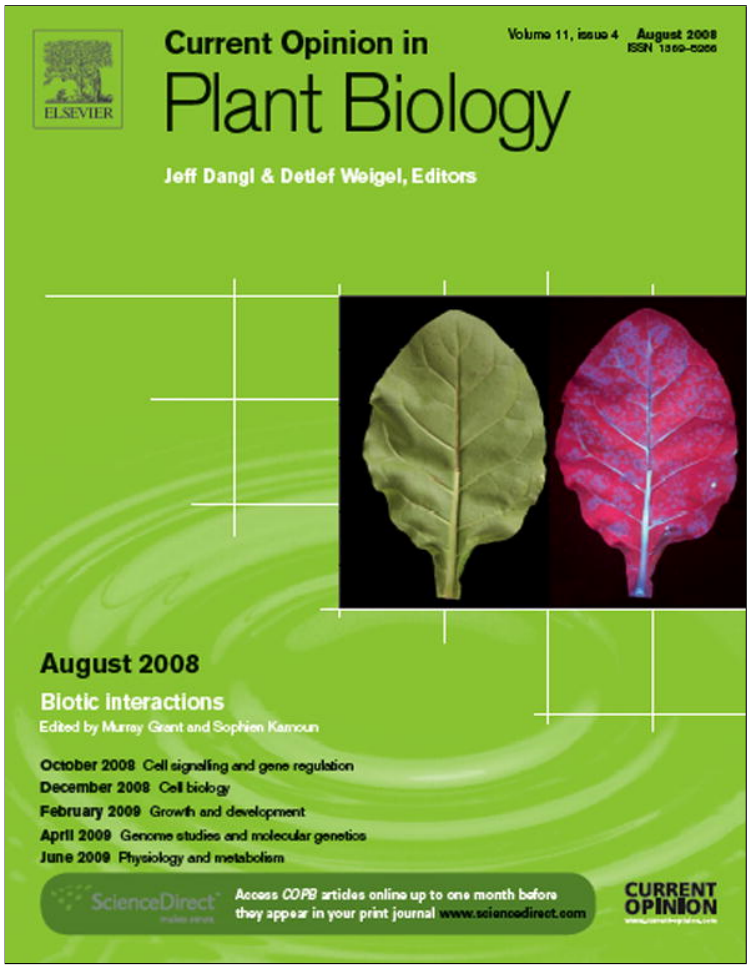

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Plant immune responses triggered by beneficial microbes

Saskia CM Van Wees, Sjoerd Van der Ent and Corné MJ Pieterse

Beneficial soil-borne microorganisms, such as plant growth promoting rhizobacteria and mycorrhizal fungi, can improve plant performance by inducing systemic defense responses that confer broad-spectrum resistance to plant pathogens and even insect herbivores. Different beneficial microbe-associated molecular patterns (MAMPs) are recognized by the plant, which results in a mild, but effective activation of the plant immune responses in systemic tissues. Evidence is accumulating that systemic resistance induced by different beneficials is regulated by similar jasmonate-dependent and ethylene-dependent signaling pathways and is associated with priming for enhanced defense.

Address
Plant-Microbe Interactions, Institute of Environmental Biology, Faculty of Science, Utrecht University, P.O. Box 800.56, 3508 TB Utrecht, The Netherlands

Corresponding author: Pieterse, Corné MJ (C.M.J.Pieterse@uu.nl)

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Introduction

Plant roots become quickly colonized by a diverse microflora of soil-borne bacteria and fungi that may have either beneficial or deleterious effects on the plant. Classical examples of symbiotic microorganisms are mycorrhizal fungi that aid in the uptake of water and minerals, notably phosphate [1], and *Rhizobium* bacteria that fix atmospheric nitrogen for the plant [2]. Several other types of beneficial soil-borne microbes, such as plant growth promoting rhizobacteria and fungi, can stimulate plant growth by suppressing plant diseases [3–6,7•] or insect herbivory [8•]. This biological control activity is exerted either directly through antagonism of soil-borne pathogens or indirectly by eliciting a plant-mediated resistance response [3,9]. The mechanisms by which beneficials and parasites activate the host's immune response not only share intriguing similarities but also display crucial differences. Here, we review the recent discoveries on the molecular mechanisms involved in beneficial microbe-induced resistance.

