

Loss of susceptibility as a novel breeding strategy for durable and broad-spectrum resistance

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Abstract Recent studies on plant immunity have suggested that a pathogen should suppress induced plant defense in order to infect a plant species, which otherwise would have been a nonhost to the pathogen. For this purpose, pathogens exploit effector molecules to interfere with different layers of plant defense responses. In this review, we summarize the latest findings on plant factors that are activated by pathogen effectors to suppress plant immunity. By looking from a different point of view into host and nonhost resistance, we propose a novel breeding strategy: disabling plant disease susceptibility genes (S-genes) to achieve durable and broad-spectrum resistance.

Keywords Effector · Effector target · Effector-triggered susceptibility · Recessive resistance · Susceptibility genes

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Introduction

Though resistance and susceptibility are opposite sides of the same coin, most studies have focused for a long time on the resistance side in search for plant resistance genes (R-genes) and other defense genes. In 2002, when *PMR6* was discovered as a gene coding for a susceptibility factor for promoting growth of powdery mildews, Eckardt (2002) questioned “Are there plant genes that are required for susceptibility to certain pathogens?” In 2005, based on the unique forms of resistance conferred by loss of function in genes like *Mlo*, *PMR6* and *eIF4E*, De Almeida Engler et al. (2005) suggested to exploit susceptibility genes as an alternative in breeding for nematode resistance. Nowadays, the field is rapidly moving toward identification of plant factors targeted by pathogen effectors and elucidation of mechanisms controlling plant disease susceptibility. Ultimately, a better understanding of the molecular basis of plant disease susceptibility can be applied in breeding for resistance against a wide spectrum of pathogens. This review, by highlighting recent studies on effector-triggered susceptibility, proposes a novel breeding strategy: exploitation of plant susceptibility genes (S-genes) for durable and broad-spectrum resistance.

Disease susceptibility genes (S-genes)

Plants are exposed to a tremendous number of potential pathogens. Many plant pathogens can infect

only a limited number of plant species that are called hosts to the given pathogen. To exploit a plant as a host, pathogens have to overcome plant defense mechanisms ranging from preformed passive barriers (e.g. physical barriers such as the cuticle of leaves) to induced defense reactions (e.g. Heath 2000; Thordal-Christensen 2003; Niks and Marcel 2009). The front line of the induced defense is triggered by pathogen-associated molecular patterns (PAMPs), also termed as PAMP-triggered immunity (PTI). PAMPs are generally conserved compounds (like chitin in fungi and flagellins of bacteria), and PTI is induced by all invading pathogens (Bittel and Robatzek 2007; Boller and He 2009; Jones and Dangl 2006). Thus, suppression of PTI is required as the first step for a pathogen to alter a plant's status from a nonhost into a host. For adapted pathogens, the suppression of PTI is achieved by the secretion of pathogen effectors to manipulate host cell functions (Jones and Dangl 2006; van der Hoorn and Kamoun 2008).

In the field of plant–microbe interactions, the study on how effectors suppress PTI to establish effector-triggered susceptibility (ETS) has moved to the center stage (Hoeftle and Hückelhoven 2008). Emerging evidence suggests that the primary function of pathogen effectors is to suppress plant innate immunity by interacting with specific host proteins (effector targets) (Nomura et al. 2005; Jones and Dangl

2006; Chisholm et al. 2006; Kamoun 2007; Van der Hoorn and Kamoun 2008). Not surprisingly, most effector targets play a positive role in plant defense machinery, like defense-signaling components (Chisholm et al. 2006; Bittel and Robatzek 2007; Speth et al. 2007; Fig. 1). For example, the effector HopAII of *Pseudomonas syringae* suppresses PTI by inactivating Arabidopsis MPK 3 and MPK6 (mitogen-activated protein kinases), two key components of the plant immune response-signaling cascade (Zhang et al. 2007).

