Abstract: Infestations of crop plants with pathogens pose a major threat to global food supply. Exploiting plant defense mechanisms to produce disease-resistant crop varieties is an important strategy to control plant diseases in modern plant breeding and can greatly reduce the application of agrochemicals. The discovery of different types of immune receptors and a detailed understanding of their activation and regulation mechanisms in the last decades has paved the way for the deployment of these central plant immune components for genetic plant disease management. This review will focus on a particular class of immune sensors, termed pattern recognition receptors (PRRs), that activate a defense program termed pattern-triggered immunity (PTI) and outline their potential to provide broad-spectrum and potentially durable disease resistance in various crop species—simply by providing plants with enhanced capacities to detect invaders and to rapidly launch their natural defense program.

Keywords: biotic stress; pattern-triggered immunity; microbe-associated molecular pattern; damage-associated molecular pattern; pattern recognition receptor; receptor-like kinase; receptor-like protein; signal transduction; disease resistance engineering

1. Introduction

Pathogens and pests of plants are a major problem in agricultural food production despite the application of plant protection chemicals [1]. Pre- and post-harvest diseases can cause significant losses in crop yield and impair crop quality. The emergence and global spreading of novel pathogens or pathogen races/strains capable of defeating existing, resistant crop cultivars, such as the wheat stem rust (Puccinia graminis f. sp. tritici) race Ug99 [2] or the kiwi fruit pathogen Pseudomonas syringae pv. actinidae [3], and the increasing resistance of many pathogen races/strains against available pesticides, illustrates the vulnerability of our current plant protection strategies and the looming risk of devastating disease outbreaks. Increasing the yield of high-quality plant products on the available arable farm land while reducing the amount of ecologically harmful agrochemicals, necessitates the development of future-oriented, sustainable agricultural production systems and effective but environment-friendly plant protection measures. In the last 20 years, the identification of a range of different molecular plant immune components has not only greatly advanced our mechanistic understanding of the plant immune system but also provided the conceptual framework to deploy these discoveries for genetic plant protection. Using selected examples, I will demonstrate in which ways PRRs and PTI can be deployed for disease resistance management in crop plants and illustrate future perspectives for molecular engineering of PRRs and PRR signaling.
2. Pattern-Triggered Immunity Forms a Robust Host Barrier to Invaders

Plants rely on genetically determined (innate) immunity to protect themselves from potentially harmful invaders such as pathogens, pests, and parasitic plants. Central to the plant immune system is a multi-layered surveillance system of various extra- and intracellular immune receptors that sense molecular features of the invader (non-self recognition) as well as perturbations of the cellular integrity provoked by the invader (altered-self recognition). Detection of such danger signals by plant immune sensors activates local and systemic defense mechanisms [4,5]. The capacity of a plant to detect invasion attempts early and to mount a defense response in time, i.e., before establishment and proliferation of the invader, largely depends on its repertoire of immune sensors capable of recognizing the invader.

2.1. Microbe-Associated Molecular Patterns (MAMPs)

Plants sense a variety of conserved microbial components with vital roles for microbial fitness as immune elicitors [4]. Because of their important functions, these components are usually conserved across microbial species and cannot readily be modulated to evade recognition without a fitness cost. Such immunogenic molecular structures are termed microbe- or pathogen-associated molecular patterns (MAMPs/PAMPs). MAMPs are chemically diverse, e.g., proteins, polysaccharides, lipids or composite molecules. Classical examples of MAMPs are microbial cell wall structures, such as chitin (fungi), beta-glucans (oomycetes), lipopolysaccharide or peptidoglycan (bacteria), or microbial proteins, such as bacterial flagellin or elongation factor thermo-unstable (EF-Tu, part of the cellular protein translation machinery) [6]. In case of larger molecular structures, a defined partial structure (epitope or pattern) of these molecules is generally sufficient to activate plant immunity. One of the best-studied examples is the flg22 epitope, which corresponds to a stretch of 22 amino acids from the highly conserved N-terminus of flagellin, a region which is important for assembly of the flagellin monomers into a functional flagellum and for bacterial motility. A synthetic flg22 peptide is sufficient to activate the same defense program as the natural flagellin protein [7]. Similarly, the peptide elf18, which corresponds to the conserved N-terminus of EF-Tu, is sufficient to trigger plant immunity [8]. The use of synthetic peptide MAMPs has greatly expedited functional studies of these proteinaceous elicitors.

