Thus, *Rps7* nonhost resistance to *Pst* in barley is mediated by one particular *Mla* resistance specificity (*Mla8*), which confers immunity to only a subset of the *Bgh* population. This reveals a shared resistance component to highly divergent rust and powdery mildew pathogens (an estimated divergence time of ascomycetes and basidiomycetes of more than 500 million years[3]), and prompts questions about the evolutionary history of resistance to both pathogens in the sister species barley and wheat, which diverged at approximately 8 million years ago[4]. Domestication of both cereal species began around 10,000 BC, each with the selection of genetically different accessions (the early forms of which are known as landraces)[5,6].

A systematic survey of barley germplasm, comprising modern cultivars, landraces and wild accessions, by Bettgenhaueser et al.[2] confirmed near-complete resistance to a wheat *Pst* isolate among the two-row elite accessions. However, one-third of the tested wild accessions proved susceptible to *Pst*, which suggests that domestication has contributed to barley being considered a 'nonhost' for *Pst*. Pathotyping of progeny of a cross between a *Pst*-susceptible barley landrace and a fully resistant barley cultivar then revealed the aforementioned genetic architecture of three *Rps* quantitative trait loci that underlie full resistance to *Pst*. This architecture with multiple *Rps* loci, each quantitatively limiting *Pst* proliferation, probably contributed to the durability of *Pst* nonhost resistance in domesticated barley. It also suggests that plant breeders have unintentionally helped to shape nonhost resistance of cultivated barley to *Pst* by the deployment of *Bgh*-resistance specificities

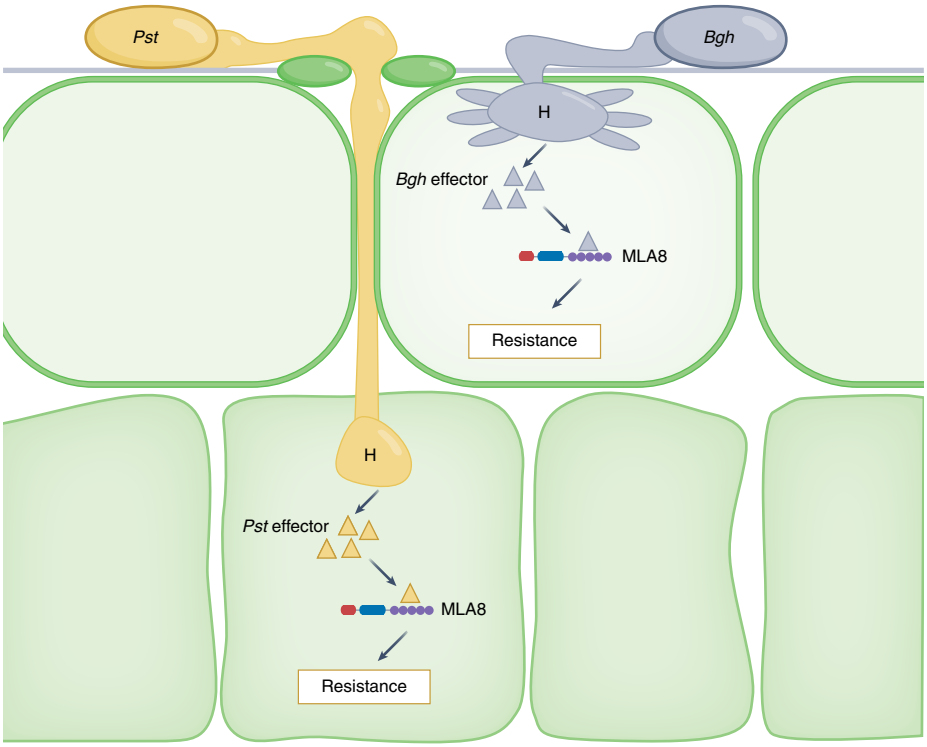

Fig. 1 | *Mla8* confers resistance to isolates of the evolutionarily diverged cereal pathogens *Pst* and *Bgh*. During infection of barley leaf epidermal cells, *Bgh* delivers effectors through the fungal haustorium (H) to promote virulence. In resistant lines, one of these *Bgh* effectors (AVR_{A8}) is recognized by the MLA8 immune receptor encoded at the *Mla* of barley. *Pst* forms rust haustoria in mesophyll cells of leaves to secrete effectors. One of these effectors is also recognized by MLA8 for resistance to *Pst* in barley.

in modern agriculture. However, *Mla8*-mediated resistance to *Bgh* has long been overcome and is effective only towards a divergent *Bgh* isolate, RACE1, which was isolated from wild barley: therefore, *Mla8* is no longer used for genetic control of powdery mildew. The existence of multiple *Rps* quantitative trait loci suggests that these can compensate for the loss of *Rps7*, so that the absence of *Rps7* alone has not yet destabilized *Pst* nonhost resistance in domesticated barley. Regardless, Bettgenhaueser et al.[2] provide an intriguing example of how breeding plants for disease resistance to one pathogen species can erode, at least formally, reproductive barriers to an unrelated nonhost pathogen.

For promoting proliferation on a given host, pathogens secrete virulence factors (known as effectors), many of which are delivered inside plant cells. A widespread class of resistance genes encodes intracellular nucleotide-binding oligomerization domain (NOD)-like receptors (NLRs) that are activated by pathogen effectors. NLRs directly bind effectors or indirectly sense the manipulation of effector host targets[7]. The highly sequence-related NLR-type immune receptors that are encoded by allelic *Mla* resistance specificities in barley detect the AVR_A effectors of *Bgh*[8–10]. Although most of the isolated AVR_A effectors are sequence-unrelated, they are predicted to adopt a common ribonucleases-like fold but lack RNase activity[10]. This, along with evidence for direct binding of at least some AVR_A effectors to matching MLA receptors, led to the hypothesis that functional diversification of multi-allelic MLA receptors may be driven by a common structural effector scaffold[9,10]. The work of Bettgenhaueser et al.[2] suggests that barley MLA8 recognizes an effector from at least two tested *Pst* isolates in addition to *Bgh* AVR_{A8}. The predicted *Pst* effector remains to be isolated to clarify whether it is conserved in *Pst* populations, whether it activates MLA8 by direct binding and whether it is structurally related to *Bgh* AVR_A effectors. Furthermore, we could ask whether this *Pst* effector and AVR_{A8} have overlapping virulence functions. The *Mla* orthologues *Sr33* from wheat[11] and *Sr50* from rye[12] confer strain-specific resistance to the wheat stem rust pathogen *Puccinia graminis* forma specialis *tritici* (*Pgt*). AvrSr50 binds directly to the wheat Sr50 NLR[13] but, unlike *Bgh* AVR_A effectors, the predicted AvrSr50 structure bears no similarity to ribonucleases. AvrSr33 remains to be isolated. Overall, this raises the possibility that ancestral *Mla* in the last common ancestor of the Triticeae has diversified in this grass family to recognize pathogen effectors of multiple agronomically relevant foliar pathogens, including *Pgt*, *Pst* and *Bgh*. This could explain why some *Mla* resistance specificities are maintained in wild barley although they are ineffective towards extant *Bgh* populations[14]. The work of Bettgenhaueser et al.[2] also raises the question of to what extent nonhost-resistance quantitative trait loci obtained by laboratory experiments with single fungal isolates and under optimized infection conditions mirror the immunity of wild barley to *Pst* in natural environments. ❐

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Competing interests

The authors declare no competing interests.