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Systemic Acquired Resistance vs Induced Systemic Resistance: A Review

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ABSTRACT

SAR and ISR are key acquired resistances in plants that play major role in imparting resistance to plants against various pathogens namely bacteria, virus, nematodes *etc*. The increasing awareness towards chemicals has led scientists to work on new mechanism of resistances. Both SAR and ISR are of future perspective for disease management. SAR require salicylic acid as transport molecule along with other complexes that include reactive oxygen species, lipid molecules whereas ISR require Jasmonic acid as signal molecule. SAR is more long lasting and broad spectrum as compared to ISR. Non-pathogenic bacteria and insectivores induce ISR. In future, disease management will be more focused on ISR and SAR.

Key words: Induced resistance, ISR, JA, Resistance, SA, SAR.

Plants have evolved a number of inducible defense mechanisms against the attack of pathogen. Recognition of a pathogen often triggers a localized resistance reaction, known as the hypersensitive response (HR), which is characterized by rapid cell death at the site of infection (Hammond-Kosack *et al*., 1996). In the 1960s, Ross showed that tobacco plants challenged with tobacco mosaic virus (TMV) subsequently developed increased resistance to secondary infection in distal tissues (Ross, 1961). This spread of resistance throughout the plant's tissues was termed systemic acquired resistance (SAR). We now know that SAR can be activated in many plant species by pathogens that cause necrosis, either as part of the HR or as a symptom of the disease. The resistance conferred is long-lasting, sometimes for the lifetime of the plant and effective against a broad spectrum of pathogens including viruses, bacteria, fungi and oomycetes (Ryals *et al*., 1996). Molecularly, SAR is characterized by the increased expression of a large number of pathogenesis-related genes (PR genes), in both local and systemic tissues. PR proteins were first described in the 1970s by Van Loon, who observed the accumulation of various novel proteins after infection of tobacco with TMV (Van Loon *et al*., 1970). Although many PR proteins have antimicrobial properties *in vitro* (Van Loon *et al*., 1999), the function of each in the defense response has not been clearly defined. It is generally thought that SAR results from the concerted effects of many PR proteins rather than a specific PR protein. Although their roles in establishing SAR are unclear, PR genes serve as useful molecular markers for the onset of SAR.

History of SAR

For over 90 years, scientists and naturalists have observed that when plants survive pathogen infection, they develop increased resistance to subsequent infections. In 1933, Chester reviewed 200 publications describing a phenomenon he termed physiological acquired immunity (Chester, 1933). At that time, scientists believed they were investigating a phenomenon analogous to the immune response in mammals. In retrospect, at least three different processes were being called acquired immunity: vira1 cross-protection, antagonism (or biocontrol) and what we now refer to as SAR. During the 30 years following Chester's review, many papers were published on the subject, but most of these were descriptive studies extending the earlier observations and none of them were practical. The first systematic study of SAR was published by A. Frank Ross in 1961. Using TMV on local lesion hosts, Ross demonstrated that infections of TMV were restricted by a prior exposure to the pathogen. This resistance was effective against not only TMV but also tobacco necrosis acquired resistance are aspects of the same response or distinct processes. In the past 30 years, SAR has been demonstrated in many plant species and the spectrum of resistance has been broadened to include not only viruses and bacteria but also many agronomically important phytopathogenic fungi (Kuć, 1982). However, our understanding of the biochemical events leading to the establishment of SAR had not progressed substantially until the past dozen years. In 1982, Kees Van Loon showed that the accumulation of a group of

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extracellular proteins called PR proteins corelated with the onset of SAR (Van Loon and Antoniw, 1982). Ray White demonstrated in 1979 that salicylic acid (SA) and certain Benzoic acid (BA) derivatives could induce both resistance and the accumulation of PR proteins (White, 1979). As a result, SA was considered as a possible endogenous signal molecule (Van Loon and Antoniw, 1982). However, progress slowed through the 1980s and the involvement of PR proteins and salicylic acid in SAR was questioned. Recently, significant progress toward understanding SAR has been made with the application of molecular biology, genetics and enhanced biochemical tools. Nevertheless, our knowledge is still rudimentary and future progress will depend on even more aggressive use of modem biological methods.

