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Review article

Signaling mechanisms underlying systemic acquired resistance to microbial pathogens☆

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ABSTRACT

Plants respond to biotic stress by inducing a variety of responses, which not only protect against the immediate diseases but also provide immunity from future infections. One example is systemic acquired resistance (SAR), which provides long-lasting and broad-spectrum protection at the whole plant level. The induction of SAR prepares the plant for a more robust response to subsequent infections from related and unrelated pathogens. SAR involves the rapid generation of signals at the primary site of infection, which are transported to the systemic parts of the plant presumably via the phloem. SAR signal generation and perception requires an intact cuticle, a waxy layer covering all aerial parts of the plant. A chemically diverse set of SAR inducers has already been identified, including hormones (salicylic acid, methyl salicylate), primary/secondary metabolites (nitric oxide, reactive oxygen species, glycerol-3-phosphate, azelaic acid, pipecolic acid, dihyroabetinal), fatty acid/lipid derivatives (18 carbon unsaturated fatty acids, galactolipids), and proteins (DIR1-Defective in Induced Resistance 1, AZI1-Azelaic acid Induced 1). Some of these are demonstrably mobile and the phloem loading routes for three of these SAR inducers is known. Here we discuss the recent findings related to synthesis, transport, and the relationship between these various SAR inducers.

1. Introduction

In plants, active defense against microbial pathogens involves the induction of elaborate defense signaling pathways. Some of these can provide protection at the site of infection (local), whereas others provide systemic resistance throughout the plant including in non-infected (distal) tissue. Local resistance includes species level resistance to non-host pathogens, basal resistance to virulent pathogens, or race-specific resistance to avirulent (Avr) pathogen isolates [1,2]. Basal immunity, or PAMP/MAMP (pathogen/microbe associated molecular patterns)-triggered immunity (PTI) is induced when pattern recognition receptors (PRRs) from the plant recognize pathogen-derived elicitors. Race-specific resistance, or effector-triggered immunity (ETI) is induced when strain-specific Avr proteins from the pathogen associate directly/indirectly with cognate plant resistant (R) proteins. PTI and ETI have been extensively reviewed in many recent articles [3–6].

Besides local defense mechanisms, plants can also activate systemic immune responses which typically confer broad-spectrum resistance at the whole plant level. Systemic defense signaling mechanisms include induced systemic resistance (ISR), which is triggered in response to root colonization by beneficial microbes [7], and systemic acquired resistance (SAR), which is activated in response to pathogen infection [8–12]. SAR is unique and highly desirable due to its exciting potential applications in sustainable and long-term crop protection. Induction of SAR involves the generation of mobile signal(s) at the site of primary infection, which translocate to distal tissue and prepare the plant against future infections. This requires careful and balanced cross-talk between various phytohormones, metabolites, and proteins [13,14]. SAR also has transgenerational benefits, and can be transferred to the immediate next generation of progeny via epigenetic changes that affect the patterns of DNA methylation at the promoter of defense-related genes [15,16]. However, it is important to note that the mechanisms via which DNA methylation regulates SAR within a single generation may differ from transgenerational SAR [17]. Although SAR is associated with a downregulation of photosynthesis and growth-related processes, it has been reported to confer a fitness advantage under conditions of high disease pressure [18,19].

Several studies have shown that the SAR mobile signal(s) are generated very rapidly; within 4–6 h of primary infection [20–23], although the kinetics of signal generation might differ depending on the experimental system used to conduct these analyses. The signal(s) then translocate acropetally, suggesting that this likely occurs via the phloem [24,25]. Phloem loading of the SAR signal(s) in turn can occur

