

Pathogen perception and deception in plant immunity by kinase fusion proteins

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Two studies describe kinase fusion proteins (KFPs) that regulate the perception and deception of wheat pathogens. These highlight the emergence of KFPs as plant immune regulators and emphasize the importance of crop wild relatives as a reservoir for resistance breeding and global food security.

Plants are the major source of food, clothing and shelter across the world. Feeding the growing world population in a changing climate and with diminishing external inputs (such as water, fertilizer and arable land) is one of the most pressing challenges facing humanity. Wheat is a major food crop that provides over 20% of calories and proteins in the human diet, as well as vitamins, dietary fibers and phytochemicals¹. Pathogens and pests result in 20% global yield losses for bread wheat annually². To implement effective genetic and biotechnological approaches to decrease losses due to disease, scientists require a foundational understanding of how plants restrict pathogens. However, the cloning of disease-resistance genes (R-genes) in the botanical tribe Triticeae (that includes wheat, barley and rye) is still challenging owing to their large and repeat-rich genomes. The recent development of genomics-based gene cloning approaches has facilitated the discovery of noncanonical R-gene families in the Triticeae³. In this issue of *Nature Genetics*, papers by Wang et al.⁴ and Yu et al.⁵ describe the identification of two wheat disease-resistance genes with novel domain architecture derived from wheat wild relatives, both containing fusions of kinases to additional domains, designated here as kinase fusion proteins (KFPs) (Fig. 1).

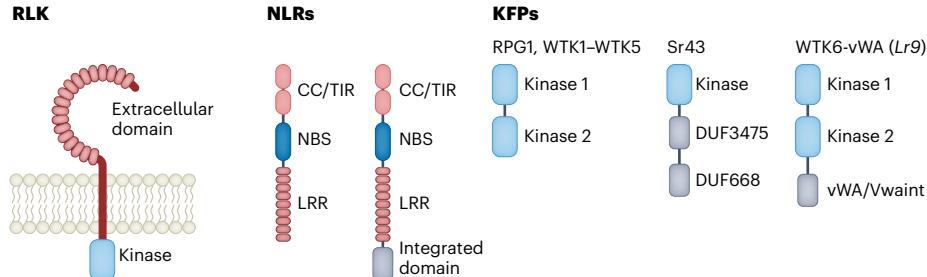
Plants have evolved an innate immune system comprised of germline-encoded immune receptors that can recognize all pathogen classes. Plant immune receptors are structurally similar to their animal counterparts and include pattern-recognition receptors as well as intracellular nucleotide-binding leucine-rich repeat (NLR) receptors (Fig. 1). Plant pattern recognition receptors are receptor-like

kinases (RLKs) or receptor-like proteins that can recognize conserved pathogen or damage-associated molecular patterns. NLR receptors recognize diverse pathogen effector proteins delivered into plant cells during infection. Both types of immune receptor have been intensely investigated over the past 30 years, resulting in a detailed understanding of plant immune signaling. However, in comparison, the role of noncanonical R-genes, some of which confer durable resistance, is relatively unexplored.

Wang et al.⁴ used mutagenesis and transcriptome sequencing to clone the leaf rust resistance genes *Lr9* and *Lr58*, which were reportedly introgressed into bread wheat from the wild grass species *Aegilops umbellulata* and *Ae. triuncialis*, respectively. *Lr9* and *Lr58* encode identical tandem kinase domains followed by fusions of von Willebrand factor A (vWA) and Vwaint domains (WTK6-vWA; Fig. 1). Further cytogenetic and haplotype analyses revealed that the two genes originated from the same *Ae. umbellulata* translocation event⁴. Notably, proteins containing vWA and Vwaint have been implicated in plant defense⁶. The cloning of the Triticeae rust R-gene *RPG1* and *Yr15* brought to light the existence of non-canonical R-genes that have tandem-kinase protein (TKP) architecture⁷, followed by the discovery of additional wheat rust and powdery mildew TKPs (*Sr60*, *Sr62*, *Pm24* and *WTK4*), designated as wheat tandem kinases (WTK1–WTK5, reviewed by Klymiuk et al.⁸) (Fig. 1). Nevertheless, WTK6-vWA is the first, to our knowledge, described TKP that holds an integrated domain (vWA/Vwaint)⁴.

Yu et al.⁵ also discovered a KFP (*Sr43*) that contains a kinase domain fused to two domains of unknown function (DUFs) (Fig. 1). Mutational analyses demonstrated that all three domains are essential for conferring resistance to wheat stem rust. The domain architecture of *Sr43* is unique, differentiating it from the approximately 283 cloned plant disease-resistance genes. DUF3475 and DUF668 exhibit amino acid similarity to PHYTOSULFOKINE SIMULATOR (PSI) proteins, which act downstream of phytosulfokine receptor-like kinases in *Arabidopsis*⁹. Phytosulfokine (PSK) receptors perceive secreted sulfated PSK plant peptide growth factors and are involved in immunomodulation⁹. Notably, both bacteria and nematodes can secrete mimics of plant sulfated peptides during infection^{10,11}. Moreover, although typical RLKs exhibit

Fig. 1 | Domain architecture of plant innate immune receptors and KFPs. Wang et al.⁴ and Yu et al.⁵ have identified rust-resistance genes from wild grass species that encode kinases fused to additional integrated domains (KFPs). These integrated domains may function as decoys for pathogen targets. CC, coiled coil; NBS, nucleotide-binding site; TIR, Toll/interleukin-1 receptor.



plasma membrane localization, Sr43 has no transmembrane domain and is localized to the nucleus, cytoplasm and plastids⁵.

Kinase proteins have an important role in plant immunity as they are powerful 'molecular switches' that can rapidly activate cellular signaling. The discoveries by Wang et al.⁴ and Yu et al.⁵ highlight the importance of KFPs for conferring disease resistance in monocots. Around 81 Triticeae resistance genes have been cloned, with the most common classes being NLRs (45) and KFPs (15)⁵. Sr43 and WTK6-vWA contain fusions and their integrated domains have been implicated in plant immune regulation and targets of pathogen effectors^{5,9,11}. NLRs can also possess integrated domains that act as decoys of effector targets. NLRs with integrated domains bind pathogen effectors, leading to the activation of a paired executor NLR and immune activation¹². Thus, it is tempting to hypothesize that integrated domains present in the KFPs Sr43 and WTK6-vWA also act as decoys of pathogen targets. This would enable a single KFP to trap effectors, with effector binding inducing kinase activation and downstream signaling. Future research that identifies corresponding pathogen effectors detected by Sr43 and WTK6-vWA will enable scientists to directly test this hypothesis.

Domestication and crop improvement have considerably reduced genetic diversity relative to that of crop wild relatives. The work by Wang et al.⁴ and Yu et al.⁵ demonstrates the importance of crop wild relatives as a source for diversifying the repertoire of non-canonical R-genes for resistance breeding and global food security. These studies also highlight the emergence of KFPs as new regulators of plant immunity.

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Competing interests

The authors declare no competing interests.