Salicylic acid

The detection of increased SA levels in systemic leaves and the phloem led many researchers to believe that SA might be a systemic signal for SAR (Dempsey *et al*., 1999). Labelling studies in TMV-infected tobacco showed that most of the SA (69%) accumulating systemically was made and exported from the inoculated leaf (Shulaev *et al*., 1995). Similarly, in cucumber infected with TNV, SA found in systemic leaves was both imported from the infected leaf as well as synthesized de novo (Meuwly *et al*., 1995). A more recent study suggests that signalling might occur through the conversion of SA to the volatile compound methyl salicylate, which could induce resistance not only in the uninfected parts of the same plant but also in neighbouring plants (Shulaev *et al*., 1997). Several experiments argue against SA being the systemic signal. Detachment of *Pseudomonas syringae*-infected cucumber leaves before SA levels had increased in the petiole did not block the development of SAR (Rasmussen *et al*., 1991). Furthermore, grafting experiments in tobacco between wild-type scions and nahG-expressing rootstocks showed that, although the rootstock was unable to accumulate SA, the SAR signal was still produced and translocated to the scion (Vernooij *et al*., 1994). The reciprocal grafting experiment showed that the systemic tissue must accumulate SA for the SAR signal to be perceived.

Lipid-based signal molecule

Exciting new work suggests that a lipid-based molecule may be the mobile signal for SAR. Maldonado *et al.* showed that the dir1 (defective in induced resistance 1) mutant has normal local resistance to pathogens but is unable to develop SAR or express PR genes in systemic leaves (Maldonado *et al*., 2002). Therefore, wild-type DIR1, which has sequence similarity to lipid transfer proteins (LTPs), might function in the generation or transmission of the mobile signal. Indeed, experiments using petiole exudate showed that the phloem sap from dir1 is deficient in the mobile signal for SAR. However, the mutant plants could still respond to a signal contained in the sap from wild-type plants, ruling out a role for DIR1 in signal perception. Furthermore, the dir1 plants have wild-type SA metabolism and a normal response to SA and INA. The similarity of DIR1 to LTPs suggests that the mobile signal for SAR might be a lipid molecule. LTPs form a multigene family in Arabidopsis with 71 predicted members (Beisson *et al*., 2003). Interestingly, they share sequence similarity with elicitins from *Phytophthora* spp., which are elicitors of plant defense responses (Blein *et al*., 2002). The extracellular location of LTPs and elicitins is consistent with a role in signalling and implies the presence of plasma membrane (PM) receptors involved in signal transduction. Indeed, wheat LTP1 binds to the same PM receptor as the Phytophthora elicitincryptogein (Buhot *et al*., 2001).

Reactive oxygen species

Early studies could detect no reactive oxygen species (ROS) production in systemic tissues during the onset of SAR (Neuenschwander *et al*., 1995). However, it has since been discovered that H_2O_2 accumulates in small groups of cells in uninoculated leaves of *Arabidopsis* after infection with an avirulent strain of P. *syringae* (Alvarez *et al*., 1998). These microbursts occur within two hours after an initial oxidative burst in the inoculated tissue and are followed by the formation of microscopic HR lesions. Using catalase to scavenge H_2O_2, or DPI (diphenyleneiodonium) to inhibit the NADPH oxidase, it was demonstrated that both the primary and secondary oxidative bursts are required for the onset of SAR. The authors propose that microbursts of ROS may activate defense responses at a low level throughout the plant and this contributes to the SAR-induced state. Transport. Girdling experiments suggested that the SAR signal produced in inoculated leaves travels in the phloem to upper leaves (Ross, 1966). If the mobile signal does travel through the phloem, the pattern of SAR induction should match the transport of sugars out of the infected leaf. When this was tested in Arabidopsis, it was observed that the movement of radioactively labelled sucrose did not exactly match the induction of SAR, SA accumulation, or PR-1 expression (Kiefer *et al*., 2003). Induction of SAR was observed outside of the normal orthostichy defining phloem movement. This suggests the small amount of phloem moving between orthostichies contains enough signal to induce SAR.

SA synthesis

It was previously assumed that SA for SAR is synthesized *via* the shikimate phenylpropanoid pathway (Lee *et al*., 1995), although this was never proven. It has recently been shown that, like bacteria, plants can also synthesize SA from chorismate via isochorismate. Expression of the bacterial enzymes catalyzing these reactions, isochorismate synthase 1 (ICS1) and isochorismate pyruvate lyase 1 (IPL1), in tobacco and Arabidopsis results in increased SA accumulation and pathogen resistance (Mauch *et al*., 2001). Using HPLC, Nawrathand Metraux isolated the SA induction-deficient Arabidopsis mutants sid1 and sid2, which failed to accumulate SA after SAR induction (Nawrath *et al*., 1999). More alleles of sid1 and sid2, called eds5 and eds16,

respectively, were identified independently by their enhanced disease-susceptibility phenotype (Dewdney *et al*., 2000).

