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## Induced Systemic Resistance and the Rhizosphere Microbiome

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**Microbial communities that are associated with plant roots are highly diverse and harbor tens of thousands of species. This so-called microbiome controls plant health through several mechanisms including the suppression of infectious diseases, which is especially prominent in disease suppressive soils. The mechanisms implicated in disease suppression include competition for nutrients, antibiosis, and induced systemic resistance (ISR). For many biological control agents ISR has been recognized as the mechanism that at least partly explains disease suppression. Implications of ISR on recruitment and functioning of the rhizosphere microbiome are discussed.**

**Keywords :** disease suppressive soils, plant pathogens, *Pseudomonas* spp.

### The rhizosphere microbiome

Plant roots growing in the dark realms of soils are certainly not solitary. They sustain a community of organisms that includes trillions of microbial cells belonging to tens of thousands of species. In this respect plants and animals are actually quite alike, as also animals live in close association with complex microbial communities. The human gut microflora is estimated to consist of  $10^{14}$  bacterial cells, ten times more than there are human cells in a body, and belonging to several thousands of species (Arumugam et al., 2011). These microorganisms in the gut play a role in nutrient uptake (Derrien et al., 2010) and obesity (Turnbaugh et al., 2006, 2009), absorption of herbal medicine (Crow, 2011), control of gastrointestinal pathogens (Khoruts et al., 2010), immunity against diseases (Fagundes et al., 2012), and they even are suggested to influence mammal behaviour (Diaz Heijtz et al., 2011; Grenham et al., 2011; Williams et

al., 2012). The collective microbiome in the plant rhizosphere is similarly important for the functioning and health of plants. Uptake of nutrients for a large part depends on microorganisms. Not only are plants directly assisted in their phosphate (Khan et al., 2009; Van der Heijden et al., 2006) and nitrogen uptake (Kraiser et al., 2011) by microorganisms, but many fungal, bacterial and archaeal taxa are also important for nutrient cycling in soil (Van der Heijden et al., 2008). Furthermore, rhizosphere microorganisms support plants through direct control of diseases and their impact on the disease defensive capacity of plants (Bakker et al., 2007, Berendsen et al., 2012) and on tolerance to abiotic stresses (Yang et al., 2008). The importance of the rhizosphere microflora for plant growth and health has been studied for decades. Rhizodeposition of carbon compounds increases microbial activity and biomass in rhizosphere soil (Hartmann et al., 2009), and interactions between members of the microbial rhizosphere community are important drivers of plant growth (Raaijmakers et al., 2009). Compared to the human gut microbiome, the microbiome associated with the plant root is staggeringly complex (Berendsen et al., 2012). Around 3000 culturable soil fungi have been described (Gams, 2007), but this number will undoubtedly increase with the application of molecular techniques (Anderson and Cairney, 2004). In sugar beet rhizosphere soil over 33,000 bacterial and archaeal operational taxonomic units (OTUs) were detected (Mendes et al., 2011). Such a microbial diversity extends the functional repertoire of the plant and its associated microbes beyond imagination. The function that we focus on in this mini-review is the ability of specific root associated microorganisms to elicit induced systemic resistance against pathogens.

### Disease suppressive soils

According to the definition by Baker and Cook (1974) disease suppressive soils are “soils in which the pathogen

