Plant Biotechnology Journal

Plant Biotechnology Journal (2023) 21, pp. 17–45 doi: 10.1111/pbi.13916

Review article

Engineering plant immune circuit: walking to the bright future with a novel toolbox

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Received 10 June 2022;
revised 20 August 2022;
accepted 23 August 2022.
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Keywords: plant immune system, engineering, CRISPR/Cas, disease resistance, receptors, *S* genes.

Summary

Plant pathogens destroy crops and cause severe yield losses, leading to an insufficient food supply to sustain the human population. Apart from relying on natural plant immune systems to combat biological agents or waiting for the appropriate evolutionary steps to occur over time, researchers are currently seeking new breakthrough methods to boost disease resistance in plants through genetic engineering. Here, we summarize the past two decades of research in disease resistance engineering against an assortment of pathogens through modifying the plant immune components (internal and external) with several biotechnological techniques. We also discuss potential strategies and provide perspectives on engineering plant immune systems for enhanced pathogen resistance and plant fitness.

Introduction

Plants have evolved a sophisticated immune system to protect against pathogen invasion. Preformed immunity, including physical and chemical barriers such as leaf trichomes, cell walls, and surface pH, is utilized early in the attack of the pathogen. However, some pathogenic organisms can overcome this immunity and cause diseases in plants. To survive, plants have evolved innate immunity as a barrier, comprising complex pathogen-interfering patterns called induced immunity, which is based on the recognition and activation of different immune receptors that sense the presence of pathogens (Deslandes and Rivas, 2012; Jones and Dangl, 2006; Zipfel and Robatzek, 2010). Transmembrane pattern recognition receptors (PRRs) are typically utilized in the first layer of this system to recognize virulence factors such as pathogen-/microbe-/damage-associated molecular patterns (PAMPs/MAMPs/DAMPs, hereafter MAMPs) to induce a basal response known as pattern-triggered immunity (PTI; Zipfel, 2009, 2014). Once PTI is activated, a series of defence responses is triggered to suppress the colonization of the pathogen (Bigeard *et al*., 2015; Torres *et al*., 2006). However, many pathogens can suppress PTI by introducing interfering molecules (called effectors) into the cell (Iswanto *et al*., 2021b; Stergiopoulos and de Wit, 2009; Tampakaki *et al*., 2010). Effectors target various host proteins to facilitate pathogen replication, colonization, and pathogenicity in plants to cause effector-triggered susceptibility (ETS; Deslandes and Rivas, 2012; Raffaele and Kamoun, 2012). In turn, plants have developed a strategy to recognize specific effectors using intracellular nucleotide-binding and leucine-rich repeat receptors (NLRs; Bonardi *et al*., 2012; Nguyen *et al*., 2021; Su *et al*., 2018; Takken *et al*., 2006). Once the plant cell has sensed the effectors, it undergoes a robust and timely effector-triggered immunity (ETI) response. ETI is often associated with programmed cell death and typically involves a hypersensitive response (HR) at the site of infection and systemic acquired resistance (SAR) in distal plant tissue to limit pathogen growth and proliferation (Cui *et al*., 2015; Durrant and Dong, 2004; Fu *et al*., 2012; Greenberg and Yao, 2004). Recent studies revealed the consequential relationship between PRR-mediated PTI and NLR-mediated ETI during bacterial infection (Ngou *et al*., 2021; Nguyen *et al*., 2021; Yuan *et al*., 2021). The continuous adaptation and evolution of PTI, ETS, and ETI have further strengthened the improvisation of both the host and pathogen to simultaneously diversify effector and resistance proteins (Delaux and Schornack, 2021; Deslandes and Rivas, 2012).

The plant immune system comprises a complicated system of immune genes with positive or negative effects. Immune receptors and positive regulators of plant immunity contribute to the recognition of intruders and help transmit signals to activate a series of downstream events after sensing the presence of the pathogen. The activation of these signalling cascades often enhances immune responses (Durrant and Dong, 2004; Fu *et al*., 2012; Greenberg and Yao, 2004; Kachroo and Robin, 2013). By contrast, genes that encode proteins that facilitate the compatibility of pathogens and plants are defined as *susceptibility* (*S*) genes (Koseoglou *et al*., 2022). *S* genes encode negative regulators of plant defence and facilitate pathogen invasion and susceptibility. Some negative regulators encoded by *S* genes also control the activation of positive regulators of plant defence under normal conditions to avoid the abnormal plant growth and autoimmune responses (Kim *et al*., 2010; Mackey *et al*., 2003).

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Crop improvement has continuously aimed to achieve higher yields and more substantial tolerance against various pathogens. Traditional breeding methods have been used to select desirable traits within crossbreeding plants. However, conventional methods have some disadvantages, such as a long production time, the need for large populations, labor-intensive procedures, and a limited gene pool. Therefore, new genome editing techniques have been developed to facilitate plant breeding and increase its efficiency, such as oligonucleotide-directed mutagenesis (ODM; Sauer *et al*., 2016), transcription activator-like effector nucleases (TALENs; Joung and Sander, 2013), zinc finger nucleases (ZFNs; Petolino, 2015), the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated (Cas) system (Cong *et al*., 2013; Iswanto *et al*., 2021a; Jinek *et al*., 2012; Shmakov *et al*., 2017; Zetsche *et al*., 2015), and modified versions on the CRISPR/Cas system, such as base editor and prime editor, according to the needs of the scientist (Anzalone *et al*., 2019; Gaudelli *et al*., 2017; Kang *et al*., 2018; Lin *et al*., 2020; Zou *et al*., 2022). Compared to traditional breeding, these techniques allow researchers to rapidly make more precise genome changes to generate plants with desirable traits (Abdallah *et al*., 2015).

Remarkable advancements in elucidating plant immune components have been utilized for the genetic engineering of crop plants. Several reviews have discussed some aspects of engineering plant resistance, but a thorough summary of the engineering of plant innate immunity from a different point of view is needed. In this review, we summarize recent advances in plant immune engineering based on important publications over the past two decades. We divide the engineering targets into three types: PTI-related receptors, ETI-related receptors, and other downstream components. We also discuss the novel concept of transferring pathogen genes into plants to counter their aggressiveness.

Engineering PTI receptors to confer broad-spectrum resistance

Overview of pattern recognition receptors

PRRs are membrane-localized receptor proteins that are divided into two types: receptor-like kinases (RLKs) and receptor-like proteins (RLPs; Boutrot and Zipfel, 2017; Couto and Zipfel, 2016; Zipfel, 2014). RLKs possess an ectodomain in the extracellular space, a transmembrane domain, and an endokinase domain in the cytoplasm. The ectodomain functions in ligand perception, while the endokinase domain is required for signal transduction and to activate defence responses in the cell (Boutrot and Zipfel, 2017). Unlike RLKs, RLPs lack an endokinase domain. Therefore, RLPs normally associate with other RLKs to sense the presence of MAMPs or DAMPs. The leucine-rich repeat (LRR) domain, epidermal growth factor-like domain, and lysin motif (LysM) have been identified as common ectodomains that guard the apoplast environment following successful infection by intruders and the onset of plant disease. The recognition signals are transduced into the cytoplasm through the endokinase domain, triggering downstream events such as protein oligomerization, auto- and transphosphorylation, and the release of negative regulators of immunity, thereby inducing PTI (Boutrot and Zipfel, 2017; de Vries, 2015). PTI responses confer broad-spectrum resistance in plants. However, in many cases, the plant lacks PRRs to recognize particular pathogens, or the current immune system is insufficient to fend off the invasion. Here, we summarize two strategies of PTI-related engineering to make more durable and sustainable resistance in the field.

Transformation-based engineering to transfer PRRs across species

The bacterial peptide elf18, derived from the well-known MAMP elongation factor thermo unstable (EF-Tu), is recognized by the RLK EF-Tu receptor (EFR) in Arabidopsis (*Arabidopsis thaliana*). EFR binds to EF-Tu to prevent the transmission of bacterial genetic material and protein synthesis, triggering basal defence responses against the bacterial pathogen (Kunze *et al*., 2004; Zipfel *et al*., 2006). Since EFR is only present in the plant family Brassicaceae, the ability of plants from other families to recognize EF-Tu is limited. In 2010, Lacombe *et al*. successfully transferred *EFR* from the cruciferous plant Arabidopsis (*AtEFR*) into the solanaceous plants *Nicotiana benthamiana* and tomato (*Solanum lycopersicum*) to induce broad-spectrum resistance to different phytopathogens (Lacombe *et al*., 2010). Moreover, potato (*Solanum tuberosum*) plants exogenously overexpressing *AtEFR* showed significant resistance to bacterial wilt caused by the bacterium *Ralstonia solanacearum* (Boschi *et al*., 2017). *AtEFR* was also recently introduced into barrel clover (*Medicago truncatula*) and orange (*Citrus sinensis*) to prevent infection by *R. solanacearum* and *Xanthomonas citri* subsp. *citri* (*Xcc*) and *Xylella fastidiosa* subsp. *pauca* (*Xfp*), respectively (Mitre *et al*., 2021; Pfeilmeier *et al*., 2019). Notably, interspecies transfer of *AtEFR* into apple (*Malus domestica*) significantly reduced the extent of tissue necrosis associated with *Erwinia amylovora* infection, which causes fire blight disease (Piazza *et al*., 2021). The success of this study demonstrates the feasibility of using biotechnological strategies to tackle the devastating fire blight disease in apple trees, which causes substantial losses to cultivated apple production worldwide. Several studies have demonstrated the power of constitutively expressing *AtEFR* to increase plant immunity in both dicotyledons and monocotyledons such as rice (*Oryza sativa*) and common wheat (*Triticum aestivum*) in response to *Xanthomonas oryzae* pv. *oryzae* and *Pseudomonas syringae* pv. *oryzae*, respectively (Lu *et al*., 2015; Schoonbeek *et al*., 2015).

Another well-studied PRR in plants is FLAGELLIN-SENSITIVE 2 (FLS2), an RLK that recognizes the most highly conserved domain of the bacterial flagellin flg22 (Chinchilla *et al*., 2006; Gomez-Gomez *et al*., 2001). Unlike EFR, FLS2 is conserved in several plant species. However, flg22 perception by FLS2 orthologs differs among species (Chinchilla *et al*., 2006). Notably, overexpressing grapevine (*Vitis vinifera*) *FLS2* (*VvFLS2*) in Arabidopsis conferred resistance against *Burkholderia phytofirmans* (Trda *et al*., 2014). Overexpressing frost grape (*V. riparia*) $FLS2^{XL}$ in *N. benthamiana* induced resistance to *Agrobacterium tumefaciens* (Furst *et al*., 2020), and overexpressing *NbFLS2* in citrus reduced susceptibility to *X. citri* (Hao *et al*., 2016).

Xa21 is a PRR that confers robust resistance to *X. oryzae* pv. *oryzae* (*Xoo*; Ronald *et al*., 1992; Song *et al*., 1995; Wang *et al*., 1996). A RaxX protein sulfated by the tyrosine sulfotransferase RaxST from *Xoo* is required to activate Xa21-mediated immunity (Pruitt *et al*., 2015). Moreover, chimeric PRRs generated using an extracellular domain of AtEFR and a kinase domain of Xa21 conferred elf18-induced signalling and quantitative immunity in Arabidopsis and *N. benthamiana*, revealing the essential role of Xa21 kinase activity in plant resistance (Holton *et al*., 2015). Indeed, introducing *Xa21* into four sweet orange cultivars conferred resistance to *Xanthomonas axonopodis* pv. *citri*, the causal agent of leaf-spotting and fruit rind-blemishing

disease. In addition, the introduction of *Xa21* via genetic transformation enhanced resistance to pathogens in other crops, such as tomato (Afroz *et al*., 2010) and banana (*Musa acuminata*; Tripathi *et al*., 2014), including against bacterial wilt pathogens and *Xanthomonas campestris* pv. *musacearum*, respectively.

Domain swapping-based engineering to enhance resistance

Engineering PRRs by domain swapping represents another promising approach for achieving disease resistance (Figure 1). Chitin-elicitor binding protein (CEBiP), a plasma membrane receptor in rice that perceives chitin from the fungal cell wall, is a glycoprotein with two LysM domains in the extracellular portion and a putative transmembrane domain (Kaku *et al*., 2006; Shinya *et al*., 2012). Xa21, a member of the RLK family, harbours a leucine-rich repeat motif and a serine–threonine kinase-like domain (Song *et al*., 1995). Two LysM domains of CEBiP and the kinase-like domain of Xa21 were combined to generate the new chimeric receptor CRXA (Figure 1). Transgenic rice plants accumulating CRXA showed more robust resistance to *Magnaporthe oryzae* than plants harbouring wild-type CEBiP, producing an HR-like response and strong disease resistance to rice blast (Kishimoto *et al*., 2010). This enhanced immune response suggests that the LysM domains of CEBiP are required for the early perception of fungal invasion (Kishimoto *et al*., 2011).

Enigmatic MAMP of *Xanthomonas* (eMax) is recognized by the receptor-like protein RECEPTOR OF eMax (ReMAX) in Arabidopsis

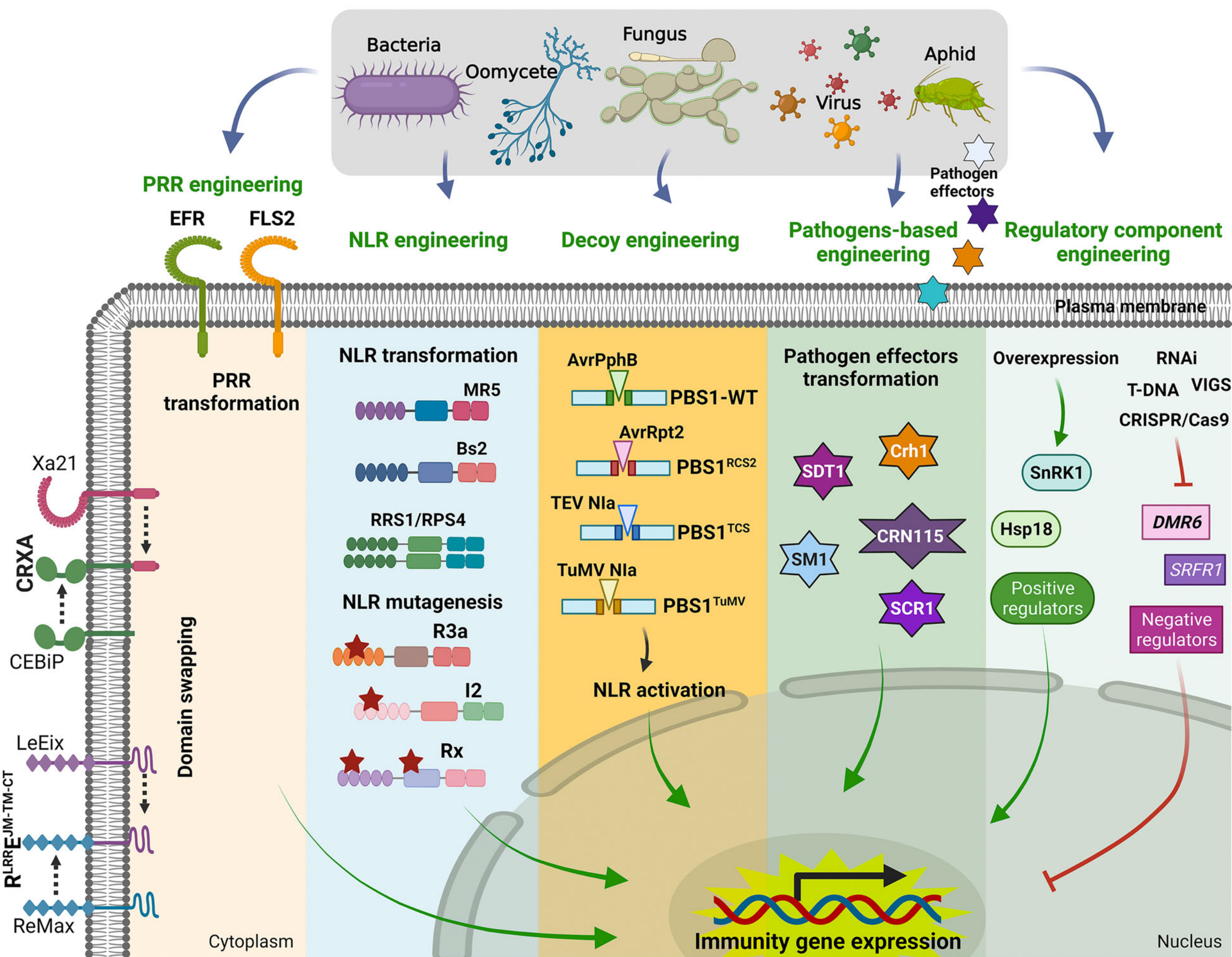

Figure 1 Biotechnological strategies to improve disease resistance in crops. *PRR engineering*: PRRs (e.g., EFR and FLS2) can be transformed across species for broadening pathogen recognition. Besides, a new chimeric of PRR can be generated through domain swapping to enhance resistance. Chimera receptor CRXA, made of two LysM domains from CEBiP and kinase domain from Xa21, induces a more robust immune response to *Magnaporthe oryzae*. The combination of the LRR domain from ReMax and JM-TM-CT domain from *Le*Eix can resist *Xanthomonas* in *Nicotiana benthamiana*. *NLR engineering*: NLRs (e.g., MR5, Bs2, and RRS1/RPS4) can be introduced inter-/intra-species through transformation to gain resistance against specific pathogens. Besides, random mutagenesis in NLR (e.g., R3a and I2) can be applied to expand effector recognition. Secondary mutation in NLR (e.g., Rx) increases its activation sensitivity to overcome the cost of over-activated NLR through primary mutagenesis. *Decoy engineering*: Arabidopsis RPS5 specifically recognizes protease effector AvrPphB by the cleavage of PBS1 and promotes a defensive response. The recognition specificity of RPS5 could be expanded by substituting AvrPphB cleavage sequence in AtPBS1 with other new proteases (e.g., AvrRpt2 from bacteria, TEV NIa protease, and TuMV NIa protease from viruses). *Pathogens-based engineering*: Pathogen effectors (e.g., SDT1, Crh1, SM1, CRN115, and SCR1) can be utilized as alternative genetic resources for a transgenic-based approach to crop disease management. *Regulatory component engineering*: Downstream regulatory components involved in immune signalling positively or negatively regulate the resistance to pathogen attack. Overexpression of positive regulators (e.g., SnRK1 and Hsp18) increases disease resistance. Alternatively, transcriptional suppression of negative regulators (e.g., DMR6 and SRFR1) through CRISPR/Cas9, VIGS, RNAi, and T-DNA can boost plant immunity. Created with www.BioRender.com.

(Jehle *et al*., 2013b). In addition, the PAMP xylanase provokes a defence response in tomato via the activity of *Lycopersicon esculentum* ethylene-inducing xylanase (LeEix). ReMAX and LeEix are RLPs containing large extracellular LRR domains, a juxtamembrane domain (JM), a transmembrane domain (TM), and a cytoplasmic tail (CT). *N. benthamiana* lacks an endogenous perception system for both eMax and xylanase. However, transgenic *N. benthamiana* plants accumulating a hybrid protein containing the ReMAX LRR and Eix2 JM-TM-CT domains successfully induced defence responses upon eMax recognition (Figure 1; Jehle *et al*., 2013a,b). One possible strategy for enhancing the basal response layer may therefore take advantage of each domain of different RLKs and RLPs to engineer upgraded versions of PRRs.

Engineering ETI receptors to enhance specific resistance

Overview of NLR receptors

Some NLRs can recognize their corresponding effectors directly via physical interactions. However, other NLRs recognize the presence of effectors via an indirect pathway (Martin *et al*., 2003). In detail, NLRs are in company with other host components targeted by effectors, thus recognizing effector presence through the modification of the host proteins. The other host components can be a decoy or a guardee (Cesari, 2018). Once the guardee/decoy undergoes a conformational change caused by pathogen effectors, the vigilant NLR is activated, thereby inducing ETI responses. In some cases, NLRs work in pairs in effector recognition, in which one NLR functions as a sensor to trap the effector while the other NLR acts as an executor to induce signalling (Cesari, 2018). Besides the effector recognition function, some "helper" NLRs commonly contribute to the signal transduction downstream after the vigilant NLR activation (Castel *et al*., 2019; Dong *et al*., 2016; Wu *et al*., 2019b).

Altering NLR structure or effector recognition mechanisms is an excellent approach for engineering ETI components to boost resistance to a specific pathogen effector. The NLR itself represents a popular target for engineering. The guardee/decoy in the indirect recognition system may also be targeted (Kim *et al*., 2016; Kourelis *et al*., 2016). A guardee is unlikely to tolerate a change due to its specific functions in plant signalling in addition to effector recognition (Cesari, 2018), whereas a decoy is a preferred engineering target by taking advantage of a mimic host target protein without any role in the plant. In the following sections, we summarize strategies and provide examples of increased plant resistance engineering that targets ETI components.

Transformation-based engineering to transfer NLRs within species

Many studies using crops or model plants have demonstrated the successful transformation of resistance genes to increase resistance against pathogens. For instance, in 2014, Broggini *et al*. proposed a transformation strategy to increase the resistance of apple to fire blight disease (Broggini *et al*., 2014). This devastating disease can destroy an entire apple/pear (*Pyrus communis*) orchard if just one plant is infected. *E. amylovora*, the causal agent of fire blight disease, contains the effector AvrPpt2^{EA}, which is recognized by the R protein FB_MR5 from apple accession Mr5. To generate resistance to *E. amylovora* in apple cultivar Gala, *FB_MR5* was transformed from apple accession *Malus* × *robusta* 5 (Mr5; Figure 1). The transgenic lines expressing *Mr5* showed significantly less severe disease symptoms compared to susceptible wild-type 'Gala'. Therefore, it is possible to isolate a single resistance-determinant gene from the native genome of apple and transfer it to a susceptible cultivar to protect it from fire blight. Although *FB_MR5* is an endogenous apple gene, exogenous T-DNA from the transformation construct is still present in transgenic apple plants, prompting researchers to design ways to remove it. In 2015, Kost *et al*. generated the first cisgenic 'Gala' apple using the same method involving *A. tumefaciens*-mediated transformation of *FB_MR5* from wild apple accession *Mr5* (Kost *et al*., 2015). Interestingly, the cisgenic apple line, displaying markedly fewer fire blight disease symptoms, carried only the cisgene FB_MR5 controlled by a copy of the MR5 promoter and no transgene due to the removal of the T-DNA by heat-induced flippase.

Transformation-based engineering can also be used for the intraspecies transfer of NLRs when the effector from the pathogen and the NLR from the resistant cultivar are known. However, in some cases, even when the cognate effector is unknown, NLR transfer can still be exploited to generate resistant cultivars. Indeed, soybean (*Glycine max*) lines overexpressing *GmKR3*, a soybean gene encoding a TIR-NB-LRR (TNL) similar to tobacco mosaic virus (TMV) resistance protein N, showed decreased susceptibility to several soybean mosaic virus strains, bean common mosaic virus, watermelon mosaic virus, and bean pod mottle virus (Xun *et al*., 2019; Table 1). Remarkably, the enhanced resistance in *GmKR3* overexpression lines did not sacrifice plant growth, including seed production and quality. In addition, overexpressing the RPM1 (RESISTANCE TO P. SYRINGAE PV MACULICOLA 1)-like resistance gene *OsRLR1* enhanced the resistance of rice to the fungus *Pyricularia oryzae* and the bacterium *Xoo* (Table 1; Du *et al*., 2021).

Transformation-based engineering to transfer NLRs from one species to another

Following the pioneering study of 2010 in which the PRR protein EFR from Arabidopsis was expressed in *N. benthamiana* and tomato (Lacombe *et al*., 2010), an increasing number of studies have reported the transfer of NLRs across species. Some studies have focused on the transfer of NLRs to increase resistance against bacteria. For example, the *bacterial spot 2* (*Bs2*) resistance gene from pepper (*Capsicum annuum*) was transferred into tomato, which is phylogenetically close to pepper, to control bacterial spot disease (Horvath *et al*., 2012). Pepper Bs2 is an R protein that senses the effector AvrBs2, which is conserved in bacterial spot-inducing *Xanthomonas* strains. Tomato plants harbouring the *Bs2* transgene exhibited a dramatic decrease in disease severity (Figure 1). Moreover, the fruit yield from tomato plants expressing *Bs2* was more than double that of non-transgenic tomatoes. A later study demonstrated that pepper Bs2-related immunity could also be engineered in a plant family other than *Solanaceae* (Sendin *et al*., 2017). Indeed, the *Bs2* gene was used to develop transgenic sweet oranges (from the Rutaceae family) with increased resistance to citrus canker disease, which is caused by *Xcc* harbouring the conserved *avrBs2*.