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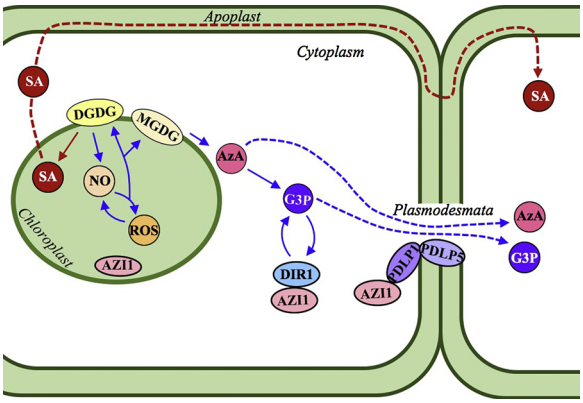

Fig. 1. Model summarizing metabolite and protein-mediated signaling during systemic acquired resistance. Pathogen infection induces the accumulation of salicylic acid (SA) and the free radicals nitric oxide (NO) and reactive oxygen species (ROS). This requires the galactolipid digalactosyldiacylglycerol (DGDG). The ROS species operate in a feedback loop with NO and catalyze the oxidative cleavage at carbon 9 of 18 carbon unsaturated fatty acids present on DGDG and monogalactosyldiacylglycerol (MGDG) to generate azelaic acid (AzA). AzA induces the expression of glycerol-3-phosphate (G3P) biosynthetic genes to generate G3P. G3P functions in a feedback loop with the lipid transfer like proteins DIR1 (Defective in induced resistance 1) and AZI1 (AZA induced 1). AZI1 interacts with the plasmodesmata (PD) localizing protein 1 (PDLP1). PDLP1 interacts with PDLP5, which regulates PD gating and the symplastic transport (dotted blue lines) of AzA and G3P. The PDLP proteins also regulate partitioning of AZI1 between the chloroplast and cytoplasm. Unlike AzA and G3P, SA is primarily transported via the apoplast (dotted red line). SA-mediated signaling (red arrows) function in parallel with NO-ROS-AZA-G3P-mediated (blue arrows) signaling to induce SAR.

either via the apoplast (space outside the plasma membrane) or the symplast (network of cytoplasm interconnected by specialized openings called plasmodesmata, PD). Importantly, these mobile signals are highly conserved because petiole exudate from pathogen-infected plants of one species can induce SAR in unrelated plant species [Kachroo et al., unpublished data; 22,23,26]. Several chemical inducers of SAR have been identified and some of these have been shown to translocate systemically. The SAR associated chemicals include, salicylic acid (SA) and its methylated derivative MeSA, [27,28] azelaic acid (AzA) [29], glycerol-3-phosphate (G3P) [22,30,31] pipecolic acid (Pip) [32], dehydroabietinal (DA) [23], and the free radicals, nitric oxide (NO) and reactive oxygen species (ROS) [33,12]. Of these, SA regulates one branch, whereas AzA, G3P, NO, and ROS regulate the other branch of SAR (Fig. 1). DA and Pip are likely to feed into the SA-dependent branch of the SAR pathway because they can induce SA accumulation [23,32]. However, a recent study suggests that Pip operates in both SA-dependent and −independent manner [19]. Many of the chemical SAR inducers require the non-specific lipid transfer-like protein (LTP), DIR1 (defective in induced resistance 1) [34] and the hybrid proline-rich protein, AZI1 (AzA induced 1) [29,35] for SAR signaling. DIR1 and AZI1 contain the conserved hydrophobic C-terminal cysteine rich domain found in LTPs [36]. DIR1 and AZI1 can form homo- and hetero-oligomers, and can also interact with the close AZI1 paralog, EARLI1 (Early Arabidopsis Aluminium Induced 1) [22,31,36]. Like *dir1* and *azi1*, *earli1* mutant plants are defective in SAR [29,34,35].