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does not establish or persist, establishes but causes little or no damage, or establishes and causes disease for a while but thereafter the disease is less important, although the pathogen may persist in the soil.” Biological factors have been identified as the most important element in disease suppression in such soils (Mazzola, 2002). A prominent example of disease suppressiveness is take-all decline (TAD). When wheat is grown continuously in the same field, take-all disease caused by *Gaeumannomyces graminis* var. *tritici* will develop over the years. However, after a severe outbreak of take-all, the soil becomes suppressive against the disease (Weller et al., 2002). This suppressiveness can be negated by heat treatment and it is transferrable to a conducive soil by mixing a small ratio of suppressive to the conducive soil (Raaijmakers and Weller, 1998). Whereas build up of 2,4-diacetylphloroglucinol producing *Pseudomonas fluorescens* populations appears to be solely responsible for take-all decline (Raaijmakers and Weller, 1998), 16S rRNA-based techniques have identified additional bacterial taxa that may be involved in take-all decline (Sanguin et al., 2009; Schreiner et al., 2010). Other well examined examples of disease suppressive soils include Fusarium wilt suppressiveness (Alabouvette, 1999), tobacco black root rot disease suppressiveness (Kyselkova et al., 2009), and *Rhizoctonia solani* suppressiveness (Mendes et al., 2011). In soil naturally suppressive to Fusarium wilt, a synergistic effect of competition for carbon by non-pathogenic *Fusarium oxysporum* and production of redox-active phenazines appears to play an important role in suppressiveness (Mazurier et al., 2009). Using a 16S rRNA taxonomic microarray several bacterial taxa, including *Pseudomonas*, *Azospirillum*, *Gluconacetobacter*, *Bulkholderia*, *Comamonas* and *Sphingomonadaceae*, were shown to be more prevalent in tobacco black root rot suppressive soil than in conducive soil (Kyselkova et al., 2009). This suggests that suppression of *Thielaviopsis basicola* in this soil is based on a microbial consortium. Similar findings have been described for a potato common scab suppressive soil (Rosenzweig et al., 2012). An in depth study of the rhizosphere microbiome of the *R. solani* suppressive soil also revealed that a consortium of microbes governs disease suppression. Using PhyloChip analysis, which allows simultaneous detection of ~60,000 bacterial and archaeal OTUs, 17 taxa belonging to the  $\beta$ -proteobacteria,  $\gamma$ -proteobacteria, and the firmicutes were identified as being closely associated with disease suppressiveness (Mendes et al., 2011). The group of Pseudomonaceae has been suggested as a player in disease suppressiveness in all aforementioned disease suppressive soils. Control of diseases by these fluorescent pseudomonads has been studied in detail over the last three to four decades (Weller, 2007). The main modes of action of disease suppression by fluorescent

*Pseudomonas* spp. are siderophore mediated competition for iron (Duijff et al., 1999), antibiosis (Raaijmakers et al., 2002), and induced systemic resistance (ISR) (Bakker et al., 2007). During the last two decades the involvement of ISR has been recognized as an important and effective mode of action for a range of bacterial and fungal biological control agents.

### ISR eliciting biocontrol agents and ISR eliciting determinants

In the early nineties, plant growth promoting rhizobacteria were studied for their abilities to elicit ISR, with special focus on *Pseudomonas* spp.. It was discovered that when certain biocontrol pseudomonads were applied and kept spatially separated from the pathogen, they still reduced disease, suggesting that the mode of action must be plant mediated (Van Peer et al., 1991; Wei et al., 1991). Induced resistance is a state of enhanced defensive capacity developed by a plant when appropriately stimulated (Van Loon et al., 1998). There is a long and growing list of both biotic and abiotic agents that can protect crops against pathogens by eliciting ISR (Da Rocha and Hammerschmidt, 2005; Reglinski and Walters, 2009). Many bacterial biocontrol agents have been implicated to elicit ISR (De Vleeschauwer and Höfte, 2009), including *Bacillus* spp. (Jourdan et al., 2009; Kloepper et al., 2004), *Pseudomonas* spp. (Bakker et al., 2007), and *Serratia* spp. (Press et al., 1997; Schuhegger et al., 2006). Fungal biocontrol agents reported to elicit ISR include *Trichoderma* spp. (Koike et al., 2001; Segarra et al., 2009), *Piriformospora indica* (Shores et al., 2010), *Penicillium simplicissimum* (Elsharkawy et al., 2012), *Phoma* sp. (Sultana et al., 2009), non-pathogenic *Fusarium oxysporum* (Fravel et al., 2003), and arbuscular mycorrhizal fungi (Pozo et al., 2009). The above mentioned list of examples of ISR eliciting microorganisms is certainly not exhaustive and one may wonder if there are biological control agents that can not elicit ISR.