The isolation and identification of MAMPs is often a challenging task. While it is relatively easy to enrich fractions of microbial extracts that trigger PTI-like defense responses in plants, the identification of the causal molecular motif is demanding and requires sophisticated biochemical and analytical skills [6,9]. This is largely due to the fact, that MAMPs are not necessarily very abundant microbial components. To detect invaders timely, host plants evolved highly sensitive immune receptors that detect MAMPs at very low concentrations (nanomolar range) [9]. Thus, although novel analytical techniques have expedited the identification of MAMPs, these are usually not routine methods applicable for high-throughput identification of MAMPs from microbial populations.

Studies on proteinaceous MAMPs are at the forefront of research because they can be produced in large amounts and high purity through recombinant expression systems or chemical synthesis, can be easily genetically modified, and are amenable to population-wide genetic studies. Once a protein motif has been identified as MAMP epitope in a microbial species/race/strain, the DNA sequence of the respective gene can be easily analyzed in silico in many species. Such bioinformatic studies in combination with functional assays have revealed that MAMP epitopes are not as strictly conserved as was initially assumed. Although the protein sequences of MAMPs are overall conserved to maintain their function, the MAMP epitopes were found to be more diversified, presumably due to the selective pressure exerted on microbes to evade host immune sensing through these epitopes [10]. flg22 epitopes from different bacterial species, for example, are sensed with different efficacy in different plant species and some flg22 motifs are not detected at all in some plant species [7,11–15]. The specific genetic fingerprints resulting from the opposing (purifying versus diversifying) selection pressure on MAMPs can, in turn, be exploited to identify putative MAMP epitopes de novo by means of bioinformatic genome surveys of microbial populations [16]. In a proof-of-concept study several candidate MAMP
epitopes identified by screening *P. syringae* and *Xanthomonas campestris* genome data were shown to elicit PTI in Arabidopsis. Hence, with the increasing availability of microbial genome data such in silico screenings will greatly speed up identification of proteinaceous MAMPs in the future and facilitate targeted screenings for MAMP epitopes in pathogen species of interest.

To date, numerous MAMPs from all microbial classes that are sensed by different plant species have been identified and the list is continuously growing (for a comprehensive summary see recent reviews [6,17,18]). In addition, immunogenic molecular patterns have also been enriched from nematodes, insects, and parasitic plants [6,18,19]. Taken together, this demonstrates the central role of MAMP sensing for plant defense against different types of invaders.

### 2.2. Damage-Associated Molecular Patterns (DAMPs)

Invaders are not only sensed by the plant immune system via their own molecular components (exogeneous elicitors) but usually also provoke the release of plant-derived signals characteristic of infection, called endogenous elicitors or damage-associated molecular patterns (DAMPs) [4]. Typical examples of DAMPs are fragments of cell wall components generated during attack by microbial cell wall-degrading enzymes, e.g., oligogalacturonides (OGs, derived from pectin) [20] or cutin monomers [21], and intracellular plant components released into the extracellular space upon cell lysis, such as extracellular ATP (eATP) [22], extracellular NAD (eNAD) [23], or intracellular proteins (e.g., Arabidopsis HMGB3) [24]. Like MAMPs, DAMPs are sensed by cell surface-resident PRRs and activate typical PTI signaling and defense responses [4].

In addition, plants release various endogenous peptide hormones into the apoplast upon wounding or pathogen attack. Because these peptides trigger typical PTI defense responses via PRR-like receptors, they are also classified as DAMPs. The systemin peptide, for instance, is produced upon wounding in tomato and contributes to plant defense against herbivorous insects [25]. Two peptide families from Arabidopsis, termed AtPEPs and AtPIPs, that are produced upon biotic stress and wounding, apparently play an important role in the amplification of PTI [26–28]. Peptides of the PEP family are found in various monocot and dicot plant species [29,30], suggesting that amplification of PTI by endogenous peptide hormones is a common strategy in plant immunity.