Successful induction of SAR also relies on "perception" of the mobile signal(s) in the distal tissue. Although this aspect of SAR is not well understood, some factors that are essential for signal perception have been identified. These include, an intact plant cuticle (a hydrophobic barrier comprised of wax and cutin monomers that surrounds all aerial surfaces of the plant), the major plant galactolipid, digalactosyldiacylglycerol (DGDG), and two PD localizing proteins PDLP1 and PDLP5. Notably, plants that are defective in these components can generate the SAR signal but are unable to perceive it [11,37–39]. However, some cuticular factors also contribute to SAR mobile signal generation [40]. Notably, at least one protein that regulates cuticle formation was detected in the phloem exudate of SAR-induced plants [41].

2. Endogenous chemical inducers of SAR

2.1. Dihydroabetinal

DA is a 20 carbon (C20) diterpenoid, which requires SA and its signaling component NPR1 (Non-Expressor of Pathogenesis Related 1) for inducing SAR [23,42,43]. In fact, DA application induces the accumulation of SA [23]. Although DA levels do not change in response to pathogen infection, it is thought to change to an "active" form by associating with proteinaceous component(s) that enable its SAR-inducing activity. These proteinaceous component(s) may include DIR1 and AZI1 because DA-induced SAR requires these proteins [23]. Thus, DIR1 and/or AZI1 might mediate the switch between inactive and active forms of DA, or the translocation of DA to distal tissues. The elucidation of the DA biosynthetic pathway and further clarification of its relationship to the other known chemical inducers of SAR should help provide better insights into the precise contribution of DA.

2.2. Pipecolic acid

The SAR inducer Pip, is a non-protein amino acid derivative of lysine, which accumulates in local and distal tissue of pathogen infected plants. Pip is possibly also transported systemically based on its significant accumulation in the petiole exudates of infected tissue [32]. In plants, L-Pip is synthesized from lysine via ALD1 (AGD2 like defense response protein) encoded aminotransferase [44–48]. ALD1 converts lysine to e-amino-a-keto caproic acid (Δ1-P2C), which in turn isomerizes to the *in planta* detectable enamine Δ2-piperideine-2 carboxylic acid (P2C) [45,46,48]. Two recent studies showed that ALD1 converts lysine to P2C, which is subsequently converted to Pip by ornathine cyclodeaminase (encoded by SARD4) [47,48]. Intriguingly, although both *ald1* and *sard4* plants were compromised in SAR [32,46,47], Pip levels in the infected leaves of these plants differed substantially. In contrast to *ald1* plants, which contained basal levels of Pip in both infected and distal leaves, the *sard4* mutant accumulated Pip in infected but not distal leaves [47]. However, another recent study showed that the distal leaves of *sard4* can accumulate low levels of Pip at later times after infection and that *sard4* plants are SAR competent [48]. This suggests that a pathogen-inducible factor can generate Pip in the infected leaves of the *sard4* mutant and enzymes other than SARD4 contribute to the conversion of P2C to Pip. The chloroplastic localization of ALD1 and SARD4 suggests that Pip is likely synthesized in the plastids [35,48]. ALD1 expression is itself induced by Pip application, as is the overexpression of another SAR component, FMO1 a flavin monooxygenase. Like the *sard4* mutant, *fmo1* plants are also compromised in Pip accumulation in the distal leaves but contain wild-type-like Pip levels in infected leaves [49]. Like *ald1*, the *fmo1* mutants are also defective in SAR [34,49]. Both *ALD1* and *FMO1* are induced in infected and systemic tissues of pathogen-infected plants, and their induction is independent of SA accumulation. Notably, ALD1-derived factors (such as Pip) appear to be key for SAR-associated transcriptional reprograming in the systemic tissue because pathogen-responsive transcriptional changes in the distal tissue are almost completely absent in *ald1* mutant plants [19].