However, some pathogen effectors suppress plant innate immunity by activating effector targets that function as negative regulators of the plant immunity system. In principle, knocking out such an effector target would release the suppression of plant defense and lead to resistance (Fig. 1). More and more examples of this group are being identified (Tables 1, 2). One of the well-characterized examples is the transmembrane MLO protein, which negatively regulates *PEN* gene-associated disease resistance to powdery mildews (Bhat et al. 2005; Panstruga 2005; Hardham et al. 2007; our unpublished data). In barley and Arabidopsis, loss-of-function mutations in *Mlo* result in efficient preinvasion resistance to adapted powdery mildews (Büschges et al. 1997; Piffanelli et al. 2004; Humphry et al. 2006). Recently, it has been shown that the tomato recessive allele *ol-2*, conferring

Role of effector target:	A		B			
	Positive role in plant defense		Negative role in plant defense			
Pathogen effector:	Present		Negative defense regulator		Susceptibility factor	
The resistance protein:	Absent		Present		Present	
Effector target:	Absent		Absent		Absent	
Expected outcome in plants:	Present	Absent (loss-of-function)	Present	Absent (loss-of-function)	Present	Absent (loss-of-function)
	Susceptibility	Susceptibility	Susceptibility	Resistance (recessive)	Susceptibility	Resistance (recessive)

Fig. 1 Comparison on effector targets with positive or negative roles in plant defense to demonstrate how to obtain resistance by knocking out susceptibility gene. Panel **a** shows that, in the absence of resistance protein, both presence and absence of the effector target (with a positive role in plant

defense) lead to susceptible plants. Panel **b** demonstrates that, in the absence of resistance protein, presence of the effector target (with a negative role in plant defense) leads to susceptible plants and that knocking out the effector target leads to resistant plants

Table 1 Cloned susceptibility genes from naturally occurring mutants

Role as a effector target	Gene	Plant species	Encoded protein	Pathogen	Reported pleiotropic phenotype	References
Negative regulator	<i>MLO</i> orthologues	Barley	Transmembrane protein	<i>Blumeria graminis</i>	Early senescence and axenic cell death	Büschges et al. (1997)
Susceptibility factor	Genes encoding isoforms of eIF4E and eIF4G	Tomato	Translation initiation factor	<i>Oidium neolyopersici</i>	Not reported	Bai et al. (2008)
	<i>Xa5</i> <i>Xa13</i>	Several species Rice Rice	Transcription factor II A- γ Membrane-localized protein	<i>Potyviridae</i> <i>Xanthomonas oryzae</i> <i>X. oryzae</i>	Not reported Pollen abortion	Diaz-Pendon et al. (2004) Robaglia and Caranta (2006) Iyer-Pascuzzi and McCouch (2007) Chu et al. (2006); Yang et al. (2006); Sugto et al. (2007)

resistance to the powdery mildew fungus *Oidium neolyopersici*, is also caused by a null mutation of the tomato *SIM1* (Bai et al. 2008; Pavan et al. 2008).

In addition to the suppression of PTI, pathogen effectors may promote disease by activating effector targets that function as susceptibility factors, like plant factors that are required by the pathogen for its growth and development (Fig. 1). Examples are isoforms of eIF4E and eIF4G functioning as translation factors for potyvirus replication and infection (Diaz-Pendon et al. 2004; Robaglia and Caranta 2006). Interestingly, all characterized recessive resistances to viruses originate from mutations in isoforms of eIF4E and eIF4G, two components of the translation initiation complex (Kang et al. 2005b; Albar et al. 2006; Robaglia and Caranta 2006). The mechanism leading to resistance is likely due to the lack of interaction between the viral effector protein VPg and the translation initiation complex (Robaglia and Caranta 2006).