Also for microbial determinants that are involved in ISR the list is growing. The first reports on bacterial determinants involved in ISR concerned *P. fluorescens* lipopolysaccharides (Leeman et al., 1995a; Van Peer et al., 1992) and siderophores (Maurhofer et al., 1994). Many more ISR elicitors have been identified by application of purified compounds and the use of mutants that lack the production of a possible eliciting compound (Bakker et al., 2003; De Vleeschauwer and Höfte, 2009). ISR elicitors that were identified using such strategies include flagella (Meziane et al., 2005), iron-regulated metabolites (Audenaert et al., 2002; De Vleeschauwer et al., 2008; Meziane et al., 2005; Ongena et al., 2005; Ran et al., 2005), the antibiotics 2,4-diacetylphloroglucinol (Iavicoli et al., 2003; Weller et

al., 2012) and pyocyanin (Audenaert et al., 2002; De Vleeschauwer et al., 2006), biosurfactants (Ongena et al., 2007; Tran et al., 2007), and volatile organic compounds (Ryu et al., 2004). Moreover, redundancy of ISR elicitors in a single biological control microorganism has been reported (Bakker et al., 2003; De Vleeschauwer and Höfte, 2009). Taking into account the high population densities of microorganisms in the rhizosphere (Katznelson et al., 1948) and the high diversity of these microbial communities (Mendes et al., 2011), on top of the many microorganisms that have the potential to elicit ISR and the variety in ISR eliciting determinants, it seems reasonable to assume that most plants are in the state of ISR. However, under field conditions ISR can effectively suppress disease (Leeman et al., 1995b, Wei et al., 1996), suggesting that untreated plants are not in the state of ISR.

### Why are not all plants in the state of ISR?

The rhizosphere microflora contains an incredible number of bacterial species (Mendes et al., 2011), and within one species different genotypes are present, as described for *Pseudomonas* spp. (Glandorf et al., 1993, 1994; Lemanceau et al., 1995). To effectively elicit ISR high population densities of a specific biocontrol strain are introduced into the soil or rhizosphere, usually around  $10^7$  colony forming units (cfu) per gram of root, see for example Van Pelt et al. (2008). Dose response studies for biological control agents revealed that high populations are needed for effective control of diseases (Bull et al., 1991; Johnson and DiLeone, 1999; Montesinos and Bonaterra, 1996; Raaijmakers and Weller, 1998). Typically bacterial population densities of at least  $10^5$  cfu per gram of root are required for control of diseases by fluorescent pseudomonads, either mediated by antibiosis (Raaijmakers and Weller, 1998), or by ISR (Raaijmakers et al., 1995). It seems unlikely that such high population densities of a specific bacterial genotype are present in the rhizospheres of plants in the field, although it has been reported for disease suppressive soils. In take-all decline soil, 2,4-diacetylphloroglucinol producing fluorescent *Pseudomonas* spp. were detected at densities above the threshold level of  $10^5$  per gram (De Souza et al., 2003; Raaijmakers and Weller, 1998). Even if one specific bacterial genotype would reach population densities above this threshold, there is specificity in ISR both on the bacterial side and the plant side (Van Loon and Bakker, 2005).

### What's in it for the eliciting bacteria?

Stimulation of ISR eliciting bacteria by plants under pathogen attack was reported by Rudrappa et al. (2008). The roots of *A. thaliana* plants infected by *P. syringae* pv.