Resistance-inducing traits of beneficial microbes

Microbial determinants that contribute to induced resistance as triggered by beneficial microbes are best studied for fluorescent *Pseudomonas* spp. In analogy to the microbe-associated molecular patterns (MAMPs) flagellin and lipopolysaccharides (LPS) of pathogenic *Pseudomonas* spp. [10], it was found that these cell surface components of beneficial *Pseudomonas* spp. are potent inducers of the host immune response [11]. Purified flagellin and LPS of the nonpathogenic resistance-inducing strains *Pseudomonas fluorescens* WCS417 and WCS374, and *Pseudomonas putida* WCS358 have differential resistance-inducing activities on Arabidopsis, tomato, and bean, suggesting host specificity in the recognition of these beneficial microbe derived MAMPs. Flagellin and LPS mutants of these rhizobacterial strains are nevertheless often as effective as the wild-type strains, suggesting that multiple MAMPs are involved in the activation of the plant's immune response [11].

Under conditions of low iron availability, most aerobic and facultative anaerobic microorganisms, including fluorescent *Pseudomonas* spp., produce low molecular weight Fe^{3+}-specific chelators, so-called siderophores. Competition for iron between fluorescent *Pseudomonas* spp. and plant pathogens is often considered to be the mode of action of these siderophores in disease suppression. However, a role for siderophores in the elicitation of resistance has been reported in several systems as well [12,13]. For instance, in tomato the *P. putida* WCS358 siderophore pseudobactin358 triggers systemic resistance, but the pseudobactin358-mutant of this strain does not [12]. In bean, however, this mutant is as effective as the wild-type strain, again indicating that induced systemic resistance (ISR) is activated by multiple MAMPs in this plant–microbe interaction. Interestingly, under low iron conditions several *Pseudomonas* spp. also produce salicylic acid (SA), a signaling molecule that is known to play an important role in the regulation of pathogen-induced systemic acquired resistance (SAR) [11,14]. Indeed, SA produced by the siderophore mutant KMPCH of *P. aeruginosa* 7NSK2 was demonstrated to induce disease resistance in tomato [15]. However, in most cases, microbially produced SA does not contribute to enhanced defense, as it is directly channeled into the production of SA-containing siderophores [16].

Antibiotics, which are produced by some beneficial microorganisms, can also function as MAMPs in triggering the immune response. An example is 2,4-diacetylphloroglucinol (DAPG) that is produced by many

fluorescent *Pseudomonas* spp. [17]. In Arabidopsis, DAPG produced by *P. fluorescens* CHA0 was demonstrated to induce resistance, while DAPG-mutants lost this ability [18]. Recently, the biosurfactant massetolide A from *P. fluorescens* SS101 was shown to trigger systemic resistance in tomato against *Phytophthora infestans*, while the *massA*-mutant was significantly less effective in controlling the disease than the wild-type strain [19•]. A similar role in the activation of host defense was demonstrated for surfactin, a lipoprotein produced by *Bacillus subtilis* [20]. Other rhizobacterially produced compounds implicated in eliciting host defense are *N*-alkylated benzylamine [21] and *N*-acyl-L-homoserine lactone [22]. Interestingly, the volatile organic compound (VOC) 2,3-butanediol produced by two *Bacillus* spp. was shown to induce resistance in Arabidopsis as well [23], demonstrating the diversity of MAMPs produced by beneficial rhizobacteria that are recognized by the plant.

MAMPs involved in systemic resistance triggered by beneficial fungi are not well studied. The nonenzymatic activity of *Trichoderma* spp.-produced cellulose and xylanase is known to elicit resistance in plants [24]. Djonović *et al.* [25•] recently demonstrated that the hydrophobin-like elicitor Sm1 of the beneficial soil-borne fungus *Trichoderma virens* induces systemic resistance in maize. Maize plants grown with *SM1*-deletion strains or *SM1*-overexpressing strains displayed decreased or enhanced levels of systemic disease protection, respectively, demonstrating its role in triggering host defense. The fungal determinants that elicit mycorrhiza-induced resistance are currently unknown [9]. However, the recently published genome sequence of the mycorrhizal fungus *Laccaria bicolor* [26••] may provide clues for the discovery of MAMPs involved in the induction of systemic resistance by these beneficials.