In this review, we refer to genes required for susceptibility as disease susceptibility genes (S-genes), such as genes coding for effector targets that function as negative defense regulators or susceptibility factor (Fig. 1). The term of plant S-gene was first introduced in the review of Eckardt (2002). Genetically, S-genes can be defined as dominant genes whose impairment will lead to recessive resistance. Recessive resistances have been known for many years (e.g. Stubbs et al. 1983). For example, the first reported resistance gene was identified by Biffen in 1905, which is recessively inherited and confers resistance to wheat yellow rust (*Puccinia striiformis*) (Singh and Singh 2005). One of the recently reported recessive resistance genes is the *rpsGZ* gene, which is effective against all races of the barley stripe rust *P. striiformis* f.sp. *hordei* (Yan and Chen 2006). Only few recessive resistance genes have been characterized for their role in plant disease establishment (Table 1). It is intriguing to know whether natural recessive resistances result from loss-of-function mutations of S-genes that code for effector targets. With increasing interest in the research topic on suppression of PTI and establishment of ETS, a considerable amount of potential S-genes has been recently identified via different experimental approaches (Table 2). Proteins encoded by S-genes have been shown or predicted to be activated by effectors for ETS. The challenge is how to exploit S-genes, in complementary to R-genes, in plant breeding for durable and broad-spectrum resistance.

Table 2 Genes experimentally identified or cloned as potential susceptibility genes

Role as an effector target	Gene	Plant species	Encoded protein	Pathogen	Reported pleiotropic phenotype	References
Negative regulator	<i>AtSR1</i>	Arabidopsis	Ca ²⁺ /calmodulin-binding transcription factor	<i>Pseudomonas syringae</i>	Chlorosis and autonomous lesions	Du et al. (2009)
	<i>BIK1</i>	Arabidopsis	Membrane-anchored protein kinase	<i>P. syringae</i>	Enhanced susceptibility to <i>Botrytis cinerea</i> and <i>Alternaria brassicicola</i> ; altered root growth	Veronese et al. (2006)
	<i>CEV1</i>	Arabidopsis	Cellulose synthase	<i>G. orontii</i> <i>G. cichoracearum</i>	Reduced size, darker green leaf color, anthocyanins accumulation	Ellis and Turner (2001) Ellis et al. (2002)
	<i>CPR5</i>	Arabidopsis	Transmembrane protein	<i>Oidium neolyopersici</i> <i>Hyaloperonospora parasitica</i>	Reduced growth; chlorotic lesions	Bowling et al. (1997) Kirik et al. (2001)
	<i>DMR6</i>	Arabidopsis	2-Oxoglutarate-Fe(II) oxygenase	<i>P. syringae</i> <i>H. parasitica</i>	Slightly rounded leaves	van Damme et al. (2005) van Damme et al. (2008)
	<i>DND1</i>	Arabidopsis	Cyclic nucleotide-gated ion channel	<i>Colletotrichum higginsianum</i> <i>P. syringae</i> <i>Xanthomonas campestris</i>	Dwarf	Yu et al. (1998) Clough et al. (2000)
	<i>DND2</i>	Arabidopsis	Cyclic nucleotide-gated ion channel	Tobacco ringspot virus <i>P. syringae</i>	Dwarf	Jurkowski et al. (2004)
	<i>EDR1</i>	Arabidopsis	Mitogen-activated protein kinase	<i>P. syringae</i> <i>G. cichoracearum</i>	Stunted plants with spontaneous lesions under drought conditions	Asai et al. (2002) Frye et al. (2001) Tang et al. (2005)
	<i>LSD1</i>	Arabidopsis	Zinc finger protein	<i>H. parasitica</i> <i>P. syringae</i>	Lesion formation	Dietrich et al. (1994) Kaminaka et al. (2006)
	<i>MLO</i> orthologues	Arabidopsis Barley	Transmembrane protein	<i>G. orontii</i> <i>G. cichoracearum</i>	Early senescence and axenic cell death	Consonni et al. (2006)
	<i>MPK4</i>	Arabidopsis	Mitogen-activated protein kinase	<i>B. graminis</i> <i>H. parasitica</i> <i>P. syringae</i>	Dwarf, curled leaves and reduced fertility	Petersen et al. (2000)