### 2.3. Pattern Recognition Receptors (PRRs)

MAMPs and DAMPs are detected by immune receptors localized at the host cell surface, called PRRs (Figure 1) [4]. PRRs are typically single-span transmembrane or membrane-anchored proteins with structurally diverse extracellular domains, such as leucine-rich repeat (LRR), Lysin-motif (LysM) or lectin domains, that bind MAMP/DAMP epitopes with high specificity and sensitivity [18]. Receptor-like kinase (RLK)-type PRRs possess a cytosolic kinase domain, which usually functions in intracellular signal transduction (Figure 1). Receptor-like protein (RLP)-type PRRs that lack active signaling domains and RLK-type PRRs with non-functional kinase domains require signaling-competent protein partners [18,31]. In general, however, PRRs (RLP-type as well as RLK-type) do not function alone but are part of multi-protein complexes where they engage with co-receptors, signaling partners and regulatory proteins that fine-tune PRR activation/deactivation for appropriate signaling output (Figure 1) [31]. Among the best-studied PRRs to date are the flg22 receptor FLS2 and the elf18 receptor EFR, both of which are LRR-type RLKs [8,32]. Many other LRR-type RLKs and RLPs also detect proteinaceous MAMPs, e.g., RLP23 senses the nlp20 epitope of necrosis- and ethylene-inducing peptide 1-like proteins (NLPs) which show a remarkably broad distribution in bacteria, fungi as well as oomycetes [33,34]. Whereas binding of a MAMP or DAMP to its respective PRR is highly specific, other receptor complex components are commonly shared by several PRRs (Figure 1) [31]. Various LRR-type PRRs (e.g., FLS2 and EFR) interact with the LRR-RLK BAK1 in a ligand-dependent manner [35]. LRR-RLP-type PRRs constitutively associate with the signaling adapter LRR-RLK SOBIR and also recruit BAK1 upon ligand binding [36]. The LysM-RLK CERK1 similarly interacts with different LysM-type PRRs [31].
Individual plant species apparently harbor numerous PRRs that sense different classes of invaders in a partially redundant manner. In this way, each invader is sensed by several PRRs. Arabidopsis, for instance, senses at least seven MAMPs from Pseudomonas bacteria through distinct PRRs [37]. Presumably, the diversity and functional redundancy of PRRs is central to the remarkable robustness of the PTI system. Some PRRs are broadly distributed across the plant kingdom (evolutionary old, e.g., FLS2) whereas others are specific to individual plant families or species (evolutionary young, e.g., EFR) [4]. As a consequence, different plant species have different but partially overlapping sets of PRRs. Just as invaders continuously evolve to evade MAMP sensing, plants continuously adapt their PRRs and evolve new PRRs that facilitate detection of novel MAMPs or of other epitopes within a MAMP. Tomato, for instance, has a second flagellin receptor, FLS3, that detects an epitope (termed flgII-28) distinct from flg22 (sensed by FLS2) [38]. Similarly, rice can sense another EF-Tu epitope (EFa50) distinct from elf18 which is sensed in Brassicaceae [39]. Thus, the genetic diversity of plants provides a rich source of PRRs not only for a multitude of different MAMPs from various kinds of invaders but also for distinct MAMP epitopes.

![Scheme of typical MAMP and DAMP-activated immune responses in plant cells.](image)

**Figure 1.** Scheme of typical MAMP and DAMP-activated immune responses in plant cells. MAMPs and DAMPs (star symbols) are sensed by specific host PRRs localized at the cell surface. Signaling pathways downstream of PRRs converge on common signaling components, for instance co-receptors (CoR) or signaling HUBs. PTI responses include for example fluxes of various ions—including the secondary messenger Ca\(^{2+}\)—across the plasma membrane, production of ROS by RBOH-type oxidases, activation of calcium-dependent and mitogen-activated protein kinases (CDPKs and MAPKs), gene expression changes, production of antimicrobial compounds, and fortification of the plant cell wall.

2.4. Pattern-Triggered Immunity (PTI)

Detection of a MAMP or DAMP by its respective PRR is highly specific. However, downstream of PRRs, signaling pathways converge on common signaling hubs, often already at the receptor complex level, because certain co-receptors (e.g., BAK1, SOBIR, and CERK1) can act in multiple receptor complexes (Figure 1) [4,5,31]. Therefore, PRRs generally activate a quite stereotypic defense program referred to as PTI. Typical PTI signaling and defense responses are, for example, the depolarization of the plasma membrane, an increase in the cytosolic concentration of the secondary messenger Ca\(^{2+}\), activation of different protein kinases, production of reactive oxygen species (ROS), induction of defense-related genes, cell wall fortifications, and production of antimicrobial enzymes and secondary metabolites as well as defense-related plant hormones (Figure 1) [4,31]. PTI is not restricted to the site of infection but establishes in a systemic manner, resulting in an increased resistance of distal, uninfected parts of the plant to secondary infection with the same or unrelated pathogens [4,40]. Plant immune components including PRRs are systemically upregulated upon elicitor sensing, which further enables the plant to respond faster and stronger to a subsequent pathogen attack [4].