Induced defense signaling pathways

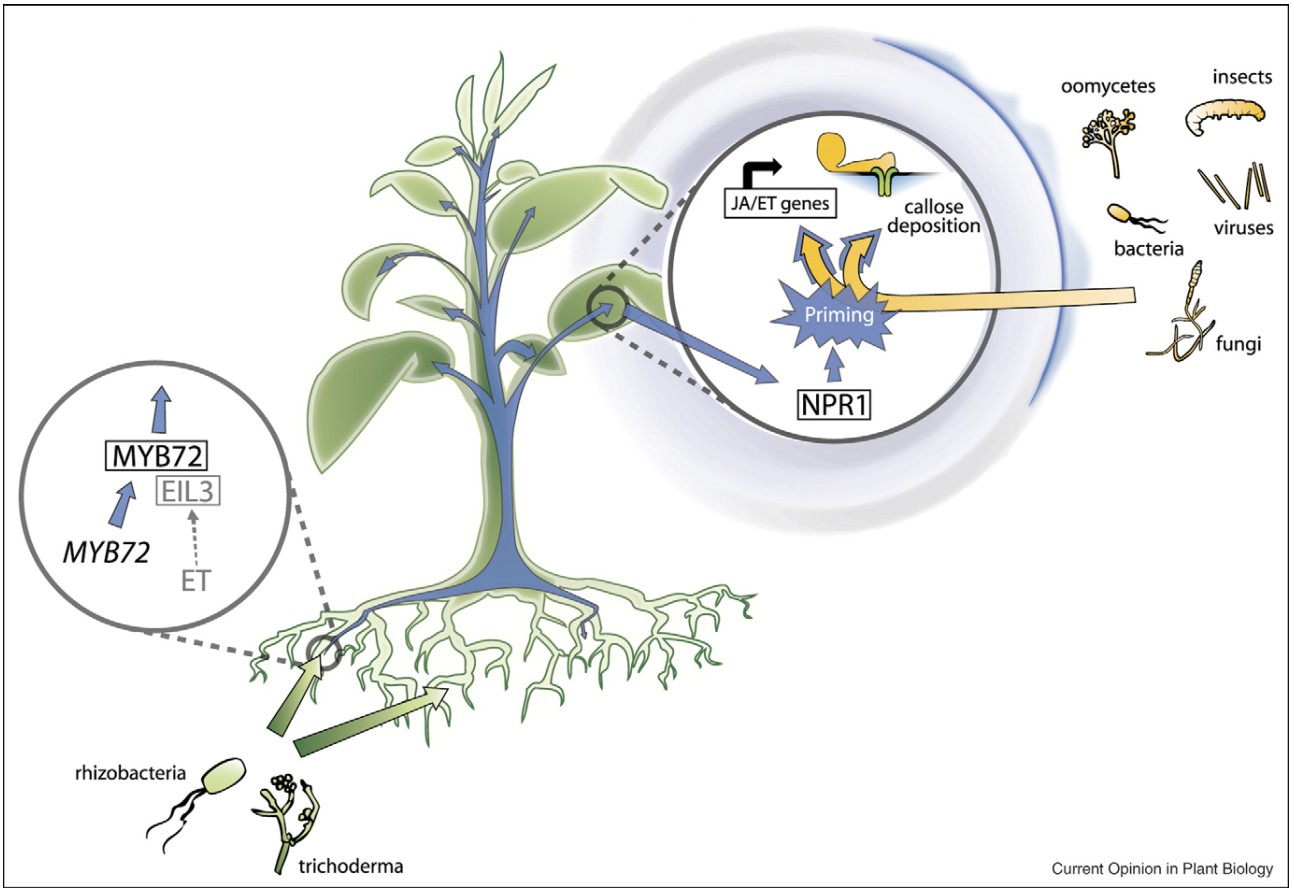
It is probable that MAMPs of beneficial microbes and pathogens are recognized in a largely similar manner, ultimately resulting in an enhanced defensive capacity of the plant. However, in plant–beneficial microbe interactions, MAMP-triggered immunity does not ward off the interacting beneficial as it remains accommodated by the plant. This suggests a high degree of coordination and a continuous molecular dialog between the plant and the beneficial organism. The local and systemic defense responses that are triggered by beneficial and parasitic microorganisms are controlled by a signaling network in which the plant hormones SA, jasmonic acid (JA), and ethylene (ET) play important roles [27]. There is ample evidence that SA, JA, and ET pathways crosscommunicate, allowing the plant to finely tune its defense response depending on the invader encountered [28•]. Well-studied examples of systemically induced resistance are SAR, which is triggered upon infection by necrosis-inducing pathogens and is dependent on SA signaling [14], and ISR, which is triggered by beneficial rhizobacteria, such as *P. fluorescens* WCS417 and requires components of the JA and ET signaling pathway [29]. Both pathogen-induced SAR and *P. fluorescens* WCS417-triggered ISR are controlled by the transcriptional regulator NPR1 ([30]; Figure 1). Because SAR is associated with NPR1-dependent *PR* gene expression [31], and ISR is not, NPR1 must differentially regulate gene expression, depending on the signaling pathway that is activated upstream of it. Hence, the NPR1 protein is integrating and responding to different hormone-dependent defense pathways [32]. Not only several other rhizobacterial strains but also some beneficial fungi have been shown to induce systemic resistance in a JA-dependent, ET-dependent, and/or NPR1-dependent manner [7•,18,19•,25•,33•,34–36] (S Van der Ent, PhD thesis, Utrecht University, 2008), while there are also some reports about dependency on SA signaling [15,37], or requirement of both ISR and SAR components [38•].