Table 2 continued

Role as an effector target	Gene	Plant species	Encoded protein	Pathogen	Reported pleiotropic phenotype	References
	<i>PMR4</i>	Arabidopsis	Callose synthase	<i>G. orontii</i> <i>G. cichoracearum</i> <i>H. parasitica</i>	Epinaetic leaves	Vogel and Somerville (2000) Nishimura et al. (2003)
	<i>RAR1</i>	Arabidopsis	Zinc-binding protein	<i>P. syringae</i>	Not reported	Shang et al. (2006)
	<i>SN1</i>	Arabidopsis	Leucine-rich nuclear protein	<i>H. parasitica</i> <i>P. syringae</i>	Reduced growth and fertility	Li et al. (1999); Mosher et al. (2006)
	<i>SON1</i>	Arabidopsis	F-box protein	<i>H. parasitica</i> <i>P. syringae</i>	Not reported	Kim and Delaney (2002)
	<i>SSI2</i>	Arabidopsis	Stearyl-acyl carrier protein desaturase	<i>H. parasitica</i>	Small rosette, curled leaves, lesions	Kachroo et al. (2001)
	<i>WRKY family members</i>	Arabidopsis Barley Pepper	WRKY transcriptional factors	<i>P. syringae</i> <i>P. syringae</i> <i>G. orontii</i> <i>Blumeria graminis</i> <i>Xanthomonas axonopodis</i>	Not reported	Shah et al. (2001) Eulgem and Somssich (2007)
	<i>ZmLOX3</i>	Maize	9-Lipoxygenase	<i>Meloidogyne incognita</i>	Slightly early senescence depending on the mutated alleles	Oh et al. (2008)
Susceptibility factor	<i>DMR1</i>	Arabidopsis	Homoserine kinase	<i>H. parasitica</i>	No effect or slightly smaller size, depending on the <i>dmr1</i> allele	van Damme et al. (2005) Van Damme (2007)
	<i>PMR5</i>	Arabidopsis	Unknown function protein	<i>Golovinomyces orontii</i>	Reduced growth, microlesions	Vogel et al. (2004)
	<i>PMR6</i>	Arabidopsis	Pectate lyase-like protein	<i>G. cichoracearum</i> <i>G. orontii</i>	Reduced growth, microlesions	Vogel et al. (2002)
	<i>TOM1 and TOM3</i>	Arabidopsis	Transmembrane proteins	<i>G. cichoracearum</i>	Not reported	Diaz-Pendon et al. (2004)
	<i>TOM2A</i>	Arabidopsis	Transmembrane protein interacting with TOM1	Tobacco mosaic virus	Not reported	Tsujimoto et al. (2003)
	<i>LOV1</i>	Arabidopsis	NB-LRR protein	<i>Cochliobolus victoriae</i>	Not reported	Sweat et al. (2008)
	<i>MAP65-3</i>	Arabidopsis	Microtubule-associated protein	<i>Meloidogyne incognita</i>	Dwarf phenotype and reduced fertility	Caillaud et al. (2008)