Other studies have focused on genetic transformation-based engineering for resistance to fungal pathogens. For instance, Arabidopsis plants harbouring the *Mildew A* (*MLA*) NLR gene from barley (*Hordeum vulgare*) were fully resistant to the barley powdery mildew fungus *Blumeria graminis* f. sp. *hordei* (*Bgh*) containing the effector AVR_{A1} (Maekawa *et al*., 2012), indicating

Table 1 Representative of positive immune regulators that were identified in crop plants

No.	Gene	Pathogen/pest	Hormone signalling	Reference
Monocotyledon				
*Brachypodium distachyon**				
1	*AtSAG101*	*Puccinia brachypodii* *M. oryzae*	SA	Wang *et al*. (2020c)
2	*BdWRKY38*	*R. solani*	SA	Kouzai *et al*. (2020)
*Haynaldia villosa**				
3	*Stpk-V*	*Bgt*, *Bgh*	SA, JA	Qian *et al*. (2017)
4	*HvSERK2*	*Bgh*	nd	Li *et al*. (2018)
5	*RLK-V1.1*	*Bgt*	nd	Hu *et al*. (2018)
6	*LecRK-V*	*Bgt*	SA	Wang *et al*. (2018c)
*Hordeum vulgare**				
7	*SnRK1*	*Bgh*	nd	Han *et al*. (2020)
8	*Sr22*, *Sr33*, *Sr35* and *Sr45*	*Pgt*	nd	Hatta *et al*. (2021)
*Oryza sativa**				
9	*SDS2*	*M. oryzae*	nd	Fan *et al*. (2018)
10	*OsWRKY67*	*M. oryzae*, *Xoo*	nd	Vo *et al*. (2017)
11	*OsMYC2*	*Xoo*	JA	Uji *et al*. (2016)
12	*OsCIPK30*	RSV	nd	Liu *et al*. (2017c)
13	*OsHsp18.0*	*Xoo*, *Xoc*	SA, JA	Ju *et al*. (2017), Kuang *et al*. (2017)
14	*OsSnRK1a*	*P. oryzae*, *C. miyabeanus*, *R. solani* *Xoo*	JA and SA	Filipe *et al*. (2018)
15	*WRKY45*	*Magnaporthe grisea* *Xoo*	SA	Shimono *et al*. (2012)
16	*OsRSR1*	*R. solani*	nd	Wang *et al*. (2021a)
17	*OsRLCK5*	*R. solani*	nd	Wang *et al*. (2021a)
18	*SWEET14*	*R. solani*	nd	Kim *et al*. (2021)
19	*DOF11*	*R. solani*	nd	Kim *et al*. (2021)
20	*OsbHLH034*	*Xoo*	JA	Onohata and Gomi (2020)
21	*Osa-miR162a*	*M. oryzae*	nd	Li *et al*. (2020b)
22	*Os6PGDH1*	*Nilaparvata lugens* (BPH)	JA and ET	Chen *et al*. (2020b)
23	*OsPDR1*	*Xoo*	JA	Zhang *et al*. (2020a)
24	*MIM156-3p*	*M. oryzae*	nd	Zhang *et al*. (2020c)
25	*OsMIM167d*	*M. oryzae*	IAA and JA	Zhao *et al*. (2020)
26	*FBL55*	*R. solani*	Auxin	Qiao *et al*. (2020)
27	*ALEX1*	*Xoo*, *Xoc*	JA	Yu *et al*. (2020)
28	*OsHsfB4d*	*Xoo*, *Xoc*	nd	Yang *et al*. (2020)
29	*OsCM*	*Xoo*	SA and JA	Jan *et al*. (2020)
30	*OsWRKY114*	*Xoo*	nd	Son *et al*. (2020)
31	*IPA1*	*Xoo*	Gibberellin (GA)	Liu *et al*. (2019)
32	*LPA1*	*R. solani*	nd	Sun *et al*. (2019)
33	*OsFWL5*	*Xoo*	JA	Li *et al*. (2019a)
34	*OsGRF8*	BPH	Flavonoid componds	Dai *et al*. (2019)
35	*OsMKK3*	BPH	JA, JA-Ile and ABA	Zhou *et al*. (2019b)
36	*OsPGIP1*	*Xoc*	JA	Wu *et al*. (2019a)
37	*HIR3*	RSV *Pto DC3000* *Xoo*	SA	Li *et al*. (2019c)
38	*AtRPS2* and *AtRPM1(D505V)*	*M. oryzae* *Xoo* BPH	nd	Li *et al*. (2019e)
39	*OsERF83*	*M. oryzae*	SA, MeJA and Ethephon (ETH)	Tezuka *et al*. (2019)
40	*OsRRK1*	BPH	nd	Ma *et al*. (2017)
41	*BAG2*	*Xoo*	nd	You *et al*. (2016)
42	*OsRLR1*	*P. oryzae* *Xoo*	nd	Du *et al*. (2021)
Saccharum spp. *hybrid**				
43	*ScPR10*	*Sporisorium scitamineum*, *Sorghum mosaic virus*	SA and MeJA	Peng *et al*. (2017)
*Triticum aestivum**				
44	*TaRCR1*	*Rhizoctonia cerealis*	nd	Zhu *et al*. (2017)
45	*ERF1-V*	*Bgt*	ET and ABA	Xing *et al*. (2017)
46	*TaPIMP2*	*Bipolaris sorokiniana*	nd	Wei *et al*. (2017)
47	*TaSnRK1α*	*F. graminearum*	nd	Jiang *et al*. (2020)

Table 1 Continued

No.	Gene	Pathogen/pest	Hormone signalling	Reference
48	*WFhb1-1*	*F. graminearum*	nd	Paudel *et al.* (2020)
49	*TaUGT6*	*F. graminearum*	nd	He *et al.* (2020)
50	*TaJAZ1*	*B. graminis*	JA	Jing *et al.* (2019)
51	*AtLTP4.4*	*F. graminearum*	nd	McLaughlin *et al.* (2021)
*Triticum urartu**				
52	*TuACO3*	*Bgt*	ET	Zheng *et al.* (2020)
Phalaenopsis aphrodite sub sp. *Formosana**				
53	*PaAGO5s*	*Cymbidium mosaic virus, Odontoglossum ringspot virus*	nd	Kuo *et al.* (2021)
*Zea mays**				
54	*ZmERF105*	*Exserohilum turcicum*	nd	Zang *et al.* (2020)
55	*LcCHI2*	*E. turcicum* *Curvularia lunata*	nd	Liu *et al.* (2020b)
56	*ZmDEF1*	*Sitophilus zeamais*	nd	Vi *et al.* (2019)
Dicotyledons				
*Brassica napus**				
57	*AtGDSL1*	*Sclerotinia sclerotiorum*	SA	Ding *et al.* (2020)
*Capsicum annuum**				
58	*Can-miRn37a*	*Colletotrichum truncatum*	nd	Mishra *et al.* (2018)
59	*CaHDZ27*	*R. solanacearum*	SA, JA, Ethephon (ETH)	Mou *et al.* (2017)
60	*CaLRR51*	*R. solanacearum*	SA, JA, Ethephon	Cheng *et al.* (2017)
*Chrysanthemum morifolium**				
61	*CmMYB19*	*Macrosiphoniella sanborni*	nd	Wang *et al.* (2017e)
62	*CmMYB15*	*M. sanborni*	nd	An *et al.* (2019)
*Citrus sinensis**				
63	*EFR*	*Xcc, Xfp*	nd	Mitre *et al.* (2021)
64	*CsPrx25*	*Xcc*	nd	Li *et al.* (2020a)
65	*CsGH3.1* and *CsGH3.1L*	*Xcc*	SA, ET	Zou *et al.* (2019)
*Cucumis sativus**				
66	*CsWRKY10*	*Corynespora cassiicola*	nd	Liu *et al.* (2020a)
67	*CsERF004*	*Pseudoperonospora cubensis, C. cassiicola*	SA, ET	Liu *et al.* (2017a)
68	*CsRSF1* and *CsRSF2*	*Sphaerotheca fuliginea*	ABA, GA	Wang *et al.* (2021c)
*Glycine max**				
69	*GmSN1*	SMV	nd	He *et al.* (2017)
70	*Rsv3*	SMV	nd	Tran *et al.* (2018)
71	*GmKR3*	SMV, *Bean common mosaic virus* (BCMV), *Watermelon mosaic virus, Bean pod mottle virus* (BPMV)	ABA	Xun *et al.* (2019)
72	*hrpZm*	*P. syringae* pv. *tabaci, P. sojae*	nd	Du *et al.* (2018)
73	*GmPAL2.1*	*P. sojae*	SA and Genistein	Zhang *et al.* (2017a)
74	*GmERF113*	*P. sojae*	nd	Zhao *et al.* (2017)
75	*OXO*	*S. sclerotiorum*	nd	Yang *et al.* (2019)
76	*GmSnRK1.1*	*P. sojae*	SA	Wang *et al.* (2019b)
77	*GmDR1*	*Fusarium virguliforme* *Tetranychus urticae* *A. glycines, Matsumura* *H. glycines*	SA and JA	Ngaki *et al.* (2021)
78	*GmPI4L*	*P. sojae*	Daidzein and genistein	Chen *et al.* (2019)
79	*AtQQS*	*H. glycines* BPMV *PsgR4* *Myzus persicae* *F. virguliforme*	nd	Qi *et al.* (2019)
80	*AtNF-YC4, GmNF-YC4-1*	*H. glycines* TuMV *Pto* DC3000 *M. persicae* *F. virguliforme*	nd	Qi *et al.* (2019)
*Gossypium hirsutum**				
81	*GhERF-IIb3*	*Xanthomonas citri* pv. *malvacearum* (*Xcm*)	JA	Cacas *et al.* (2017)

Table 1 Continued

No.	Gene	Pathogen/pest	Hormone signalling	Reference
82	*miR398*, *miR2950*	Cotton leaf curl Multan virus (CLCuMuV)	nd	Akmal *et al*. (2017)
83	*GhLAC15*	*Verticillium dahliae*	nd	Zhang *et al*. (2019)
84	*ghr-miR164*	*V. dahliae*	nd	Hu *et al*. (2020)
85	*GhMORG1*	*F. oxysporum*	nd	Wang *et al*. (2020a)
86	*ZmASN*	*Bemisia tabaci*	nd	Gul *et al*. (2020)
87	*GhPAP1D*	*Helicoverpa armigera* *Tetranychus cinnabarinus*	Anthocyanin	Li *et al*. (2019d)
*Ipomoea batatas**				
88	*IbBBX24*	*Fusarium oxysporum* f. sp *batatas*	JA	Zhang *et al*. (2020b)
*Malus domestica**				
89	*MdERF11*	*Botryosphaeria dothidea*	SA	Wang *et al*. (2020b)
90	*MdMYB88*, *MdMYB124*	*Alternaria alternata* *Valsa mali*	nd	Geng *et al*. (2020)
91	*MdMYB73*	*B. dothidea*	SA	Gu *et al*. (2021)
92	*MdUGT88F1*	*V. mali*	SA	Zhou *et al*. (2019a)
93	*MdATG18a*	*Diplocarpon mali*	SA	Sun *et al*. (2018)
*Manihot esculenta**				
94	*MeNR1*, *MeNR2*	*Xanthomonas axonopodis* pv. *manihotis*	nd	Yan *et al*. (2021)
*Populus tremula**				
95	*PtDefensin*	*Septotis populiperda*	JA	Wei *et al*. (2020)
Populus alba var. *pyramidalis**				
96	*PalbHLH1*, *PalMYB90*	*B. cinerea*, *Dothiorella gregaria*	Flavonoid compounds	Bai *et al*. (2019)
*Solanum lycopersicum**				
97	*SlMAPK3*	TYLCV	SA, JA	Li *et al*. (2017)
98	*CsI*	TYLCV	nd	Choe *et al*. (2021)
99	*SlMYC1*	*T. urticae*	JA	Hua *et al*. (2021)
100	*SlMYB75*	*B. cinerea*	JA	Liu *et al*. (2021b)
101	*lncRNA39026*	*P. infestans*	nd	Hou *et al*. (2020)
102	*Pti4/5/6*	*Pto* DC3000	nd	Wang *et al*. (2021d)
103	*SlWRKY8*	*Pto* DC3000	SA, ABA	Gao *et al*. (2020)
*Solanum tuberosum**				
104	*StMPK7*	*P. infestans*, *Phytophthora parasitica*	SA	Zhang *et al*. (2021)
105	*StRac1*	*P. infestans*	nd	Zhang *et al*. (2020d)
*Vitis pseudoreticulata**				
106	*VpRH2*	*Uncinula necator*	nd	Wang *et al*. (2017c)
107	*VpEIFP1*	*Golovinomyces cichoracearum*	nd	Wang *et al*. (2017b)
108	*VpSTS29/STS2*	*U. necator*	SA	Xu *et al*. (2019)

*Indicated for the applied plant.

that AVR_{A1}-mediated resistance via MLA in monocot barley was recapitulated in the transgenic dicot Arabidopsis. Whereas wheat contains many *Stem rust* (*Sr*) resistance genes against the fungus *Puccinia graminis* f. sp. *tritici* (*Pgt*), barley contains a limited number of genetically determined resistance genes. The transformation of the wheat NLR genes *Sr22*, *Sr33*, *Sr35*, and *Sr45* successfully increased resistance to stem rust in barley (Table 1; Hatta *et al*., 2021). The transgenic barley plants showed no agronomically negative effects in the absence of disease. Another example is the transfer of the NLR gene *Ve1* from tomato to tobacco (*Nicotiana tabacum*) and cotton (*Gossypium hirsutum*; Song *et al*., 2018b). In detail, Song *et al*. successfully increased the resistance of tobacco and cotton against *Verticillium* spp. strains via the effector Ave1 recognition by tomato Ve1. In Arabidopsis, the NLR proteins RESISTANT TO P. SYRINGAE 4 (RPS4) and RESISTANT TO RALSTONIA SOLANACEARUM 1 (RRS1) recognize three distinct effectors: PopP2, AvrRps4, and an unknown *Colletotrichum* effector (Birker *et al*., 2009; Narusaka *et al*., 2009). Transferring the *RPS4/RRS1* pair from Arabidopsis conferred resistance to the fungal pathogen *Colletotrichum higginsianum* in *Brassicaceae* and protected cucumber (*Cucumis sativus*, a member of the *Cucurbitaceae*) against *C. orbiculare* (Figure 1; Narusaka *et al*., 2013). Transgenic tomato plants expressing *RPS4/RRS1* also specifically recognized the PopP2 and AvrRps4 effectors (Narusaka *et al*., 2013). These findings expand our knowledge of the roles of NLR-type genes in recognizing and conferring resistance to distinct pathogens. The specific recognizing mechanism is highly conserved, as vigilant NLR protein pairs were formed between different species. Therefore, transferring NLR genes to other species represents a powerful strategy for genetic engineering for enhanced plant immunity.

Random mutagenesis of NLRs enhances plant responses to effectors

Each NLR can recognize only a few effectors. Therefore, the limitation of ETI is that the plant must develop a new NLR to recognize a newly evolved effector secreted from the pathogen. To address this issue, scientists have performed random mutagenesis to broaden the effector recognition capacity of an NLR. For example, the potato R protein R3a was subjected to random

mutagenesis (Segretin *et al*., 2014) to alter its response to the pathogenic effector AVR3a from the oomycete *Phytophthora infestans*. In detail, wild-type R3a responds effectively to AVR3a^{KI} but weakly to its variant AVR3a^{EM} (Armstrong *et al*., 2005; Bos *et al*., 2009), which causes virulence in R3a-containing potato plants. Through a random mutagenesis screening of R3a, Segretin *et al*. obtained eight mutant R3a proteins with single amino acid mutations that showed sufficient recognition of virulent AVR3a^{EM} and even other isoforms. These eight mutations were located across the R3a protein, but mainly in LRR domains (Figure 1). Interestingly, R3a^{N336Y}, harbouring a mutation in a nearby pocket of the NB, conferred resistance to the effector PcAVR3a4 from the vegetable pathogen *P. capsici*.

Furthermore, based on the R3a case study in potato, the authors applied the previously identified mutations in *R3a* to its ortholog in tomato, *NLR I2*, which confers resistance to the fungal pathogen *Fusarium oxysporum* f. sp. *lycopersici* (Figure 1; Giannakopoulou *et al*., 2015). Whereas wild-type I2 conferred a weak response to AVR3a, the I2^{I141N} mutant significantly enhanced the response to AVR3a. Moreover, I2^{I141N} partially mediated resistance against *P. infestans* and showed a broad-spectrum response to effector Avr2 variants from *F. oxysporum* f. sp. *lycopersici*. This finding suggests that it is possible to engineer NLR via mutation to confer resistance to distantly related pathogens. The knowledge obtained from studying an NLR in one plant may thus be applied to improve the resistance conferred by orthologous NLRs in other plants.

In some cases, broadening the effector recognition of an NLR through mutagenesis comes at a cost, i.e., yield-compromising and trailing necrosis caused by autoimmunity. For instance, in the case of potato Rx protein, which mediates resistance to potato virus X (PVX), mutations in the LRR domain of *Rx* confer resistance to both PVX and the phylogenetically unrelated poplar mosaic virus (PopMV). In response to PopMV, one *Rx* mutant showed a trailing necrosis phenotype that annihilated the plant, while plants carrying wild-type *Rx* displayed mild disease symptoms. However, the researchers overcame this cost by performing secondary mutagenesis (Harris *et al*., 2013). Specifically, the authors conducted random mutagenesis in the N terminus of the *Rx* mutant with impaired broad-host recognition. Four mutations located close to the NB pocket were identified, conferring more robust resistance to PopMV. Moreover, stable transgenic plants expressing one of these secondary *Rx* mutants showed resistance to PVX and PopMV, which previously induced trailing necrosis in transgenic plants harbouring the primary *Rx* mutant (Figure 1). These findings demonstrate that the recognition of an NLR can be improved by stepwise mutagenesis. The stepwise mutagenesis has been recently applied for Sw-5b, an NLR recognizing the movement protein NSm from Tomato spotted wilt virus (TSWV), to confer resistance against several TSWV variants and American-type tospoviruses (Huang *et al*., 2021). However, since the gain-of-function mutations arose from random mutagenesis, no rational design strategy has thus far been proposed to engineer NLRs with new recognition specificities, which represents an obstacle to NLR engineering.

Utilizing a decoy system to expand the effector recognition specificity of an NLR

The classical gene-for-gene hypothesis posits that a single R protein recognizes only one avirulence effector. The concept that NLRs could be engineered to recognize several unrelated effectors had been challenging until the decoy engineering of Arabidopsis AVRPPHB SUSCEPTIBLE 1 (PBS1) was proposed (Kim *et al*., 2016). In nature, the Arabidopsis NLR RPS5 perceives the cleavage products of the decoy host protein PBS1 following its cleavage by the protease type III effector AvrPphB to trigger a defence response (DeYoung *et al*., 2012; Qi *et al*., 2014). Targeting PBS1, Kim and colleagues replaced the cleavage sequence targeted by AvrPphB with those of AvrRpt2, tobacco etch virus (TEV) NIa protease, or turnip mosaic virus (TuMV) NIa protease. In response to each tested protease, the corresponding engineered PBS1 successfully activated RPS5-mediated ETI (Kim *et al*., 2016; Figure 1). Notably, unlike engineering to target an R protein, decoy engineering provides a safe and predictable method for protein modification. Indeed, except for effector recognition, decoy PBS1 has no other biological function in the plant; therefore, PBS1 decoy engineering will not have any additional side effects on plants.

The decoy PBS1-based engineering strategy is suitable for plant species containing Arabidopsis PBS1 orthologs and an endogenous R protein that recognizes AvrPphB. Alternatively, the Arabidopsis *RPS5*-engineered *PBS1* cassette can be transferred into crop plants. In addition, the target pathogens must be able to take advantage of the host protease function for their virulence activity to use this strategy. PBS1 orthologs have been characterized in several crops such as wheat, barley, soybean, and potato (Bai *et al*., 2022; Carter *et al*., 2019; Helm *et al*., 2019; Sun *et al*., 2017). To date, the PBS1 decoy approach was successfully used to limit soybean mosaic virus (SMV) and potato virus Y (PVY) in soybean and potato, respectively (Bai *et al*., 2022; Helm *et al*., 2019). The successful engineering of soybean PBS1 (GmPBS1) and potato PBS1 (StPBS1) did not require the identification of the corresponding R protein. Therefore, PBS1-based decoy engineering is expected to be widely applied to crops without the need to identify the responsible R protein for protease effector-mediated resistance.

Unlike a decoy, a guardee is not considered to be a good target for engineering due to its other functions besides effector recognition. For example, a T-DNA knockout mutant of the guardee gene *RPM1 INTERACTING PROTEIN 4* (*RIN4*) caused seedling lethality due to the failure to suppress RPS2 autoactivation (Mackey *et al*., 2003). Therefore, engineering the guardee RIN4 could alter its function, posing a challenge for researchers. However, a recent study of natural RIN4 variants created an opportunity to overcome that challenge (Kim *et al*., 2022). In detail, natural RIN4 variants require RIN4-specific motifs, asparagine/tyrosine (NY) or aspartic acid/phenylalanine (DF), to regulate distinct NLRs. In general, while NY-type RIN4s suppress the autoactivation of Arabidopsis RPM1 and RPS2, DF-type RIN4s activate apple FB_MR5-mediated resistance. More importantly, the conserved H167 residue in various RIN4s plays a key role in regulating multiple NLRs. The idea of expanding NLR recognition specificity by combining two motifs proved to be fruitful, since three of six engineered chimeric RIN4 proteins designed using two full-length NY-type RIN4s and three C-terminal DF-type RIN4s suppressed RPM1/RPS2 autoactivation and activated the R protein FB_MR5. When co-expressed with *RPM1* and *RPS2*, the constructs encoding the tested RIN4 chimeric proteins triggered AvrRpm1- and AvrRpt2-mediated resistance, respectively. Since RIN4 is conserved among species, but with several polymorphisms (Kim *et al*., 2022), it might be possible to engineer chimeric RIN4 to broaden the specificity of NLR recognition in plants of interest.

Engineering crop resistance by targeting the regulators of plant innate immunity

Enhancing the expression of positive regulators of plant innate immunity for broad-spectrum resistance

Genetic transformation is the most commonly employed strategy compared to several other biotechnological approaches, as it permits researchers to insert specific gene sequences into a host plant and to enhance the expression of positive regulatory components in plant defence. During defence responses, phytohormone signalling, particularly jasmonic acid (JA), ethylene (ET), salicylic acid (SA), abscisic acid (ABA), auxin, cytokinin (CK), gibberellin (GA), and brassinosteroid (BR) signalling, is somehow induced, indicating that these plant hormones play significant roles in plant defence responses (Bari and Jones, 2009; Berens *et al*., 2017).

JA and ET primarily control resistance against necrotrophic pathogens. By contrast, SA is a primary regulator of defence against biotrophic and hemibiotrophic pathogens and is also required to establish SAR (Durrant and Dong, 2004). Hence, many researchers have utilized various regulatory components from these phytohormone signalling networks to reduce host susceptibility to specific pathogens. Table 1 lists positive immune regulators that were engineered in crops over the past 5 years and conferred disease resistance against several pathogens. For instance, overexpressing *SNF1-related protein kinase 1* (*SnRK1*), encoding a key regulator of cellular metabolism, positively affected SA and JA signalling pathways and enhanced resistance against necrotrophic and biotrophic fungal pathogens such as *Fusarium graminearum*, *Bgh*, *M. oryzae*, *Cochliobolus miyabeanus*, *Rhizoctonia solani*, and *Plasmodiophora brassicae* in various crops (Table 1).

The activation of incompatible plant-pathogen interactions mediated by SA and JA signalling is also applicable for many bacteria. *SnRK1* has been utilized to generate broad-spectrum disease resistance. *SnRK1* was also reported to decrease susceptibility to bacterial leaf blight *Xoo* in various rice cultivars. In addition to *SnRK1*, many regulatory components in the SA signalling pathway are involved in the plant defence response against bacteria (Filipe *et al*., 2018). Overexpressing *Heat shock protein 18.0* (*Hsp18.0*) activated SA signalling and positively regulated resistance to *Xoo* and *X. oryzae* pv. *oryzicola* (*Xoc*), the causal agent of bacterial leaf streak in rice. Conversely, suppressing this gene increased susceptibility to *Xoo* and *Xoc* and decreased free SA levels, suggesting that *OsHsp18.0*-mediated resistance functions via an SA-dependent signalling pathway (Ju *et al*., 2017; Kuang *et al*., 2017). The decreased susceptibility of the transgenic rice lines to *Xoo* and *Xoc* was not solely due to increased SA levels but also to increased JA and GA levels (Table 1; Onohata and Gomi, 2020; Zhang *et al*., 2020a). Consistent with these findings, the enhanced transcriptional regulatory activity of *SnRK1* that confers resistance to *Xoo* involves three phytohormone signalling pathways. Thus, defence responses against the leaf blight pathogens seem to be coordinately regulated by SA, JA and GA signalling pathways.

Engineering of *S* genes to enhance crop resistance

The engineering of durable, broad-spectrum resistance involves the loss of function of *S* genes. Pathogens target and exploit *S* genes to establish a compatible interaction with the host. Therefore, the mutation or loss of function of *S* genes can limit the ability of the pathogen to cause infection and disease (Moniruzzaman *et al*., 2020). Recent advances in crop protection have led to the identification and targeting of an assortment of *S* genes in vegetables and other crops that play critical roles in plant susceptibility to a wide range of pathogens and pests. Table 2 shows a summary of representative *S* genes identified in crops over the past decade. One significant constraint to yield production in rice is blast disease caused by the hemibiotrophic fungus *M. oryzae*. Over the past decade, powerful biotechnology approaches aimed at exploring the rice blast disease circuitry have led to the discovery of various *S* genes involved in *M. oryzae* infection. Interestingly, some *S* genes of *M. oryzae* were also designated as *S* genes of the biotrophic bacterium *Xoo* (Table 2). Even though numerous rice genes have been identified and defined as *S* genes to *Xoo*, their roles in *M. oryzae* infection have not yet been tested (Table 2). Thus, future studies on the pathogenicity of *Xoo* and *M. oryzae* could help elucidate the connection between *M. oryzae* and *Xoo S* genes. Besides interacting with bacteria and fungi, *S* genes play roles in plant-virus interactions. For example, knockout of *ARGONAUTE 2* (*OsAGO2*) and *SQUAMOSA PROMOTER BINDING PROTEIN-LIKE 9* (*OsSPL9*) conferred resistance against rice black-streaked dwarf virus (RBSDV) and rice stripe virus (RSV), respectively (Wang *et al*., 2021e; Yao *et al*., 2019). Soybean *MITOGEN-ACTIVATED PROTEIN KINASE 6* (*MPK6*), tomato *eIF4E2*, and *Pelota* genes also function as *S* genes that interact with plant viruses. Suppression of *MPK6* expression decreased susceptibility to SMV (Liu *et al*., 2014), whereas knockout mutations of *eIF4E2* and *Pelo* conferred resistance against pepper veinal mottle virus (PVMV) and tomato yellow leaf curl virus (TYLCV), respectively (Moury *et al*., 2020; Pramanik *et al*., 2021).

The biotrophic fungus *B. graminis* causes powdery mildew, one of the most destructive foliar diseases of cereals, thereby significantly reducing crop productivity. Three *S* genes from barley, *cysteine-rich RLK 1* (*HvCRK1*), *Microrchidia 1* (*HvMORC1*), and *HvMORC6a*, were recently shown to contribute to susceptibility to *Bgh*, as transcriptional suppression of *HvCRK1* and knockout of *HvMORC1/MvMORC6a* enhanced resistance to *Bgh* (Table 2; Galli *et al*., 2021; Rayapuram *et al*., 2012). *S* genes to *B. graminis* f. sp. *Tritici* (*Bgt*) from wheat have also been characterized, including *BONZAI 1* (*BON1*), *BON3*, *ENHANCED DISEASE RESISTANCE 1* (*EDR1*), and *DOMAINS REARRANGED METHYLASE 2* (*DRM2*); the downregulation of any of these four genes led to significantly reduced powdery mildew symptoms (Table 2; Geng *et al*., 2019; Zhang *et al*., 2017b; Zou *et al*., 2018). Therefore, *S* genes play a role in disease susceptibility to a wide range of pathogens.