Local immune responses triggered by beneficial microbes

Only few plant–beneficial microbe interactions leading to enhanced systemic resistance have been studied for locally induced changes in plant gene expression or metabolism. In most cases only weak, transient, or strictly localized defense-associated responses were elicited, which differs greatly from the massive induction of defense responses triggered during plant–pathogen interactions [39–41,42••]. Transcriptome analysis of Arabidopsis expressing WCS417-ISR revealed a set of 94 genes that were differentially expressed locally in the roots [39]. Knockout mutant analysis of a subset of these WCS417-responsive genes showed that the transcription factor (TF) MYB72 is required in early signaling steps of ISR [43••]. Arabidopsis *myb72* mutants were incapable of mounting ISR against both SA-controlled and JA-controlled pathogens, indicating that MYB72 is essential to establish broad-spectrum ISR. Overexpression of MYB72 was not sufficient for the expression of ISR. Hence, MYB72 was assumed to act in concert with another signaling component. MYB72 interacted with the EIN3-like TF EIL3 *in vitro*, making EIL3 a potential candidate in this respect [43••]. The interaction with EIL3 links MYB72 function to the ET response pathway involved in ISR, which was previously demonstrated to orchestrate ISR in the roots ([44]; Figure 1). Interestingly, resistance induced in Arabidopsis by the beneficial fungus *Trichoderma asperellum* T34 also appeared to be dependent on MYB72 (S Van der Ent, PhD thesis, Utrecht University, 2008), suggesting that MYB72 functions as a node of convergence in induced defense triggered by soil-borne beneficial microorganisms.

In the case of plant–mycorrhizal symbiosis, significantly more local changes take place. For instance, defense-related compounds like chitinases and glucanases have

Figure 1



Model for the ISR signaling pathway. Recognition of MAMPs of beneficial rhizosphere-colonizing microorganisms, such as *Pseudomonas fluorescens* WCS417 or *Trichoderma asperellum* T34, leads to a local activation of the transcription factor gene *MYB72* in the roots. Subsequently, MYB72 putatively interacts with the transcription factor EIL3. Downstream of, or in parallel with MYB72/EIL3, a so far unidentified ET signaling component is required in the roots for the onset of ISR in the leaves. The ISR signal transduction cascade requires NPR1, probably in the systemic tissue. Systemically, induction of ISR is associated with priming for enhanced expression of a set of JA-responsive and/or ET-responsive genes and increased formation of callose-containing papillae at the site of attempted pathogen entry. Attack by pathogens or insects, as depicted on the right side of the figure, activates defense responses in the plant (yellow arrows), which is accelerated in ISR-primed plants (combined blue and yellow arrows). Artwork: Wouter Boog.

been shown to accumulate locally in mycorrhizal roots of tomato [9]. In rice, 40% of the mycorrhiza-responsive genes were also responsive to infection by fungal pathogens, indicating that the responses to beneficial and pathogenic fungi partly overlap [45]. Interestingly, some of the initial responses of *Medicago truncatula* to the mycorrhizal fungus *Glomus mosseae* and to the beneficial rhizobacterium *P. fluorescens* C7R12 have been shown to be overlapping as well [46]. Both beneficial microbes failed to elicit these shared responses in the symbiosis-defective mutant *dmi3*, which is affected in the calcium-dependent and calmodulin-dependent protein kinase DMI3 [46]. Again, this suggests that the signaling pathways triggered by very different beneficial microbes converge.

