

A new blueprint for plant pathogen resistance

A signaling cascade downstream of a leucine-rich repeat receptor kinase identified in *Arabidopsis* offers new options for engineering crop disease resistance.

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Every year, a large fraction of worldwide crop production falls prey to viral, bacterial, or fungal infection. Such infections not only cause severe losses in world food production, but also can damage human health by contaminating crops with potent carcinogens and toxins. Traditionally, farmers have controlled crop disease through the application of fungicides and pesticides, but these chemicals pose environmental and health problems in themselves if used indiscriminately. Genetic modification allows disease-resistance traits to be introduced into crop plants, usually by overexpression of antimicrobial proteins (e.g., chitinase) or by induction of key plant defense pathways through signaling molecules (e.g., salicylic acid, jasmonic acid, or ethylene). A paper published recently in *Nature* by Sheen and colleagues¹ describes an additional signaling pathway, the flagellin mitogen-activated protein kinase (MAPK) cascade, that has considerable potential for the engineering of crops with broad-spectrum resistance against fungal and bacterial pathogens.

Plant defense against pathogens is a complex multistep process including the expression of an array of defense genes, the production of a variety of antimicrobial substances, and programmed cell death at the site of attack². In the 1940s, Flor found in genetic experiments that a single dominant plant disease-resistance locus, *R*, conferred upon flax plants a resistance to infection by rust fungus, and that the fungus' virulence also was dependent on a single fungal gene, *Avr* (ref. 3). On the basis of these data, generally summarized by the "gene-for-gene" concept of incompatible plant-pathogen interactions, workers set out to identify the underlying mechanisms.

Many *R* and *Avr* genes have now been identified. Whereas the *Avr* genes encode a variety of structurally and functionally different proteins, many plant *R* proteins

share extensive similarity with insect and animal receptors (Fig. 1) that are required for the onset of the innate immune response and are involved in the sensing of pathogen-derived factors, called PAMPs (for pathogen-associated molecular patterns⁴). Although the defense genes in animals and plants differ considerably, signal transduction connecting the activation of

the receptors to the induction of the defense responses shows some similarities between kingdoms.

In both animals and plants, kinases of the MAPKs class are activated by PAMPs. MAPK pathways are typically multiprotein complexes containing at minimum a MAPK, a MAPK kinase (MAPKK), and a MAPKK kinase (MAPKKK)⁵. MAPKs are ideal intracellular mediators of information, because they shuttle between cytoplasm and nucleus, and among their targets are several classes of transcription factors. Thus, MAPKs represent the mechanistic link between information transfer through the interior of the cell and the transcriptional response in the nucleus.

In their *Nature* paper, Sheen and colleagues confirm previous studies in various plant systems, including both monocot⁶