Translating *S* gene engineering from Arabidopsis to crops

Initial research to increase disease resistance in the model plant Arabidopsis by downregulating *S* genes laid the foundation for crop improvement. For example, DOWNY MILDEW-RESISTANT 6 (DMR6) was first identified as a negative regulator of plant innate immunity via EMS mutagenesis of the highly susceptible Arabidopsis mutant *enhanced disease susceptibility1-2* (*eds1-2*) in the accession Landsberg *erecta*. The growth of *Hyaloperonospora parasitica* was highly constrained in the resulting *dmr6* mutants (Van Damme *et al*., 2005). Moreover, overexpressing *DMR6* in the Columbia-0 accession enhanced susceptibility to *P. syringae* pv. *tomato* DC3000 (*Pto* DC3000) and *Hyaloperonospora arabidopsidis*. Remarkably, the mutation in *DMR6* strongly enhanced

Table 2 Representative of *S* genes identified in crop plants (2011–2021)

No.	Gene	Method	Pathogen/pest	Reference
Monocotyledon				
*Hordeum vulgare**				
1	*HvCRK1*	RNAi	*Bgh*	Rayapuram *et al.* (2012)
2	*HvMORC1*, *HvMORC6a*	CRISPR/Cas9	*Bgh* *F. graminearum*	Galli *et al.* (2021)
Musa spp.*				
3	*MusaDMR6*	CRISPR/Cas9	*Xcm*	Tripathi *et al.* (2021)
*Oryza sativa**				
4	*OsAGO2*	CRISPR/Cas9, transposon insertion	RBSDV	Wang *et al.* (2021e)
5	*OsMADS26*	RNAi	*M. oryzae* *Xoo*	Khong *et al.* (2015)
6	*OsDCL1*	RNAi	*M. oryzae*	Zhang *et al.* (2015a)
7	*GF14e*	RNAi	*Xoo*	Manosalva *et al.* (2011)
8	*OsGLIP1*, *OsGLIP2*	RNAi	*Xoo* *M. oryzae*	Gao *et al.* (2017)
9	*OsNramp6*	T-DNA	*M. oryzae*	Peris-Peris *et al.* (2017)
10	*SPL33*	EMS	*M. oryzae* *Xoo*	Wang *et al.* (2017d)
11	*OsDjA6*	RNAi	*M. oryzae*	Zhong *et al.* (2018)
12	*OsCUL3a*	EMS	*M. oryzae* *Xoo*	Liu *et al.* (2017b)
13	*OsCPK4*	T-DNA	*M. oryzae* *Xoo*	Wang *et al.* (2018b)
14	*OsWRKY28*	T-DNA	*M. oryzae*	Delteil *et al.* (2012)
15	*OsEDR1*	RNAi, T-DNA	*Xoo*	Shen *et al.* (2011)
16	*OsERF922*	RNAi	*M. oryzae*	Liu *et al.* (2012)
17	*OsNPR1*	Antisense expression	*C. suppressalis*	Li *et al.* (2013)
18	*CPK18*	RNAi	*M. oryzae*	Xie *et al.* (2014)
19	*LMR*	RNAi and EMS	*M. oryzae* *Xoo*	Fekih *et al.* (2015)
20	*OsHDT701*	RNAi	*M. oryzae* *Xoo*	Ding *et al.* (2012)
21	*OsMESL*	T-DNA, CRISPR/Cas9, RNAi	*Xoo* *R. solani*	Hu *et al.* (2021)
22	*OsTrxm*	CRISPR/Cas9	*Xoo* *R. solani*	Hu *et al.* (2021)
23	*OsSULTR3;6*	CRISPR/Cas9	*Xoc*	Xu *et al.* (2021)
24	*DEP1*	RNAi, T-DNA insertion	*R. solani*	Miao Liu *et al.* (2021)
25	*Osa-miR1873*	miR1873	*M. oryzae*	Zhou *et al.* (2020)
26	*OsSPL9*	CRISPR/Cas9	RSV	Yao *et al.* (2019)
27	*OsMPK15*	CRISPR/Cas9	*M. oryzae* *Xoo*	Hong *et al.* (2019)
28	*Os8N3*	CRISPR/Cas9	*Xoo*	Kim *et al.* (2019)
29	*OsHCAR*	CRISPR/Cas9	*Xoo*	Kampire *et al.* (2021)
30	*OsPG1*	CRISPR/Cas9	*Xoo*	Cao *et al.* (2021)
31	*OsVOZ1/OsVOZ2*	CRISPR/Cas9, RNAi	*M. oryzae*	Wang *et al.* (2021b)
*Triticum aestivum**				
32	*TaNAC1*	VIGS	*Pst*	Wang *et al.* (2015)
33	*Ta-A/N-Inv1*	VIGS	*Pst*	Liu *et al.* (2015)
34	*TaBON1 and TaBON3*	VIGS	*Bgt*	Zou *et al.* (2018)
35	*TaWRKY49*	VIGS	*Pst*	Wang *et al.* (2017a)
36	*TaEDR1*	RNAi, VIGS, CRISPR/Cas9	*Bgt*	Zhang *et al.* (2017b)
37	*TaLSD1*	VIGS	*Pst*	Guo *et al.* (2013)
38	*TaEIL1*	VIGS	*Pst*	Duan *et al.* (2013)
39	*TaNAC21/22*	VIGS	*Pst*	Feng *et al.* (2014)
40	*TaDIR-B1*	VIGS, EMS	*Fusarium pseudograminearum*	Yang *et al.* (2021)
41	*TaSTP13*	VIGS	*Pst*	Huai *et al.* (2020)
42	*TaHRC*	RNAi, CRISPR/Cas9	*F. graminearum*	Su *et al.* (2019)
43	*TaCSN5*	RNAi	*Pst*	Bai *et al.* (2021)
44	*TaADF3*	VIGS	*Pst*	Tang *et al.* (2015)
45	*DRM2*	VIGS	*Bgt*	Geng *et al.* (2019)
*Zea mays**				
46	*ZmLOX3*	Mu-transposable element-insertional mutagenesis	*Colletotrichum graminicola*	Constantino *et al.* (2013)

Table 2 Continued

No.	Gene	Method	Pathogen/pest	Reference
47	*ZmFBL41*	Transposon insertion	*R. solani*	Li *et al.* (2019b)
Dicotyledons				
*Brassica napus**				
48	*BnCRT1a*	EMS, CRISPR/Cas9	*Verticillium longisporum*	Probsting *et al.* (2020)
*Capsicum annuum**				
49	*CaMLO2*	VIGS	*Xanthomonas campestris* pv. *vesicatoria* (*Xcv*)	Kim *et al.* (2014)
50	*CaWRKY58*	VIGS	*R. solanacearum*	Wang *et al.* (2013)
51	*CaGRP1*	VIGS	*Xcv*	Kim *et al.* (2015)
*Citrus sinensis**				
52	*CsWRKY22*	RNAi	*Xcc*	Long *et al.* (2021)
53	*CsDMR6*	CRISPR/Cas9	*Xcc*	Parajuli *et al.* (2022)
54	*CsTCTP1 or CsTCTP2*	VIGS	*S. fuliginea*	Meng *et al.* (2018)
55	*CsMLO1 or CsMLO2*	VIGS	*C. cassiicola*	Yu *et al.* (2019a,b)
56	*CYP6CY14*, *CYP6CY22*, *CYP6UN1*	RNAi	*Aphis gossypii*	Chen *et al.* (2020a)
*Fragaria × ananassa**				
57	*FaWRKY25*	RNAi	*B. cinerea*	Jia *et al.* (2020)
*Glycine max**				
58	*Gm-NDR1-1*	RNAi	*Meloidogyne incognita*	McNeece *et al.* (2017)
59	*GmMPK6*	VIGS	*P. manshurica* SMV	Liu *et al.* (2014)
*Gossypium barbadense**				
60	*GbWRKY1*	VIGS	*V. dahliae* *B. cinerea*	Li *et al.* (2014a)
61	*GbMPK3*	RNAi	*V. dahliae*	Long *et al.* (2020)
*Gossypium hirsutum**				
62	*HDTF1*	VIGS	*V. dahliae* *B. cinerea*	Gao *et al.* (2016)
63	*GhSSI2*	VIGS	*V. dahliae* *F. oxysporum*	Mo *et al.* (2021)
64	*GhADF6*	VIGS	*V. dahliae*	Sun *et al.* (2021)
65	*GhNAC100*	VIGS	*V. dahliae*	Hu *et al.* (2020)
66	*GhBsr-k1*	VIGS	*V. dahliae* *F. oxysporum*	Li *et al.* (2021)
*Malus domestica**				
67	*MdMLO19*	RNAi	*Podosphaera leucotricha*	Pessina *et al.* (2016)
*Solanum lycopersicum**				
68	*SlWRKY70*	VIGS	*Macrosiphum euphorbiae* *Meloidogyne javanica*	Atamian *et al.* (2012)
69	*SlSR1*, *SlSR3L*	VIGS	*B. cinerea* *Pto* DC3000	Li *et al.* (2014b)
70	*eIF4E2*	EMS	PVMV	Moury *et al.* (2020)
71	*SlSRFR1*	CRISPR/Cas9	*Pto* DC3000	Son *et al.* (2021)
72	*SlPelo*	CRISPR/Cas9	TYLCV	Pramanik *et al.* (2021)
73	*SlMlo1*	CRISPR/Cas9	*Oidium neolycopersici*	Pramanik *et al.* (2021)
74	*SlDMR1*	RNAi	*O. neolycopersici*	Huibers *et al.* (2013)
75	*SlDMR6*	CRISPR/Cas9	*Pto* DC3000 *X. gardneri* *X. perforans* *P. capsici* *P. neolycopersici*	Thomazella *et al.* (2021)
Solanum lycopersicum, *Solanum tuberosum**				
76	*StDND1*	RNAi	*P. infestans* *O. neolycopersici* *Golovinomyces orontii*	Sun *et al.* (2016a)
*Solanum tuberosum**				
77	*StDND1*	CRISPR/Cas9	*P. infestans*	Kieu *et al.* (2021)
78	*StCHL1*	CRISPR/Cas9	*P. infestans*	Kieu *et al.* (2021)
79	*StDMR6-1*	RNAi CRISPR/Cas9	*P. infestans* *P. infestans*	Sun *et al.* (2016b) Kieu *et al.* (2021)
80	*StERF3*	RNAi	*P. infestans*	Tian *et al.* (2015)

*Indicated for the applied plant.

Table 3 List of *S* genes from *Arabidopsis thaliana* for potential resistance improvement in crops

No.	Gene name	Gene ID	Method	Pathogen/pest	Reference
Pathogen: Bacteria					
1	*AtHMAD1*	AT1G51090	T-DNA insertion	*Pto* DC3000	Imran *et al*. (2016)
2	*ORM1*	AT1G01230	T-DNA insertion	*P. syringae*	Li *et al*. (2016)
3	*ORM2*	AT5G42000	artificial microRNA	*P. syringae*	
4	*CBP60a*	AT5G62570	T-DNA insertion	*P. syringae* pv. *maculicola*	Truman *et al*. (2013)
5	*LECRK-I.7*	AT5G60270	T-DNA insertion	*P. brassicae*, *P. capsici*	Wang *et al*. (2014)
6	*LecRK-V.5*	AT3G59700	T-DNA insertion, OX	*Pto* DC3000	Desclos-Theveniau *et al*. (2012), Wang *et al*. (2014)
7	*AtLIK1*	AT3G14840	T-DNA insertion	*Pto* DC3000	Le *et al*. (2014)
8	*PAT1*	AT1G79090	T-DNA insertion	*Pto* DC3000	Roux *et al*. (2015)
9	*PBL13*	AT5G35580	T-DNA insertion	*Pto* DC3000	Lin *et al*. (2015)
10	*PICC*	AT2G32240	Knockout	*Pto* DC3000	Venkatakrishnan *et al*. (2013)
11	*EIJ1*	AT2G24860	T-DNA insertion	*Pto* DC3000	Liu *et al*. (2021a)
12	*EIL1*	AT2G27050	PCR-based Screen knockout	*Pto* DC3000	Chen *et al*. (2009)
13	*AtG3BP-LIKE*	AT5G48650	T-DNA insertion	*Pto* DC3000	Abulfaraj *et al*. (2018)
14	*IAN9*	AT1G33970	CRISPR/Cas9	*Pto* DC3000	Wang *et al*. (2019c)
15	*IAP1*	AT1G18660	T-DNA insertion	*Pto* DC3000	
16	*ATG5*	AT5G17290	Autophagy knock-out	*Pto* DC3000	Lenz *et al*. (2011)
17	*ATG10*	AT3G07525	Autophagy knock-out	*Pto* DC3000	
18	*ATG18a*	AT3G62770	RNAi, T-DNA insertion	*Pto* DC3000	
19	*MIEL1*	AT5G18650	T-DNA insertion	*Pto* DC3000	Marino *et al*. (2013)
20	*MOM1*	AT1G08060	TGS mutants	*Pto* DC3000	Cambiagno *et al*. (2018)
21	*MKP2*	AT3G06110	T-DNA insertion	*R. solanacearum*	Lumbreras *et al*. (2010)
22	*At NFXL1*	AT5G50440	T-DNA insertion	*Pto* DC3000	Zhang *et al*. (2011)
23	*AtMEMB12*	AT1G10170	T-DNA insertion	*Pto* DC3000	Asano *et al*. (2008)
24	*AtNUDT7*	AT4G12720	T-DNA insertion	*Pto* DC3000	Ge *et al*. (2007)
25	*AtPLA2-α*	AT2G26560	T-DNA insertion	*Pto* DC3000	Froidure *et al*. (2010)
26	*AtPRN2*	AT2G43120	T-DNA insertion	*R. solanacearum*	Zhang *et al*. (2014)
27	*PROSCOOP12*	AT5G44585	T-DNA insertion	*E. amylovora*	Gully *et al*. (2019)
28	*AtPUB13*	AT3G46510	T-DNA insertion	*Pto* DC3000	Antignani *et al*. (2015)
29	*AtCBRLK1*	AT1G11350	T-DNA insertion	*Pto* DC3000	Kim *et al*. (2009a)
30	*SEF*	AT5G37055	T-DNA insertion	*Pto* DC3000	March-Diaz *et al*. (2008)
31	*PIE1*	AT3G12810			
Pathogen: Fungus					
32	*ABA2*	AT1G52340	Amino acid substitution	*G. cichoracearum*	Xiao *et al*. (2017)
33	*ABA3*	AT1G16540	Amino acid substitution	*G. cichoracearum*	Xiao *et al*. (2017)
34	*ATG2*	AT3G19190	EMS, T-DNA insertion	*G. cichoracearum*	Wang *et al*. (2011)
35	*RWA2*	AT3G06550	T-DNA insertion	*B. cinerea*	Manabe *et al*. (2011)
36	*EXO70B1*	AT5G58430	T-DNA insertion	*G. cichoracearum*	Zhao *et al*. (2015)
37	*EDR2*	AT4G19040	EMS	*Erysiphe cichoracearum*	Tang *et al*. (2005)
38	*EDR4*	AT5G05190	EMS	*G. cichoracearum*	Wu *et al*. (2015)
39	*AtGRXS13*	AT1G03850	T-DNA insertion	*B. cinerea*	La Camera *et al*. (2011)
40	*MED20*	AT2G28230	T-DNA insertion	*F. oxysporum*	Fallath *et al*. (2017)
41	*MED8*	AT2G03070	T-DNA insertion	*F. oxysporum*	Kidd *et al*. (2009)
42	*MED25, PFT1*	AT1G25540	T-DNA insertion	*F. oxysporum*	Kidd *et al*. (2009)
43	*AtMLO2*	AT1G11310	T-DNA insertion	*B. cinerea*	Consonni *et al*. (2010)
44	*MYB3R4*	AT5G11510	T-DNA insertion	*G. orontii*	Chandran *et al*. (2010)
45	*AtMYB46*	AT5G12870	T-DNA insertion	*B. cinerea*	Ramirez *et al*. (2011)
46	*AtMYB44*	AT5G67300	T-DNA insertion	*Alternaria brassicicola*	Shim *et al*. (2013)
47	*OCP3*	AT5G11270	EMS	*B. cinerea*, *Plectosphaerella cucumerina*	Coego *et al*. (2005)
48	*PAD4*	AT3G52430	EMS	*G. cichoracearum*	Neubauer *et al*. (2020)
49	*PMR6*	AT3G54920	T-DNA insertion	*E. cichoracearum*	Vogel *et al*. (2002)
50	*PUB25*	AT3G11840	T-DNA insertion	*B. cinerea*	Wang *et al*. (2018a)
51	*PUB26*	AT3G19380	T-DNA insertion	*B. cinerea*	
52	*PUX2*	AT2G01650	T-DNA insertion	*G. cichoracearum*	Chandran *et al*. (2009)
53	*AtSEX1*	AT1G10760	T-DNA insertion	*E. cruciferarum*	Engelsdorf *et al*. (2013)
54	*PGM*	AT1G78050			
55	*ADG1*	AT5G48300			
56	*At2OGO*	ND	CRISPR/Cas9	*F. graminearum*	Low *et al*. (2020)
Pathogen: Virus					
57	*ACS6*	AT4G11280	T-DNA insertion	TMV	Chen *et al*. (2013b)
58	*AtTOR*	AT1G50030	RNAi	CaMV	Schepetilnikov *et al*. (2011)
59	*BIR1*	AT5G48380	T-DNA insertion	*Tobacco rattle virus*	Guzman-Benito *et al*. (2019)

Table 3 Continued

No.	Gene name	Gene ID	Method	Pathogen/pest	Reference
60	*CBP20*	AT5G44200	T-DNA insertion	*Plum pox virus* (PPV)	Pasin *et al.* (2020)
61	*CBP80, ABH1*	AT2G13540	T-DNA insertion	PPV	
62	*CDKC;2*	AT5G64960	T-DNA insertion	CaMV	Cui *et al.* (2007)
63	*CYCT1;5*	AT5G45190	T-DNA insertion	CaMV	Cui *et al.* (2007)
64	*AtDBP1*	AT2G25620	T-DNA insertion	PPV, TuMV	Castello *et al.* (2010)
65	*PCaP1, MDP25*	AT4G20260	T-DNA insertion	TuMV	Cheng *et al.* (2020)
66	*NISP*	AT4G30240	T-DNA insertion	*Begomovirus*	Gouveia-Mageste *et al.* (2021)
67	*PAP85*	AT3G22640	RNAi	TMV	Chen *et al.* (2013a)
Pathogen: Oomycete					
68	*AtERF019*	AT1G22810	CRISPR/Cas9	*P. parasitica*	Lu *et al.* (2020)
69	*IOS1*	AT1G51800	T-DNA insertion	*H. arabidopsidis*	Hok *et al.* (2011)
70	*AtOBE1*	AT3G07780	T-DNA insertion	*H. arabidopsidis*	Mukhtar *et al.* (2011)
71	*NPR3*	AT5G45110	T-DNA insertion	*H. parasitica*	Zhang *et al.* (2006)
Pathogen: Nematode					
72	*AtWRKY23*	AT2G47260	RNAi	*H. schachtii*	Grunewald *et al.* (2008)
73	*STP12*	AT4G21480	T-DNA insertion	*H. schachtii*	Hofmann *et al.* (2009)
74	*PME3*	AT3G14310	T-DNA insertion	*H. schachtii*	Hewezi *et al.* (2008)
75	*RPE*	AT5G61410	T-DNA insertion	*M. incognita*	Favery *et al.* (1998)
Pests: Arthropods					
76	*AtWSCP*	AT1G72290	T-DNA insertion	*Porcellio scaber, Armadillidium vulgare*	Boex-Fontvieille *et al.* (2015)
77	*AGO1*	AT1G48410	EMS	*M. persicae*	Kettles *et al.* (2013)
78	*DCL1*	AT1G01040	T-DNA insertion	*M. persicae*	Kettles *et al.* (2013)
79	*HRL1*	AT4G23660	EMS	*S. exigua*	Mewis *et al.* (2005)
80	*ETR1*	AT1G66340	EMS	*S. exigua*	Mewis *et al.* (2005)
81	*LOX5*	AT3G22400	T-DNA insertion	*M. persicae*	Nalam *et al.* (2012)
Multiple pathogens					
82	*LIF2*	AT4G00830	T-DNA insertion	*Pto* DC3000 *B. cinerea*	Le Roux *et al.* (2014)
83	*AtLYK3*	AT1G51940	T-DNA insertion	*Pectobacterium carotovorum* *B. cinerea*	Paparella *et al.* (2014)
84	*RTP1*	AT1G70260	T-DNA insertion, RNAi	*G. cichoracearum* *P. parasitica*	Pan *et al.* (2016)
85	*AtMED18*	AT2G22370	T-DNA insertion	*F. oxysporum* TuMV, CaMV, AltMV, *Cytomegalovirus* (CMV)	Fallath *et al.* (2017) Hussein *et al.* (2020)
86	*AtSSI2*	AT2G43710	EMS	CMV *M. persicae*	Sekine *et al.* (2004) Louis *et al.* (2010)
87	*PGL3*	AT5G24400	T-DNA insertion	*P. syringae* pv. *maculicola* *H. arabidopsidis*	Xiong *et al.* (2009)

resistance to *H. arabidopsidis* without any growth defects in the plants (Zeilmaker *et al.*, 2015). DMR6 is a SA 5-hydroxylase (S5H) that catalyses the formation of 2,5-DHBA (an aromatic compound in green plants) from SA (Zhang *et al.*, 2017c). Since DMR6 plays an important role in regulating plant defence responses in Arabidopsis, its orthologs have been successfully targeted in many different crops (Table 2). For example, a loss-of-function mutant of *SlDMR6* in tomato generated by CRISPR/Cas9-mediated mutagenesis showed broad-spectrum resistance to pathogens, including *Pto* DC3000, *X. gardneri*, *X. perforans*, *P. capsici*, and *Pseudoidium neolycopersici* (Thomazella *et al.*, 2021). Knockout mutants of sweet basil (*Ocimum basilicum*) *ObDMR6* using CRISPR/Cas9-mediated mutagenesis exhibited enhanced resistance to downy mildew caused by *Peronospora belbahrii* (Hasley *et al.*, 2021). Knockdown of *StDMR6* in potato by RNAi (Sun *et al.*, 2016b) and knockout of this gene by CRISPR/Cas9 (Kieu *et al.*, 2021) conferred resistance to *P. infestans*, which causes late blight disease. A mutation in the banana ortholog *MusaDMR6* generated by CRISPR/Cas9 enhanced resistance to banana xanthomonas wilt (BXW) caused by *Xanthomonas campestris* pv. *musacearum* (*Xcm*; Tripathi *et al.*, 2021). In two citrus *cultivars*, 'Duncan' grapefruit and Carrizo citrange, the m*utation of CsDMR6* via CRISPR/Cas9 led to significantly increased resistance to the bacterial disease citrus canker caused by *X. citri* ssp. *citri* (*Xcc*; Parajuli *et al.*, 2022). These findings highlight the benefits of engineering disease resistance by disabling disease *S* genes using genome-editing techniques in which CRISPR/Cas is a dominant tool.

SUPPRESSOR OF rps4-RLD 1 (SRFR1) is a negative regulator of ETI-associated transcriptional immune responses in Arabidopsis (Kwon *et al.*, 2004, 2009). SRFR1 functions as a scaffold protein in association with the defence regulator EDS1 and other TNL proteins, such as RPS4, RPS6, and SUPPRESSOR OF NPR1-1 CONSTITUTIVE 1 (SNC1), to regulate downstream plant immune signalling (Bhattacharjee *et al.*, 2011; Kim *et al.*, 2010). Mutations in *SRFR1* enhanced resistance to the *Pto* DC3000-expressing effectors *avrRps4* or *hopA1* in Arabidopsis in the absence of functional RPS4 or RPS6, respectively (Kim *et al.*, 2009b,c; Kwon *et al.*, 2009), as well as resistance to the generalist chewing insect beet armyworm (*Spodoptera exigua*) and sugar beet cyst

Table 4 List of effector genes and RNA molecules from pathogens that enhanced resistance in crops

No.	Gene	Gene source	Method	Applied plant	Pathogen	Reference
Effector genes						
1	*MoSDT1*	*M. oryzae*	OE	*O. sativa*	*M. oryzae*	Wang *et al*. (2019a)
2	*MoSM1*	*M. oryzae*	OE	*O. sativa*	*M. oryzae* *Xoo*	Hong *et al*. (2017)
3	*PsCRN115*	*P. sojae*	OE	*N. benthamiana*	*Phytophthora capsica*, *P. parasitica*	Zhang *et al*. (2015b)
4	*BcCrh1*	*B. cinerea*	OE	*N. benthamiana*, *A. thaliana*, *S. lycopersicum*, *P. vulgaris*	*B. cinerea*	Bi *et al*. (2021)
5	*PstSCR1*	*Pst*	Transiently expressed	*N. benthamiana*	*P. infentans*, *P. hyoscyami* f. sp. *tabacina*	Dagvadorj *et al*. (2017)
RNA molecules						
6	*Bmp3*	*B. cinerea*	dsRNA-based control	*L. sativa*	*B. cinerea*	Spada *et al*. (2021)
7	*CYP51A*, *CYP51B*, *CYP51C*	*F. graminearum*	dsRNA-based control	*H. vulgare*	*F. graminearum*	Koch *et al*. (2016)
8	*Myo5*	*F. asiaticum*	dsRNA-based control	*T. aestivum*	*F. asiaticum*	Song *et al*. (2018a)
9	*Bc-DCL1*, *Bc-DCL2*	*B. cinerea*	OE, sRNAs-and dsRNA-based control	*A. thaliana*, *S. lycopersicum*, *Fragaria* × *ananassa*, *L. sativa*, *A. cepa* and *Rosa hybrida*	*B. cinerea*	Wang *et al*. (2016)
10	*Amino acyl tRNA ligase* (SS1G_01703) *thioredoxin reductase* (SS1G_05899), *TIM44* (SS1G_06487)	*S. sclerotiorum*	dsRNA-based control	*B. napus*, *A. thaliana*	*S. sclerotiorum*, *B. cinerea*	McLoughlin *et al*. (2018)
11	*Faβ2Tub-3*	*F. asiaticum*	dsRNA-based control	*T. aestivum* *C. sativus* *H. vulgare* *G. max*	*F. asiaticum* *B. cinerea* *M. oryzae* *C. truncatum*	Gu *et al*. (2019)
12	*BCMVNIb*, *BCMVCP*	BCMV	dsRNA-based control	*N. benthamiana*, *V. unguiculata*	BCMV	Worrall *et al*. (2019)
13	*CsCYP15C1*	*C. suppressalis*	dsRNA-based control	*O. sativa*	*C. suppressalis*	Sun *et al*. (2020)

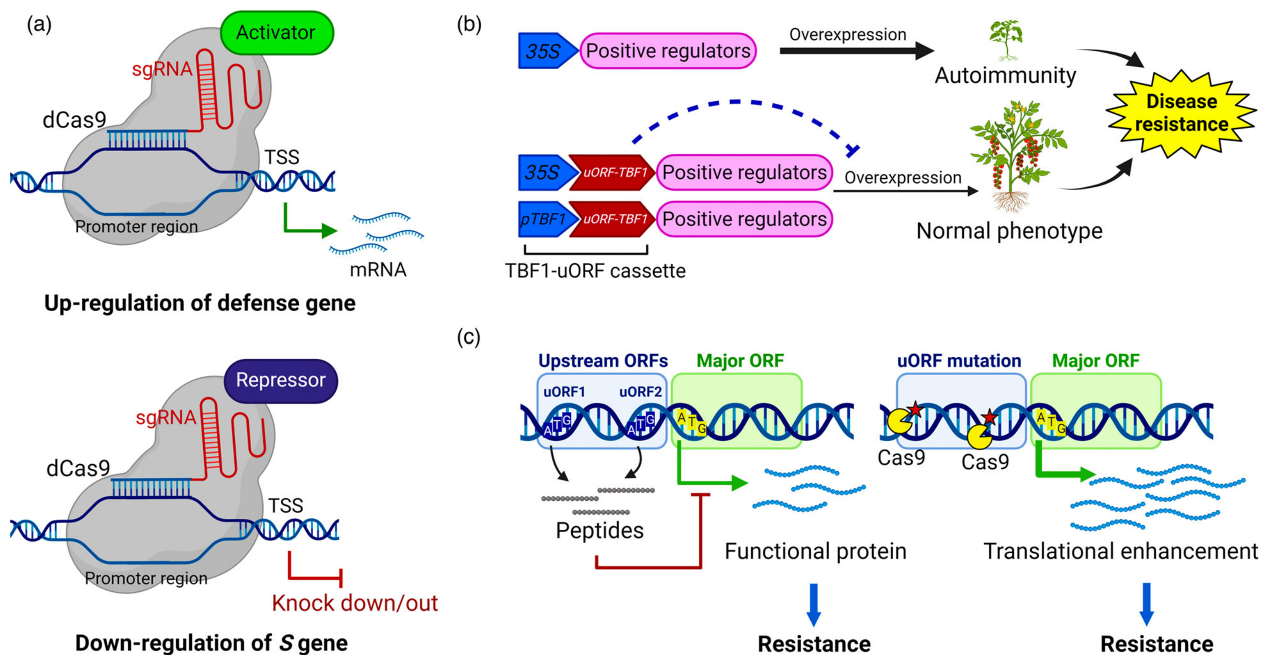

Figure 2 Multiple strategies to engineer disease resistance by targeting the promoter region of immune-related genes. (a) Using dCas9 to control the transcriptional expression of the target genes. dCas9 is fused with a transcriptional activator or repressor. Specific gRNA(s) specifically guide(s) the complex of dCas9 and the activator or repressor to the promoter region of the target gene to up-regulate or down-regulate its transcriptional level, leading to disease resistance enhancement in the plant. (b) Using uORF of TBF1 gene to overcome growth defect issue in plant disease engineering. Overexpressing some positive regulators of immunity somehow causes an autoimmune response, which affects plant growth. Incorporating uORF sequences of the TBF gene enables to compromise of normal phenotype without changing disease resistance traits of the plant. (c) Using CRISPR/Cas9 to remove uORF sequences of a positive regulator gene efficiently increases the translational level, leading to disease resistance enhancement. Created with www.BioRender.com.

nematode (*Heterodera schachtii*; Figure 3; Nguyen *et al*., 2016). Knowledge of Arabidopsis *SRFR1* prompted the editing of tomato *SRFR1* (*SlSRFR1*) with the CRISPR/Cas9 system. Interestingly, this approach not only enhanced disease resistance against *Pto* DC3000, but it also revealed the antagonistic functions of Arabidopsis SRFR1 and tomato SRFR1 as negative regulators of the response to hemibiotrophic pathogens (*Pto* DC3000) and positive regulators of the response to necrotrophic pathogens (*F. oxysporum* f. sp. *lycopersici* and *Botrytis cinerea*), respectively (Table 2 and Figure 3; Son *et al*., 2021). Targeting *SRFR1* orthologs in other crop plants could offer a new means of engineering enhanced disease resistance.