Although PTI is a temperate immune response that usually does not culminate in a hypersensitive response (HR, a programmed cell death reaction), it nevertheless constitutes a robust host barrier...
effective against commensals and non-adapted pathogens and maintains a basal level of immunity during infection with adapted pathogens [5]. The vital role of PTI is illustrated by the following observations: (i) Loss of individual PRRs renders plants more susceptible to infection with microbes harboring the respective MAMP [5,41,42]; (ii) Treatment of plants with MAMPs to activate PTI (which depends on the presence of a functional, matching PRR) results in enhanced resistance to subsequent local or systemic infection [5,40–42]; (iii) For successful host colonization pathogens need to overcome PTI by evading MAMP sensing or by releasing effectors that subvert PTI through interfering with MAMP/DAMP detection or downstream signaling and defense responses (adapted pathogens). If the effector repertoire of the pathogen sufficiently suppresses host immunity, the pathogen can establish itself in the host and cause disease (effector-triggered susceptibility, ETS) [5,43].

MAMPs are not specific to pathogens. Accordingly, commensal and beneficial microbes are also sensed by PRRs unless they have adapted their MAMP epitopes to evade detection [44,45]. Indeed, it is now evident that PTI restricts not only the growth of pathogenic microbes but also controls colonization of plant tissues with commensal and beneficial microbes [44–47]. Presumably, the diversity and functional redundancy of PRRs in combination with signal amplification through feedback-induction of genes encoding PRRs and PTI signaling components and diverse plant hormones is key to the apparent robustness of the PTI system. Indeed, breaching of host immunity against natural commensal bacteria requires inactivation of multiple PRRs simultaneously or of co-receptors shared by several PRRs [46]. In conclusion, the PRR class of immune sensors and PTI form a robust protective barrier against various types of plant colonizers and are central to plant health.

3. Prospects of Deploying PTI for Broad-Spectrum Disease Resistance Engineering in Crops

It has been known for decades that microbial and plant-derived elicitors (now usually called MAMPs and DAMPs) trigger defense responses in diverse plant species [48–51]. However, only with the molecular identification of PRRs it was possible to unravel the perception and cellular signaling mechanisms in sufficient detail to eventually exploit this central layer of the plant immune system for genetic plant protection in a purposive manner.

3.1. Pattern- versus Effector-Triggered Immunity

Because of the conserved nature and broad occurrence of MAMPs in different microbes, sensing of MAMPs to activate PTI enables the host to detect and efficiently control a wide range of microbes [4]. Adapted pathogens employ effectors to dampen PTI and to modulate host cell metabolism for their own needs. Plants, in turn, evolved immune sensors, called resistance (R) proteins that detect microbial effectors directly or indirectly by monitoring the effector targets, thus turning effectors into avirulence factors. This results in effector-triggered immunity (ETI), which includes overall similar defense responses like PTI but usually develops faster and in a stronger fashion and is mostly accompanied by an HR [5]. Since effector genes are typically specific to certain pathogen races, while R genes are limited to certain plant cultivars, this form of resistance is called race-specific or gene-for-gene resistance. In a co-evolutionary arms-race with their hosts, pathogens may be able to overcome R-gene mediated ETI relatively easy [5,52]. Mostly, recognized effectors are not essential and/or functional redundant allowing microbes to evade recognition by diversifying or even losing them. Alternatively, microbes may produce novel effectors that e.g. suppress the same or other PTI components or R protein signaling [5,52]. To date, plant resistance breeding widely relies on race-specific resistance mechanisms, largely because effectors and R genes typically result in complete or near-complete resistance. The selective pressure exerted on pathogen populations by ETI, however, may result in rapid resistance breaching in the field by the appearance of novel pathogen races/strains [52]. PTI, by contrast, enables defense against a broad spectrum of pathogens and presumably is more durable because of the evolutionary constraints on MAMP modulation and the quantitative resistance conferred by PRRs which reduces the selective pressure on the pathogen.
3.2. PRR Transfer Between Plants Species