2.3. Salicylic acid and MeSA

The phytohormone SA is well known for its role in mediating plant defense against pathogens [50]. SA, a small phenolic compound, is synthesized via the shikimic acid pathway, with chorismic acid serving as an important precursor that can be converted to SA via two distinct branches. Both branches contribute to SA biosynthesis and are required for SAR [51–54]. In one branch, chorismic acid is converted to SA via phenylalanine and cinnamic acid intermediates by the key enzyme phenylalanine ammonia lyase (PAL). In the other branch, chorismic acid is converted to SA via isochorismic acid by the enzyme

isochorismate synthase (ICS1/SID2) [53,55]. Mutations in either *ICS* or *PAL* are sufficient to compromise SAR [51–53], indicating that SA synthesis is essential for SAR.

SA accumulates in pathogen infected tissue [20,56–58], and most studies have shown that the levels of SA in the distal tissue are significantly lower than in infected tissue [11]. This is consistent with the notion that nearly 70% of the SA in distal tissue is that which is transported from the infected tissue, and only a small percentage of SA is transported from infected to distal tissue during SAR [37,59,60]. Nonetheless, the low levels of SA in the distal tissues appear to be important for SAR. Recent work has shown that the intracellular movement of SA occurs via the apoplastic compartment [37]. This is surprising given that the molecular mass of SA (138.12 Da) is well below the size exclusion limit of PD (800–1000 Da) [57–59]. Thus, it appears that the acidic SA must transverse the plasma membrane to exit the cell for phloem loading. Interestingly, both pathogen infection and exogenous SA application reduce PD permeability and thereby the movement of solutes via the PD [37,64]. SA reduces PD aperture by inducing the expression of PD-Localizing Protein 5 (PDLP5), which in turn induces callose deposition at the PD resulting in PD closure [64,65]. This raises the possibility that pathogen-responsive SA accumulation in infected cells could inhibit the intercellular movement of SAR signals via the PD. This cross regulation of signaling molecules is a hallmark of plant signal transduction pathways and likely promotes a fine control of SAR induction particularly since many of the signaling molecules are conserved metabolites essential for the normal growth physiology of the plant.

Although SA itself is transported systemically, MeSA the biologically inactive derivative of SA, may also function in delivering SA to distal tissue. Like SA, pathogen infection induces the accumulation of MeSA in both local and distal tissues. Due to its volatile nature, MeSA can function as an airborne defense signal [66,67], although it also accumulates in the phloem during SAR. MeSA is synthesized from SA by SA methyltransferases (SAMT/BSMT), and SAMT is required for the phloem accumulation of MeSA [67–70]. Upon translocation to the distal tissue MeSA is converted back to SA via MeSA esterase activity of the SA binding protein (SABP) 2. Mutations in either SAMT or SABP2 were shown to compromise SAR [71–73]. Furthermore, SAR is inhibited by the synthetic SA analog, tetraFA (2,2,2,20-tetra-fluoroacetophenone), which inhibits the esterase activity of SABP2 [74]. Grafting studies in tobacco have shown that SABP2 activity is essential in the distal, but not in the infected tissue, for SAR to be induced [70,75]. Thus, MeSA must be converted to SA in the distal tissue during SAR. However, MeSA is required 48 and 72 h post primary infection [22,23,74], which is much later than the time frame of translocation of the mobile signal. This makes MeSA an unlikely candidate for the primary mobile signal in SAR. This is also true for SA, which accumulates later than the time frame of mobile signal movement. Moreover, neither accumulation, nor transport of SA alone, is sufficient to induce SAR [37,51,52,76]. This reinforces the view that SA signaling functions in parallel with the AzA/G3P-derived branch to regulate SAR. The requirement for MeSA in SAR was questioned by another study that showed normal SAR in mutant plants defective in *BSMT1*, which encodes a benzoic acid/SA methyl transferase [72]. The Chaturvedi et al. [23] study also suggested variability in the SAR response of the *bsmt1* mutant. Subsequently, Liu et al. [73] showed that prolonged exposure to light after pathogen infection could compensate for the lack of *BSMT1* in the Arabidopsis SAR response, suggesting that environmental factors might be invovled in the regulation of MeSA levels.