Breakthrough in our understanding of SA biosynthesis came when SID2/EDS16 was cloned and shown to encode a putative chloroplast-localized ICS1 (Wildermuth *et al*., 2001). Mutations of the ICS1 gene, in sid2 and eds16, reduce SA accumulation after infection to only 5-10% of wild-type levels and compromise both basal and systemic resistance. This demonstrates that the isochorismate pathway in plants is the main source of SA synthesis during SAR. Consistent with this conclusion, ICS1 expression is induced by infection in both local and systemic tissues. Wildermuth *et al.* proposed that the phenylpropanoid pathway is responsible for the rapid production of SA associated with local cell death, whereas the isochorismate pathway is more important for sustained SA synthesis during the development of SAR. Since SA synthesis is not completely abolished in sid2 plants, some SA must be produced either through the activity of another ICS-like protein, such as ICS2 or through the phenylpropanoid pathway. *Arabidopsis* ICS1 contains a putative plastid transit sequence, suggesting that SA synthesis occurs in the plastid. Interestingly, EDS5/SID1 encodes another protein required for SA accumulation that has sequence similarity to the multidrug and toxin extrusion (MATE) family of transporter proteins (Nawrath *et al*., 2002).

Signal transduction of SAR

The first step in the development of SAR is the recognition of pathogen infection by a plant. Once the plant reacts to the pathogen, signals are released that trigger resistance in adjacent as well as distant tissues. Importantly, not a plant- pathogen interactions lead to SAR induction. Compatible interactions can lead to SAR induction; thus, the pathogen need not induce a gene-for-gene resistance reaction (Kuć, 1982). Currently there is no common denominator that can be used to group 'inducing pathogens," and this area needs further clarification. SA has been proposed as one signal leading to SAR because its concentration rises dramatically after pathogen infection (Malamy *et al*., 1990). The most compelling evidence that implicates SA as a signal in SAR comes from experiments using transgenic tobacco to express the enzyme salicylate hydroxylase, encoded by the nahG gene from *Pseudomonas putida* (Gaffney *et al*., 1993). This enzyme catalyzes the conversion of SA to catechol, which is not an active SAR inducer. The NahG-expressing plants do not accumulate SA in response to pathogen infection and are unable to induce a SAR response to viral, bacterial or fungal pathogens. These experiments implicate the direct involvement of SA in SAR signaling, but they do not address whether SA is a long-distance, phloem-mobile signal for SAR. However, experiments by Hammerschmidt and co-workers suggest that SA may not be a systemic signal. In this study SA and acidic peroxidase levels (encoded by a SAR gene in cucumber) were measured in various tissues of cucumber after removal of a leaf infiltrated with *Pseudomonas syringae* (Rasmussen *et al*., 1991). Surprisingly, the inducing leaf could be removed 4 to 8 h post-inoculation, before significant SA accumulation, without preventing the systemic induction of either SA or SAR gene expression. Although SAR was not directly measured, this result suggests the existence of a systemic signal that is distinct from SA.

PR proteins

Pathogenesis-related proteins, often called PR proteins, are a structurally diverse group of plant proteins that are toxic to invading fungal pathogens. They are widely distributed in plants in trace amounts but are produced in much greater concentrations following pathogen attack or stress. PR proteins exist in plant cells intracellularly and also in the intercellular spaces, particularly in the cell walls of different tissues. Varying types of PR proteins have been isolated from each of several crop plants. Different plant organs, *e.g*., leaves, seeds and roots, may produce different sets of PR proteins. Different PR proteins appear to be expressed differentially in their hosts in the field when temperatures become stressful, low or high, for extended periods. The several groups of PR proteins have been classified according to their function, serological relationship, amino acid sequence, molecular weight and certain other properties. PR proteins are either extremely acidic or extremely basic and therefore are highly soluble and reactive. 17 families of PR proteins are recognized. The better-known PR proteins are PR1 proteins (antioomycete and antifungal), PR2 (β-1,3-glucanases), PR3 (chitinases), PR4 proteins (antifungal), PR6 (proteinase inhibitors) thaumatin-like proteins, defensins, thionins, lysozymes, osmotinlike proteins, lipoxygenases, cysteine-rich proteins, glycine-rich proteins, proteinases, chitosanases and peroxidases. There are often numerous isoforms of each PR protein in various host plants (Agrios, 2005).