As demonstrated by the above examples, successful studies in Arabidopsis have paved the way for the editing of *S* genes to enhance disease resistance in crops. With this in mind, we compiled a list of *S* genes that were mutated to improve plant resistance in Arabidopsis but that have not yet been targeted in any crop (Table 3). We categorized these *S* genes into seven groups, based on the pathogen to which the mutation in the gene confers resistance: bacterium, fungus, virus, oomycete, nematode, arthropod, and multiple pathogens. Notably, the mutation of many *S* genes causes a broad range of resistance to multiple pathogens (Table 3). For instance, Mediator Complex Subunit 18 (MED18) is a multifunctional protein that regulates plant immunity, flowering time, and responses to plant hormones (Lai *et al*., 2014). Mutating Arabidopsis *MED18* via T-DNA insertion strongly enhanced plant immunity in response to the fungus *F. oxysporum* (Fallath *et al*., 2017) and to many viruses such as TuMV, cauliflower mosaic virus (CaMV), Alternanthera mosaic *virus* (AltMV), and CMV (Table 3; Hussein *et al*., 2020). Therefore, orthologs of Arabidopsis *MED18* in other crops that are generally affected by fungi and viruses represent potential targets for engineering to reduce crop losses in the future. The mutation of *LHP-INTERACTING FACTOR 2* (*LIF2*), which controls flowering time and cell fate in Arabidopsis (Latrasse *et al*., 2011), also enhanced resistance to both the hemibiotrophic bacterium *Pto* DC3000 and the necrotrophic ascomycete *B. cinerea* (Table 3; Le Roux *et al*., 2014). Based on the success of generating new disease resistance traits by knocking down/out the *S* genes *DMR6* and *SRFR1* from model plants into crop plants (Table 2 and Figure 3; Son *et al*., 2021; Thomazella *et al*., 2021), the information in Table 3 could serve as a guide for improving productivity via plant immune engineering simply by targeting *S* genes.

Alternative ways to engineer disease resistance: introducing pathogen molecules into plants

Plant disease management in the agricultural sector principally relies on breeding disease-resistant varieties, chemical applications, biological control and cultural practices. Identifying new disease-resistance resources and selecting new resistant cultivars with broad-spectrum resistance are the most economical, practical, and effective methods for disease control and prevention. However, the disease resistance of plant varieties against specific pathogens is often limited by the existence of regulatory components that suppress defence responses. Intriguingly, recent studies have identified an assortment of effector proteins that conferred

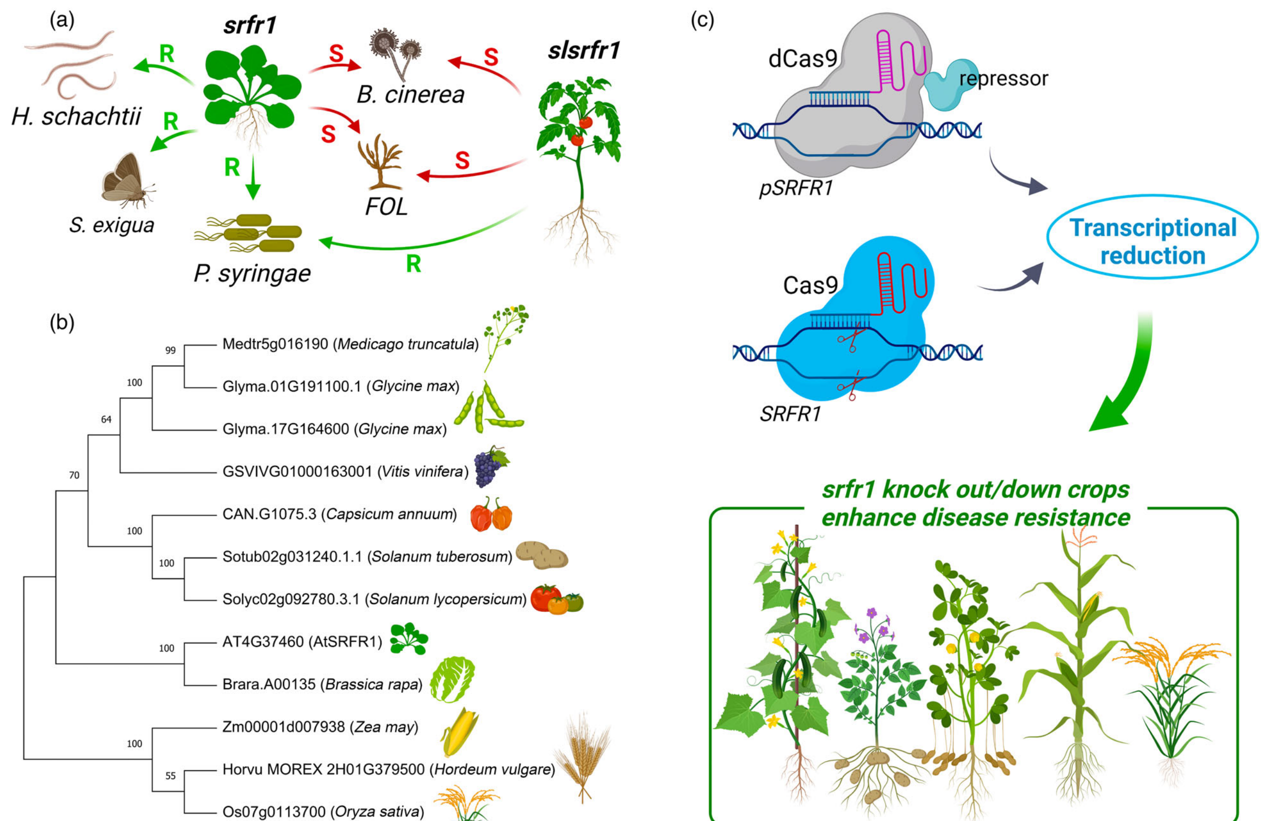

Figure 3 SRFR1 engineering as a case study of modifying gene encoding a negative regulator/S protein. (a) Summary of defence responses in the loss-of-function mutant *srfr1* in Arabidopsis and tomato. Mutation of *SRFR1* in Arabidopsis induces disease resistance to *Heterodera schachtii*, *Spodoptera exigua*, and *Pto* DC3000 expressing *AvrRps4*. However, *srfr1* enhanced disease susceptibility to *Fusarium oxysporum* f. sp. *lycopersici* (*FOL*) and *Botrytis cinerea*. Consistently, mutation of *SlSRFR1* enhances resistance to *Pto* DC3000 and enhances susceptibility to *FOL* and *B. cinerea*. Enhancement of resistance and susceptibility are indicated by green and red arrows, respectively. (b) Neighbour-joining phylogenetic tree based on the amino acid alignment of full-length products of Arabidopsis SRFR1 (AtSRFR1) and its orthologs in other crops. AtSRFR1 sequence was obtained from The Arabidopsis Information Resource (TAIR10, arabidopsis.org), and SRFR1-related protein sequences were obtained from the Dicots PLAZA 4.0 and Monocots PLAZA 5.0. Eleven different SRFR1-like homologous were shown in the figure. The phylogenetic tree with 12 amino acid sequences was made using MEGAX. Amino acid sequences were aligned using the MUSCLE alignment method, and the result was collected to generate a phylogenetic tree with the neighbour-joining model. Clades were assessed using 1000 bootstrap repeats. (c) Transcriptional reduction of *SRFR1* homologous in crops to generate new disease resistance by using CRISPR/Cas9 and CRISPR/dCas9 systems. Created with www.BioRender.com.

improved disease resistance when expressed in transgenic plants. For instance, overexpressing *Phytophthora sojae* crinkling and necrosis (CRN) effector (*PsCRN115*; Zhang *et al*., 2015b), small cysteine-rich effector (*PstSCR1*) from *Puccinia striiformis* f. sp. *tritici* (*Pst*; Dagvadorj *et al*., 2017), *B. cinerea* Congo red hypersensitivity effector (*BcCrh1*; Bi *et al*., 2021), and *M. oryzae* SM1 and systemic defence trigger 1 effectors (*MoSM1* and *MoSDT1*; Hong *et al*., 2017; Wang *et al*., 2019a) significantly improved disease resistance in various crops (Table 4). Thus, pathogen effectors could be used as genetic resources for a transgenic-based approach to disease management in crops.

However, the approval of transgenic plants or genetically modified (GM) plants is controversial. The most important consideration for GM plant cultivation is their impact on human health and environmental sustainability. Consequently, GM plants and their products must undergo adequate screening and extensive safety testing before commercialization. Thus, transgenic-based breeding is relatively time-consuming and costly. One alternative method that does not produce GM plants involves spray-induced gene silencing (SIGS) using exogenously applied double-stranded RNA (dsRNA), short interfering RNA (siRNA), or hairpin RNA (hpRNA). This technique has been applied to enhance resistance against pathogens and pests in several plants (Table 4). For example, the application of dsRNAs or siRNAs to target *F. graminearum* genes, such as *Cytochrome P450 monooxygenase 51A* (*CYP51A*), *CYP51B*, and *CYP51C*, suppressed fungal growth in barley (Koch *et al*., 2016). Similarly, exogenously applied dsRNA targeting *myosin5* of *Fusarium asiaticum* reduced fungal virulence in wheat (Song *et al*., 2018a). The exogenous application of dsRNAs targeting numerous genes of *B. cinerea*, including *Bmp3*, *DCL1*, *DCL2*, *amino acyl tRNA ligase*, *thioredoxin reductase*, and *TIM44*, significantly decreased the severity of grey mould disease in various fruits and vegetables (McLoughlin *et al*., 2018; Spada *et al*., 2021; Wang *et al*., 2016). SIGS is not only compatible with fungi, but it has also been used to target a gene from the moth *Chilo suppressalis* (striped rice stemborer) and several viral components (Sun *et al*., 2020; Worrall *et al*., 2019). Therefore, RNAi-based biocontrol holds great potential for managing devastating diseases and engineering plant innate immunity.

Perspectives

Strategies for targeting PRR and NLR receptors: from broad-spectrum perception to specific resistance

In general, most plants are resistant to most pathogens, so disease is the exception. A susceptible plant may not contain the proper PRR found in resistant plants to recognize the pathogen. Taking advantage of gene transfer techniques, scientists have introgressed *PRR* genes from resistant to susceptible plants (Figure 1; Lacombe *et al.*, 2010; Piazza *et al.*, 2021). The exogenous PRRs functioned well in the previously susceptible plants, providing these plants with resistance against a range of pathogens. To enhance the response of a PRR to a PAMP of interest, domain swapping can be performed. The idea of combining a PAMP recognition ectodomain from one PRR with an endokinase domain from another PRR has proven to be successful, since the chimeric PRRs exhibited more robust resistance to the target pathogen compared to the original receptor lacking a kinase domain (Figure 1; Kishimoto *et al.*, 2010). Therefore, PRRs can be transferred from one plant to another or engineered by domain swapping based on the domains of other receptors.

Notably, NLRs are mainly engineered to perceive a specific effector. An NLR normally recognizes a specific cognate effector: recognizing multiple effectors is the exception. If an NLR that is responsible for perceiving a particular effector is known, the NLR could be introduced from resistant plants into susceptible ones. The transfer of NLR genes has been carried out within and across species (Figure 1). Although overexpressing an NLR gene can induce an autoimmune response (Li *et al.*, 2007; Stokes *et al.*, 2002), in some cases, an NLR gene can be overexpressed in a plant to obtain resistance without any side effects (Du *et al.*, 2021; Xun *et al.*, 2019). Because NLRs recognize specific effectors, researchers have tried to expand the recognition specificity of NLRs using several methods. The first such method was random mutagenesis of the LRR domain (responsible for effector recognition; Giannakopoulou *et al.*, 2015; Segretin *et al.*, 2014). Some randomly mutated NLRs conferred enhanced immunity and resistance to another pathogen. Although a mutagenized NLR can lead to a growth defect in the plant, secondary stepwise mutagenesis can be utilized to overcome this issue. However, information about the effects of mutated residues from a mutagenized NLR might not be applicable to another NLR due to the random mutagenesis strategy itself. Secondly, the domain-swapping strategy for PRRs prompted the idea of domain engineering in NLRs. In detail, in the cases that NLRs work in pairs to recognize effectors, some NLRs that act as sensors but not executors contain an integrated decoy domain for effector recognition. Promising approaches for NLR engineering are introducing the integrated decoy domain into an executor NLR or replacing/incorporating the integrated decoy domain with other decoys/effector targets in a sensor NLR. Indeed, a recent study of the sensor/executer NLR pair RGA5/RGA4 revealed that this strategy is achievable (Cesari *et al.*, 2022). After all, scientists need to consider the partners of NLR in effector recognition and downstream components of NLRs-mediated resistance to apply NLR engineering in crops. Some NLR introductions could become successful due to the identity between signalling components in the target plants and those in the studied plants. Otherwise, NLR introductions could not be accomplished.

NLRs are not the only targets of ETI-based engineering. Based on an indirect recognition system, a guardee or decoy protein targeted by a pathogenic effector could be engineered to expand the recognition specificity of a corresponding NLR. In this review, we discussed the engineering of the novel guardee RIN4 and the decoy PBS1. When RIN4 was engineered, the chimeras generated from RIN4s with two functional motifs regulated multiple NLRs (Kim *et al.*, 2022). Crops such as soybean and grape contain RIN4 homologues with variable RIN4-specific motifs (Kim *et al.*, 2022); these motifs might function in NLR-mediated resistance that has not yet been characterized. It would be fascinating to explore their functions and engineer a chimeric RIN4 for the regulation of multiple NLRs. When PBS1 was engineered, swapping the PBS1 cleavage site of the effector AvrPphB with other sites cleaved by other effectors expanded the recognition capacity of RPS5 (Figure 1; Kim *et al.*, 2016). This finding suggests that we can engineer crop resistance against any pathogen that takes advantage of a protease as part of its effector repertoire as long as the target crop exhibits PBS1-mediated immunity.

Two examples of applications for decoy engineering (Bai *et al.*, 2022; Helm *et al.*, 2019) revealed the challenge of translating this strategy into crops: (i) crops might harbour more than one PBS1 orthologs that impede the identification of the actual decoy protein for engineering (Helm *et al.*, 2019); (ii) modifying endogenous decoy genes raises a technical tricky in crops. Therefore, to apply PBS1 decoy engineering, first, the actual native PBS1 decoy must be carefully identified. Second, validated genome editing tools should be considered to generate desirable modifications efficiently. Nowadays, new plant genome editing techniques detailed in Engineering PRRs, NLRs, and regulators of plant innate immunity by CRISPR/Cas-mediated gene editing section allow the installation of precise mutation. Everything has its challenges; however, every challenge is possible to solve.

Moreover, the successful engineering of PBS1 sheds light on the concept that other target proteins could perhaps be engineered to be cleaved by protease effectors. We suspect that if negative immune regulators are engineered to be cleaved by a specific protease effector, they will become dysfunctional in immunity suppression in the presence of pathogens that harbour the protease. Therefore, depending on the pathogens and protease effectors they contain, engineering negative immune regulators by adding a cleavage site represents a possible approach for resistance engineering based on the case study of PBS1.

How can the expression levels of plant immune regulators be modified as needed?

Besides immune receptors, downstream immune regulators represent potential targets for resistance engineering. Immune regulators positively or negatively regulate disease resistance upon pathogen attack. One basic strategy is to transcriptionally and translationally boost the activities of positive immune regulators. Overexpression systems are commonly used in this approach (Table 1). However, overexpressing genes in plants sometimes leads to slower development due to over-active immunity (Stokes *et al.*, 2002; Tong *et al.*, 2017). To modify the expression levels and abundance of positive immune regulators, the use of native or pathogen-specific promoters is recommended. The translation of TL1-BINDING TRANSCRIPTION FACTOR 1 (TBF1), a transcription factor that functions in the switch from plant growth to defence upon defence activation in Arabidopsis, was shown to be modulated by an upstream open reading frame (uORF; Figure 2a; Xu *et al.*, 2017). Generally, an uORF located in the 5′ untranslated region of a major open

reading frame of a gene serves as a translational control factor to precisely fine-tune the translation of the encoded protein. Based on this finding, Xu *et al*. developed a 'TBF1-cassette' consisting of the immune-inducible promoter and two pathogen-responsive uORFs from the *TBF1* promoter region. This cassette constrained the translation of the autoactivated immune receptor *snc1-1* in Arabidopsis and the positive immune regulator AtNPR1 in rice. The characterization of more genes exhibiting a similar type of translation regulation is expected to increase the available repertoire of uORFs. The combination of uORF cassettes with positive immune regulators might function efficiently in crops, resulting in enhanced resistance and normal plant growth.

Another method for resistance engineering is to modify effector targets or negative regulators of the immune system. Specifically, pathogenic effectors interact with and modify host proteins for their virulence function (Jones and Dangl, 2006), and negative regulators suppress immunity during pathogen infection. Therefore, effector targets or negative regulators of immunity could be repressed to boost plant defence. To date, several methods have been used to accomplish this type of suppression, such as T-DNA insertion to knockout target genes and VIGS or RNAi to knockdown these genes (Table 2). In some cases, knockout/knockdown of negative regulators leads to defective growth and abnormal phenotype by the uncontrolled positive immune regulators. For example, in the Arabidopsis Col-0 ecotype, a T-DNA knockout in *AtSRFR1* led to defective development but not in the RLD ecotype. It is explained that SRFR1 suppresses the autoimmunity induced by the NLR SNC1 (that does not function in RLD; Kim *et al*., 2010). Interestingly, unlike the T-DNA knockout of *AtSRFR1*/Col-0, the mutation of *SlSRFR1* enhanced defence against a bacterial pathogen with mild growth defects in tomato (Son *et al*., 2021). These studies revealed that the challenge of engineering immune regulators in one plant due to the growth-defence tradeoff could be overcome in other plant species. Therefore, identifying and engineering the orthologs of immune regulators remains a promising strategy (Figure 3).

Plant pathologists have long focused on fighting enemies (pathogens) and cherishing allies (plants). Surprisingly, however, using a pathogen component to improve plant resistance can sometimes be successful. Table 4 lists several immune regulators originating from pathogen species that have been used to enhance plant defence responses. Some effectors may be used as critical genetic resources for the transgenic improvement of plant disease resistance. However, the process of genetically modifying crops remains controversial, not only due to technical limitations but also because many consumers are apprehensive about consuming GM products. The emergence of RNAi technology utilizing exogenous dsRNAs, siRNAs, and hpRNAs could be viewed as a viable alternative, as it is more eco-friendly, sustainable, and broadly acceptable than genetic engineering/transformation. Additionally, RNAi-based biocontrol could be utilized for pre- and post-harvest disease management in vegetables and other crops. However, the number of target genes that could be used for RNAi-based biocontrol and our understanding of how plants or pathogens absorb exogenous dsRNA are still limited. These issues pose challenges that could hinder the use of RNA molecules on a large scale or in open-field conditions. In summary, RNAi-based biocontrol represents a promising approach to managing devastating plant diseases, but additional studies are needed to overcome the limitations of this technology.

Engineering PRRs, NLRs, and regulators of plant innate immunity by CRISPR/Cas-mediated gene editing

Plants that were engineered using either transgenic or cisgenic strategies still contain exogenous genetic material, precluding their use as non-GM crops. The CRISPR/Cas system has recently emerged as a powerful engineering method to generate T-DNA-free plants. This system was developed based on the bacterial immune system, using the Cas nuclease to bind to and cleave exogenous DNA sequences from viruses (Terns and Terns, 2011; Wiedenheft *et al*., 2012). A single guide RNA (sgRNA) accompanies a Cas nuclease to a specific target sequence to generate DNA double-strand breaks. This event triggers a natural repair mechanism of the host cell via two pathways: homology-directed repair (HDR) and non-homologous end-joining (Malzahn *et al*., 2017), resulting in a modified host DNA sequence. The versatility of the CRISPR/Cas system allows users to create knockout mutants, insert donor DNA, edit the bases of a target sequence, or control the expression of target genes. This section focuses on the CRISPR/Cas-based genome editing approach and its potential for disease resistance engineering.

CRISPR-based tools open the door to immune receptor engineering, which was previously impossible. We discussed LRR domain swapping and NLR mutagenesis in a previous section. These methods could theoretically be performed using CRISPR/Cas. For LRR domain swapping, CRISPR/Cas could be used to insert donor DNA encoding the desired additional domain. CRISPR/Cas-mediated insertion is challenging, depending on the length of donor template DNA. Recently, the improvement of HDR efficiency in the plant has been validated (Vu *et al*., 2020, 2021). Therefore, it might be possible to perform LRR domain swapping using an improved CRISPR/Cas system in the future. For NLR mutagenesis, CRISPR/Cas could be used to precisely edit specific target bases to obtain the amino acid sequence of interest. However, more studies of NLR mutagenesis or NLR crystallization are needed to provide references for CRISPR/Cas-mediated NLR editing. In addition, two recent successful applications of PBS1 decoy engineering are overexpression of modified *PBS1* in transgenic soybean and potato (Bai *et al*., 2022; Helm *et al*., 2019), which are regarded as GM organisms. This disadvantage inhibits the approval of engineered plants in global markets. CRISPR/Cas-based modification can produce T-DNA free in the engineered plants providing the desired resistance traits without foreign DNA.

CRISPR/Cas9 has been widely used to engineer immune regulators, especially negative immune regulators. CRISPR/Cas9 can be used to induce mutations or a premature stop codon to knock out a gene of interest (Tables 2 and 3). *SRFR1* and *DMR6* are two recent examples of negative regulator genes that were knocked out to gain resistance in tomato (Son *et al*., 2021; Thomazella *et al*., 2021). Using CRISPR/Cas9 to knockout genes of interest and applying information about the orthologs of negative regulators will facilitate disease resistance engineering.

The DNA-binding activity of the gRNA-Cas9 complex provides an excellent system for altering the expression of genes of interest, especially genes encoding immune regulators. A transcriptional repressor or activator could be combined with dead Cas9 (dCas9) to suppress or enhance the gene expression of a target negative/positive regulator of immunity without introducing DNA double-strand breaks (DSBs; Figure 2b; Moradpour and Abdulah, 2020; Selma *et al*., 2019). Based on this knowledge, to

enhance the expression level of a positive immune regulator in the plant, targeting the promoter region of the gene using dCas9 represents a promising approach. When the gene encoding the positive regulator contains a uORF(s), standard CRISPR/Cas9-induced mutation could be utilized to repress uORF-mediated translational suppression, resulting in the enhanced production of the positive immunity regulator (Figure 2c). Notably, compared to the traditional CRISPR/Cas system, base-editor and prime editor are the most recent evolution of this technology to generate desired mutations without DSBs (Anzalone *et al*., 2019; Kang *et al*., 2018; Komor *et al*., 2016; Lin *et al*., 2020; Nishida *et al*., 2016). Combining engineering strategies mentioned in this manuscript and upgraded versions of new genome editing techniques opens the new door to engineering plant innate immunity wisely.

In summary, our present understanding of plant immune components and current engineering strategies is being utilized to enhance plant resistance. Although every strategy has its advantages and disadvantages, the choice of a suitable strategy could greatly facilitate crop engineering for improved disease resistance. With rapid advances in our understanding of plant immunity, we predict that new engineering strategies will be developed, promising a bright future for crop protection.

Acknowledgements

We apologize for not being able to cite the research of all our colleagues in this review. We thank Dr. Geon Hui Son for the critical review of the manuscript and members of Kim laboratory for discussion.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

U.T.V. and S.H.K. designed the manuscript structure. U.T.V., A.B.B.I., Q.-M.N., and S.H.K. wrote the manuscript. U.T.V., A.B.B.I., Q.-M.N., H.K., J.L., and J.M. generated the figures and tables. All authors read and approved the manuscript.

Funding

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (No. 2021R1I1A3054417), the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT; No. 2022R1A5A1031361), and grants from the New Breeding Technologies Development Program (project no. PJ01653202) and the BioGreen21 Agri-Tech Innovation Program (project no. PJ015756), Rural Development Administration, Republic of Korea.

References

Abdallah, N.A., Prakash, C.S. and McHughen, A.G. (2015) Genome editing for crop improvement: challenges and opportunities. *GM Crops Food*, **6**, 183–205.

Abulfaraj, A.A., Mariappan, K., Bigeard, J., Manickam, P., Blilou, I., Guo, X., Al-Babili, S. *et al*. (2018) The Arabidopsis homolog of human G3BP1 is a key regulator of stomatal and apoplastic immunity. *Life Sci. Alliance*, **1**, e201800046.

Afroz, A., Chaudhry, Z., Rashid, U., Ali, G.M., Nazir, F., Iqbal, J. and Khan, M.R. (2010) Enhanced resistance against bacterial wilt in transgenic tomato (*Lycopersicon esculentum*) lines expressing the Xa21 gene. *Plant Cell Tiss. Org. Cult.* **104**, 227–237.

Akmal, M., Baig, M.S. and Khan, J.A. (2017) Suppression of cotton leaf curl disease symptoms in *Gossypium hirsutum* through over expression of host-encoded miRNAs. *J. Biotechnol.* **263**, 21–29.

An, C., Sheng, L., Du, X., Wang, Y., Zhang, Y., Song, A., Jiang, J. *et al*. (2019) Overexpression of CmMYB15 provides *Chrysanthemum* resistance to aphids by regulating the biosynthesis of lignin. *Hortic. Res.* **6**, 84.

Antignani, V., Klocko, A.L., Bak, G., Chandrasekaran, S.D., Dunivin, T. and Nielsen, E. (2015) Recruitment of PLANT U-BOX13 and the PI4Kbeta1/beta2 phosphatidylinositol-4 kinases by the small GTPase RabA4B plays important roles during salicylic acid-mediated plant defense signaling in Arabidopsis. *Plant Cell*, **27**, 243–261.

Anzalone, A.V., Randolph, P.B., Davis, J.R., Sousa, A.A., Koblan, L.W., Levy, J.M., Chen, P.J. *et al*. (2019) Search-and-replace genome editing without double-strand breaks or donor DNA. *Nature*, **576**, 149–157.

Armstrong, M.R., Whisson, S.C., Pritchard, L., Bos, J.I., Venter, E., Avrova, A.O., Rehmany, A.P. *et al*. (2005) An ancestral oomycete locus contains late blight avirulence gene Avr3a, encoding a protein that is recognized in the host cytoplasm. *Proc. Natl. Acad. Sci. USA*, **102**, 7766–7771.

Asano, T., Masuda, D., Yasuda, M., Nakashita, H., Kudo, T., Kimura, M., Yamaguchi, K. *et al*. (2008) AtNFXL1, an Arabidopsis homologue of the human transcription factor NF-X1, functions as a negative regulator of the trichothecene phytotoxin-induced defense response. *Plant J.* **53**, 450–464.

Atamian, H.S., Eulgem, T. and Kaloshian, I. (2012) SlWRKY70 is required for Mi-1-mediated resistance to aphids and nematodes in tomato. *Planta*, **235**, 299–309.

Bai, Q., Duan, B., Ma, J., Fen, Y., Sun, S., Long, Q., Lv, J. *et al*. (2019) Coexpression of PalbHLH1 and PalMYB90 genes from *Populus alba* enhances pathogen resistance in poplar by increasing the flavonoid content. *Front. Plant Sci.* **10**, 1772.