The importance of SA in SAR is reiterated by the fact that many SA signaling components are also essential for SAR [77,78]. For example, NPR1, the central regulator of SA signaling, is required for SAR [42,79,80–82]. In the absence of SA, NPR1 resides in the cytoplasm as an oligomer [83]. Upon SA accumulation, the oligomers dissociate, and the NPR1 monomers are transported into the nucleus [83,84]. Here, NPR1 interacts with TGA proteins, which belong to the basic leucine zipper (bZIP) protein family of transcription factors and binds TGACG motifs to activate defense-related transcription [85–91]. SA accumulation also promotes the interaction between NPR1 and TGA proteins [86,92].

2.4. Free radicals

NO is a well-known gaseous signaling molecule that regulates many physiological processes in plants both directly and by *S*-nitrosylation (post translational modification of cysteine residues to *S*-nitrocysteine) of key proteins. In plant defense, *S*-nitrosylation of NPR1 and TGA factors promotes their nuclear translocation and DNA binding activity, respectively [93]. However, NO can also promote NPR1 oligomerization and thereby its inactivation through thiol *S*-nitrosylation [84]. These contrasting effects of NO on NPR1 may be dependent on the intracellular concentration of NO because NO-induced SAR is highly concentration-dependent [33]. Thus, too low or too high levels of NO can inhibit SAR. In plants, NO can be directly synthesized from nitrate by the nitrate reductases, NIA1 and NIA2, which are functionally non-redundant in SAR. In addition, the GTPase AtNOA1 (NO associated protein 1) also contributes to NO levels via an unknown mechanism [94–96], and is partially redundant with the NIA isoforms. Thus, *noa1 nia1* or *noa1 nia2* double mutant plants are fully compromised in pathogen-responsive NO accumulation and the onset of SAR [33,95]. Mutations in NOX1 (NO overproducer) and GSNOR1 (*S*-Nitrosoglutathione Reductase), which result in increased endogenous levels of NO also impair SAR [33]. In plants, *S*-nitrosoglutathione (GSNO) serves as a mobile reservoir of NO [97]. GSNOR regulates the turnover of GSNO by reducing GSNO to GSSG (oxidized glutathione) and NH_3 [98]. In Arabidopsis, GSNO levels increase in response to wounding or SA application. GSNO is also detected in the systemic tissue of wounded plants suggesting a possible role for GSNO as a mobile signal during wounding [97]. Pathogen-induced NO accumulation is also reduced in plants defective for the respiratory burst oxidase homologs (RBOH), RBOHD and RBOHF [33]. RBOH generate reactive oxygen species (ROS), and RBOHD and RBOHF are functionally non-redundant in SAR-related ROS generation and thereby the onset of SAR. Like NO, ROS-mediated SAR is also concentration-dependent [33].

2.5. Azelaic acid

NO and ROS both contribute to the biosynthesis of the SAR inducer, AzA. AzA is a C9 dicarboxylic acid which is generated by the hydrolysis of C18 fatty acids (FAs) carrying a double bond at carbon 9. These include, oleic acid (18:1) and its desaturated derivatives, linoleic acid (18:2) and linolenic acid (18:3). Because these FAs are essential for plant survival and they function redundantly in AzA biosynthesis, it is difficult to generate plants lacking AzA; mutations abrogating the synthesis of all three unsaturated FAs are lethal. Cleavage of the double bond between carbon 9 and 10 of 18:1/18:2/18:3 results in the formation of 9-oxononanoic acid (ONA, a monocarboxylic acid), which is then oxidized to AzA [33,99,100]. Different ROS species function additively in the hydrolysis of these C18 FAs specifically present on the major plant lipids digalactosyldiacylglycerol (DGDG) and monogalatosyldiacylglycerol (MGDG). Thus, plants defective in DGDG (*dgd1*, mutation in DGDG synthase) or MGDG (*mgd1*, MGDG synthase) synthesis cannot generate sufficient AzA in response to pathogen infection [101]. Interestingly, DGDG, but not MGDG, is also important for pathogen-induced NO and SA accumulation in the chloroplasts. Thus, DGDG is required for the biosynthesis/accumulation of both NO and AzA. Importantly, petiole exudate from *dgd1* plants can induce SAR in wild-type plants, indicating the presence of a yet unknown SAR-inducing signal, which functions upstream of SA and NO-ROS-AzA-G3P branches, and requires the DGDG lipid for SAR induction. Furthermore, the sugar composition of the DGDG lipid appears to be crucial for SAR because an altered form of DGDG carrying one glucose and one