The sequence of events from pathogen recognition to defense gene induction

Induced disease resistance in plants by chemicals

Various chemicals have been discovered that seem to act at various points in these defense activating networks and mimic all or parts of the biological activation of resistance. Of these, only a few have reached commercialization. The best-studied resistance activator is acibenzolar-S-methyl (BION). Probenazole (ORYZEMATE) is used mainly on rice against rice blast and bacterial leaf blight (Watanabe, 1977). D, L-β-aminobutyric acid (BABA) or it's 3-(S)-enantiomer has been reported to activate disease resistance, especially against downy mildews in various crops (Tosi *et al*., 1998). 2, 2-Dichloro-3, 3-dimethylcyclopropane carboxylic acid (WL 28325) has been known for more than 20 years as a specific and systemic research compound against rice leaf blast. It shows low direct fungitoxicity against pathogen P. *oryzae and* treated plants respond more quickly and in a resistant manner to infection (Langcake *et al*., 1983). The impact of different SAR chemical inducers *viz*. Phosphoric acid, Salicylic acid, Naphthalene acetic acid (NAA), Benzoic acid, Benzothiadiazole, Dichloro-iso nicotinic acid (INA) and

Kinetin at 0.05%, 0.10% and 0.15% concentrations along with check with water and standard fungicide metalaxyl + mancozeb @0.25% concentration. They found that among all chemicals Benzothiadiazole was most effective in delaying the appearance of first symptoms of the disease by 11 days @ 0.10 to 0.15% followed by Salicylic acid which delay the appearance of first symptoms by 9 days as compared to water (Peerzada *et al.*, 2020).

Induced resistance

The term induced resistance is a generic term for the induced state of resistance in plants triggered by biological or chemical inducers, which protects non-exposed plant parts against future attack by pathogenic microbes and herbivorous insects (Kuc, 1982). Plants can develop induced resistance as a result of infection by a pathogen, in response to insect herbivory, upon colonization of the roots by specific beneficial microbes or after treatment with specific chemicals. The induced state of resistance is characterized by the activation of latent defense mechanisms that are expressed upon a subsequent challenge from a pathogen or insect herbivore. Induced resistance is expressed not only locally at the site of induction but also systemically in plant parts that are spatially separated from the inducer, hence the term ISR. Generally, induced resistance confers an enhanced level of protection against a broad spectrum of attackers (Walters *et al.*, 2013). Induced resistance is regulated by a network of interconnected signalling pathways in which plant hormones play a major regulatory role (Pieterse *et al.*, 2012). The signalling pathways that regulate induced resistance elicited by beneficial microbes, pathogens and insects share signalling components. Therefore, we first highlight the important principles of pathogen- and insect-induced resistance before reviewing the current status of ISR mediated by beneficial soil borne microbes.

The plant immune system and induced resistance

In the past decade, ground breaking conceptual advances in the understanding of the evolutionary development of the plant immune system (Ross, 1961) placed our knowledge on induced resistance in a clear perspective. In the current concept of the plant immune system, pattern-recognition receptors (PRRs) have evolved to recognize common microbial compounds, such as bacterial flagellin or fungal chitin, called pathogen- or microbe-associated molecular patterns (PAMPs or MAMPs) (Boller *et al.*, 2009). Plants also respond to endogenous plant-derived signals that arise from damage caused by the enemy invasion, called damage-associated molecular patterns (DAMPs) (Boller *et al.*, 2009). Pattern recognition is translated into the first line of defense called PAMP-triggered immunity (PTI), which keeps most potential invaders in check (Dodds *et al.*, 2010). Successful pathogens have evolved to minimize host immune stimulation and utilize virulence effector molecules to bypass this first line of defense, by either suppressing PTI signalling or preventing detection by the host (Bardoel *et al.*, 2011, De Jonge *et al.*, 2010).

In turn, plants acquired a second line of defense in which resistance (R) NB-LRR (nucleotide-binding-leucine-rich repeat) receptor proteins mediate recognition of attacker-specific effector molecules, resulting in effector-triggered immunity (ETI) (Dodds *et al.*, 2010). ETI is a manifestation of gene-for-gene resistance (Flor, 1971), which is often accompanied by a programmed cell death at the site of infection that prevents further ingress of biotrophic pathogens that thrive on living host tissue. The onset of PTI and ETI often triggers an induced resistance in tissues distal from the site of infection and involves one or more long-distance signals that propagate an enhanced defensive capacity in still undamaged plant parts (Dempsey and Klessig, 2012). This well-characterized form of pathogen-induced resistance is commonly known as systemic acquired resistance (SAR) (Slaughter *et al.*, 2012) and confers enhanced resistance against a broad spectrum of pathogens. As with the pathogen recognition system, plants also recognize herbivorous insects, most likely through a similar signalling concept.