Bai, X., Huang, X., Tian, S., Peng, H., Zhan, G., Goher, F., Guo, J. *et al*. (2021) RNAi-mediated stable silencing of TaCSN5 confers broad-spectrum resistance to *Puccinia striiformis* f. sp. *tritici*. *Mol. Plant Pathol.* **22**, 410–421.

Bai, R., Li, H., Du, W., Niu, N., Li, W., Gao, Q., Yao, C. *et al*. (2022) Decoy engineering of the receptor-like cytoplasmic kinase StPBS1 to defend against virus infection in potato. *Mol. Plant Pathol.* **23**, 901–908.

Bari, R. and Jones, J.D. (2009) Role of plant hormones in plant defence responses. *Plant Mol. Biol.* **69**, 473–488.

Berens, M.L., Berry, H.M., Mine, A., Argueso, C.T. and Tsuda, K. (2017) Evolution of hormone signaling networks in plant defense. *Annu. Rev. Phytopathol.* **55**, 401–425.

Bhattacharjee, S., Halane, M.K., Kim, S.H. and Gassmann, W. (2011) Pathogen effectors target Arabidopsis EDS1 and alter its interactions with immune regulators. *Science*, **334**, 1405–1408.

Bi, K., Scalschi, L., Jaiswal, N., Mengiste, T., Fried, R., Sanz, A.B., Arroyo, J. *et al*. (2021) The *Botrytis cinerea* Crh1 transglycosylase is a cytoplasmic effector triggering plant cell death and defense response. *Nat. Commun.* **12**, 2166.

Bigeard, J., Colcombet, J. and Hirt, H. (2015) Signaling mechanisms in pattern-triggered immunity (PTI). *Mol. Plant*, **8**, 521–539.

Birker, D., Heidrich, K., Takahara, H., Narusaka, M., Deslandes, L., Narusaka, Y., Reymond, M. *et al*. (2009) A locus conferring resistance to *Colletotrichum higginsianum* is shared by four geographically distinct Arabidopsis accessions. *Plant J.* **60**, 602–613.

Boex-Fontvieille, E., Rustgi, S., von Wettstein, D., Reinbothe, S. and Reinbothe, C. (2015) Water-soluble chlorophyll protein is involved in herbivore resistance activation during greening of *Arabidopsis thaliana*. *Proc. Natl. Acad. Sci. USA*, **112**, 7303–7308.

Bonardi, V., Cherkis, K., Nishimura, M.T. and Dangl, J.L. (2012) A new eye on NLR proteins: focused on clarity or diffused by complexity? *Curr. Opin. Immunol.* **24**, 41–50.

Bos, J.I., Chaparro-Garcia, A., Quesada-Ocampo, L.M., McSpadden Gardener, B.B. and Kamoun, S. (2009) Distinct amino acids of the *Phytophthora infestans* effector AVR3a condition activation of R3a hypersensitivity and suppression of cell death. *Mol. Plant Microbe Interact.* **22**, 269–281.

Boschi, F., Schvartzman, C., Murchio, S., Ferreira, V., Siri, M.I., Galvan, G.A., Smoker, M. *et al*. (2017) Enhanced bacterial wilt resistance in potato through expression of Arabidopsis EFR and introgression of quantitative resistance from *Solanum commersonii*. *Front. Plant Sci.* **8**, 1642.

Boutrot, F. and Zipfel, C. (2017) Function, discovery, and exploitation of plant pattern recognition receptors for broad-spectrum disease resistance. *Annu. Rev. Phytopathol.* **55**, 257–286.

Broggini, G.A., Wohner, T., Fahrentrapp, J., Kost, T.D., Flachowsky, H., Peil, A., Hanke, M.V. *et al*. (2014) Engineering fire blight resistance into the apple cultivar 'Gala' using the FB_MR5 CC-NBS-LRR resistance gene of *Malus* x *robusta* 5. *Plant Biotechnol. J.* **12**, 728–733.

Cacas, J.L., Pre, M., Pizot, M., Cissoko, M., Diedhiou, I., Jalloul, A., Doumas, P. *et al*. (2017) GhERF-IIb3 regulates the accumulation of jasmonate and leads to enhanced cotton resistance to blight disease. *Mol. Plant Pathol.* **18**, 825–836.

Cambiagno, D.A., Nota, F., Zavallo, D., Rius, S., Casati, P., Asurmendi, S. and Alvarez, M.E. (2018) Immune receptor genes and pericentromeric transposons as targets of common epigenetic regulatory elements. *Plant J.* **96**, 1178–1190.

Cao, Y., Zhang, Y., Chen, Y., Yu, N., Liaqat, S., Wu, W., Chen, D. *et al*. (2021) OsPG1 encodes a polygalacturonase that determines cell wall architecture and affects resistance to bacterial blight pathogen in rice. *Rice (N Y)*, **14**, 36.

Carter, M.E., Helm, M., Chapman, A.V.E., Wan, E., Restrepo Sierra, A.M., Innes, R.W., Bogdanove, A.J. *et al*. (2019) Convergent evolution of effector protease recognition by Arabidopsis and barley. *Mol. Plant Microbe Interact.* **32**, 550–565.

Castel, B., Ngou, P.M., Cevik, V., Redkar, A., Kim, D.S., Yang, Y., Ding, P. *et al*. (2019) Diverse NLR immune receptors activate defence via the RPW8-NLR NRG1. *New Phytol.* **222**, 966–980.

Castello, M.J., Carrasco, J.L. and Vera, P. (2010) DNA-binding protein phosphatase AtDBP1 mediates susceptibility to two potyviruses in Arabidopsis. *Plant Physiol.* **153**, 1521–1525.

Cesari, S. (2018) Multiple strategies for pathogen perception by plant immune receptors. *New Phytol.* **219**, 17–24.

Cesari, S., Xi, Y., Declerck, N., Chalvon, V., Mammri, L., Pugniere, M., Henriquet, C. *et al*. (2022) New recognition specificity in a plant immune receptor by molecular engineering of its integrated domain. *Nat. Commun.* **13**, 1524.

Chandran, D., Tai, Y.C., Hather, G., Dewdney, J., Denoux, C., Burgess, D.G., Ausubel, F.M. *et al*. (2009) Temporal global expression data reveal known and novel salicylate-impacted processes and regulators mediating powdery mildew growth and reproduction on Arabidopsis. *Plant Physiol.* **149**, 1435–1451.

Chandran, D., Inada, N., Hather, G., Kleindt, C.K. and Wildermuth, M.C. (2010) Laser microdissection of Arabidopsis cells at the powdery mildew infection site reveals site-specific processes and regulators. *Proc. Natl. Acad. Sci. USA*, **107**, 460–465.

Chen, H., Xue, L., Chintamanani, S., Germain, H., Lin, H., Cui, H., Cai, R. *et al*. (2009) ETHYLENE INSENSITIVE3 and ETHYLENE INSENSITIVE3-LIKE1 repress SALICYLIC ACID INDUCTION DEFICIENT2 expression to negatively regulate plant innate immunity in Arabidopsis. *Plant Cell*, **21**, 2527–2540.

Chen, C.E., Yeh, K.C., Wu, S.H., Wang, H.I. and Yeh, H.H. (2013a) A vicilin-like seed storage protein, PAP85, is involved in tobacco mosaic virus replication. *J. Virol.* **87**, 6888–6900.

Chen, L., Zhang, L., Li, D., Wang, F. and Yu, D. (2013b) WRKY8 transcription factor functions in the TMV-cg defense response by mediating both abscisic acid and ethylene signaling in Arabidopsis. *Proc. Natl. Acad. Sci. USA*, **110**, E1963–E1971.

Chen, X., Fang, X., Zhang, Y., Wang, X., Zhang, C., Yan, X., Zhao, Y. *et al*. (2019) Overexpression of a soybean 4-coumaric acid: coenzyme A ligase (GmPI4L) enhances resistance to *Phytophthora sojae* in soybean. *Funct. Plant Biol.* **46**, 304–313.

Chen, A., Zhang, H., Shan, T., Shi, X. and Gao, X. (2020a) The overexpression of three cytochrome P450 genes CYP6CY14, CYP6CY22 and CYP6UN1 contributed to metabolic resistance to dinotefuran in melon/cotton aphid, *Aphis gossypii* Glover. *Pestic. Biochem. Physiol.* **167**, 104601.

Chen, L., Kuai, P., Ye, M., Zhou, S., Lu, J. and Lou, Y. (2020b) Overexpression of a cytosolic 6-phosphogluconate dehydrogenase gene enhances the resistance of rice to *Nilaparvata lugens*. *Plants (Basel)*, **9**, 1529.

Cheng, W., Xiao, Z., Cai, H., Wang, C., Hu, Y., Xiao, Y., Zheng, Y. *et al*. (2017) A novel leucine-rich repeat protein, CaLRR51, acts as a positive regulator in the response of pepper to *Ralstonia solanacearum* infection. *Mol. Plant Pathol.* **18**, 1089–1100.

Cheng, G., Yang, Z., Zhang, H., Zhang, J. and Xu, J. (2020) Remorin interacting with PCaP1 impairs Turnip mosaic virus intercellular movement but is antagonised by VPg. *New Phytol.* **225**, 2122–2139.

Chinchilla, D., Bauer, Z., Regenass, M., Boller, T. and Felix, G. (2006) The Arabidopsis receptor kinase FLS2 binds flg22 and determines the specificity of flagellin perception. *Plant Cell*, **18**, 465–476.

Choe, S., Choi, B., Kang, J.H. and Seo, J.K. (2021) Tolerance to tomato yellow leaf curl virus in transgenic tomato overexpressing a cellulose synthase-like gene. *Plant Biotechnol. J.* **19**, 657–659.

Coego, A., Ramirez, V., Gil, M.J., Flors, V., Mauch-Mani, B. and Vera, P. (2005) An Arabidopsis homeodomain transcription factor, OVEREXPRESSOR OF CATIONIC PEROXIDASE 3, mediates resistance to infection by necrotrophic pathogens. *Plant Cell*, **17**, 2123–2137.

Cong, L., Ran, F.A., Cox, D., Lin, S., Barretto, R., Habib, N., Hsu, P.D. *et al*. (2013) Multiplex genome engineering using CRISPR/Cas systems. *Science*, **339**, 819–823.

Consonni, C., Bednarek, P., Humphry, M., Francocci, F., Ferrari, S., Harzen, A., Loren, V. *et al*. (2010) Tryptophan-derived metabolites are required for antifungal defense in the Arabidopsis mlo2 mutant. *Plant Physiol.* **152**, 1544–1561.

Constantino, N.N., Mastouri, F., Damarwinasis, R., Borrego, E.J., Moran-Diez, M.E., Kenerley, C.M., Gao, X. *et al*. (2013) Root-expressed maize lipoxygenase 3 negatively regulates induced systemic resistance to *Colletotrichum graminicola* in shoots. *Front. Plant Sci.* **4**, 510.

Couto, D. and Zipfel, C. (2016) Regulation of pattern recognition receptor signalling in plants. *Nat. Rev. Immunol.* **16**, 537–552.

Cui, X., Fan, B., Scholz, J. and Chen, Z. (2007) Roles of Arabidopsis cyclin-dependent kinase C complexes in cauliflower mosaic virus infection, plant growth, and development. *Plant Cell*, **19**, 1388–1402.

Cui, H., Tsuda, K. and Parker, J.E. (2015) Effector-triggered immunity: from pathogen perception to robust defense. *Annu. Rev. Plant Biol.* **66**, 487–511.

Dagvadorj, B., Ozketen, A.C., Andac, A., Duggan, C., Bozkurt, T.O. and Akkaya, M.S. (2017) A *Puccinia striiformis* f. sp. *tritici* secreted protein activates plant immunity at the cell surface. *Sci. Rep.* **7**, 1141.

Dai, Z., Tan, J., Zhou, C., Yang, X., Yang, F., Zhang, S., Sun, S. *et al*. (2019) The OsmiR396-OsGRF8-OsF3H-flavonoid pathway mediates resistance to the brown planthopper in rice (*Oryza sativa*). *Plant Biotechnol. J.* **17**, 1657–1669.

Delaux, P.M. and Schornack, S. (2021) Plant evolution driven by interactions with symbiotic and pathogenic microbes. *Science*, **371**, eaba6605.

Delteil, A., Blein, M., Faivre-Rampant, O., Guellim, A., Estevan, J., Hirsch, J., Bevitori, R. *et al*. (2012) Building a mutant resource for the study of disease resistance in rice reveals the pivotal role of several genes involved in defence. *Mol. Plant Pathol.* **13**, 72–82.

Desclos-Theveniau, M., Arnaud, D., Huang, T.Y., Lin, G.J., Chen, W.Y., Lin, Y.C. and Zimmerli, L. (2012) The Arabidopsis lectin receptor kinase LecRK-V.5 represses stomatal immunity induced by *Pseudomonas syringae* pv. tomato DC3000. *PLoS Pathog.* **8**, e1002513.

Deslandes, L. and Rivas, S. (2012) Catch me if you can: bacterial effectors and plant targets. *Trends Plant Sci.* **17**, 644–655.

DeYoung, B.J., Qi, D., Kim, S.H., Burke, T.P. and Innes, R.W. (2012) Activation of a plant nucleotide binding-leucine rich repeat disease resistance protein by a modified self protein. *Cell. Microbiol.* **14**, 1071–1084.

Ding, B., Bellizzi Mdel, R., Ning, Y., Meyers, B.C. and Wang, G.L. (2012) HDT701, a histone H4 deacetylase, negatively regulates plant innate immunity by modulating histone H4 acetylation of defense-related genes in rice. *Plant Cell*, **24**, 3783–3794.

Ding, L.N., Li, M., Guo, X.J., Tang, M.Q., Cao, J., Wang, Z., Liu, R. *et al*. (2020) Arabidopsis GDSL1 overexpression enhances rapeseed *Sclerotinia sclerotiorum* resistance and the functional identification of its homolog in *Brassica napus*. *Plant Biotechnol. J.* **18**, 1255–1270.

Dong, O.X., Tong, M., Bonardi, V., El Kasmi, F., Woloshen, V., Wunsch, L.K., Dangl, J.L. *et al*. (2016) TNL-mediated immunity in Arabidopsis requires complex regulation of the redundant ADR1 gene family. *New Phytol.* **210**, 960–973.

Du, Q., Yang, X., Zhang, J., Zhong, X., Kim, K.S., Yang, J., Xing, G. *et al*. (2018) Over-expression of the *Pseudomonas syringae* harpin-encoding gene hrpZm confers enhanced tolerance to *Phytophthora* root and stem rot in transgenic soybean. *Transgenic Res.* **27**, 277–288.

Du, D., Zhang, C., Xing, Y., Lu, X., Cai, L., Yun, H., Zhang, Q. *et al*. (2021) The CC-NB-LRR OsRLR1 mediates rice disease resistance through interaction with OsWRKY19. *Plant Biotechnol. J.* **19**, 1052–1064.

Duan, X., Wang, X., Fu, Y., Tang, C., Li, X., Cheng, Y., Feng, H. *et al*. (2013) TaEIL1, a wheat homologue of AtEIN3, acts as a negative regulator in the wheat-stripe rust fungus interaction. *Mol. Plant Pathol.* **14**, 728–739.

Durrant, W.E. and Dong, X. (2004) Systemic acquired resistance. *Annu. Rev. Phytopathol.* **42**, 185–209.

Engelsdorf, T., Horst, R.J., Prols, R., Proschel, M., Dietz, F., Huckelhoven, R. and Voll, L.M. (2013) Reduced carbohydrate availability enhances the susceptibility of Arabidopsis toward *Colletotrichum higginsianum*. *Plant Physiol.* **162**, 225–238.

Fallath, T., Kidd, B.N., Stiller, J., Davoine, C., Bjorklund, S., Manners, J.M., Kazan, K. *et al*. (2017) MEDIATOR18 and MEDIATOR20 confer susceptibility to *Fusarium oxysporum* in *Arabidopsis thaliana*. *PLoS ONE*, **12**, e0176022.

Fan, J., Bai, P., Ning, Y., Wang, J., Shi, X., Xiong, Y., Zhang, K. *et al*. (2018) The monocot-specific receptor-like kinase SDS2 controls cell death and immunity in rice. *Cell Host Microbe*, **23**, 498–510.e5.

Favery, B., Lecomte, P., Gil, N., Bechtold, N., Bouchez, D., Dalmasso, A. and Abad, P. (1998) RPE, a plant gene involved in early developmental steps of nematode feeding cells. *EMBO J.* **17**, 6799–6811.

Fekih, R., Tamiru, M., Kanzaki, H., Abe, A., Yoshida, K., Kanzaki, E., Saitoh, H. *et al*. (2015) The rice (*Oryza sativa* L.) LESION MIMIC RESEMBLING, which encodes an AAA-type ATPase, is implicated in defense response. *Mol. Genet. Genomics*, **290**, 611–622.

Feng, H., Duan, X., Zhang, Q., Li, X., Wang, B., Huang, L., Wang, X. *et al*. (2014) The target gene of tae-miR164, a novel NAC transcription factor from the NAM subfamily, negatively regulates resistance of wheat to stripe rust. *Mol. Plant Pathol.* **15**, 284–296.

Filipe, O., De Vleesschauwer, D., Haeck, A., Demeestere, K. and Hofte, M. (2018) The energy sensor OsSnRK1a confers broad-spectrum disease resistance in rice. *Sci. Rep.* **8**, 3864.

Froidure, S., Canonne, J., Daniel, X., Jauneau, A., Briere, C., Roby, D. and Rivas, S. (2010) AtsPLA2-alpha nuclear relocalization by the Arabidopsis transcription factor AtMYB30 leads to repression of the plant defense response. *Proc. Natl. Acad. Sci. USA*, **107**, 15281–15286.

Fu, Z.Q., Yan, S., Saleh, A., Wang, W., Ruble, J., Oka, N., Mohan, R. *et al*. (2012) NPR3 and NPR4 are receptors for the immune signal salicylic acid in plants. *Nature*, **486**, 228–232.

Furst, U., Zeng, Y., Albert, M., Witte, A.K., Fliegmann, J. and Felix, G. (2020) Perception of *Agrobacterium tumefaciens* flagellin by FLS2(XL) confers resistance to crown gall disease. *Nat. Plants*, **6**, 22–27.

Galli, M., Martiny, E., Imani, J., Kumar, N., Koch, A., Steinbrenner, J. and Kogel, K.H. (2021) CRISPR/SpCas9-mediated double knockout of barley microrchidia MORC1 and MORC6a reveals their strong involvement in plant immunity, transcriptional gene silencing and plant growth. *Plant Biotechnol. J.* **20**, 89–102.

Gao, W., Long, L., Xu, L., Lindsey, K., Zhang, X. and Zhu, L. (2016) Suppression of the homeobox gene HDTF1 enhances resistance to *Verticillium dahliae* and *Botrytis cinerea* in cotton. *J. Integr. Plant Biol.* **58**, 503–513.

Gao, M., Yin, X., Yang, W., Lam, S.M., Tong, X., Liu, J., Wang, X. *et al*. (2017) GDSL lipases modulate immunity through lipid homeostasis in rice. *PLoS Pathog.* **13**, e1006724.

Gao, Y.F., Liu, J.K., Yang, F.M., Zhang, G.Y., Wang, D., Zhang, L., Ou, Y.B. *et al*. (2020) The WRKY transcription factor WRKY8 promotes resistance to pathogen infection and mediates drought and salt stress tolerance in *Solanum lycopersicum*. *Physiol. Plant.* **168**, 98–117.

Gaudelli, N.M., Komor, A.C., Rees, H.A., Packer, M.S., Badran, A.H., Bryson, D.I. and Liu, D.R. (2017) Programmable base editing of A*T to G*C in genomic DNA without DNA cleavage. *Nature*, **551**, 464–471.

Ge, X., Li, G.J., Wang, S.B., Zhu, H., Zhu, T., Wang, X. and Xia, Y. (2007) AtNUDT7, a negative regulator of basal immunity in Arabidopsis, modulates two distinct defense response pathways and is involved in maintaining redox homeostasis. *Plant Physiol.* **145**, 204–215.

Geng, S., Kong, X., Song, G., Jia, M., Guan, J., Wang, F., Qin, Z. *et al*. (2019) DNA methylation dynamics during the interaction of wheat progenitor *Aegilops tauschii* with the obligate biotrophic fungus *Blumeria graminis* f. sp. *tritici*. *New Phytol.* **221**, 1023–1035.

Geng, D., Shen, X., Xie, Y., Yang, Y., Bian, R., Gao, Y., Li, P. *et al*. (2020) Regulation of phenylpropanoid biosynthesis by MdMYB88 and MdMYB124 contributes to pathogen and drought resistance in apple. *Hortic. Res.* **7**, 102.

Giannakopoulou, A., Steele, J.F., Segretin, M.E., Bozkurt, T.O., Zhou, J., Robatzek, S., Banfield, M.J. *et al*. (2015) Tomato I2 immune receptor can be engineered to confer partial resistance to the oomycete *Phytophthora infestans* in addition to the fungus *Fusarium oxysporum*. *Mol. Plant Microbe Interact.* **28**, 1316–1329.

Gomez-Gomez, L., Bauer, Z. and Boller, T. (2001) Both the extracellular leucine-rich repeat domain and the kinase activity of FSL2 are required for flagellin binding and signaling in Arabidopsis. *Plant Cell*, **13**, 1155–1163.

Gouveia-Mageste, B.C., Martins, L.G.C., Dal-Bianco, M., Machado, J.P.B., da Silva, J.C.F., Kim, A.Y., Yazaki, J. *et al*. (2021) A plant-specific syntaxin-6 protein contributes to the intracytoplasmic route for the begomovirus CabLCV. *Plant Physiol.* **187**, 158–173.

Greenberg, J.T. and Yao, N. (2004) The role and regulation of programmed cell death in plant-pathogen interactions. *Cell. Microbiol.* **6**, 201–211.

Grunewald, W., Karimi, M., Wieczorek, K., Van de Cappelle, E., Wischnitzki, E., Grundler, F., Inze, D. *et al*. (2008) A role for AtWRKY23 in feeding site establishment of plant-parasitic nematodes. *Plant Physiol.* **148**, 358–368.

Gu, K.X., Song, X.S., Xiao, X.M., Duan, X.X., Wang, J.X., Duan, Y.B., Hou, Y.P. *et al*. (2019) A beta2-tubulin dsRNA derived from *Fusarium asiaticum* confers plant resistance to multiple phytopathogens and reduces fungicide resistance. *Pestic. Biochem. Physiol.* **153**, 36–46.

Gu, K.D., Zhang, Q.Y., Yu, J.Q., Wang, J.H., Zhang, F.J., Wang, C.K., Zhao, Y.W. *et al*. (2021) R2R3-MYB transcription factor MdMYB73 confers increased resistance to the fungal pathogen *Botryosphaeria dothidea* in apples via the salicylic acid pathway. *J. Agric. Food Chem.* **69**, 447–458.

Gul, A., Hussain, G., Iqbal, A., Rao, A.Q., Din, S.U., Yasmeen, A., Shahid, N. *et al*. (2020) Constitutive expression of asparaginase in *Gossypium hirsutum* triggers insecticidal activity against *Bemisia tabaci*. *Sci. Rep.* **10**, 8958.

Gully, K., Pelletier, S., Guillou, M.C., Ferrand, M., Aligon, S., Pokotylo, I., Perrin, A. *et al*. (2019) The SCOOP12 peptide regulates defense response and root elongation in *Arabidopsis thaliana*. *J. Exp. Bot.* **70**, 1349–1365.

Guo, J., Bai, P., Yang, Q., Liu, F., Wang, X., Huang, L. and Kang, Z. (2013) Wheat zinc finger protein TaLSD1, a negative regulator of programmed cell death, is involved in wheat resistance against stripe rust fungus. *Plant Physiol. Biochem.* **71**, 164–172.

Guzman-Benito, I., Donaire, L., Amorim-Silva, V., Vallarino, J.G., Esteban, A., Wierzbicki, A.T., Ruiz-Ferrer, V. *et al*. (2019) The immune repressor BIR1 contributes to antiviral defense and undergoes transcriptional and post-transcriptional regulation during viral infections. *New Phytol.* **224**, 421–438.

Han, X., Zhang, L., Zhao, L., Xue, P., Qi, T., Zhang, C., Yuan, H. *et al*. (2020) SnRK1 phosphorylates and destabilizes WRKY3 to enhance barley immunity to powdery mildew. *Plant Commun.* **1**, 100083.

Hao, G., Pitino, M., Duan, Y. and Stover, E. (2016) Reduced susceptibility to *Xanthomonas citri* in transgenic citrus expressing the FLS2 receptor from *Nicotiana benthamiana*. *Mol. Plant Microbe Interact.* **29**, 132–142.

Harris, C.J., Slootweg, E.J., Goverse, A. and Baulcombe, D.C. (2013) Stepwise artificial evolution of a plant disease resistance gene. *Proc. Natl. Acad. Sci. USA*, **110**, 21189–21194.

Hasley, J.A.R., Navet, N. and Tian, M. (2021) CRISPR/Cas9-mediated mutagenesis of sweet basil candidate susceptibility gene ObDMR6 enhances downy mildew resistance. *PLoS ONE*, **16**, e0253245.

Hatta, M.A.M., Arora, S., Ghosh, S., Matny, O., Smedley, M.A., Yu, G., Chakraborty, S. *et al*. (2021) The wheat Sr22, Sr33, Sr35 and Sr45 genes confer resistance against stem rust in barley. *Plant Biotechnol. J.* **19**, 273–284.

He, H., Yang, X., Xun, H., Lou, X., Li, S., Zhang, Z., Jiang, L. *et al*. (2017) Over-expression of GmSN1 enhances virus resistance in Arabidopsis and soybean. *Plant Cell Rep.* **36**, 1441–1455.

He, Y., Wu, L., Liu, X., Jiang, P., Yu, L., Qiu, J., Wang, G. *et al*. (2020) TaUGT6, a novel UDP-glycosyltransferase gene enhances the resistance to FHB and DON accumulation in wheat. *Front. Plant Sci.* **11**, 574775.

Helm, M., Qi, M., Sarkar, S., Yu, H., Whitham, S.A. and Innes, R.W. (2019) Engineering a decoy substrate in soybean to enable recognition of the soybean mosaic virus NIa protease. *Mol. Plant Microbe Interact.* **32**, 760–769.

Hewezi, T., Howe, P., Maier, T.R., Hussey, R.S., Mitchum, M.G., Davis, E.L. and Baum, T.J. (2008) Cellulose binding protein from the parasitic nematode *Heterodera schachtii* interacts with Arabidopsis pectin methylesterase: cooperative cell wall modification during parasitism. *Plant Cell*, **20**, 3080–3093.

Hofmann, J., Hess, P.H., Szakasits, D., Blochl, A., Wieczorek, K., Daxbock-Horvath, S., Bohlmann, H. *et al*. (2009) Diversity and activity of sugar transporters in nematode-induced root syncytia. *J. Exp. Bot.* **60**, 3085–3095.

Hok, S., Danchin, E.G., Allasia, V., Panabieres, F., Attard, A. and Keller, H. (2011) An Arabidopsis (malectin-like) leucine-rich repeat receptor-like kinase contributes to downy mildew disease. *Plant Cell Environ.* **34**, 1944–1957.

Holton, N., Nekrasov, V., Ronald, P.C. and Zipfel, C. (2015) The phylogenetically-related pattern recognition receptors EFR and XA21 recruit similar immune signaling components in monocots and dicots. *PLoS Pathog.* **11**, e1004602.

Hong, Y., Yang, Y., Zhang, H., Huang, L., Li, D. and Song, F. (2017) Overexpression of MoSM1, encoding for an immunity-inducing protein from *Magnaporthe oryzae*, in rice confers broad-spectrum resistance against fungal and bacterial diseases. *Sci. Rep.* **7**, 41037.