One feature makes PRRs particularly attractive targets for genetic engineering of plant immunity: signaling networks downstream of PRRs are sufficiently conserved (Figure 1), not only within but also between plant families and even between monocot and dicot classes, to facilitate functional transfer of PRRs between them [53–55]. Apparently, PRRs can plug into the existing signaling network by engaging with conserved interacting signaling partners (e.g., SOBIR, BAK1 or CERK1) (Figure 2) [54,55]. Because PRRs as the ligand binding components of PTI receptor complexes determine the epitope specificity, introducing a PRR with a novel epitope specificity can confer recognition of this epitope onto previously insensitive plant species. In this way, plants can be equipped with additional MAMP sensing capacities to enhance disease resistance to pathogen classes harboring the respective MAMPs (Figure 2). These can either be PRRs for MAMPs not yet sensed by the recipient plant or for additional epitopes within a given MAMP (e.g., flgII-28/FLS3). A breakthrough study utilizing the Brassicaceae-specific EFR receptor has proven the general feasibility of this strategy [53], which was subsequently shown for multiple PRRs in various plant species (summarized in [6,56]). EFR-transgenic tomato (Solanum lycopersicum) and Nicotiana benthamiana plants gained immune responsiveness to the elf18 epitope and were more resistant to several major bacterial pathogens carrying this epitope including Ralstonia solanacearum, P. syringae, Xanthomonas perforans, and Agrobacterium tumefaciens [53]. EFR was subsequently also successfully transferred into monocots, such as wheat (Triticum aestivum) and rice (Oryza sativa) [55,57]. Similarly, transfer of the rice PRR XA21, which detects the RaxX protein from Xanthomonas oryzae pv. oryzae, to banana (Musa sp.) and sweet orange (Citrus sinensis) confers increased resistance against different Xanthomonas spp. [58,59] and expression of the PRR ELR from a wild potato species renders cultivated potato (Solanum tuberosum) more resistant to the oomycete pathogen Phytophthora infestans [60]. Taken together, these results demonstrate that addition of only a single PRR can already significantly enhance resistance of plants to adapted pathogens. Given that these pathogens are equipped with an arsenal of effectors to dampen PTI, this is quite astonishing and suggests that increased pathogen sensing provides a substantial advantage to the plant, possibly because of a stronger and/or faster onset of defense reactions.

![Figure 2. Schematic representation of potential PRR transfer and engineering options. PRR-mediated sensing of MAMPs/DAMPs (star symbols) and PRR signaling capacities can be enhanced by optimization of endogenous PRRs or introduction of novel, chimeric or even “designer” PRRs. This equips plants with additional MAMP/DAMP sensing and improved signaling capacities and results in enhanced PTI against a broad spectrum of invaders.](image-url)
for instance through screening for altered resistance against the pathogen of interest in loss- or gain-of-function mutants or natural accessions, or through heterologous expression in suitable model plants (e.g., Arabidopsis thaliana or N. benthamiana) [64–69].

A major concern of introducing novel PRRs into plant species is that this might negatively affect beneficial interactions of these plant species with their natural microbiota and/or symbiotic interactions, such as legume-rhizobia or mycorrhizal interactions. Transgenic Medicago plants expressing EFR from Arabidopsis, however, are apparently not defective in symbiosis and are more resistant to the root pathogen R. solanacearum. Although the EFR transgenic plants showed a delay in nodule formation the final extent of nodulation and nitrogen fixation of the EFR transgenics was comparable to the wild-type plants [70]. Potentially, adapted symbionts have evolved efficient strategies to evade or suppress host PTI at various levels.

While to date mostly strong, constitutive promoters (e.g., viral promoters such as the 35S promoter of cauliflower mosaic virus, plant ubiquitin or actin promoters) are used to drive heterologous PRR expression in plants because of their universal functionality in diverse plant species and different plant tissues, this can result in unwanted side effects on general plant performance. Overexpression of RLKs, for instance, may trigger their activation in the absence of ligand and lead to growth defects because of constitutive activation of PTI or interference with developmental signaling [71]. This can be overcome by using plant promoters from e.g. endogenous PRR genes that drive PRR expression in plant tissues preferentially targeted by the pathogen of interest (e.g., root) or at sites of pathogen entry (e.g. stomata guard cells) and are strongly induced above the basal level upon infection [72,73].

The growing interest in PTI in recent years already led to the identification of numerous PRRs from different model and wild plant species and there is more to come (summarized in [6,17]). Natural diversity provides plant breeders with a versatile genetic tool box for crop improvement. Relevant PRR genes can be introduced, for instance, from wild relatives through classical breeding strategies. However, this is usually a lengthy process, bears the risk of co-segregation of unfavorable traits (linkage drag), and is not applicable to all crop species (e.g., banana, which is sterile) [56,74]. Alternatively, modern genetic engineering tools facilitate direct transfer of PRR genes across plant families beyond the constraints of sexual compatibility with the advantage that PRR genes can be quickly introduced into elite crop varieties as single traits (Figure 2). Additionally, this allows to utilize virtually any plant species as source of PRR genes. In conclusion, PRR transfer has great potential for conferring broad-spectrum and potentially durable resistance traits onto crop plants.