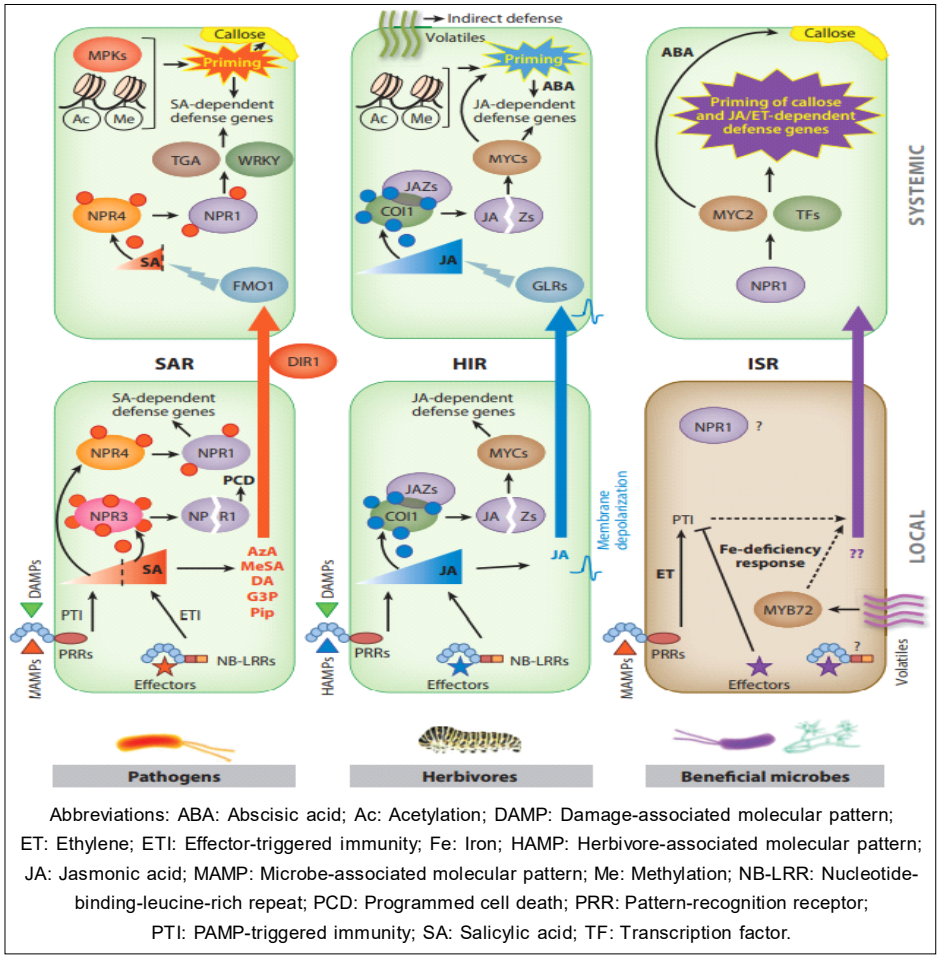
Induced systemic resistance: Early signalling events

Root colonization

Initiation of ISR requires beneficial microbes to efficiently colonize the root system of host plants (Lugtenberg *et al.*, 2009). For the establishment of a successful mutualistic association, host plants and microbes need to respond to reciprocal signals and accordingly prioritize their responses so as to develop a lifestyle that provides mutual benefits. In the well-studied mycorrhizal and rhizobial symbioses, host-secreted strigolactones and flavonoids stimulate the production of symbiotic Sym and Nod factors by the microbes, which in turn activate a common symbiosis (Sym) signaling pathway in plant roots that is necessary for the establishment of a successful symbiotic relationship (Oldroyd and Kamilova, 2009). How non-symbiotic PGPR and PGPF establish a prolonged mutualistic interaction with plant roots is less well characterized, but a picture is emerging that a molecular dialog is also essential for these mutualistic interactions (Shoresh *et al.*, 2010).

Schematic representation of molecular components and mechanisms involved in pathogen-induced systemic acquired resistance (SAR), herbivore-induced resistance (HIR) and induced systemic resistance (ISR) triggered by beneficial soilborne microbes (Fig 1).

Many free-living PGPR actively responds to root exudates by adjusting their transcriptional program toward traits involved in chemotaxis, root colonization and energy metabolism (Matilla *et al.*, 2007). Once established on the root epidermis, PGPR epiphytes typically form biofilms in which multicellular communities are enclosed within an extracellular matrix of self-produced polymeric substances, mainly exopolysaccharides (EPS) and mucilage (Rudrappa *et al.*, 2008). Within the EPS matrix, bacterial cells integrate host and self-derived signals and function in unison to coordinate the production and release of compounds related



Abbreviations: ABA: Abscisic acid; Ac: Acetylation; DAMP: Damage-associated molecular pattern; ET: Ethylene; ETI: Effector-triggered immunity; Fe: Iron; HAMP: Herbivore-associated molecular pattern; JA: Jasmonic acid; MAMP: Microbe-associated molecular pattern; Me: Methylation; NB-LRR: Nucleotide-binding-leucine-rich repeat; PCD: Programmed cell death; PRR: Pattern-recognition receptor; PTI: PAMP-triggered immunity; SA: Salicylic acid; TF: Transcription factor.