*tomato* secreted elevated levels of malic acid, and in a dose dependent manner malic acid stimulated binding to and biofilm formation on the roots by the ISR eliciting *Bacillus subtilis* strain FB17. In this situation the plant offers a more hospitable rhizosphere environment to the bacteria and in return the plant benefits from protection offered by the bacteria. Rhizobacteria-mediated ISR affects activity and growth of pathogenic microorganisms and may also affect the growth and activity of the indigenous rhizosphere microflora and introduced biological control agents. ISR eliciting microbes may modulate defense responses of the plant to their own benefit (Zamioudis and Pieterse, 2012). In this context it is interesting that in the rhizosphere of *Arabidopsis* mutant *myb72*, that can not express *Pseudomonas*- or *Trichoderma*-mediated ISR (Segarra et al., 2009; Van der Ent et al., 2008), population densities of strains of fluorescent *Pseudomonas* spp. that are able to trigger ISR in wild-type *Arabidopsis* are much lower than their rhizosphere populations in the wild-type (Doornbos et al., 2009). This suggests cross communication between the plant and the ISR-eliciting bacteria, resulting in rewards for the plant, that becomes less susceptible to pathogen attack, and the bacteria, that establish higher population densities. Whereas in the absence of pathogens the state of induced resistance poses slight fitness costs on the plant, when pathogens are present the benefits of induced resistance greatly outweigh the costs (Van Hulten et al., 2006).

In *Arabidopsis*, a possible impact of the constitutive expression of induced resistance on bacterial community structure and diversity in the rhizosphere was studied (Hein et al., 2008). However, differences in bacterial diversity that were observed in this study could not be related to the expression of induced resistance. Application of defense inducing phytohormones salicylic acid and jasmonic acid did not result in major shifts in *Arabidopsis* rhizosphere bacterial communities (Doornbos et al., 2011). In the rhizospheres of *Arabidopsis* accessions RLD and WS-0, bacterial communities are distinct from those of Col-0 and five other accessions (Micallef et al., 2009). These data do suggest a possible impact of defense signaling on bacterial community structure, since RLD and WS-0 are relatively insensitive to ethylene and impaired in the expression of ISR compared to the other accessions (Ton et al., 1999, 2001).

Recent studies have provided exciting evidence that plants under attack recruit beneficial microbes in their rhizospheres, for example in *Arabidopsis* under attack of a bacterial pathogen (Rudrappa et al., 2008) or in pepper that is being fed upon by aphids (Lee et al., 2012). Such recruitment of beneficial microbes is also evident in monocultures of wheat, in which after an initial outbreak of take-all disease, disease suppressiveness caused by 2,4-diacetylphloroglucinol producing pseudomonads develops (Weller et al., 2002).

Support for a cry for help hypothesis can also be found in a recent study by Mavrodi et al. (2012) in which 2,4-diacetylphloroglucinol producing pseudomonads were recruited in the rhizosphere of wheat under irrigated conditions and under dry conditions phenazine producing pseudomonads were recruited. *G. graminis* var. *tritici*, that is sensitive to 2,4-diacetylphloroglucinol, is the major pathogen under irrigated conditions, whereas *R. solani*, sensitive to phenazines, is the major pathogen under dry conditions.

### Concluding remarks

Despite a century long history of rhizosphere research (Hartmann et al., 2008) we are still at the beginning of understanding the complex plant-microbe interactions in this dynamic environment (Bisseling et al., 2009). ISR is a powerful mode of action of biological control of plant diseases, but widespread practical applications in agriculture require a rigorous knowledge of the ISR eliciting microbes and their interactions with the rhizosphere microbiome. Positive interactions may occur, as for example antagonistic activity against plant pathogens by combinations of apparently non-antagonistic soil bacteria (De Boer et al., 2007). But also less expected negative effects in which harmless or even beneficial microbes assist incoming pathogens (Venturi and Passos de Silva, 2012). The complexity of the microbiome and the fact that most members are as yet uncultivated (Vartoukian et al., 2010) calls for new approaches. Exciting developments that will enable in depth studies of the functioning of the rhizosphere microbiome include the use of PhyloChips to study the composition of microbial communities (Hazen et al., 2010; Mendes et al., 2011), development of metatranscriptomics (Helbling et al., 2012; Mark et al., 2005), and metabolic profiling of root exudates (Van Dongen et al., 2009). Knowing the advantages and disadvantages of specific interactions will enable sensible applications to control diseases in a sustainable manner.

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