Priming for enhanced defense

In contrast to the systemic immune responses that are triggered upon pathogen attack, systemic resistance conferred by beneficial microorganisms is generally not associated with substantial reprogramming of the transcriptome. Instead, the systemic changes in gene expression are either relatively mild [42••,47,48•] or not detectable at all [39]. However, a common feature of ISR responses induced by beneficial microorganisms is priming for enhanced defense. In primed plants, defense responses are not activated directly, but are accelerated upon pathogen or insect attack, resulting in enhanced resistance to the attacker encountered [49•,50]. In Arabidopsis, rhizobacteria-mediated ISR is often associated with priming for enhanced expression of JA/ET-respon-

sive genes and increased deposition of callose at the site of pathogen entry [8•,33•,39,43••,51,52] (Figure 1). Both priming phenomena were abolished in the ISR mutants *myb72* and *npr1* [43••], demonstrating the key role of priming in ISR. Some beneficial rhizobacteria, such as *Paenibacillus alvei* K165 prime for enhanced SA-dependent defenses [37], while others, such as selected endophytic actinobacteria, are able to prime both the SA and the JA/ET pathway [38•].

Like beneficial rhizobacteria, certain plant growth promoting fungi have also been reported to induce priming in plants. Cucumber plants preinoculated with the beneficial fungus *T. asperellum* T203 developed a JA/ET-dependent systemic resistance that was associated with potentiated *PR* gene expression in response to pathogen challenge [35]. A similar observation was noted in Arabidopsis following colonization of the roots by a beneficial *Penicillium* sp. [7•]. The endophytic fungus *Piriformospora indica* induced systemic resistance in barley without priming for JA-mediated, ET-mediated, or SA-mediated defenses, but was associated with the activation of the glutathione–ascorbate cycle, indicating an increased antioxidative capacity [5]. In some cases, shoots of mycorrhizal plants showed changes in defense-related gene expression in the absence of a pathogen [42••], but in other cases priming seems to be the dominant mechanism involved in mycorrhiza-induced systemic resistance [9]. For instance, colonization of tomato roots by mycorrhizal fungi systemically provided protection against *Phytophthora parasitica* infection without direct accumulation of PR proteins. However, upon pathogen attack, mycorrhized plants significantly accumulated more PR proteins than nonmycorrhized plants [53]. Although JA emerged as an important regulator of mycorrhization [54], it remains to be elucidated whether JA serves as the endogenous signal in the mycorrhiza-induced primed state.

Conclusions

Progress in research on plant immune responses that are triggered by beneficial microorganisms shows that the establishment of mutualistic associations usually involves mutual recognition and a high degree of coordination between the plant and the beneficial organism. Various MAMPs from beneficial microbes have been identified that, in analogy to MAMPs of pathogens, play crucial roles in the onset of the plant's immune response. There seems to be considerable redundancy in the ability of MAMPs from beneficials to induce resistance, which is also common to MAMPs of pathogens [55]. Recognition of different pathogen-derived MAMPs has been shown to elicit similar cellular responses, suggesting an early point of convergence in the corresponding signaling pathways. Recently, the receptor-like kinase BAK1 (brassinosteroid-associated kinase 1) was identified as a potentially important regulator in this signaling convergence [56••]. It is tempting to speculate that redundancy in MAMP recognition guarantees robustness of induced immune response.

The signaling networks that are activated by the plant in response to parasitic and beneficial organisms overlap; this indicates that the regulation of the adaptive response of the plant is finely balanced between protection against aggressors and acquisition of benefits. In the roots, the TF MYB72 and the protein kinase DMI3 have emerged as signaling nodes in which defense signaling pathways triggered by different types of beneficial microorganisms converge. Systemic resistance induced by beneficial microorganisms appears to be predominantly regulated by the JA/ET pathway based on priming for enhanced defense, rather than on direct activation of defense. This is not illogical, because activation of inducible defenses involves major costs that affect plant growth and reproduction [57], and this is inconsistent with the beneficial nature of these plant–microbe interactions. Through the study of the costs and benefits of priming in Arabidopsis, it was recently shown that the fitness costs of priming are lower than those of constitutively activated defenses, such as those expressed in the constitutive SAR-expressing mutant *cpr1* [58••]. Intriguingly, the fitness benefits of priming outweighed its costs under pathogen pressure, which suggests that priming functions as an ecological adaptation of the plant to respond faster to its hostile environment.

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