Fig 1: Schematic representation of molecular components and mechanisms involved in pathogen-induced systemic acquired resistance (SAR), herbivore-induced resistance (HIR) and induced systemic resistance (ISR) triggered by beneficial soilborne microbes. Solid black lines indicate established interactions; dashed black lines indicate hypothetical interactions. Coloured arrows indicate systemic translocation of long-distance molecular or electric signals (indicated in the same colour at the base of the arrows). Source: Pieterse *et al.*, 2014.

to plant growth promotion, nutrition and ISR. Conceptually, this matrix can be considered as the mutualistic interface through which host plants and beneficial exchange solutes and chemical information. PGPR endophytes commonly enter the root interior through cracks in the newly emerged lateral roots or utilize root hairs and the apical zone as entry points. This mode of entry is facilitated by cell wall-degrading exo-enzymes, such as cellulase and pectinase (Reinhold-Hurek and Hurek, 2011).

Although well known for their ability to adapt in the rhizosphere of various hosts, endophytic PGPF has evolved sophisticated strategies to colonize the intercellular space of the epidermal cortical root layer (Shoresh *et al.*, 2010). The fungal endophyte *P. indica* is a typical generalist with the unique ability to colonize the inter-and intracellular space of a wide range of mono- and dicotyledonous plants. In order to adapt to highly variable host environments, this fungus can adopt alternative lifestyles that are determined by host-specific metabolic cues (Lahrmann *et al.*, 2013). Endophytic *Trichoderma* spp. preferentially colonize the root hairs, where they typically form structures analogous to the appressorium of plant-pathogenic fungi (97). In the *Trichoderma virens* Gv29-8-maize interaction, it was shown that plant-derived sucrose and a sucrose-dependent signaling network in the fungus are crucial for the establishment of a mutualistic association (Vargas *et al.*, 2011). Upon root colonization, *Pseudomonas*, *Bacillus* and *Trichoderma* strains have been shown to initiate an auxin-dependent root developmental program that results in abundant lateral root formation, increased root hair length and enhanced plant biomass production (Zamioudis *et al.*, 2013). Sahu *et al.* (2020) isolated twenty-one bacterial endophytes from roots, leaves and shoots of Holy basil (*Ocimumten uiflorum*). Based on 16s RNA gene sequencing, these isolates were putatively identified belonging to *Bacillus spp*. Among them, 8 were found to be reducing sheath blight disease incidence to a varying extent. Rice plants challenged with *R. solani* and inoculated with *Bacillus altitudinis* exhibited the least value

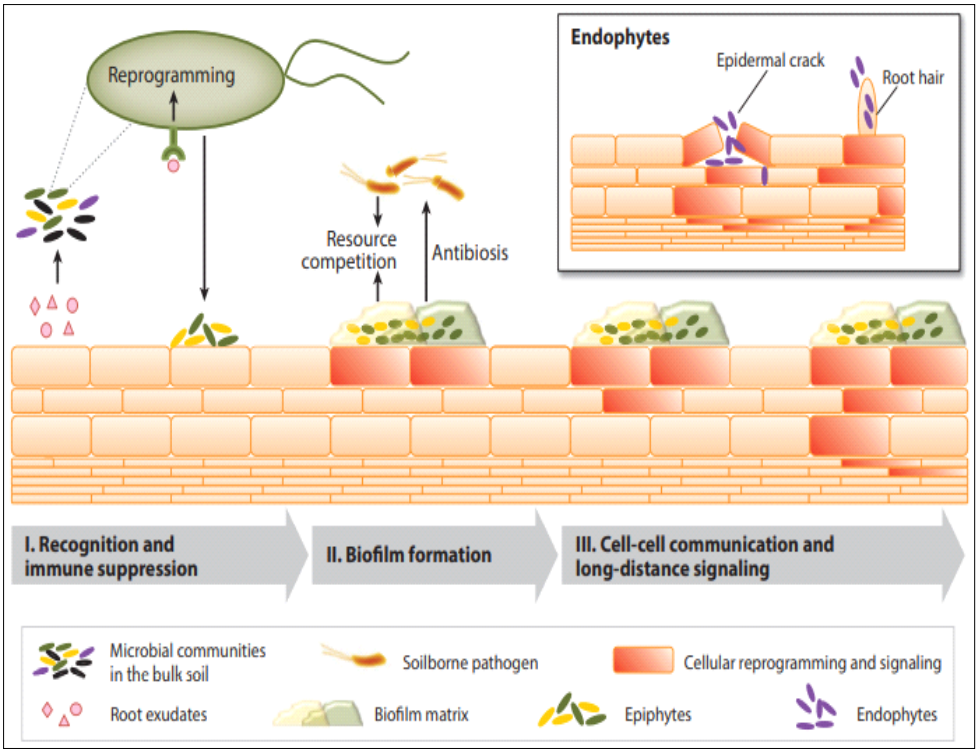


Fig 2: Main phases involved in root colonization by beneficial soilborne bacteria and their functions. Source: Pieterse *et al.*, 2014.