Hong, Y., Liu, Q., Cao, Y., Zhang, Y., Chen, D., Lou, X., Cheng, S. *et al*. (2019) The OsMPK15 negatively regulates *Magnaporthe oryza* and Xoo disease resistance via SA and JA signaling pathway in rice. *Front. Plant Sci.* **10**, 752.

Horvath, D.M., Stall, R.E., Jones, J.B., Pauly, M.H., Vallad, G.E., Dahlbeck, D., Staskawicz, B.J. *et al*. (2012) Transgenic resistance confers effective field level control of bacterial spot disease in tomato. *PLoS ONE*, **7**, e42036.

Hou, X., Cui, J., Liu, W., Jiang, N., Zhou, X., Qi, H., Meng, J. *et al*. (2020) LncRNA39026 enhances tomato resistance to *Phytophthora infestans* by decoying miR168a and inducing PR gene expression. *Phytopathology*, **110**, 873–880.

Hu, P., Liu, J., Xu, J., Zhou, C., Cao, S., Zhou, W., Huang, Z. *et al*. (2018) A malectin-like/leucine-rich repeat receptor protein kinase gene, RLK-V, regulates powdery mildew resistance in wheat. *Mol. Plant Pathol.* **19**, 2561–2574.

Hu, G., Lei, Y., Liu, J., Hao, M., Zhang, Z., Tang, Y., Chen, A. *et al*. (2020) The ghr-miR164 and GhNAC100 modulate cotton plant resistance against *Verticillium dahlia*. *Plant Sci.* **293**, 110438.

Hu, B., Zhou, Y., Zhou, Z., Sun, B., Zhou, F., Yin, C., Ma, W. *et al*. (2021) Repressed OsMESL expression triggers reactive oxygen species-mediated broad-spectrum disease resistance in rice. *Plant Biotechnol. J.* **19**, 1511–1522.

Hua, B., Chang, J., Wu, M., Xu, Z., Zhang, F., Yang, M., Xu, H. *et al*. (2021) Mediation of JA signalling in glandular trichomes by the woolly/SlMYC1 regulatory module improves pest resistance in tomato. *Plant Biotechnol. J.* **19**, 375–393.

Huai, B., Yang, Q., Wei, X., Pan, Q., Kang, Z. and Liu, J. (2020) TaSTP13 contributes to wheat susceptibility to stripe rust possibly by increasing cytoplasmic hexose concentration. *BMC Plant Biol.* **20**, 49.

Huang, H., Huang, S., Li, J., Wang, H., Zhao, Y., Feng, M., Dai, J. *et al*. (2021) Stepwise artificial evolution of an Sw-5b immune receptor extends its resistance spectrum against resistance-breaking isolates of tomato spotted wilt virus. *Plant Biotechnol. J.* **19**, 2164–2176.

Huibers, R.P., Loonen, A.E., Gao, D., Van den Ackerveken, G., Visser, R.G. and Bai, Y. (2013) Powdery mildew resistance in tomato by impairment of SlPMR4 and SlDMR1. *PLoS ONE*, **8**, e67467.

Hussein, N.K., Sabr, L.J., Lobo, E., Booth, J., Ariens, E., Detchanamurthy, S. and Schenk, P.M. (2020) Suppression of Arabidopsis mediator subunit-encoding MED18 confers broad resistance against DNA and RNA viruses while MED25 is required for virus defense. *Front. Plant Sci.* **11**, 162.

Imran, Q.M., Falak, N., Hussain, A., Mun, B.G., Sharma, A., Lee, S.U., Kim, K.M. *et al*. (2016) Nitric oxide responsive heavy metal-associated gene AtHMAD1 contributes to development and disease resistance in *Arabidopsis thaliana*. *Front. Plant Sci.* **7**, 1712.

Iswanto, A.B.B., Shelake, R.M., Vu, M.H., Kim, J.Y. and Kim, S.H. (2021a) Genome editing for plasmodesmal biology. *Front. Plant Sci.* **12**, 679140.

Iswanto, A.B.B., Vu, M.H., Pike, S., Lee, J., Kang, H., Son, G.H., Kim, J.Y. *et al*. (2021b) Pathogen effectors: what do they do at plasmodesmata? *Mol. Plant Pathol.* **23**, 795–804.

Jan, R., Khan, M.A., Asaf, S., Lee, I.J., Bae, J.S. and Kim, K.M. (2020) Overexpression of OsCM alleviates BLB stress via phytohormonal accumulation and transcriptional modulation of defense-related genes in *Oryza sativa*. *Sci. Rep.* **10**, 19520.

Jehle, A.K., Furst, U., Lipschis, M., Albert, M. and Felix, G. (2013a) Perception of the novel MAMP eMax from different *Xanthomonas* species requires the Arabidopsis receptor-like protein ReMAX and the receptor kinase SOBIR. *Plant Signal. Behav.* **8**, e27408.

Jehle, A.K., Lipschis, M., Albert, M., Fallahzadeh-Mamaghani, V., Furst, U., Mueller, K. and Felix, G. (2013b) The receptor-like protein ReMAX of Arabidopsis detects the microbe-associated molecular pattern eMax from *Xanthomonas*. *Plant Cell*, **25**, 2330–2340.

Jia, S., Wang, Y., Zhang, G., Yan, Z. and Cai, Q. (2020) Strawberry FaWRKY25 transcription factor negatively regulated the resistance of strawberry fruits to *Botrytis cinerea*. *Genes (Basel)*, **12**, 56.

Jiang, C., Hei, R., Yang, Y., Zhang, S., Wang, Q., Wang, W., Zhang, Q. *et al*. (2020) An orphan protein of *Fusarium graminearum* modulates host immunity by mediating proteasomal degradation of TaSnRK1alpha. *Nat. Commun.* **11**, 4382.

Jinek, M., Chylinski, K., Fonfara, I., Hauer, M., Doudna, J.A. and Charpentier, E. (2012) A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. *Science*, **337**, 816–821.

Jing, Y., Liu, J., Liu, P., Ming, D. and Sun, J. (2019) Overexpression of TaJAZ1 increases powdery mildew resistance through promoting reactive oxygen species accumulation in bread wheat. *Sci. Rep.* **9**, 5691.

Jones, J.D. and Dangl, J.L. (2006) The plant immune system. *Nature*, **444**, 323–329.

Joung, J.K. and Sander, J.D. (2013) TALENs: a widely applicable technology for targeted genome editing. *Nat. Rev. Mol. Cell Biol.* **14**, 49–55.

Ju, Y., Tian, H., Zhang, R., Zuo, L., Jin, G., Xu, Q., Ding, X. *et al*. (2017) Overexpression of OsHSP18.0-CI enhances resistance to bacterial leaf streak in rice. *Rice (N Y)*, **10**, 12.

Kachroo, A. and Robin, G.P. (2013) Systemic signaling during plant defense. *Curr. Opin. Plant Biol.* **16**, 527–533.

Kaku, H., Nishizawa, Y., Ishii-Minami, N., Akimoto-Tomiyama, C., Dohmae, N., Takio, K., Minami, E. *et al*. (2006) Plant cells recognize chitin fragments for defense signaling through a plasma membrane receptor. *Proc. Natl. Acad. Sci. USA*, **103**, 11086–11091.

Kampire, M.G., Sanglou, R.K., Wang, H., Kazeem, B.B., Wu, J.L. and Zhang, X. (2021) A novel allele encoding 7-hydroxymethyl chlorophyll a reductase confers bacterial blight resistance in rice. *Int. J. Mol. Sci.* **22**, 7585.

Kang, B.C., Yun, J.Y., Kim, S.T., Shin, Y., Ryu, J., Choi, M., Woo, J.W. *et al*. (2018) Precision genome engineering through adenine base editing in plants. *Nat. Plants*, **4**, 427–431.

Kettles, G.J., Drurey, C., Schoonbeek, H.J., Maule, A.J. and Hogenhout, S.A. (2013) Resistance of *Arabidopsis thaliana* to the green peach aphid, *Myzus persicae*, involves camalexin and is regulated by microRNAs. *New Phytol.* **198**, 1178–1190.

Khong, G.N., Pati, P.K., Richaud, F., Parizot, B., Bidzinski, P., Mai, C.D., Bes, M. *et al*. (2015) OsMADS26 negatively regulates resistance to pathogens and drought tolerance in rice. *Plant Physiol.* **169**, 2935–2949.

Kidd, B.N., Edgar, C.I., Kumar, K.K., Aitken, E.A., Schenk, P.M., Manners, J.M. and Kazan, K. (2009) The mediator complex subunit PFT1 is a key regulator of jasmonate-dependent defense in Arabidopsis. *Plant Cell*, **21**, 2237–2252.

Kieu, N.P., Lenman, M., Wang, E.S., Petersen, B.L. and Andreasson, E. (2021) Mutations introduced in susceptibility genes through CRISPR/Cas9 genome editing confer increased late blight resistance in potatoes. *Sci. Rep.* **11**, 4487.

Kim, H.S., Jung, M.S., Lee, S.M., Kim, K.E., Byun, H., Choi, M.S., Park, H.C. *et al*. (2009a) An S-locus receptor-like kinase plays a role as a negative regulator in plant defense responses. *Biochem. Biophys. Res. Commun.* **381**, 424–428.

Kim, S.H., Kwon, S.I., Bhattacharjee, S. and Gassmann, W. (2009b) Regulation of defense gene expression by Arabidopsis SRFR1. *Plant Signal. Behav.* **4**, 149–150.

Kim, S.H., Kwon, S.I., Saha, D., Anyanwu, N.C. and Gassmann, W. (2009c) Resistance to the *Pseudomonas syringae* effector HopA1 is governed by the TIR-NBS-LRR protein RPS6 and is enhanced by mutations in SRFR1. *Plant Physiol.* **150**, 1723–1732.

Kim, S.H., Gao, F., Bhattacharjee, S., Adiasor, J.A., Nam, J.C. and Gassmann, W. (2010) The Arabidopsis resistance-like gene SNC1 is activated by mutations in SRFR1 and contributes to resistance to the bacterial effector AvrRps4. *PLoS Pathog.* **6**, e1001172.

Kim, D.S., Choi, H.W. and Hwang, B.K. (2014) Pepper mildew resistance locus O interacts with pepper calmodulin and suppresses *Xanthomonas* AvrBsT-triggered cell death and defense responses. *Planta*, **240**, 827–839.

Kim, D.S., Kim, N.H. and Hwang, B.K. (2015) GLYCINE-RICH RNA-BINDING PROTEIN1 interacts with RECEPTOR-LIKE CYTOPLASMIC PROTEIN KINASE1 and suppresses cell death and defense responses in pepper (*Capsicum annuum*). *New Phytol.* **205**, 786–800.

Kim, S.H., Qi, D., Ashfield, T., Helm, M. and Innes, R.W. (2016) Using decoys to expand the recognition specificity of a plant disease resistance protein. *Science*, **351**, 684–687.

Kim, Y.A., Moon, H. and Park, C.J. (2019) CRISPR/Cas9-targeted mutagenesis of Os8N3 in rice to confer resistance to *Xanthomonas oryzae* pv. *oryzae*. *Rice (N Y)*, **12**, 67.

Kim, P., Xue, C.Y., Song, H.D., Gao, Y., Feng, L., Li, Y. and Xuan, Y.H. (2021) Tissue-specific activation of DOF11 promotes rice resistance to sheath blight disease and increases grain weight via activation of SWEET14. *Plant Biotechnol. J.* **19**, 409–411.

Kim, H., Prokchorchik, M. and Sohn, K.H. (2022) Investigation of natural RIN4 variants reveals a motif crucial for function and provides an opportunity to broaden NLR regulation specificity. *Plant J.* **110**, 58–70.

Kishimoto, K., Kouzai, Y., Kaku, H., Shibuya, N., Minami, E. and Nishizawa, Y. (2010) Perception of the chitin oligosaccharides contributes to disease resistance to blast fungus *Magnaporthe oryzae* in rice. *Plant J.* **64**, 343–354.

Kishimoto, K., Kouzai, Y., Kaku, H., Shibuya, N., Minami, E. and Nishizawa, Y. (2011) Enhancement of MAMP signaling by chimeric receptors improves disease resistance in plants. *Plant Signal. Behav.* **6**, 449–451.

Koch, A., Biedenkopf, D., Furch, A., Weber, L., Rossbach, O., Abdellatef, E., Linicus, L. *et al*. (2016) An RNAi-based control of *Fusarium graminearum* infections through spraying of long dsRNAs involves a plant passage and is controlled by the fungal silencing machinery. *PLoS Pathog.* **12**, e1005901.

Komor, A.C., Kim, Y.B., Packer, M.S., Zuris, J.A. and Liu, D.R. (2016) Programmable editing of a target base in genomic DNA without double-stranded DNA cleavage. *Nature*, **533**, 420–424.

Koseoglou, E., van der Wolf, J.M., Visser, R.G.F. and Bai, Y. (2022) Susceptibility reversed: modified plant susceptibility genes for resistance to bacteria. *Trends Plant Sci.* **27**, 69–79.

Kost, T.D., Gessler, C., Jansch, M., Flachowsky, H., Patocchi, A. and Broggini, G.A. (2015) Development of the first cisgenic apple with increased resistance to fire blight. *PLoS ONE*, **10**, e0143980.

Kourelis, J., van der Hoorn, R.A.L. and Sueldo, D.J. (2016) Decoy engineering: the next step in resistance breeding. *Trends Plant Sci.* **21**, 371–373.

Kouzai, Y., Shimizu, M., Inoue, K., Uehara-Yamaguchi, Y., Takahagi, K., Nakayama, R., Matsuura, T. *et al*. (2020) BdWRKY38 is required for the incompatible interaction of *Brachypodium distachyon* with the necrotrophic fungus *Rhizoctonia solani*. *Plant J.* **104**, 995–1008.

Kuang, J., Liu, J., Mei, J., Wang, C., Hu, H., Zhang, Y., Sun, M. *et al*. (2017) A class II small heat shock protein OsHsp18.0 plays positive roles in both biotic and abiotic defense responses in rice. *Sci. Rep.* **7**, 11333.

Kunze, G., Zipfel, C., Robatzek, S., Niehaus, K., Boller, T. and Felix, G. (2004) The N terminus of bacterial elongation factor Tu elicits innate immunity in Arabidopsis plants. *Plant Cell*, **16**, 3496–3507.

Kuo, S.Y., Hu, C.C., Huang, Y.W., Lee, C.W., Luo, M.J., Tu, C.W., Lee, S.C. *et al*. (2021) Argonaute 5 family proteins play crucial roles in the defence against Cymbidium mosaic virus and Odontoglossum ringspot virus in *Phalaenopsis aphrodite* subsp. *formosana*. *Mol. Plant Pathol.* **22**, 627–643.

Kwon, S.I., Koczan, J.M. and Gassmann, W. (2004) Two Arabidopsis srfr (suppressor of rps4-RLD) mutants exhibit avrRps4-specific disease resistance independent of RPS4. *Plant J.* **40**, 366–375.

Kwon, S.I., Kim, S.H., Bhattacharjee, S., Noh, J.J. and Gassmann, W. (2009) SRFR1, a suppressor of effector-triggered immunity, encodes a conserved tetratricopeptide repeat protein with similarity to transcriptional repressors. *Plant J.* **57**, 109–119.

La Camera, S., L'Haridon, F., Astier, J., Zander, M., Abou-Mansour, E., Page, G., Thurow, C. *et al*. (2011) The glutaredoxin ATGRXS13 is required to facilitate *Botrytis cinerea* infection of *Arabidopsis thaliana* plants. *Plant J.* **68**, 507–519.

Lacombe, S., Rougon-Cardoso, A., Sherwood, E., Peeters, N., Dahlbeck, D., van Esse, H.P., Smoker, M. *et al*. (2010) Interfamily transfer of a plant pattern-recognition receptor confers broad-spectrum bacterial resistance. *Nat. Biotechnol.* **28**, 365–369.

Lai, Z., Schluttenhofer, C.M., Bhide, K., Shreve, J., Thimmapuram, J., Lee, S.Y., Yun, D.J. *et al*. (2014) MED18 interaction with distinct transcription factors regulates multiple plant functions. *Nat. Commun.* **5**, 3064.

Latrasse, D., Germann, S., Houba-Herin, N., Dubois, E., Bui-Prodhomme, D., Hourcade, D., Juul-Jensen, T. *et al*. (2011) Control of flowering and cell fate by LIF2, an RNA binding partner of the polycomb complex component LHP1. *PLoS ONE*, **6**, e16592.

Le Roux, C., Del Prete, S., Boutet-Mercey, S., Perreau, F., Balague, C., Roby, D., Fagard, M. *et al*. (2014) The hnRNP-Q protein LIF2 participates in the plant immune response. *PLoS ONE*, **9**, e99343.

Le, M.H., Cao, Y., Zhang, X.C. and Stacey, G. (2014) LIK1, a CERK1-interacting kinase, regulates plant immune responses in Arabidopsis. *PLoS ONE*, **9**, e102245.

Lenz, H.D., Haller, E., Melzer, E., Kober, K., Wurster, K., Stahl, M., Bassham, D.C. *et al*. (2011) Autophagy differentially controls plant basal immunity to biotrophic and necrotrophic pathogens. *Plant J.* **66**, 818–830.

Li, Y., Yang, S., Yang, H. and Hua, J. (2007) The TIR-NB-LRR gene SNC1 is regulated at the transcript level by multiple factors. *Mol. Plant Microbe Interact.* **20**, 1449–1456.

Li, R., Afsheen, S., Xin, Z., Han, X. and Lou, Y. (2013) OsNPR1 negatively regulates herbivore-induced JA and ethylene signaling and plant resistance to a chewing herbivore in rice. *Physiol. Plant.* **147**, 340–351.

Li, C., He, X., Luo, X., Xu, L., Liu, L., Min, L., Jin, L. *et al*. (2014a) Cotton WRKY1 mediates the plant defense-to-development transition during infection of cotton by *Verticillium dahliae* by activating JASMONATE ZIM-DOMAIN1 expression. *Plant Physiol.* **166**, 2179–2194.

Li, X., Huang, L., Zhang, Y., Ouyang, Z., Hong, Y., Zhang, H., Li, D. *et al*. (2014b) Tomato SR/CAMTA transcription factors SlSR1 and SlSR3L negatively regulate disease resistance response and SlSR1L positively modulates drought stress tolerance. *BMC Plant Biol.* **14**, 286.

Li, J., Yin, J., Rong, C., Li, K.E., Wu, J.X., Huang, L.Q., Zeng, H.Y. *et al*. (2016) Orosomucoid proteins interact with the small subunit of serine palmitoyltransferase and contribute to sphingolipid homeostasis and stress responses in Arabidopsis. *Plant Cell*, **28**, 3038–3051.

Li, Y., Qin, L., Zhao, J., Muhammad, T., Cao, H., Li, H., Zhang, Y. *et al*. (2017) SlMAPK3 enhances tolerance to tomato yellow leaf curl virus (TYLCV) by regulating salicylic acid and jasmonic acid signaling in tomato (*Solanum lycopersicum*). *PLoS ONE*, **12**, e0172466.

Li, Y., Li, Q., Guo, G., He, T., Gao, R., Faheem, M., Huang, J. *et al*. (2018) Transient overexpression of HvSERK2 improves barley resistance to powdery mildew. *Int. J. Mol. Sci.* **19**, 1226.

Li, B., Sun, S., Gao, X., Wu, M., Deng, Y., Zhang, Q., Li, X. *et al*. (2019a) Overexpression a "fruit-weight 2.2-like" gene OsFWL5 improves rice resistance. *Rice (N Y)*, **12**, 51.

Li, N., Lin, B., Wang, H., Li, X., Yang, F., Ding, X., Yan, J. *et al*. (2019b) Natural variation in ZmFBL41 confers banded leaf and sheath blight resistance in maize. *Nat. Genet.* **51**, 1540–1548.

Li, S., Zhao, J., Zhai, Y., Yuan, Q., Zhang, H., Wu, X., Lu, Y. *et al*. (2019c) The hypersensitive induced reaction 3 (HIR3) gene contributes to plant basal resistance via an EDS1 and salicylic acid-dependent pathway. *Plant J.* **98**, 783–797.

Li, X., Ouyang, X., Zhang, Z., He, L., Wang, Y., Li, Y., Zhao, J. *et al*. (2019d) Over-expression of the red plant gene R1 enhances anthocyanin production and resistance to bollworm and spider mite in cotton. *Mol. Genet. Genomics*, **294**, 469–478.

Li, Z., Huang, J., Wang, Z., Meng, F., Zhang, S., Wu, X., Zhang, Z. *et al*. (2019e) Overexpression of Arabidopsis nucleotide-binding and leucine-rich repeat genes RPS2 and RPM1(D505V) confers broad-spectrum disease resistance in rice. *Front. Plant Sci.* **10**, 417.

Li, Q., Qin, X., Qi, J., Dou, W., Dunand, C., Chen, S. and He, Y. (2020a) CsPrx25, a class III peroxidase in *Citrus sinensis*, confers resistance to citrus

bacterial canker through the maintenance of ROS homeostasis and cell wall lignification. *Hortic. Res.* **7**, 192.

Li, X.P., Ma, X.C., Wang, H., Zhu, Y., Liu, X.X., Li, T.T., Zheng, Y.P. *et al*. (2020b) Osa-miR162a fine-tunes rice resistance to *Magnaporthe oryzae* and yield. *Rice (N Y)*, **13**, 38.

Li, Y., Zhou, Y., Dai, P., Ren, Y., Wang, Q. and Liu, X. (2021) Cotton Bsr-k1 modulates lignin deposition participating in plant resistance against *Verticillium dahliae* and *Fusarium oxysporum*. *Plant Growth Regul.* **95**, 283–292.

Lin, Z.J., Liebrand, T.W., Yadeta, K.A. and Coaker, G. (2015) PBL13 is a serine/threonine protein kinase that negatively regulates Arabidopsis immune responses. *Plant Physiol.* **169**, 2950–2962.

Lin, Q., Zong, Y., Xue, C., Wang, S., Jin, S., Zhu, Z., Wang, Y. *et al*. (2020) Prime genome editing in rice and wheat. *Nat. Biotechnol.* **38**, 582–585.

Liu, D., Chen, X., Liu, J., Ye, J. and Guo, Z. (2012) The rice ERF transcription factor OsERF922 negatively regulates resistance to *Magnaporthe oryzae* and salt tolerance. *J. Exp. Bot.* **63**, 3899–3911.

Liu, J.Z., Braun, E., Qiu, W.L., Shi, Y.F., Marcelino-Guimaraes, F.C., Navarre, D., Hill, J.H. *et al*. (2014) Positive and negative roles for soybean MPK6 in regulating defense responses. *Mol. Plant Microbe Interact.* **27**, 824–834.

Liu, J., Han, L., Huai, B., Zheng, P., Chang, Q., Guan, T., Li, D. *et al*. (2015) Down-regulation of a wheat alkaline/neutral invertase correlates with reduced host susceptibility to wheat stripe rust caused by *Puccinia striiformis*. *J. Exp. Bot.* **66**, 7325–7338.

Liu, D., Xin, M., Zhou, X., Wang, C., Zhang, Y. and Qin, Z. (2017a) Expression and functional analysis of the transcription factor-encoding gene CsERF004 in cucumber during *Pseudoperonospora cubensis* and *Corynespora cassiicola* infection. *BMC Plant Biol.* **17**, 96.

Liu, Q., Ning, Y., Zhang, Y., Yu, N., Zhao, C., Zhan, X., Wu, W. *et al*. (2017b) OsCUL3a negatively regulates cell death and immunity by degrading OsNPR1 in rice. *Plant Cell*, **29**, 345–359.

Liu, Z., Li, X., Sun, F., Zhou, T. and Zhou, Y. (2017c) Overexpression of OsCIPK30 enhances plant tolerance to rice stripe virus. *Front. Microbiol.* **8**, 2322.

Liu, M., Shi, Z., Zhang, X., Wang, M., Zhang, L., Zheng, K., Liu, J. *et al*. (2019) Inducible overexpression of Ideal Plant Architecture1 improves both yield and disease resistance in rice. *Nat. Plants*, **5**, 389–400.

Liu, M., Zhang, Q., Wang, C., Meng, T., Wang, L., Chen, C. and Ren, Z. (2020a) CsWRKY10 mediates defence responses to *Botrytis cinerea* infection in *Cucumis sativus*. *Plant Sci.* **300**, 110640.

Liu, X., Yu, Y., Liu, Q., Deng, S., Jin, X., Yin, Y., Guo, J. *et al*. (2020b) A Na_2CO_3-responsive chitinase gene from *Leymus chinensis* improve pathogen resistance and saline-alkali stress tolerance in transgenic tobacco and maize. *Front. Plant Sci.* **11**, 504.

Liu, H., Li, Y., Hu, Y., Yang, Y., Zhang, W., He, M., Li, X. *et al*. (2021a) EDS1-interacting J protein 1 is an essential negative regulator of plant innate immunity in Arabidopsis. *Plant Cell*, **33**, 153–171.

Liu, M., Zhang, Z., Xu, Z., Wang, L., Chen, C. and Ren, Z. (2021b) Overexpression of SlMYB75 enhances resistance to *Botrytis cinerea* and prolongs fruit storage life in tomato. *Plant Cell Rep.* **40**, 43–58.

Long, L., Xu, F.C., Zhao, J.R., Li, B., Xu, L. and Gao, W. (2020) GbMPK3 overexpression increases cotton sensitivity to *Verticillium dahliae* by regulating salicylic acid signaling. *Plant Sci.* **292**, 110374.

Long, Q., Du, M., Long, J., Xie, Y., Zhang, J., Xu, L., He, Y. *et al*. (2021) Transcription factor WRKY22 regulates canker susceptibility in sweet orange (*Citrus sinensis* Osbeck) by enhancing cell enlargement and CsLOB1 expression. *Hortic. Res.* **8**, 50.

Louis, J., Leung, Q., Pegadaraju, V., Reese, J. and Shah, J. (2010) PAD4-dependent antibiosis contributes to the ssi2-conferred hyper-resistance to the green peach aphid. *Mol. Plant Microbe Interact.* **23**, 618–627.

Low, Y.C., Lawton, M.A. and Di, R. (2020) Validation of barley 2OGO gene as a functional orthologue of Arabidopsis DMR6 gene in *Fusarium* head blight susceptibility. *Sci. Rep.* **10**, 9935.

Lu, F., Wang, H., Wang, S., Jiang, W., Shan, C., Li, B., Yang, J. *et al*. (2015) Enhancement of innate immune system in monocot rice by transferring the dicotyledonous elongation factor Tu receptor EFR. *J. Integr. Plant Biol.* **57**, 641–652.

Lu, W., Deng, F., Jia, J., Chen, X., Li, J., Wen, Q., Li, T. *et al*. (2020) The *Arabidopsis thaliana* gene AtERF019 negatively regulates plant resistance to *Phytophthora parasitica* by suppressing PAMP-triggered immunity. *Mol. Plant Pathol.* **21**, 1179–1193.

Lumbreras, V., Vilela, B., Irar, S., Sole, M., Capellades, M., Valls, M., Coca, M. *et al*. (2010) MAPK phosphatase MKP2 mediates disease responses in Arabidopsis and functionally interacts with MPK3 and MPK6. *Plant J.* **63**, 1017–1030.

Ma, Y., Zhao, Y., Shangguan, X., Shi, S., Zeng, Y., Wu, Y., Chen, R. *et al*. (2017) Overexpression of OsRRK1 changes leaf morphology and defense to insect in rice. *Front. Plant Sci.* **8**, 1783.