R-genes and S-genes

To combat the pathogens that succeed in establishment of ETS, host plants have evolved a race-specific immunity, a well-described host resistance mechanism that is governed by dominant R-genes (e.g. Speth et al. 2007; Hoefle and Hükelhoven 2008; Wladimir et al. 2008). Hundreds of R-genes have been cloned and most of them encode proteins with an N-terminal nucleotide-binding (NB) site and C-terminal leucine-rich repeats (LRRs) (Takken et al. 2006). R-genes encode proteins that recognize pathogen effectors to establish effector-triggered immunity. This recognition triggers a cascade of defense responses, mediated by a complex-signaling network in which plant hormones, like salicylic acid (SA) and jasmonic acid (JA), play a major role and the resistance is manifested as localized hypersensitive response at the site of infection (Robert-Seilaniantz et al. 2007; Bruce and Pickett 2007; Bari and Jones 2009). It is generally assumed that most R-proteins function in a tripartite module (van der Hoorn et al. 2002), where the R-protein guards a specific effector target (also known as virulence target), and in doing so can detect modifications induced by the pathogen effector. Effector targets required for R-protein function are recently categorized into two subgroups, decoy and guardee (Van der Hoorn and Kamoun 2008). An effector target is termed as a decoy if it has no function in host defense or susceptibility in absence of its cognate R-protein. In the decoy model, operative effector targets play a role in enhancing pathogen fitness in plants lacking the R-protein. A gene is considered an S-gene if it codes for the operative target that plays a negative role in plant defense (Fig. 1). One example is the pepper *upa20* gene that encodes a regulator of cell enlargement (Zhou and Chai 2008). In susceptible plants, AvrBs3, which is a type-III effector secreted by *Xanthomonas campestris* pv *vesicatoria*, mimics the eukaryotic transcription factor to activate *upa20* gene to promote disease (Kay et al. 2007). In resistant plants, AvrBs3 also activates the promoter of the pepper *Bs3* gene (promoter of the *Bs3* gene = *pBs3*), which leads to the specific expression of the R-gene *Bs3* and disease resistance. Obviously, *upa20* is an S-gene, of which loss-of-function mutants would lead to resistance in plants lacking the *Bs3* gene. *pBs3* is regarded as a decoy that is required for the R-gene *Bs3* to trap AvrBs3 for resistance (Van der

Hoorn and Kamoun 2008; Zhou and Chai 2008). A guardee is used to term an effector target that, upon attack by a pathogen effector, enhances pathogen fitness in plants absent for the R-protein and triggers innate immunity in plants carrying the R-protein (Van der Hoorn and Kamoun 2008). Genes coding for gardees that play a negative role in plant defense can also be categorized as S-genes (Fig. 1). In summary, in the R-gene network, both operative targets and gardees are considered as products of S-genes if they play a negative role in plant defense as presented in Fig. 1.

The above described concept on effector-triggered immunity, which is activated by the recognition of pathogen effectors by plant R-proteins, is mainly based on findings obtained from plant interactions with biotrophic pathogens. For necrotrophic pathogens, host-specific-toxins are defined as pathogen effectors that induce toxicity and promote disease only in host species (Friesen et al. 2008). It is well-known that host-specific-toxins are host selective because they are typically active only in plants that serve as hosts for the pathogens (Wolpert et al. 2002). As a mirror image of effector-triggered immunity of biotrophic pathogen, the necrotrophic pathogen produces an effector that is recognized by a host receptor to trigger susceptibility (Friesen et al. 2008). Thus, plant genes coding for host receptors that are recognized by host-specific-toxins of necrotrophic pathogens are S-genes. One example is the Arabidopsis *LOVI* gene-conferring susceptibility to Victorian blight caused by *Cochliobolus victoriae*. The *LOVI* gene is an unusual finding of S-genes as it encodes a NB-LRR protein (Sweat et al. 2008), which is the largest protein family of R-proteins (Takken et al. 2006). Thus, the identification of *LOVI* provokes a potential cross-link between plant R- and S-genes, suggesting that an R-gene-conferring resistance to one pathogen also can confer susceptibility to another pathogen.

Nonhost-like resistance

For a long time, resistance conferred by loss of function of the barley *Mlo* gene has been considered as a unique type of plant immunity (Schulze-Lefert and Vogel 2000; Elliot et al. 2002; Hükelhoven 2005). Only recently, the comparison between non-host resistance and *mlo*-based immunity in barley and

Arabidopsis has led to the conclusion that *mlo*-based resistance and nonhost resistance are “two faces of the same coin” (Humphry et al. 2006), as both types of resistance share analogous features like prehaustorial resistance mechanisms to powdery mildews (Trujillo et al. 2004; Ellis 2006). Besides, *mlo*-based resistance requires all the three described *PEN* genes for nonhost resistance in *Arabidopsis* and the *Ror2* genes (homolog of *PEN1*) in barley (Consonni et al. 2006; Humphry et al. 2006; Hardham et al. 2007). It has been demonstrated that mutations in these genes that affect nonhost resistance to powdery mildews compromise *mlo*-based resistance and vice versa (Consonni et al. 2006; Humphry et al. 2006; Hardham et al. 2007; Lipka et al. 2005; 2008). Thus, the absence of the key host protein (MLO) appears to convert a compatible interaction between an adapted powdery mildew and its respective host plant into an incompatible interaction having similar molecular mechanisms of nonhost resistance (Humphry et al. 2006).