galactose moiety instead of two galactose moieties is nonfunctional in SAR [101].

AzA accumulates in the petiole exudates of pathogen-infected plants [29], and at least some (< 7%) of it translocates to the distal tissues, although AzA can also be transported in the absence of pathogen infection [31,102]. Interestingly, the majority of AzA in the distal tissue is present as a derivatized product, suggesting that AzA may be derivatized before transport or rapidly converted to a derivative upon transport [31]. Recent studies show that intracellular transport of free AzA occurs symplastically through the PD [37]. AzA requires DIR1, AZI1, and EARLI1 for SAR induction [29,35].

2.6. Glycerol-3-phosphate

AzA induces SAR by inducing G3P biosynthesis via the upregulation of G3P biosynthetic genes [31]. G3P accumulates in petiole exudates as well as in local and distal tissue, as early as 6 h post pathogen infection. G3P is a three carbon, phosphorylated sugar derivative that is an obligatory component of glycolysis and glycerolipid biosynthesis in all organisms. G3P is synthesized from glycerol by glycerokinase (GK) [103], or reduction of dihydroxyacetone phosphate by glycerol-3-phosphate dehydrogenase (G3Pdh). Arabidopsis encodes multiple G3Pdh isoforms present in different subcellular locations [22,104–107]. Mutants defective in G3P synthesis are compromised in SAR, and this defect can be restored by the exogenous application of G3P [22]. Exogenous G3P also induces SAR in wild type plants, but not in *dir1* or *azi1* mutant plants indicating DIR1/AZI1 are required for G3P-induced SAR. In fact, the *dir1* and *azi1* mutants do not accumulate G3P in response to pathogen-infection. Conversely, the DIR1/AZI1 proteins are unstable in G3P biosynthetic mutant backgrounds, and the systemic movement of the DIR1 protein requires G3P [22]. Thus, G3P and DIR1/AZI1 appear to function in a feedback regulatory loop. Unlike DA or Pip, G3P-induced SAR is not associated with an increase in SA levels in local or distal tissue [22,31,101]. However, G3P application might promote the conversion of MeSA to SA in distal tissue because it induces the expression of a *SABP2*-like gene and represses *AtBSMT1* [22]. It is possible that this enables the plant to maintain threshold levels of SA in distal tissue, and reiterates the critical role for basal rather than induced levels of SA, in SAR. Indeed, G3P cannot induce SAR in *sid2* (mutation in the SA synthesizing isochorishmate synthase1, *ICS1*) plants [22], which contain significantly lower levels of basal SA compared to wild-type plants. Importantly, localized application of G3P induces transcriptional changes in distal tissue indicating a role for G3P in systemic transcriptional reprogramming [22].