Mackey, D., Belkhadir, Y., Alonso, J.M., Ecker, J.R. and Dangl, J.L. (2003) Arabidopsis RIN4 is a target of the type III virulence effector AvrRpt2 and modulates RPS2-mediated resistance. *Cell*, **112**, 379–389.

Maekawa, T., Kracher, B., Vernaldi, S., Loren, V., van Themaat, E. and Schulze-Lefert, P. (2012) Conservation of NLR-triggered immunity across plant lineages. *Proc. Natl. Acad. Sci. USA*, **109**, 20119–20123.

Malzahn, A., Lowder, L. and Qi, Y. (2017) Plant genome editing with TALEN and CRISPR. *Cell Biosci.* **7**, 21.

Manabe, Y., Nafisi, M., Verhertbruggen, Y., Orfila, C., Gille, S., Rautengarten, C., Cherk, C. *et al*. (2011) Loss-of-function mutation of REDUCED WALL ACETYLATION2 in Arabidopsis leads to reduced cell wall acetylation and increased resistance to *Botrytis cinerea*. *Plant Physiol.* **155**, 1068–1078.

Manosalva, P.M., Bruce, M. and Leach, J.E. (2011) Rice 14-3-3 protein (GF14e) negatively affects cell death and disease resistance. *Plant J.* **68**, 777–787.

March-Diaz, R., Garcia-Dominguez, M., Lozano-Juste, J., Leon, J., Florencio, F.J. and Reyes, J.C. (2008) Histone H2A.Z and homologues of components of the SWR1 complex are required to control immunity in Arabidopsis. *Plant J.* **53**, 475–487.

Marino, D., Froidure, S., Canonne, J., Ben Khaled, S., Khafif, M., Pouzet, C., Jauneau, A. *et al*. (2013) Arabidopsis ubiquitin ligase MIEL1 mediates degradation of the transcription factor MYB30 weakening plant defence. *Nat. Commun.* **4**, 1476.

Martin, G.B., Bogdanove, A.J. and Sessa, G. (2003) Understanding the functions of plant disease resistance proteins. *Annu. Rev. Plant Biol.* **54**, 23–61.

McLaughlin, J.E., Darwish, N.I., Garcia-Sanchez, J., Tyagi, N., Trick, H.N., McCormick, S., Dill-Macky, R. *et al*. (2021) A lipid transfer protein has antifungal and antioxidant activity and suppresses *Fusarium* head blight disease and DON accumulation in transgenic wheat. *Phytopathology*, **111**, 671–683.

McLoughlin, A.G., Wytinck, N., Walker, P.L., Girard, I.J., Rashid, K.Y., de Kievit, T., Fernando, W.G.D. *et al*. (2018) Identification and application of exogenous dsRNA confers plant protection against *Sclerotinia sclerotiorum* and *Botrytis cinerea*. *Sci. Rep.* **8**, 7320.

McNeece, B.T., Pant, S.R., Sharma, K., Niruala, P., Lawrence, G.W. and Klink, V.P. (2017) A *Glycine max* homolog of NON-RACE SPECIFIC DISEASE RESISTANCE 1 (NDR1) alters defense gene expression while functioning during a resistance response to different root pathogens in different genetic backgrounds. *Plant Physiol. Biochem.* **114**, 60–71.

Meng, X., Yu, Y., Zhao, J., Cui, N., Song, T., Yang, Y. and Fan, H. (2018) The two translationally controlled tumor protein genes, CsTCTP1 and CsTCTP2, are negative modulators in the *Cucumis sativus* defense response to *Sphaerotheca fuliginea*. *Front. Plant Sci.* **9**, 544.

Mewis, I., Appel, H.M., Hom, A., Raina, R. and Schultz, J.C. (2005) Major signaling pathways modulate Arabidopsis glucosinolate accumulation and response to both phloem-feeding and chewing insects. *Plant Physiol.* **138**, 1149–1162.

Miao Liu, J., Mei, Q., Yun Xue, C., Yuan Wang, Z., Pin Li, D., Xin Zhang, Y. and Hu Xuan, Y. (2021) Mutation of G-protein gamma subunit DEP1 increases planting density and resistance to sheath blight disease in rice. *Plant Biotechnol. J.* **19**, 418–420.

Mishra, R., Mohanty, J.N., Chand, S.K. and Joshi, R.K. (2018) Can-miRn37a mediated suppression of ethylene response factors enhances the resistance of chilli against anthracnose pathogen *Colletotrichum truncatum* L. *Plant Sci.* **267**, 135–147.

Mitre, L.K., Teixeira-Silva, N.S., Rybak, K., Magalhaes, D.M., de Souza-Neto, R.R., Robatzek, S., Zipfel, C. *et al*. (2021) The Arabidopsis immune receptor

EFR increases resistance to the bacterial pathogens *Xanthomonas* and *Xylella* in transgenic sweet orange. *Plant Biotechnol. J.* **19**, 1294–1296.

Mo, S., Zhang, Y., Wang, X., Yang, J., Sun, Z., Zhang, D., Chen, B. *et al*. (2021) Cotton GhSSI2 isoforms from the stearoyl acyl carrier protein fatty acid desaturase family regulate *Verticillium* wilt resistance. *Mol. Plant Pathol.* **22**, 1041–1056.

Moniruzzaman, M., Zhong, Y., Yan, H., Yuanda, L., Jiang, B. and Zhong, G. (2020) Exploration of susceptible genes with clustered regularly interspaced short palindromic repeats–tissue-specific knockout (CRISPR-TSKO) to enhance host resistance. *Crit. Rev. Plant Sci.* **39**, 387–417.

Moradpour, M. and Abdulah, S.N.A. (2020) CRISPR/dCas9 platforms in plants: strategies and applications beyond genome editing. *Plant Biotechnol. J.* **18**, 32–44.

Mou, S., Liu, Z., Gao, F., Yang, S., Su, M., Shen, L., Wu, Y. *et al*. (2017) CaHDZ27, a homeodomain-leucine zipper I protein, positively regulates the resistance to *Ralstonia solanacearum* infection in pepper. *Mol. Plant Microbe Interact.* **30**, 960–973.

Moury, B., Lebaron, C., Szadkowski, M., Ben Khalifa, M., Girardot, G., Bolou Bi, B.A., Kone, D. *et al*. (2020) Knock-out mutation of eukaryotic initiation factor 4E2 (eIF4E2) confers resistance to pepper veinal mottle virus in tomato. *Virology*, **539**, 11–17.

Mukhtar, M.S., Carvunis, A.R., Dreze, M., Epple, P., Steinbrenner, J., Moore, J., Tasan, M. *et al*. (2011) Independently evolved virulence effectors converge onto hubs in a plant immune system network. *Science*, **333**, 596–601.

Nalam, V.J., Keeretaweep, J., Sarowar, S. and Shah, J. (2012) Root-derived oxylipins promote green peach aphid performance on Arabidopsis foliage. *Plant Cell*, **24**, 1643–1653.

Narusaka, M., Shirasu, K., Noutoshi, Y., Kubo, Y., Shiraishi, T., Iwabuchi, M. and Narusaka, Y. (2009) RRS1 and RPS4 provide a dual resistance-gene system against fungal and bacterial pathogens. *Plant J.* **60**, 218–226.

Narusaka, M., Kubo, Y., Hatakeyama, K., Imamura, J., Ezura, H., Nanasato, Y., Tabei, Y. *et al*. (2013) Interfamily transfer of dual NB-LRR genes confers resistance to multiple pathogens. *PLoS ONE*, **8**, e55954.

Neubauer, M., Serrano, I., Rodibaugh, N., Bhandari, D.D., Bautor, J., Parker, J.E. and Innes, R.W. (2020) Arabidopsis EDR1 protein kinase regulates the association of EDS1 and PAD4 to inhibit cell death. *Mol. Plant Microbe Interact.* **33**, 693–703.

Ngaki, M.N., Sahoo, D.K., Wang, B. and Bhattacharyya, M.K. (2021) Overexpression of a plasma membrane protein generated broad-spectrum immunity in soybean. *Plant Biotechnol. J.* **19**, 502–516.

Ngou, B.P.M., Ahn, H.K., Ding, P. and Jones, J.D.G. (2021) Mutual potentiation of plant immunity by cell-surface and intracellular receptors. *Nature*, **592**, 110–115.

Nguyen, P.D., Pike, S., Wang, J., Nepal Poudel, A., Heinz, R., Schultz, J.C., Koo, A.J. *et al*. (2016) The Arabidopsis immune regulator SRFR1 dampens defences against herbivory by *Spodoptera exigua* and parasitism by *Heterodera schachtii*. *Mol. Plant Pathol.* **17**, 588–600.

Nguyen, Q.M., Iswanto, A.B.B., Son, G.H. and Kim, S.H. (2021) Recent advances in effector-triggered immunity in plants: new pieces in the puzzle create a different paradigm. *Int. J. Mol. Sci.* **22**, 4709.

Nishida, K., Arazoe, T., Yachie, N., Banno, S., Kakimoto, M., Tabata, M., Mochizuki, M. *et al*. (2016) Targeted nucleotide editing using hybrid prokaryotic and vertebrate adaptive immune systems. *Science*, **353**, aaf8729.

Onohata, T. and Gomi, K. (2020) Overexpression of jasmonate-responsive OsbHLH034 in rice results in the induction of bacterial blight resistance via an increase in lignin biosynthesis. *Plant Cell Rep.* **39**, 1175–1184.

Pan, Q., Cui, B., Deng, F., Quan, J., Loake, G.J. and Shan, W. (2016) RTP1 encodes a novel endoplasmic reticulum (ER)-localized protein in Arabidopsis and negatively regulates resistance against biotrophic pathogens. *New Phytol.* **209**, 1641–1654.

Paparella, C., Savatin, D.V., Marti, L., De Lorenzo, G. and Ferrari, S. (2014) The Arabidopsis LYSIN MOTIF-CONTAINING RECEPTOR-LIKE KINASE3 regulates the cross talk between immunity and abscisic acid responses. *Plant Physiol.* **165**, 262–276.

Parajuli, S., Huo, H., Gmitter, F.G., Jr., Duan, Y., Luo, F. and Deng, Z. (2022) Editing the CsDMR6 gene in citrus results in resistance to the bacterial disease citrus canker. *Hortic. Res.* **9**, uhac082.

Pasin, F., Shan, H., Garcia, B., Muller, M., San Leon, D., Ludman, M., Fresno, D.H. *et al*. (2020) Abscisic acid connects phytohormone signaling with RNA metabolic pathways and promotes an antiviral response that is evaded by a self-controlled RNA virus. *Plant Commun.* **1**, 100099.

Paudel, B., Zhuang, Y., Galla, A., Dahal, S., Qiu, Y., Ma, A., Raihan, T. *et al*. (2020) WFhb1-1 plays an important role in resistance against *Fusarium* head blight in wheat. *Sci. Rep.* **10**, 7794.

Peng, Q., Su, Y., Ling, H., Ahmad, W., Gao, S., Guo, J., Que, Y. *et al*. (2017) A sugarcane pathogenesis-related protein, ScPR10, plays a positive role in defense responses under *Sporisorium scitamineum*, SrMV, SA, and MeJA stresses. *Plant Cell Rep.* **36**, 1427–1440.

Peris-Peris, C., Serra-Cardona, A., Sanchez-Sanuy, F., Campo, S., Arino, J. and San Segundo, B. (2017) Two NRAMP6 isoforms function as iron and manganese transporters and contribute to disease resistance in rice. *Mol. Plant Microbe Interact.* **30**, 385–398.

Pessina, S., Angeli, D., Martens, S., Visser, R.G., Bai, Y., Salamini, F., Velasco, R. *et al*. (2016) The knock-down of the expression of MdMLO19 reduces susceptibility to powdery mildew (*Podosphaera leucotricha*) in apple (*Malus domestica*). *Plant Biotechnol. J.* **14**, 2033–2044.

Petolino, J.F. (2015) Genome editing in plants via designed zinc finger nucleases. *In Vitro Cell Dev. Biol. Plant*, **51**, 1–8.

Pfeilmeier, S., George, J., Morel, A., Roy, S., Smoker, M., Stransfeld, L., Downie, J.A. *et al*. (2019) Expression of the *Arabidopsis thaliana* immune receptor EFR in *Medicago truncatula* reduces infection by a root pathogenic bacterium, but not nitrogen-fixing rhizobial symbiosis. *Plant Biotechnol. J.* **17**, 569–579.

Piazza, S., Campa, M., Pompili, V., Costa, L.D., Salvagnin, U., Nekrasov, V., Zipfel, C. *et al*. (2021) The Arabidopsis pattern recognition receptor EFR enhances fire blight resistance in apple. *Hortic. Res.* **8**, 204.

Pramanik, D., Shelake, R.M., Park, J., Kim, M.J., Hwang, I., Park, Y. and Kim, J.Y. (2021) CRISPR/Cas9-mediated generation of pathogen-resistant tomato against tomato yellow leaf curl virus and powdery mildew. *Int. J. Mol. Sci.* **22**, 1878.

Probsting, M., Schenke, D., Hossain, R., Hader, C., Thurau, T., Wighardt, L., Schuster, A. *et al*. (2020) Loss of function of CRT1a (calreticulin) reduces plant susceptibility to *Verticillium longisporum* in both *Arabidopsis thaliana* and oilseed rape (*Brassica napus*). *Plant Biotechnol. J.* **18**, 2328–2344.

Pruitt, R.N., Schwessinger, B., Joe, A., Thomas, N., Liu, F., Albert, M., Robinson, M.R. *et al*. (2015) The rice immune receptor XA21 recognizes a tyrosine-sulfated protein from a Gram-negative bacterium. *Sci. Adv.* **1**, e1500245.

Qi, D., Dubiella, U., Kim, S.H., Sloss, D.I., Dowen, R.H., Dixon, J.E. and Innes, R.W. (2014) Recognition of the protein kinase AVRPPHB SUSCEPTIBLE1 by the disease resistance protein RESISTANCE TO PSEUDOMONAS SYRINGAE5 is dependent on s-acylation and an exposed loop in AVRPPHB SUSCEPTIBLE1. *Plant Physiol.* **164**, 340–351.

Qi, M., Zheng, W., Zhao, X., Hohenstein, J.D., Kandel, Y., O'Conner, S., Wang, Y. *et al*. (2019) QQS orphan gene and its interactor NF-YC4 reduce susceptibility to pathogens and pests. *Plant Biotechnol. J.* **17**, 252–263.

Qian, C., Cui, C., Wang, X., Zhou, C., Hu, P., Li, M., Li, R. *et al*. (2017) Molecular characterisation of the broad-spectrum resistance to powdery mildew conferred by the Stpk-V gene from the wild species *Haynaldia villosa*. *Plant Biol.* **19**, 875–885.

Qiao, L., Zheng, L., Sheng, C., Zhao, H., Jin, H. and Niu, D. (2020) Rice siR109944 suppresses plant immunity to sheath blight and impacts multiple agronomic traits by affecting auxin homeostasis. *Plant J.* **102**, 948–964.

Raffaele, S. and Kamoun, S. (2012) Genome evolution in filamentous plant pathogens: why bigger can be better. *Nat. Rev. Microbiol.* **10**, 417–430.

Ramirez, V., Agorio, A., Coego, A., Garcia-Andrade, J., Hernandez, M.J., Balaguer, B., Ouwerkerk, P.B. *et al*. (2011) MYB46 modulates disease susceptibility to *Botrytis cinerea* in Arabidopsis. *Plant Physiol.* **155**, 1920–1935.

Rayapuram, C., Jensen, M.K., Maiser, F., Shanir, J.V., Hornshoj, H., Rung, J.H., Gregersen, P.L. *et al*. (2012) Regulation of basal resistance by a powdery mildew-induced cysteine-rich receptor-like protein kinase in barley. *Mol. Plant Pathol.* **13**, 135–147.

Ronald, P.C., Albano, B., Tabien, R., Abenes, L., Wu, K.S., McCouch, S. and Tanksley, S.D. (1992) Genetic and physical analysis of the rice bacterial blight disease resistance locus, Xa21. *Mol. Gen. Genet.* **236**, 113–120.

Roux, M.E., Rasmussen, M.W., Palma, K., Lolle, S., Regue, A.M., Bethke, G., Glazebrook, J. *et al*. (2015) The mRNA decay factor PAT1 functions in a pathway including MAP kinase 4 and immune receptor SUMM2. *EMBO J.* **34**, 593–608.

Sauer, N.J., Mozoruk, J., Miller, R.B., Warburg, Z.J., Walker, K.A., Beetham, P.R., Schopke, C.R. *et al*. (2016) Oligonucleotide-directed mutagenesis for precision gene editing. *Plant Biotechnol. J.* **14**, 496–502.

Schepetilnikov, M., Kobayashi, K., Geldreich, A., Caranta, C., Robaglia, C., Keller, M. and Ryabova, L.A. (2011) Viral factor TAV recruits TOR/S6K1 signalling to activate reinitiation after long ORF translation. *EMBO J.* **30**, 1343–1356.

Schoonbeek, H.J., Wang, H.H., Stefanato, F.L., Craze, M., Bowden, S., Wallington, E., Zipfel, C. *et al*. (2015) Arabidopsis EF-Tu receptor enhances bacterial disease resistance in transgenic wheat. *New Phytol.* **206**, 606–613.

Segretin, M.E., Pais, M., Franceschetti, M., Chaparro-Garcia, A., Bos, J.I., Banfield, M.J. and Kamoun, S. (2014) Single amino acid mutations in the potato immune receptor R3a expand response to *Phytophthora* effectors. *Mol. Plant Microbe Interact.* **27**, 624–637.

Sekine, K.T., Nandi, A., Ishihara, T., Hase, S., Ikegami, M., Shah, J. and Takahashi, H. (2004) Enhanced resistance to cucumber mosaic virus in the *Arabidopsis thaliana* ssi2 mutant is mediated via an SA-independent mechanism. *Mol. Plant Microbe Interact.* **17**, 623–632.

Selma, S., Bernabe-Orts, J.M., Vazquez-Vilar, M., Diego-Martin, B., Ajenjo, M., Garcia-Carpintero, V., Granell, A. *et al*. (2019) Strong gene activation in plants with genome-wide specificity using a new orthogonal CRISPR/Cas9-based programmable transcriptional activator. *Plant Biotechnol. J.* **17**, 1703–1705.

Sendin, L.N., Orce, I.G., Gomez, R.L., Enrique, R., Grellet Bournonville, C.F., Noguera, A.S., Vojnov, A.A. *et al*. (2017) Inducible expression of Bs2 R gene from *Capsicum chacoense* in sweet orange (*Citrus sinensis* L. Osbeck) confers enhanced resistance to citrus canker disease. *Plant Mol. Biol.* **93**, 607–621.

Shen, X., Liu, H., Yuan, B., Li, X., Xu, C. and Wang, S. (2011) OsEDR1 negatively regulates rice bacterial resistance via activation of ethylene biosynthesis. *Plant Cell Environ.* **34**, 179–191.

Shim, J.S., Jung, C., Lee, S., Min, K., Lee, Y.W., Choi, Y., Lee, J.S. *et al*. (2013) AtMYB44 regulates WRKY70 expression and modulates antagonistic interaction between salicylic acid and jasmonic acid signaling. *Plant J.* **73**, 483–495.

Shimono, M., Koga, H., Akagi, A., Hayashi, N., Goto, S., Sawada, M., Kurihara, T. *et al*. (2012) Rice WRKY45 plays important roles in fungal and bacterial disease resistance. *Mol. Plant Pathol.* **13**, 83–94.

Shinya, T., Motoyama, N., Ikeda, A., Wada, M., Kamiya, K., Hayafune, M., Kaku, H. *et al*. (2012) Functional characterization of CEBiP and CERK1 homologs in Arabidopsis and rice reveals the presence of different chitin receptor systems in plants. *Plant Cell Physiol.* **53**, 1696–1706.

Shmakov, S., Smargon, A., Scott, D., Cox, D., Pyzocha, N., Yan, W., Abudayyeh, O.O. *et al*. (2017) Diversity and evolution of class 2 CRISPR-Cas systems. *Nat. Rev. Microbiol.* **15**, 169–182.

Son, S., An, H.K., Seol, Y.J., Park, S.R. and Im, J.H. (2020) Rice transcription factor WRKY114 directly regulates the expression of OsPR1a and chitinase to enhance resistance against *Xanthomonas oryzae* pv. *oryzae*. *Biochem. Biophys. Res. Commun.* **533**, 1262–1268.

Son, G.H., Moon, J., Shelake, R.M., Vuong, U.T., Ingle, R.A., Gassmann, W., Kim, J.Y. *et al*. (2021) Conserved opposite functions in plant resistance to biotrophic and necrotrophic pathogens of the immune regulator SRFR1. *Int. J. Mol. Sci.* **22**, 6427.

Song, W.Y., Wang, G.L., Chen, L.L., Kim, H.S., Pi, L.Y., Holsten, T., Gardner, J. *et al*. (1995) A receptor kinase-like protein encoded by the rice disease resistance gene, Xa21. *Science*, **270**, 1804–1806.

Song, X.S., Gu, K.X., Duan, X.X., Xiao, X.M., Hou, Y.P., Duan, Y.B., Wang, J.X. *et al*. (2018a) Secondary amplification of siRNA machinery limits the application of spray-induced gene silencing. *Mol. Plant Pathol.* **19**, 2543–2560.

Song, Y., Liu, L., Wang, Y., Valkenburg, D.J., Zhang, X., Zhu, L. and Thomma, B. (2018b) Transfer of tomato immune receptor Ve1 confers Ave1-dependent *Verticillium* resistance in tobacco and cotton. *Plant Biotechnol. J.* **16**, 638–648.

Spada, M., Pugliesi, C., Fambrini, M. and Pecchia, S. (2021) Silencing of the Slt2-type MAP kinase Bmp3 in *Botrytis cinerea* by application of exogenous dsRNA affects fungal growth and virulence on *Lactuca sativa*. *Int. J. Mol. Sci.* **22**, 5362.

Stergiopoulos, I. and de Wit, P.J. (2009) Fungal effector proteins. *Annu. Rev. Phytopathol.* **47**, 233–263.

Stokes, T.L., Kunkel, B.N. and Richards, E.J. (2002) Epigenetic variation in Arabidopsis disease resistance. *Genes Dev.* **16**, 171–182.

Su, J., Spears, B.J., Kim, S.H. and Gassmann, W. (2018) Constant vigilance: plant functions guarded by resistance proteins. *Plant J.* **93**, 637–650.

Su, Z., Bernardo, A., Tian, B., Chen, H., Wang, S., Ma, H., Cai, S. *et al*. (2019) A deletion mutation in TaHRC confers Fhb1 resistance to *Fusarium* head blight in wheat. *Nat. Genet.* **51**, 1099–1105.

Sun, K., Wolters, A.M., Loonen, A.E., Huibers, R.P., van der Vlugt, R., Goverse, A., Jacobsen, E. *et al*. (2016a) Down-regulation of Arabidopsis DND1 orthologs in potato and tomato leads to broad-spectrum resistance to late blight and powdery mildew. *Transgenic Res.* **25**, 123–138.

Sun, K., Wolters, A.M., Vossen, J.H., Rouwet, M.E., Loonen, A.E., Jacobsen, E., Visser, R.G. *et al*. (2016b) Silencing of six susceptibility genes results in potato late blight resistance. *Transgenic Res.* **25**, 731–742.

Sun, J., Huang, G., Fan, F., Wang, S., Zhang, Y., Han, Y., Zou, Y. *et al*. (2017) Comparative study of Arabidopsis PBS1 and a wheat PBS1 homolog helps understand the mechanism of PBS1 functioning in innate immunity. *Sci. Rep.* **7**, 5487.

Sun, X., Huo, L., Jia, X., Che, R., Gong, X., Wang, P. and Ma, F. (2018) Overexpression of MdATG18a in apple improves resistance to *Diplocarpon mali* infection by enhancing antioxidant activity and salicylic acid levels. *Hortic. Res.* **5**, 57.

Sun, Q., Li, T.Y., Li, D.D., Wang, Z.Y., Li, S., Li, D.P., Han, X. *et al*. (2019) Overexpression of Loose Plant Architecture 1 increases planting density and resistance to sheath blight disease via activation of PIN-FORMED 1a in rice. *Plant Biotechnol. J.* **17**, 855–857.

Sun, Y., Wang, P., Abouzaid, M., Zhou, H., Liu, H., Yang, P., Lin, Y. *et al*. (2020) Nanomaterial-wrapped dsCYP15C1, a potential RNAi-based strategy for pest control against Chilo suppressalis. *Pest Manag. Sci.* **76**, 2483–2489.

Sun, Y., Zhong, M., Li, Y., Zhang, R., Su, L., Xia, G. and Wang, H. (2021) GhADF6-mediated actin reorganization is associated with defence against *Verticillium dahliae* infection in cotton. *Mol. Plant Pathol.* **22**, 1656–1667.

Takken, F.L., Albrecht, M. and Tameling, W.I. (2006) Resistance proteins: molecular switches of plant defence. *Curr. Opin. Plant Biol.* **9**, 383–390.

Tampakaki, A.P., Skandalis, N., Gazi, A.D., Bastaki, M.N., Sarris, P.F., Charova, S.N., Kokkinidis, M. *et al*. (2010) Playing the "Harp": evolution of our understanding of hrp/hrc genes. *Annu. Rev. Phytopathol.* **48**, 347–370.

Tang, D., Ade, J., Frye, C.A. and Innes, R.W. (2005) Regulation of plant defense responses in Arabidopsis by EDR2, a PH and START domain-containing protein. *Plant J.* **44**, 245–257.

Tang, C., Deng, L., Chang, D., Chen, S., Wang, X. and Kang, Z. (2015) TaADF3, an actin-depolymerizing factor, negatively modulates wheat resistance against *Puccinia striiformis*. *Front. Plant Sci.* **6**, 1214.

Terns, M.P. and Terns, R.M. (2011) CRISPR-based adaptive immune systems. *Curr. Opin. Microbiol.* **14**, 321–327.

Tezuka, D., Kawamata, A., Kato, H., Saburi, W., Mori, H. and Imai, R. (2019) The rice ethylene response factor OsERF83 positively regulates disease resistance to *Magnaporthe oryzae*. *Plant Physiol. Biochem.* **135**, 263–271.

Thomazella, D.P.T., Seong, K., Mackelprang, R., Dahlbeck, D., Geng, Y., Gill, U.S., Qi, T. *et al*. (2021) Loss of function of a DMR6 ortholog in tomato confers broad-spectrum disease resistance. *Proc. Natl. Acad. Sci. USA*, **118**, e2026152118.

Tian, Z., He, Q., Wang, H., Liu, Y., Zhang, Y., Shao, F. and Xie, C. (2015) The potato ERF transcription factor StERF3 negatively regulates resistance to *Phytophthora infestans* and salt tolerance in potato. *Plant Cell Physiol.* **56**, 992–1005.

Tong, M., Kotur, T., Liang, W., Vogelmann, K., Kleine, T., Leister, D., Brieske, C. *et al*. (2017) E3 ligase SAUL1 serves as a positive regulator of PAMP-triggered immunity and its homeostasis is monitored by immune receptor SOC3. *New Phytol.* **215**, 1516–1532.

Torres, M.A., Jones, J.D. and Dangl, J.L. (2006) Reactive oxygen species signaling in response to pathogens. *Plant Physiol.* **141**, 373–378.

Tran, P.T., Widyasari, K., Seo, J.K. and Kim, K.H. (2018) Isolation and validation of a candidate Rsv3 gene from a soybean genotype that confers strain-specific resistance to soybean mosaic virus. *Virology*, **513**, 153–159.

Trda, L., Fernandez, O., Boutrot, F., Heloir, M.C., Kelloniemi, J., Daire, X., Adrian, M. *et al*. (2014) The grapevine flagellin receptor VvFLS2 differentially recognizes flagellin-derived epitopes from the endophytic growth-promoting bacterium *Burkholderia phytofirmans* and plant pathogenic bacteria. *New Phytol.* **201**, 1371–1384.