The functional characterization of S-genes (Tables 1, 2) has revealed that they encode proteins that are required by pathogens either for their growth process on the parasitized plant or for negative regulation of plant defense responses. These two events are indispensable for would-be pathogens to establish and maintain the infection process in plants. Consequently, the loss of function of such S-genes is expected to result in resistance against the pathogen. It has been shown (Tables 1, 2) that such resistance can be effective even towards different, unrelated, pathogens. Moreover, when tested against different genetic variants of a pathogen, it has been often proven to be race nonspecific (Stein and Somerville 2002; Bai et al. 2005; Kang et al. 2005a). Little information is available relative to the durability of resistances conferred by loss of function of S-genes. However, resistances conferred by mutations of *Mlo* in barley and *eIF4E* in pepper are still effective in the field after more than 30 and 50 years from their introduction in agriculture, respectively (Lyngkjaer et al. 2000; Kang et al. 2005a). Thus, loss of susceptibility has the potential to result in resistance that shares the “hallmarks of nonhost resistance” (Humphry et al. 2006): durability and broad-spectrum. In this review, we refer to *mlo*-based resistance as nonhost-like resistance defined as durable and broad-spectrum resistance with similar defense mechanisms underlying nonhost resistance.

S-genes in breeding for nonhost-like resistance

In spite of promoting pathogen proliferation and disease establishment, S-genes have not been excluded by evolution. Evidence suggests that certain S-genes, besides being involved in plant-pathogen interactions, are required for the correct functioning of other important aspects of plant physiology. For example, the rice *Xa13* gene is required for both the growth of bacteria *X. oryzae* and plant pollen development (Chu et al. 2006). The dual function of such S-genes provides a unique opportunity for exploring the functional overlap between signal pathways for plant developments and pathogen-induced susceptibility.

Loss of function of S-genes, which encode for susceptibility factors, does not alter normal plant development. Few S-genes belonging to this category (Table 1) have been successfully employed in cultivation, which include resistance conferred by loss-of-function mutations of *Xa5*, *Xa13* and *eIF4G* in rice; and *eIF4E* in many crops including barley, pepper, lettuce, melon and pea (Candresse et al. 2002; Nicaise et al. 2003; Gao et al. 2004a, b; Kang et al. 2005a; Morales et al. 2005; Nieto et al. 2006; Iyer-Pascuzzi and McCouch 2007; Rakotomalala et al. 2008; Tyrka et al. 2008). While, loss-of-function mutations of genes encoding negative regulators are in many cases accompanied by adverse pleiotropic effects due to constitutive defense activation, such as reduced growth and lesion-mimic phenotypes (Table 1). It has been reported that the extent of pleiotropic effects depends considerably on the environmental conditions as well as on plant species. For example, early senescence-like leaf chlorosis has been reported to occur in barley *mlo* mutants under certain conditions, while, no obvious pleiotropic phenotypes have been discovered yet in tomato *mlo* mutants (Bai et al. 2008). Although pleiotropic effects have been reported together with barley *mlo* mutants (Büschges et al. 1997), *mlo* resistance is by far the most used powdery mildew resistance source in spring barley grown in Europe (Lyngkjaer et al. 2000). The maize *lox3-4* mutant, carrying a true null allele of the *ZmLOX* gene, showed slightly shorter plants with earlier senescence comparing with the near-isogenic wild types. Throughout all stages of plant development, no other visible abnormalities were observed in *lox3-4* mutants, suggesting the

potential use of the S-gene, *ZmLOX*, in breeding for nematode resistance (Gao et al. 2008).

