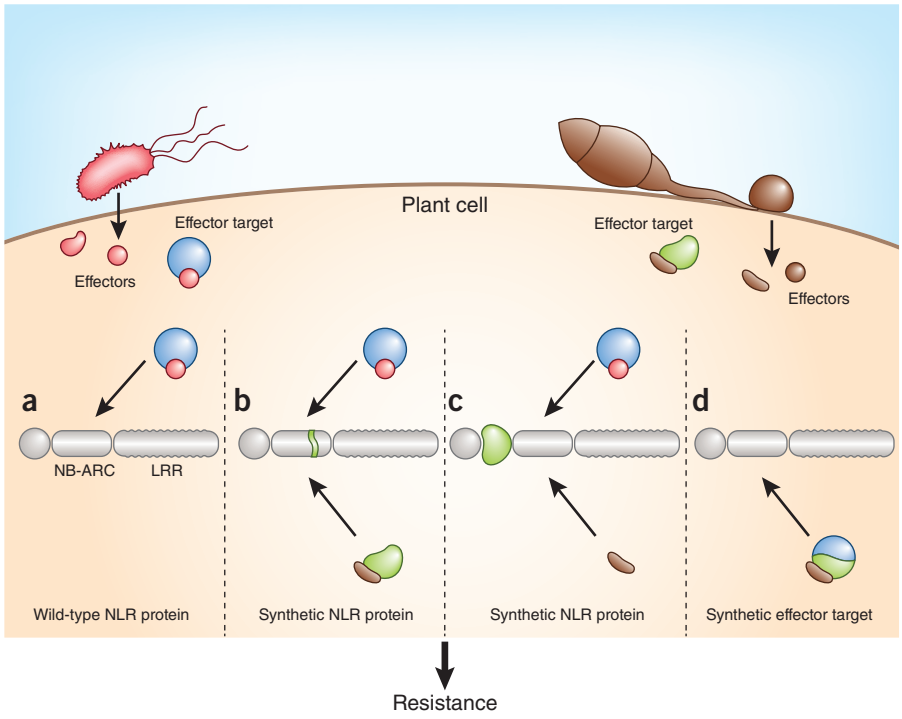

Figure 1 Engineering the plant immune system. Two phylogenetically unrelated pathogens secrete effectors into the plant cell cytoplasm. (**a**) The wild-type NLR protein perceives secreted effectors (red circle) from a pathogen with high specificity. Activation of the NLR protein triggers immune responses that result in plant resistance. Synthetic NLR proteins can be engineered to respond to effectors from different pathogens using two general approaches. (**b**,**c**) Single amino acid changes in the NLR protein (light green line) (**b**) or integration of an effector target domain (light green oval shape) in the NLR protein (**c**). (**d**) Modification of the effector target (dark and light green circle) results in a specificity switch to a different effector (brown shape). Red and brown shapes represent effectors secreted by pathogens. Light and dark green oval shapes represent effector targets in the host.

mosaic virus in addition to a *Pseudomonas syringae* protease effector. This resulted in activation of RPS5 and a specificity switch of RPS5/PBS1 to the different pathogens *in planta*.

The strategy proposed by Kim *et al.*[1] has some limitations. First, PBS1 functions inside plant cells, so it can be engineered to confer resistance only to pathogens that secrete a host-translocated protease, for example, barley powdery mildew fungus BEC1019 (ref. 8). However, most agronomically important pathogens, including oomycetes and rust fungi, are not known to secrete host-translocated proteases. Second, any mechanism of resistance must block pathogen colonization quickly and effectively. Although Kim *et al.*[1] switched RPS5/PBS1 specificity from *Pseudomonas syringae* to *Turnip mosaic virus*, systemic spread of the virus was not prevented, and infection with the virus resulted in a trailing necrosis phenotype[1]. Such a phenotype would preclude commercial applications of the system. Third, the RPS5/PBS1 proteins are present in the plasma membrane and therefore might have to be redirected to other cellular compartments to respond to effectors that have different subcellular localizations. Finally, plant pathogen effectors are typically functionally redundant and tend to be dispensable. Thus, the ability of a pathogen to overcome NLR-protein-mediated resistance is not necessarily dependent on the mechanism by which a particular effector is detected, but is rather a product of the exceptional capacity of these pathogens to carry nimble and rapidly evolving effector repertoires[9]. Owing to these large repertoires, multiple versions of engineered PBS1 might need to be combined to maximize the potential for durable resistance.

To date, plant biotechnologists have focused on engineering broad-specificity immune receptors, in order to keep pace with rapidly evolving plant pathogens. Engineered immune receptors have been developed[3,10] and have become important tools for the development of resistant crops. By manipulating the pathogen targets in the host, Kim *et al.*[1] have substantially expanded the options for engineering synthetic plant immunity. The importance of basic research into plant immunity for devising different approaches to subvert and expand plant immunity should not be underestimated.

COMPETING FINANCIAL INTERESTS
The authors declare competing financial interests: details are available in the online version of the paper.

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