3.3. PRR Engineering

During co-evolution with host plants, pathogens modulate MAMP epitopes to evade host immunity whereas plants adapt their PRRs [16]. Hence, there is a natural diversity of PRRs that recognize slightly different variants of a given MAMP epitope. Ecotype collections of plant species harboring a particular PRR are thus a rich source of PRR variants with enhanced sensing capacities for these epitope variants (Figure 2) [75,76]. Additionally, in vitro evolution of PRRs can be applied to produce PRRs with altered ligand specificities [77]. With the increasing availability of PRR ectodomain structures and computational modelling tools ligand binding sites of PRRs can be modified in a directed manner to perceive a desired epitope variant or may eventually even be designed de novo (Figure 2). Potentially, ligand binding sites can be engineered at the native gene locus through CRISPR/Cas-mediated genome editing.

Some PRRs may not be able to integrate optimally with the endogenous signaling adapters upon transfer in more distantly related plant species. In such cases, full signaling competence can be restored by exchanging the transmembrane and/or intracellular signaling domain with a related PRR from the recipient species (Figure 2) [54,62]. Such chimeric PRRs have been shown to be fully functional and can be further exploited to combine different ligand binding specificities with different downstream signaling capacities (Figure 2). Some PRRs naturally induce a stronger immune response including an HR, such as the rice RLKs XA21 [78]. Sensing of chitin fragments by the rice PRR CEBiP,
by contrast, does not result in HR [79]. A chimeric receptor combining the chitin-sensing ectodomain from CEBiP with the intracellular signaling domain of Xa21 activates HR upon chitin sensing and enhances resistance to the rice pathogen *Magnaporthe oryzae*, a pathogen that does not naturally activate Xa21 signaling [80].

### 3.4. Exploiting DAMP Signalling

Transfer and engineering of PRRs sensing DAMPs are also possible given that the respective DAMP is produced in the recipient species during infection with the pathogen of interest. Expression of the Arabidopsis eATP receptor DORN1 (also known as P2K1) in potato, for instance, enhances resistance to *P. infestans* [22,81]. Alternatively, plants can be engineered to produce the desired DAMP upon infection with diverse pathogens, for instance, by introducing a microbial enzyme producing the DAMP under control of a pathogen-responsive promoter. In this way, any pathogen that induces transcription of the transgene will trigger PTI independent of the ability to produce this DAMP itself. A promising example is the production of elicitor-active OG fragments through the balanced action of a microbial polygalacturonase (PG) and a plant PG inhibitor. Pathogen-inducible expression of this OG factory in Arabidopsis increased resistance to *Botrytis cinerea*, *Pectobacterium carotovorum* and *P. syringae* infections [82]. Such pathogen-responsive *in situ* production of DAMP signals in combination with providing the respective PRR could be a generally applicable strategy to boost PTI in any plant species and to confer resistance to a wide range of pathogens.

### 4. Conclusions

Most PRRs known to date have been identified from model species such as Arabidopsis, rice and recently also increasingly from tomato and potato [6,17]. These rather limited studies already illustrate the enormous resource of plant immune sensors available in different plant species that just await discovery. With novel genetic and computational tools at hand we can now exploit this natural genetic tool box for providing plants with expanded capacities to sense any kind of undesired invaders and strengthen their natural defense to resist them. Moreover, a mechanistic understanding of PRR function enables us to accelerate PRR evolution artificially, to modify PRRs in a targeted manner or even design novel PRRs.

Although PTI is generally more difficult for pathogens to overcome than ETI, pathogens will, albeit presumably on a longer time scale, eventually succeed. Hence, the deployment of single PRRs still poses the risk that pathogen populations eventually adapt their MAMP epitopes or their effector repertoire, particularly if the selection pressure on pathogen populations is constantly high. To deploy PRR engineering in a durable manner, combination of several PRR and R genes (stacking or pyramiding) appears to be a promising strategy as pathogens are unlikely to overcome several immune receptors at the same time. Possibly, resistant varieties equipped with different PRR/R gene combinations can be used in alternation to lower the selective pressure of the individual components on pathogen populations. If utilized in a thoughtful manner, these genetic tools have great power for developing truly durable and sustainable plant disease management practices.

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