Tripathi, J.N., Lorenzen, J., Bahar, O., Ronald, P. and Tripathi, L. (2014) Transgenic expression of the rice Xa21 pattern-recognition receptor in banana (*Musa* sp.) confers resistance to *Xanthomonas campestris* pv. *musacearum*. *Plant Biotechnol. J.* **12**, 663–673.

Tripathi, J.N., Ntui, V.O., Shah, T. and Tripathi, L. (2021) CRISPR/Cas9-mediated editing of DMR6 orthologue in banana (*Musa* spp.) confers enhanced resistance to bacterial disease. *Plant Biotechnol. J.* **19**, 1291–1293.

Truman, W., Sreekanta, S., Lu, Y., Bethke, G., Tsuda, K., Katagiri, F. and Glazebrook, J. (2013) The CALMODULIN-BINDING PROTEIN60 family includes both negative and positive regulators of plant immunity. *Plant Physiol.* **163**, 1741–1751.

Uji, Y., Taniguchi, S., Tamaoki, D., Shishido, H., Akimitsu, K. and Gomi, K. (2016) Overexpression of OsMYC2 results in the up-regulation of early JA-rresponsive genes and bacterial blight resistance in rice. *Plant Cell Physiol.* **57**, 1814–1827.

Van Damme, M., Andel, A., Huibers, R.P., Panstruga, R., Weisbeek, P.J. and Van den Ackerveken, G. (2005) Identification of Arabidopsis loci required for susceptibility to the downy mildew pathogen *Hyaloperonospora parasitica*. *Mol. Plant Microbe Interact.* **18**, 583–592.

Venkatakrishnan, S., Mackey, D. and Meier, I. (2013) Functional investigation of the plant-specific long coiled-coil proteins PAMP-INDUCED COILED-COIL (PICC) and PICC-LIKE (PICL) in *Arabidopsis thaliana*. *PLoS ONE*, **8**, e57283.

Vi, T.X.T., Nguyen, T.N.L., Pham, T.T.N., Nguyen, H.Q., Nguyen, T.H.Y., Tu, Q.T., Le, V.S. *et al*. (2019) Overexpression of the ZmDEF1 gene increases the resistance to weevil larvae in transgenic maize seeds. *Mol. Biol. Rep.* **46**, 2177–2185.

Vo, K.T.X., Kim, C.Y., Hoang, T.V., Lee, S.K., Shirsekar, G., Seo, Y.S., Lee, S.W. *et al*. (2017) OsWRKY67 plays a positive role in basal and XA21-mediated resistance in rice. *Front. Plant Sci.* **8**, 2220.

Vogel, J.P., Raab, T.K., Schiff, C. and Somerville, S.C. (2002) PMR6, a pectate lyase-like gene required for powdery mildew susceptibility in Arabidopsis. *Plant Cell*, **14**, 2095–2106.

de Vries, S.C. (2015) Plant receptor complexes. *Sci. Signal.* **8**, fs15.

Vu, T.V., Sivankalyani, V., Kim, E.J., Doan, D.T.H., Tran, M.T., Kim, J., Sung, Y.W. *et al*. (2020) Highly efficient homology-directed repair using CRISPR/Cpf1-geminiviral replicon in tomato. *Plant Biotechnol. J.* **18**, 2133–2143.

Vu, T.V., Doan, D.T.H., Tran, M.T., Sung, Y.W., Song, Y.J. and Kim, J.Y. (2021) Improvement of the LbCas12a-crRNA system for efficient gene targeting in tomato. *Front. Plant Sci.* **12**, 722552.

Wang, G.L., Song, W.Y., Ruan, D.L., Sideris, S. and Ronald, P.C. (1996) The cloned gene, Xa21, confers resistance to multiple *Xanthomonas oryzae* pv. *oryzae* isolates in transgenic plants. *Mol. Plant Microbe Interact.* **9**, 850–855.

Wang, Y., Nishimura, M.T., Zhao, T. and Tang, D. (2011) ATG2, an autophagy-related protein, negatively affects powdery mildew resistance and mildew-induced cell death in Arabidopsis. *Plant J.* **68**, 74–87.

Wang, Y., Dang, F., Liu, Z., Wang, X., Eulgem, T., Lai, Y., Yu, L. *et al*. (2013) CaWRKY58, encoding a group I WRKY transcription factor of *Capsicum annuum*, negatively regulates resistance to *Ralstonia solanacearum* infection. *Mol. Plant Pathol.* **14**, 131–144.

Wang, Y., Bouwmeester, K., Beseh, P., Shan, W. and Govers, F. (2014) Phenotypic analyses of Arabidopsis T-DNA insertion lines and expression profiling reveal that multiple L-type lectin receptor kinases are involved in plant immunity. *Mol. Plant Microbe Interact.* **27**, 1390–1402.

Wang, F., Lin, R., Feng, J., Chen, W., Qiu, D. and Xu, S. (2015) TaNAC1 acts as a negative regulator of stripe rust resistance in wheat, enhances susceptibility to *Pseudomonas syringae*, and promotes lateral root development in transgenic *Arabidopsis thaliana*. *Front. Plant Sci.* **6**, 108.

Wang, M., Weiberg, A., Lin, F.M., Thomma, B.P., Huang, H.D. and Jin, H. (2016) Bidirectional cross-kingdom RNAi and fungal uptake of external RNAs confer plant protection. *Nat. Plants*, **2**, 16151.

Wang, J., Tao, F., Tian, W., Guo, Z., Chen, X., Xu, X., Shang, H. *et al*. (2017a) The wheat WRKY transcription factors TaWRKY49 and TaWRKY62 confer differential high-temperature seedling-plant resistance to *Puccinia striiformis* f. sp. tritici. *PLoS ONE*, **12**, e0181963.

Wang, J., Yao, W., Wang, L., Ma, F., Tong, W., Wang, C., Bao, R. *et al*. (2017b) Overexpression of VpEIFP1, a novel F-box/Kelch-repeat protein from wild Chinese *Vitis pseudoreticulata*, confers higher tolerance to powdery mildew by inducing thioredoxin z proteolysis. *Plant Sci.* **263**, 142–155.

Wang, L., Xie, X., Yao, W., Wang, J., Ma, F., Wang, C., Yang, Y. *et al*. (2017c) RING-H2-type E3 gene VpRH2 from *Vitis pseudoreticulata* improves resistance to powdery mildew by interacting with VpGRP2A. *J. Exp. Bot.* **68**, 1669–1687.

Wang, S., Lei, C., Wang, J., Ma, J., Tang, S., Wang, C., Zhao, K. *et al*. (2017d) SPL33, encoding an eEF1A-like protein, negatively regulates cell death and defense responses in rice. *J. Exp. Bot.* **68**, 899–913.

Wang, Y., Sheng, L., Zhang, H., Du, X., An, C., Xia, X., Chen, F. *et al*. (2017e) CmMYB19 over-expression improves aphid tolerance in *Chrysanthemum* by promoting lignin synthesis. *Int. J. Mol. Sci.* **18**, 619.

Wang, J., Grubb, L.E., Wang, J., Liang, X., Li, L., Gao, C., Ma, M. *et al*. (2018a) A regulatory module controlling homeostasis of a plant immune kinase. *Mol. Cell*, **69**, 493–504.e6.

Wang, J., Wang, S., Hu, K., Yang, J., Xin, X., Zhou, W., Fan, J. *et al*. (2018b) The kinase OsCPK4 regulates a buffering mechanism that fine-tunes innate immunity. *Plant Physiol.* **176**, 1835–1849.

Wang, Z., Cheng, J., Fan, A., Zhao, J., Yu, Z., Li, Y., Zhang, H. *et al*. (2018c) LecRK-V, an L-type lectin receptor kinase in *Haynaldia villosa*, plays positive role in resistance to wheat powdery mildew. *Plant Biotechnol. J.* **16**, 50–62.

Wang, C., Li, C., Duan, G., Wang, Y., Zhang, Y. and Yang, J. (2019a) Overexpression of *Magnaporthe oryzae* systemic defense trigger 1 (MoSDT1) confers improved rice blast resistance in rice. *Int. J. Mol. Sci.* **20**, 4762.

Wang, L., Wang, H., He, S., Meng, F., Zhang, C., Fan, S., Wu, J. *et al*. (2019b) GmSnRK1.1, a sucrose non-fermenting-1(SNF1)-related protein kinase, promotes soybean resistance to *Phytophthora sojae*. *Front. Plant Sci.* **10**, 996.

Wang, Y., Li, Y., Rosas-Diaz, T., Caceres-Moreno, C., Lozano-Duran, R. and Macho, A.P. (2019c) The IMMUNE-ASSOCIATED NUCLEOTIDE-BINDING 9 protein is a regulator of basal immunity in *Arabidopsis thaliana*. *Mol. Plant Microbe Interact.* **32**, 65–75.

Wang, C., Guo, H., He, X., Zhang, S., Wang, J., Wang, L., Guo, D. *et al*. (2020a) Scaffold protein GhMORG1 enhances the resistance of cotton to *Fusarium oxysporum* by facilitating the MKK6-MPK4 cascade. *Plant Biotechnol. J.* **18**, 1421–1433.

Wang, J.H., Gu, K.D., Han, P.L., Yu, J.Q., Wang, C.K., Zhang, Q.Y., You, C.X. *et al*. (2020b) Apple ethylene response factor MdERF11 confers resistance to fungal pathogen *Botryosphaeria dothidea*. *Plant Sci.* **291**, 110351.

Wang, N., Song, N., Tang, Z., Wang, X., Kang, Z., Dai, L. and Wang, B. (2020c) Constitutive expression of Arabidopsis senescence associated gene 101 in *Brachypodium distachyon* enhances resistance to *Puccinia brachypodii* and *Magnaporthe oryzae*. *Plants (Basel)*, **9**, 1316.

Wang, A., Shu, X., Jing, X., Jiao, C., Chen, L., Zhang, J., Ma, L. *et al*. (2021a) Identification of rice (*Oryza sativa* L.) genes involved in sheath blight resistance via a genome-wide association study. *Plant Biotechnol. J.* **19**, 1553–1566.

Wang, J., Wang, R., Fang, H., Zhang, C., Zhang, F., Hao, Z., You, X. *et al*. (2021b) Two VOZ transcription factors link an E3 ligase and an NLR immune receptor to modulate immunity in rice. *Mol. Plant*, **14**, 253–266.

Wang, X., Chen, Q., Huang, J., Meng, X., Cui, N., Yu, Y. and Fan, H. (2021c) Nucleotide-binding leucine-rich repeat genes CsRSF1 and CsRSF2 are positive modulators in the *Cucumis sativus* defense response to *Sphaerotheca fuliginea*. *Int. J. Mol. Sci.* **22**, 3986.

Wang, Y., Feng, G., Zhang, Z., Liu, Y., Ma, Y., Wang, Y., Ma, F. *et al*. (2021d) Overexpression of Pti4, Pti5, and Pti6 in tomato promote plant defense and fruit ripening. *Plant Sci.* **302**, 110702.

Wang, Z., Chen, D., Sun, F., Guo, W., Wang, W., Li, X., Lan, Y. *et al*. (2021e) ARGONAUTE 2 increases rice susceptibility to rice black-streaked dwarf virus infection by epigenetically regulating HEXOKINASE 1 expression. *Mol. Plant Pathol.* **22**, 1029–1040.

Wei, X., Shan, T., Hong, Y., Xu, H., Liu, X. and Zhang, Z. (2017) TaPIMP2, a pathogen-induced MYB protein in wheat, contributes to host resistance to common root rot caused by *Bipolaris sorokiniana*. *Sci. Rep.* **7**, 1754.

Wei, H., Movahedi, A., Xu, C., Sun, W., Wang, X., Li, D. and Zhuge, Q. (2020) Overexpression of PtDefensin enhances resistance to Septotis populiperda in transgenic poplar. *Plant Sci.* **292**, 110379.

Wiedenheft, B., Sternberg, S.H. and Doudna, J.A. (2012) RNA-guided genetic silencing systems in bacteria and archaea. *Nature*, **482**, 331–338.

Worrall, E.A., Bravo-Cazar, A., Nilon, A.T., Fletcher, S.J., Robinson, K.E., Carr, J.P. and Mitter, N. (2019) Exogenous application of RNAi-inducing double-stranded RNA inhibits aphid-mediated transmission of a plant virus. *Front. Plant Sci.* **10**, 265.

Wu, G., Liu, S., Zhao, Y., Wang, W., Kong, Z. and Tang, D. (2015) ENHANCED DISEASE RESISTANCE4 associates with CLATHRIN HEAVY CHAIN2 and modulates plant immunity by regulating relocation of EDR1 in Arabidopsis. *Plant Cell*, **27**, 857–873.

Wu, T., Peng, C., Li, B., Wu, W., Kong, L., Li, F., Chu, Z. *et al*. (2019a) OsPGIP1-mediated resistance to bacterial leaf streak in rice is beyond responsive to the polygalacturonase of *Xanthomonas oryzae* pv. *oryzicola*. *Rice (N Y)*, **12**, 90.

Wu, Z., Li, M., Dong, O.X., Xia, S., Liang, W., Bao, Y., Wasteneys, G. *et al*. (2019b) Differential regulation of TNL-mediated immune signaling by redundant helper CNLs. *New Phytol.* **222**, 938–953.

Xiao, X., Cheng, X., Yin, K., Li, H. and Qiu, J.L. (2017) Abscisic acid negatively regulates post-penetration resistance of Arabidopsis to the biotrophic powdery mildew fungus. *Sci. China Life Sci.* **60**, 891–901.

Xie, K., Chen, J., Wang, Q. and Yang, Y. (2014) Direct phosphorylation and activation of a mitogen-activated protein kinase by a calcium-dependent protein kinase in rice. *Plant Cell*, **26**, 3077–3089.

Xing, L., Di, Z., Yang, W., Liu, J., Li, M., Wang, X., Cui, C. *et al*. (2017) Overexpression of ERF1-V from *Haynaldia villosa* can enhance the resistance of wheat to powdery mildew and increase the tolerance to salt and drought stresses. *Front. Plant Sci.* **8**, 1948.

Xiong, Y., DeFraia, C., Williams, D., Zhang, X. and Mou, Z. (2009) Characterization of Arabidopsis 6-phosphogluconolactonase T-DNA insertion mutants reveals an essential role for the oxidative section of the plastidic pentose phosphate pathway in plant growth and development. *Plant Cell Physiol.* **50**, 1277–1291.

Xu, G., Yuan, M., Ai, C., Liu, L., Zhuang, E., Karapetyan, S., Wang, S. *et al*. (2017) uORF-mediated translation allows engineered plant disease resistance without fitness costs. *Nature*, **545**, 491–494.

Xu, W., Ma, F., Li, R., Zhou, Q., Yao, W., Jiao, Y., Zhang, C. *et al*. (2019) VpSTS29/STS2 enhances fungal tolerance in grapevine through a positive feedback loop. *Plant Cell Environ.* **42**, 2979–2998.

Xu, X., Xu, Z., Li, Z., Zakria, M., Zou, L. and Chen, G. (2021) Increasing resistance to bacterial leaf streak in rice by editing the promoter of susceptibility gene OsSULRT3;6. *Plant Biotechnol. J.* **19**, 1101–1103.

Xun, H., Yang, X., He, H., Wang, M., Guo, P., Wang, Y., Pang, J. *et al*. (2019) Over-expression of GmKR3, a TIR-NBS-LRR type R gene, confers resistance to multiple viruses in soybean. *Plant Mol. Biol.* **99**, 95–111.

Yan, Y., Wang, P., Wei, Y., Bai, Y., Lu, Y., Zeng, H., Liu, G. *et al*. (2021) The dual interplay of RAV5 in activating nitrate reductases and repressing catalase activity to improve disease resistance in cassava. *Plant Biotechnol. J.* **19**, 785–800.

Yang, X., Yang, J., Wang, Y., He, H., Niu, L., Guo, D., Xing, G. *et al*. (2019) Enhanced resistance to sclerotinia stem rot in transgenic soybean that overexpresses a wheat oxalate oxidase. *Transgenic Res.* **28**, 103–114.

Yang, W., Ju, Y., Zuo, L., Shang, L., Li, X., Li, X., Feng, S. *et al*. (2020) OsHsfB4d binds the promoter and regulates the expression of OsHsp18.0-CI to resistant against *Xanthomonas oryzae*. *Rice (N Y)*, **13**, 28.

Yang, X., Zhong, S., Zhang, Q., Ren, Y., Sun, C. and Chen, F. (2021) A loss-of-function of the dirigent gene TaDIR-B1 improves resistance to *Fusarium* crown rot in wheat. *Plant Biotechnol. J.* **19**, 866–868.

Yao, S., Yang, Z., Yang, R., Huang, Y., Guo, G., Kong, X., Lan, Y. *et al*. (2019) Transcriptional regulation of miR528 by OsSPL9 orchestrates antiviral response in rice. *Mol. Plant*, **12**, 1114–1122.

You, Q., Zhai, K., Yang, D., Yang, W., Wu, J., Liu, J., Pan, W. *et al*. (2016) An E3 ubiquitin ligase-BAG protein module controls plant innate immunity and broad-spectrum disease resistance. *Cell Host Microbe*, **20**, 758–769.

Yu, G., Chen, Q., Wang, X., Meng, X., Yu, Y., Fan, H. and Cui, N. (2019a) Mildew resistance locus O genes CsMLO1 and CsMLO2 are negative modulators of the *Cucumis sativus* defense response to *Corynespora cassiicola*. *Int. J. Mol. Sci.* **20**, 4793.

Yu, G., Wang, X., Chen, Q., Cui, N., Yu, Y. and Fan, H. (2019b) Cucumber mildew resistance locus O interacts with calmodulin and regulates plant cell death associated with plant immunity. *Int. J. Mol. Sci.* **20**, 2995.

Yu, Y., Zhou, Y.F., Feng, Y.Z., He, H., Lian, J.P., Yang, Y.W., Lei, M.Q. *et al*. (2020) Transcriptional landscape of pathogen-responsive lncRNAs in rice unveils the role of ALEX1 in jasmonate pathway and disease resistance. *Plant Biotechnol. J.* **18**, 679–690.

Yuan, M., Jiang, Z., Bi, G., Nomura, K., Liu, M., Wang, Y., Cai, B. *et al*. (2021) Pattern-recognition receptors are required for NLR-mediated plant immunity. *Nature*, **592**, 105–109.

Zang, Z., Lv, Y., Liu, S., Yang, W., Ci, J., Ren, X., Wang, Z. *et al*. (2020) A novel ERF transcription factor, ZmERF105, positively regulates maize resistance to *Exserohilum turcicum*. *Front. Plant Sci.* **11**, 850.

Zeilmaker, T., Ludwig, N.R., Elberse, J., Seidl, M.F., Berke, L., Van Doorn, A., Schuurink, R.C. *et al*. (2015) DOWNY MILDEW RESISTANT 6 and DMR6-LIKE OXYGENASE 1 are partially redundant but distinct suppressors of immunity in Arabidopsis. *Plant J.* **81**, 210–222.

Zetsche, B., Gootenberg, J.S., Abudayyeh, O.O., Slaymaker, I.M., Makarova, K.S., Essletzbichler, P., Volz, S.E. *et al*. (2015) Cpf1 is a single RNA-guided endonuclease of a class 2 CRISPR-Cas system. *Cell*, **163**, 759–771.

Zhang, Y., Cheng, Y.T., Qu, N., Zhao, Q., Bi, D. and Li, X. (2006) Negative regulation of defense responses in Arabidopsis by two NPR1 paralogs. *Plant J.* **48**, 647–656.

Zhang, X., Zhao, H., Gao, S., Wang, W.C., Katiyar-Agarwal, S., Huang, H.D., Raikhel, N. *et al*. (2011) Arabidopsis argonaute 2 regulates innate immunity via miRNA393(*)-mediated silencing of a Golgi-localized SNARE gene, MEMB12. *Mol. Cell*, **42**, 356–366.

Zhang, B., Tremousaygue, D., Denance, N., van Esse, H.P., Horger, A.C., Dabos, P., Goffner, D. *et al*. (2014) PIRIN2 stabilizes cysteine protease XCP2 and increases susceptibility to the vascular pathogen *Ralstonia solanacearum* in Arabidopsis. *Plant J.* **79**, 1009–1019.

Zhang, D., Liu, M., Tang, M., Dong, B., Wu, D., Zhang, Z. and Zhou, B. (2015a) Repression of microRNA biogenesis by silencing of OsDCL1 activates the basal resistance to *Magnaporthe oryzae* in rice. *Plant Sci.* **237**, 24–32.

Zhang, M., Ahmed Rajput, N., Shen, D., Sun, P., Zeng, W., Liu, T., Juma Mafurah, J. *et al*. (2015b) A *Phytophthora sojae* cytoplasmic effector mediates disease resistance and abiotic stress tolerance in *Nicotiana benthamiana*. *Sci. Rep.* **5**, 10837.

Zhang, C., Wang, X., Zhang, F., Dong, L., Wu, J., Cheng, Q., Qi, D. *et al*. (2017a) Phenylalanine ammonia-lyase2.1 contributes to the soybean response towards *Phytophthora sojae* infection. *Sci. Rep.* **7**, 7242.

Zhang, Y., Bai, Y., Wu, G., Zou, S., Chen, Y., Gao, C. and Tang, D. (2017b) Simultaneous modification of three homoeologs of TaEDR1 by genome editing enhances powdery mildew resistance in wheat. *Plant J.* **91**, 714–724.

Zhang, Y., Zhao, L., Zhao, J., Li, Y., Wang, J., Guo, R., Gan, S. *et al*. (2017c) S5H/DMR6 encodes a salicylic acid 5-hydroxylase that fine-tunes salicylic acid homeostasis. *Plant Physiol.* **175**, 1082–1093.

Zhang, Y., Wu, L., Wang, X., Chen, B., Zhao, J., Cui, J., Li, Z. *et al*. (2019) The cotton laccase gene GhLAC15 enhances *Verticillium* wilt resistance via an increase in defence-induced lignification and lignin components in the cell walls of plants. *Mol. Plant Pathol.* **20**, 309–322.

Zhang, H., Jing, W., Zheng, J., Jin, Y., Wu, D., Cao, C., Dong, Y. *et al*. (2020a) The ATP-binding cassette transporter OsPDR1 regulates plant growth and pathogen resistance by affecting jasmonates biosynthesis in rice. *Plant Sci.* **298**, 110582.

Zhang, H., Zhang, Q., Zhai, H., Gao, S., Yang, L., Wang, Z., Xu, Y. *et al*. (2020b) IbBBX24 promotes the jasmonic acid pathway and enhances *Fusarium* wilt resistance in sweet potato. *Plant Cell*, **32**, 1102–1123.

Zhang, L.L., Li, Y., Zheng, Y.P., Wang, H., Yang, X., Chen, J.F., Zhou, S.X. *et al*. (2020c) Expressing a target mimic of miR156fhl-3p enhances rice blast disease resistance without yield penalty by improving SPL14 expression. *Front. Genet.* **11**, 327.

Zhang, Z., Zhang, X., Na, R., Yang, S., Tian, Z., Zhao, Y. and Zhao, J. (2020d) StRac1 plays an important role in potato resistance against *Phytophthora infestans* via regulating H_2O_2 production. *J. Plant Physiol.* **253**, 153249.

Zhang, H., Li, F., Li, Z., Cheng, J., Chen, X., Wang, Q., Joosten, M. *et al*. (2021) Potato StMPK7 is a downstream component of StMKK1 and promotes resistance to the oomycete pathogen *Phytophthora infestans*. *Mol. Plant Pathol.* **22**, 644–657.

Zhao, T., Rui, L., Li, J., Nishimura, M.T., Vogel, J.P., Liu, N., Liu, S. *et al*. (2015) A truncated NLR protein, TIR-NBS2, is required for activated defense responses in the exo70B1 mutant. *PLoS Genet.* **11**, e1004945.

Zhao, Y., Chang, X., Qi, D., Dong, L., Wang, G., Fan, S., Jiang, L. *et al*. (2017) A novel soybean ERF transcription factor, GmERF113, increases resistance to *Phytophthora sojae* infection in soybean. *Front. Plant Sci.* **8**, 299.

Zhao, Z.X., Feng, Q., Cao, X.L., Zhu, Y., Wang, H., Chandran, V., Fan, J. *et al*. (2020) Osa-miR167d facilitates infection of *Magnaporthe oryzae* in rice. *J. Integr. Plant Biol.* **62**, 702–715.

Zheng, H., Dong, L., Han, X., Jin, H., Yin, C., Han, Y., Li, B. *et al*. (2020) The TuMYB46L-TuACO3 module regulates ethylene biosynthesis in einkorn wheat defense to powdery mildew. *New Phytol.* **225**, 2526–2541.

Zhong, X., Yang, J., Shi, Y., Wang, X. and Wang, G.L. (2018) The DnaJ protein OsDjA6 negatively regulates rice innate immunity to the blast fungus *Magnaporthe oryzae*. *Mol. Plant Pathol.* **19**, 607–614.

Zhou, K., Hu, L., Li, Y., Chen, X., Zhang, Z., Liu, B., Li, P. *et al*. (2019a) MdUGT88F1-mediated phloridzin biosynthesis regulates apple development and Valsa canker resistance. *Plant Physiol.* **180**, 2290–2305.

Zhou, S., Chen, M., Zhang, Y., Gao, Q., Noman, A., Wang, Q., Li, H. *et al*. (2019b) OsMKK3, a stress-responsive protein kinase, positively regulates rice resistance to *Nilaparvata lugens* via phytohormone dynamics. *Int. J. Mol. Sci.* **20**, 3023.

Zhou, S.X., Zhu, Y., Wang, L.F., Zheng, Y.P., Chen, J.F., Li, T.T., Yang, X.M. *et al*. (2020) Osa-miR1873 fine-tunes rice immunity against *Magnaporthe oryzae* and yield traits. *J. Integr. Plant Biol.* **62**, 1213–1226.

Zhu, X., Lu, C., Du, L., Ye, X., Liu, X., Coules, A. and Zhang, Z. (2017) The wheat NB-LRR gene TaRCR1 is required for host defence response to the necrotrophic fungal pathogen *Rhizoctonia cerealis*. *Plant Biotechnol. J.* **15**, 674–687.

Zipfel, C. (2009) Early molecular events in PAMP-triggered immunity. *Curr. Opin. Plant Biol.* **12**, 414–420.

Zipfel, C. (2014) Plant pattern-recognition receptors. *Trends Immunol.* **35**, 345–351.

Zipfel, C. and Robatzek, S. (2010) Pathogen-associated molecular pattern-triggered immunity: veni, vidi...? *Plant Physiol.* **154**, 551–554.

Zipfel, C., Kunze, G., Chinchilla, D., Caniard, A., Jones, J.D., Boller, T. and Felix, G. (2006) Perception of the bacterial PAMP EF-Tu by the receptor EFR restricts *Agrobacterium*-mediated transformation. *Cell*, **125**, 749–760.

Zou, B., Ding, Y., Liu, H. and Hua, J. (2018) Silencing of copine genes confers common wheat enhanced resistance to powdery mildew. *Mol. Plant Pathol.* **19**, 1343–1352.

Zou, X., Long, J., Zhao, K., Peng, A., Chen, M., Long, Q., He, Y. *et al*. (2019) Overexpressing GH3.1 and GH3.1L reduces susceptibility to *Xanthomonas citri* subsp. citri by repressing auxin signaling in citrus (*Citrus sinensis* Osbeck). *PLoS ONE*, **14**, e0220017.

Zou, J., Meng, X., Liu, Q., Shang, M., Wang, K., Li, J., Yu, H. *et al*. (2022) Improving the efficiency of prime editing with epegRNAs and high-temperature treatment in rice. *Sci. China Life Sci.* 1–4.