Future perspectives

The *mlo* mutant was originally discovered in barley more than 60 years ago and it was considered as a unique form of resistance in barley. The identification of *mlo* mutants in other plant species including Arabidopsis, tomato and most probably also pea and grape showed that it is more common in nature than previously anticipated (Consonni et al. 2006; Fondevilla et al. 2006; Bai et al. 2008; Feechan et al. 2008). Till now, potential S-genes have been characterized mainly in Arabidopsis (Table 2). To exploit S-genes for resistance breeding, two questions need to be addressed: (1) are there S-gene orthologues across cultivated plant species? and (2) how to obtain and apply loss-of-function mutants of S-genes in resistance breeding? A targeted approach based on comparative genetics/genomics would provide answers to these questions. Firstly, sequence homology to characterized S-genes should be identified by, for example, mining available sequence databases in a certain plant species. Secondly, the potential S-gene candidates should be functionally characterized by gene-silencing techniques such as virus-induced gene silencing (VIGS) and/or RNA interference (RNAi) to observe altered phenotypes for susceptibility to a certain pathogen as well as other agricultural traits. VIGS is a transient gene knocking out, which can be performed nowadays in many plant species for a large-scale functional analysis (Ratcliff et al. 2001; Liu et al. 2002; Hileman et al. 2005; Burch-Smith et al. 2006). To obtain stable-silencing effect, RNAi can be performed (reviewed by Waterhouse and Helliwell 2003). Once the function of a S-gene is confirmed, loss-of-function mutations of the S-gene can be achieved by insertional mutagenesis (Krysan et al. 1999; Parinov et al. 1999; Speulman et al. 1999) and TILLING (targeting induced local lesions in genomes) (Colbert et al. 2001). The application of TILLING is particularly promising, as it combines high efficiency in the identification of mutations of interest with the advantage of being a nontransgenic technology. Alternatively, natural S-gene alleles, which can be obtained by screening genetic resource of a certain plant species and are insensitive to

effector manipulation but yet retain their intrinsic function, would be ideal alleles for recessive resistances.

Conclusions

In summary, resistance can be achieved in different ways: one of them is by the presence of corresponding R-genes to recognize pathogen effectors and another one is by the absence of S-genes. We refer to genes required for susceptibility as S-genes. In this review, we focused on S-genes encoding effector targets that function as either susceptibility factors or negative defense-regulators (Fig. 1). Loss of function of S-genes will lead to resistance that inherits recessively in normal plants and dominantly in plants of which the S-gene is silenced by using RNAi technique.

In practice, the majority of the resistance breeding programs have aimed to introgress R-genes from wild species into crop plants. Dominant resistance is highly effective and often race specific. In most cases, resistance conferred by R-genes can be overcome by pathogens resulting in outbreaks of large epidemics, which 'burst' the once 'booming' cultivars (Van der Hoorn et al. 2002; Panstruga and Dodds 2009). Repeated boom-and-burst cycles in agriculture continuously force breeders to introduce cultivars with new resistance traits. In contrast to R-genes, it has been shown that loss of function in S-genes often leads to durable and broad-spectrum resistance, such as *mlo*-based resistance. Thus, exploitation of S-gene alleles, which are insensitive to manipulation by pathogen effectors, provides an alternative breeding strategy that is complementary to the R-gene conferred resistance.

Nonhost resistance has often been proposed to be a unique alternative for host resistance and exploitation of genes for nonhost resistance in breeding requires genetic compatibilities between the host and the nonhost species (Niks and Marcel 2009). As this is the exception rather than the rule, genes for nonhost resistance are rarely used in breeding. Despite its durable and broad-spectrum characters, our knowledge on nonhost resistance is limited. Current studies in understanding the genetic factors and molecular mechanisms underlying plant nonhost resistance bear great potentials for target employment of this valuable trait to control host pathogens (Nünberger and

Lipka 2005; Schweizer 2007). To this aspect, this review proposed an alternative breeding strategy for nonhost-like resistance by eliminating plant S-genes. This breeding strategy is expected to result in durable and broad-spectrum resistance that resembles nonhost resistance.

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