Consistent with the systemic transcriptional reprogramming, G3P translocates to distal tissue, primarily in the form of an unidentified G3P derivative, and this requires the DIR1 protein [22]. Like AzA, intercellular transport of G3P occurs preferentially through the PD [37]. The movement of G3P and AzA via PD, correlates with PD localization and systemic movement of at least some portion of the cellular pool of DIR1 [22,31,108]. Although transient expression assays suggest that some DIR1 may also be targeted for secretion to the cell wall, only the cytosolic fraction of DIR1 appears to be important for SAR [109]. Likewise, AZI1, which is also required for AzA/G3P-mediated SAR also localizes to the PD, although a small amount of this protein is also detected in the chloroplast [35,37,110]. Notably, AZI1 requires the PD localizing PDLP1 and PDLP5 proteins for its stability and appropriate subcellular localization; AZI1 protein levels are reduced and localizes primarily to the chloroplast in *pdlp1* or *pdlp5* mutant plants [37]. The reduced stability and altered subcellular localization of AZI1 may be responsible for the SAR defect of *pdlp1* and *pdlp5* plants. Clearly, PD aperture is tightly regulated during SAR because both increased (via knockout mutation in *PDLP5*) and decreased PD (overexpression of *PDLP5*) permeability inhibit SAR [37,65,108]. Notably, inducible expression of AZI1 only in local tissue of *azi1* mutant plants is sufficient to restore SAR [35]. Although this does not rule out the possibility of the locally induced AZI1 moving into distal leaves, it raises the possibility that long-distance mobility of AZI1 or AZI1-derived signal may not be relevant to SAR [35]. Certainly, transiently expressed AZI1 did not exhibit systemic transport in the absence of pathogen infection based on fluorescence/Western blotting assays [111].

Besides DIR1, EARLI1 and PDLP1/5, AZI1 also interacts with Mitogen Activated Protein Kinase 3 (MPK3) and a mutation in MPK3 also impairs SAR [112]. In addition to plant defense signaling, AZI1 also plays a role in salt stress response [111–113] suggesting that AZI1, and by extension LTPs in general, likely contribute to diverse cellular processes. AZI1 is thought to undergo post translational modifications such as phosphorylation and proline hydroxylation based on differences in expected protein size and gel mobility [111]. It is possible that differential post translational modifications of AZI1 in response to different physiological stimuli enable its function in multiple modes of plant stress responses.

3. Conclusions

Parallel operation and transport of chemical signals NO-ROS-AZA-G3P and SA during SAR is likely advantageous as it confers plasticity to the plant cells that are simultaneously engaged in multiple physiological processes. The availability of multiple points at which the NO- and SA-derived pathways can be co-regulated could facilitate a tighter control of SAR. Additionally, multiple SAR-inducing signals could function additively to facilitate SAR in distal tissue where the signal levels are significantly lower than in infected tissue. The different transport route of SA as compared to AzA or G3P likely provides multiple avenues for controlling the transport of these defense chemicals and thereby minimizes the chances of non-specific activation of defense processes in systemic tissue. Despite several key advances, numerous aspects of SAR need further clarification. This includes the importance of transport versus *de novo* synthesis of free radicals in the distal leaves. Is phloem transport relevant in the context of gaseous/volatile SAR signals such as NO and MeSA? Does signaling via the NO-ROS-AzA-G3P branch intercept with signaling via the SA branch? What check points regulate the two parallel branches? What is the bioactive compound(s) that G3P is derivatized to and how does it relate to the bioactive DA complex? What role do DIR1 and AZI1 play in the SAR bioactivity of the G3P derivative(s)? What is the biosynthetic pathway and the precise contribution of DA in SAR? How do DA and Pip relate to the other known SAR signaling molecules? How are the various SAR associated proteins and metabolites partitioned subcellularly? How do SA and the PDLPs regulate PD permeability and transport of metabolite-protein complexes via PD?

What aspects of cuticle development are associated with SAR? How do cuticular components regulate SAR signal perception in the distal tissue? Are cuticle defective mutants defective in the generation of any of the known SAR inducers and can these chemicals induce SAR in cuticle defective plants? To what extent do changes in FA/lipid flux in the cuticle defective mutants affect their ability to induce SAR? Sustainable deployment of this unique mode of resistance for protecting field crops will not only depend on clarifying these aspects but also the development of tools that will enable the measurement of precise spatial and temporal changes in the various SAR inducing metabolites and proteins.

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