of percent infected tillers, recorded maximum induction of defense-related enzymes (phenyl ammonia-lyase, peroxidase and polyphenol followed by *Bacillus tequilensis*.

Fig 2 depicts the main phases involved in root colonization by beneficial soilborne bacteria and their functions. (I) Plant roots selectively secrete organic compounds that function as semiochemicals for the assembly of the root microbiome. Selected bacterial strains from the bulk soil communities specifically respond to host signals and reprogram to express traits related to root colonization. Microbes that have evolved as endophytes commonly enter the root interior through cracks in the root epidermis or through root hairs (inset). In phase I, local immune responses in host roots are transiently suppressed by epiphytic or endophytic plant growth-promoting rhizobacteria (PGPR), allowing bacteria to propagate on the root epidermis or intracellularly. (II) Once PGPR is established on the root, cell wall polysaccharides from the host function as environmental cues to promote biofilm formation on the root surface. Within the biofilm matrix, individual members and/or microbial consortia integrate host and self-derived signals to activate processes in the plant that lead to enhanced plant growth and induced systemic resistance (ISR). In addition, root microbiota protects root tissues against soilborne pathogens *via* the production of antibiotics and competition for nutrients and niches. (III) Early root responses to beneficial microbes are locally expressed in the epidermis and are subsequently communicated to the inner cell layers and to the aboveground plant parts via yet elusive long-distance molecules, where these signals confer ISR.

Jasmonic acid and ethylene in control of induced systemic resistance

Along with SA, the plant hormones JA and ethylene (ET) are also important regulators of the plant immune system (Thomma *et al.*, 2001). By using Arabidopsis mutants impaired in JA or ET signaling, it was demonstrated that JA and ET are central players in the regulation of rhizobacteria-mediated ISR (114). JA signaling mutants jar1, jin1 and coi1 and diverse ET signaling mutants, including etr1, ein2, ein3 and eir1, were shown to be defective in P. fluorescens WCS417r-ISR (Pozo *et al.*, 2008). In accordance with its dependency on JA and ET signaling, rhizobacteria-mediated ISR was shown to be effective against attackers that are sensitive to JA/ET-dependent defenses, including necrotrophic pathogens and insect herbivores (Pineda *et al.*, 2010). However, negative effects of beneficial microbes on plant-insect interactions have been reported as well (Pineda *et al.*, 2013). The synthesis of Jasmonic acid is discussed in Fig 3.

Beneficial microbes triggering the systemic acquired resistance pathway although ISR by beneficial microbes is often regulated through SA-independent mechanisms, several PGPR has been reported to trigger an SA-dependent type of ISR that resembles pathogen-induced SAR. For instance, an SA-producing mutant of PGPR strain *Pseudomonas aeruginosa* 7NSK2 was shown to confer enhanced disease resistance in wild-type beans and tomato

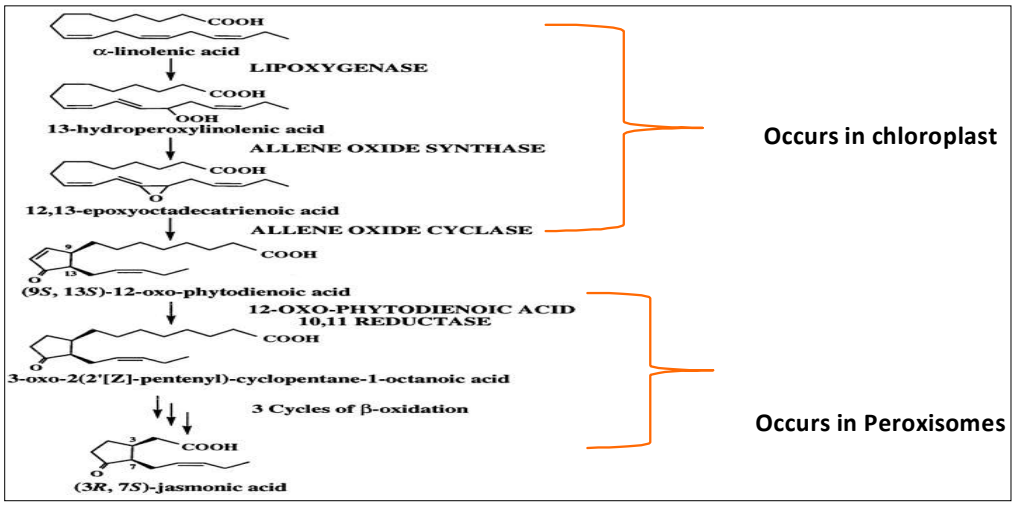


Fig 3: Synthesis of jasmonic acid.