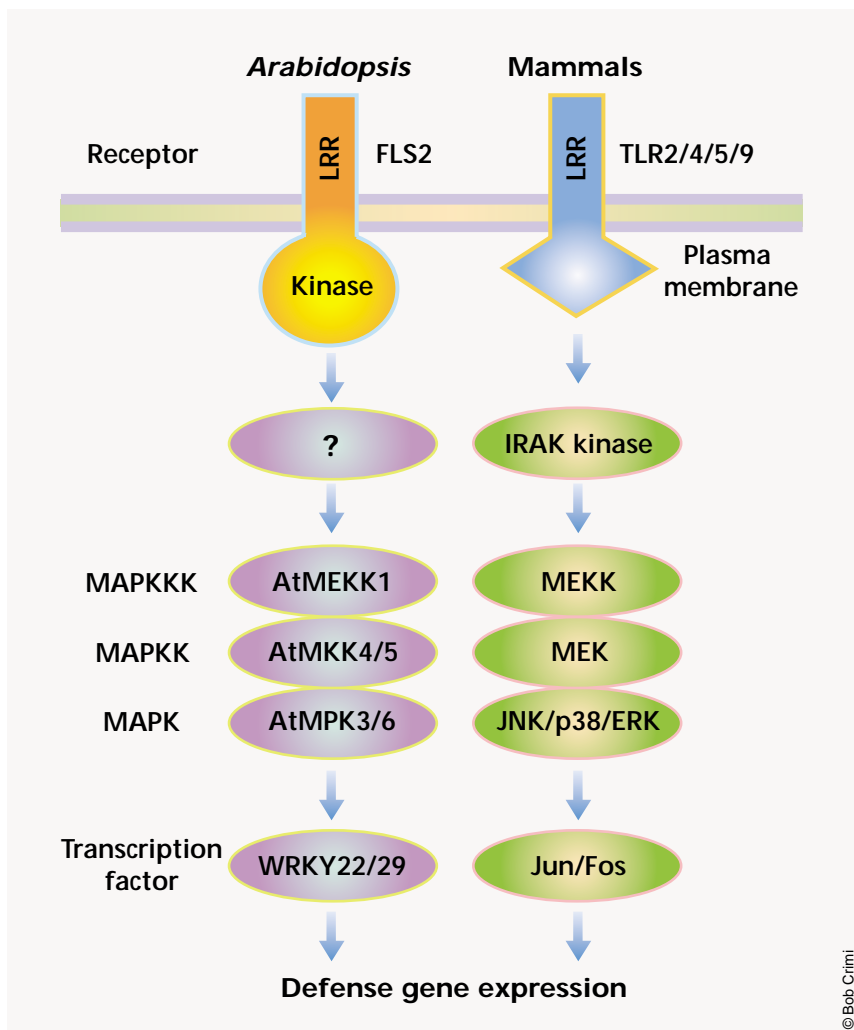


Figure 1. Model of signal transduction in plants and mammals leading to the expression of defense genes. In both cases, signaling is initiated by leucine-rich repeat (LRR)-type membrane receptors that either contain intrinsic kinase activity (e.g., *FLS2*) or are coupled to cytoplasmic kinases (e.g., IRAK). Although signal transduction is mediated through multiple kinase cascades, for simplicity only the MAPK cascades are shown. At the gene level, expression of defense genes is regulated through specific transcription factors that are themselves regulated by the MAPKs.

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and dicot species⁷⁻⁹, demonstrating that specific MAPKs are involved in pathogen signaling. Their work combines a transient expression assay with a genetic approach in which they identify the *FLS2* gene as a putative sensor of flagellin, a protein from bacterial flagella. The resulting data place the MAPKs into register with two closely related MAPKKs and with a MAPKKK in a linear pathway downstream of *FLS2* (Fig. 1). The targets of the MAPK pathway are proposed to be two plant-specific transcription factors of the WRKY family. Confirmation of the biological importance of this pathway is provided by the fact that transient overexpression of active AtMEKK1, AtMKK4, AtMKK5, or one of the WRKYs confers resistance to *Arabidopsis thaliana* leaves upon infection by the bacterial pathogen *Pseudomonas syringae* or the fungal pathogen *Botrytis cinerea*¹.

What is the biotechnological significance of these findings? *R* genes are mostly specific for a certain PAMP and resistance of host plants is usually lost as soon as the pathogen sheds or mutates the respective *Avr* gene, which frequently occurs due to

the high selection pressure on the pathogen. The ability to engineer a single signaling pathway that confers resistance to various pathogens would therefore be clearly advantageous, allowing the creation of crop plants resistant to a wide spectrum of pathogens in the near future. This can be achieved either by classical breeding methods assisted by molecular marker guidance or by more direct engineering of crop plants with variants of active MAPKKKs, MAPKKs, or the WRKY transcription factors.

Before joining in the shouts of joy, we should consider whether it may be premature to declare the problem completely solved. Sheen and colleagues have seen pathogen resistance only in leaves upon transient overexpression of the active MAPKKK, MAPKKs and WRKY genes. A previous report showed that overexpression of active MAPKK in tobacco leaves in the absence of pathogen attack can lead to programmed cell death¹⁰. Overexpression of any of these potent regulators might thus be counterproductive or even lethal. Moreover, studies in which crop plants have been engineered for abiotic stress tol-

erance have shown repeatedly that overexpression of stress genes may not be beneficial to the plant but rather may substantially decrease yield. Several problems therefore need to be resolved before the procedure developed by Sheen and coworkers can be turned into a reliable procedure for generating pathogen-resistant crop plants. Nevertheless, with increasing concerns about the environmental and health impact of fungicides in agriculture, the availability of a new pathway by which to engineer pathogen-resistant crops should be welcome news indeed.

1. Asai, T. *et al.* *Nature* **415**, 977–983 (2002).
2. Agrios, G.N. *Plant Pathology*, edn. 4 (Academic Press, San Diego, 1997).
3. Flor, H.H. *Annu. Rev. Phytopathol.* **9**, 275–296 (1971).
4. Dangl, J.L. & Jones, J.D.G. *Nature* **411**, 826–833 (2001).
5. Hirt, H. (ed.). *MAP Kinases in Plant Signal Transduction* (Springer, Heidelberg; 2000).
6. He, C. *et al.* *Mol. Plant Microbe Int.* **12**, 1064–1073 (1999).
7. Ligterink, W. *et al.* *Science* **276**, 2054–2057 (1997).
8. Romeis, W. *et al.* *Plant Cell* **11**, 273–287 (1999).
9. Nühse, T. *et al.* *J. Biol. Chem.* **275**, 7521–7526 (2000).
10. Yang, K.-Y. *et al.* *Proc. Natl. Acad. Sci. USA* **98**, 741–746 (2001).