but not in SA-non accumulating NahG tomato (De Meyer *et al.*,1999). Also, PGPR *P. fluorescens* P3 over expressing the SA biosynthesis gene cluster of *P. aeruginosa* PAO1 was demonstrated to elicit SA-dependent SAR (Maurhofer *et al.*,1998). Although many rhizobacteria have the capacity to produce SA, it is usually not the causal agent of the observed systemic resistance (Djavaheri *et al.*, 2012). This is likely caused by the fact that rhizobacteria-produced SA is often not released in the rhizosphere but becomes incorporated into SA moiety-containing siderophores that are produced under iron-limiting conditions to improve uptake of ferric iron (Fe^{3+}), which makes SA unavailable for triggering the SAR pathway (Bakker *et al.*, 2014). In the cases that beneficial microbes trigger SA-dependent SAR, reactive oxygen species that accumulate at the site of tissue colonization seem to be important elicitors (Audenaert *et al.*, 2002).

Crosstalk between SA and JA

Both synergistic and antagonistic interactions between SA and JA have been reported, suggesting that the interaction is either concentration dependent or tissue specific. Application of low concentrations of SA and JA resulted in synergistic expression of both the SA target *PR1* and the JA marker *PDF1.2* and *Thi1.2*. Abundant molecular evidence shows that the JA- and SA-signalling pathways exhibit negative crosstalk (Thaler *et al.*, 2012). For instance, SA-mediated suppression of JA-responsive gene expression has been shown in Arabidopsis thaliana, Lima bean, tomato and tobacco plants (Koornneef *et al.*, 2008). The transcription factor WRKY70 and the defence-regulating protein NPR1 were shown to play dual roles in regulating SA-mediated activation of SA-dependent defences as well as SA-mediated suppression of JA-dependent defences (Pieterse *et al.*, 2009). Moreover, SA and MeJA treatments applied at different concentrations and time intervals and using SA-inducible PR-1 and MeJA-inducible PDF1.2 and VSP2 as marker genes, revealed the molecular kinetics of SA-JA negative crosstalk in *Arabidopsis* (Koornneef *et al.*, 2008). A concentration as low as 0.0001mM SA suppressed MeJA-induced PDF1.2 transcription in *Arabidopsis* plants and this suppression was lost between 30 and 48 hpa (Koornneef *et al.*, 2008). However, no suppressive effect of JA on transcription of the SA-responsive gene PR-1 was found in *A. thaliana*.

CONCLUSION

Our understanding of SAR and ISR has increased considerably over recent years as we have begun to elucidate the molecular mechanisms underlying this response. Many of the processes contributing to SAR and ISR are clearly required in both local and systemic tissues and contribute to basal disease resistance. These include the synthesis of SA, JA and Ethylene changes in redox status and the induction of defense gene expression. In local tissue, the trigger for these changes is the recognition of the invading pathogen, whereas in systemic tissue they are induced by the perception of a systemic signal. There is evidence for the negative and positive feedback of SA signaling and cross-talk between different signaling pathways, adding to the complexity of the defense response. As well as the central role played by NPR1-mediated signaling, there is growing evidence for an NPR1-independent pathway(s) that contributes to defense gene induction. Challenges for the future include the identification of the mobile signal for SAR, to which we are one step closer after the identification of DIR1. Induction of SAR to control infection of crop plants is already being used in the field by application of BTH and it has been suggested that NPR1 overexpression is another viable strategy. A better understanding of the SAR signaling pathway will certainly lead to new environmentally friendly methods of crop protection. Understanding the biochemical and molecular basis for SAR and ISR may lead to the development of both low-usage-rate fungicides that act by stimulating natural disease resistance mechanisms and improved crop varieties. Furthermore, SAR and ISR will undoubtedly serve

as a paradigm for environmentally regulated signal-transduction systems and a sustainable approach for disease resistance. SAR and ISR will lead to a reduction in reliance on chemicals for disease management.

Conflict of interest

All authors declare that they have no conflict of interest.

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