УДК 632.938+502.753

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INDUCTION OF SYSTEMIC RESISTANCE IN PLANTS

When a pathogen is perceived by a host plant, a series of defense responses can be activated. One of these are «local» defenses that occur rapidly at the site of pathogen invasion. Another are «systemic» defenses that are induced in uninoculated parts of the plant. Recently, molecular genetic studies have revealed genes that are signaling components of systemic resistance pathways. Cloning of these genes and characterization of the function of their proteins is now providing insights to processes regulating plant defense against pathogens. Evidence that «systemic» defenses are important for resistance is that when the way is blocked in transgenic plants or in mutants, the plant's defense is compromised. When the pathway is stimulated by exogenous compounds or in mutants, the host resistance is strengthened. A detailed understanding of this pathway is important for both practical and theoretical reasons.

Introduction. Plants have developed a number of strategies to defend themselves against microbial attack. These include early responses such as production of reactive oxygen species (ROS), which can lead to cell death [1]. Thus, the pathogen may be «trapped» in dead cells and appears to be prevented from spreading from the site of initial infection. Other defense responses are also switched on such as synthesis hydrolytic enzymes to inhibit the growth of the pathogen, changes in physiology [2], e.g. strengthening of the cell wall through deposition of lignin. Molecules released or generated during microbial invasion, so-called elicitors, are thought to act as the chemical cues that are perceived by the plant and activate defense responses.

Further local responses in the surrounding cells include *de novo* synthesis of phytoalexins, which are defined as antimicrobial, low-molecular-weight compounds that are produced after infection [3–5]. Collectively, plants produce a remarkably diverse array of over 100,000 low-molecular-mass natural products, also known as secondary metabolites. Most are derived from the isoprenoid, phenylpropanoid, alkaloid or fatty acid/polycetide pathways [6]. Among this rich diversity only about 200 substances were described as phytoalexins driven by selection for acquisition of improved defense against pathogen attack.

Recent advances in our understanding of the mechanisms underlying the expression of plant disease resistance have allowed to follow the course of events through 1) The perception of a signal by a plant cell. 2) The intracellular transduction of this recognition signal. 3) The synthesis of defense molecules. 4) Transport of defense molecules to strategic sites [7]. The multicomponent defense responses occur both in the plant organ originally attacked (local response) and in distant, yet unaffected, parts (systemic response). The last one is so-called systemic acquired resistance (SAR) [8, 9].

Phenomenon of SAR. Interactions between plants and pathogens can lead either to a successful infection (compatible response) or resistance (incompatible response). In the last case, infection by viruses, bacteria or fungi will elicit a set of localized responses in and around the infected host cells. Caused by these local responses, a signal spreads through the plant and induces subtle changes in gene expression in yet uninfected plant parts. The systemic response involves the de novo production of pathogenesis-related (PR) proteins [10, 11].

A protein is classified as a SAR protein when its presence or activity correlates tightly with maintenance of the resistance state [9]. Originally, PR proteins were detected and defined as being absent in healthy plants but accumulating in large amounts after infection. They have now been found in more than 40 species belonging to at least 13 families [12]. Two groups of PR proteins can be distinguished. Acidic PR proteins are predominantly localized in the intercellular spaces. Basic PR proteins are functionally similar but have different molecular masses and amino acid sequences and are mainly localized in the vacuole.

It was first shown for tobacco that some of PR proteins have chitinase or β-1,3-glucanase activity [13]. Since many fungi contain chitin and β-1,3-glucans as major structural components of their cell walls, it was suggested that the accumulation of chitinases and β-1,3-glucanases plays an important role in plant defense. Basic, vacuolar isoforms of β-1,3-glucanase possessed in general higher specific activity that acidic intercellular isoforms. In addition to the potential antifungal activity, a role for β-1,3-glucanases in morphogenesis was suggested — in view of their expression in flowers and roots [14]. Since chitin does not seem to occur in plants, it looks like chitinases produced by plants upon infection by pathogens play an important role in active defense against pathogens. Plants over-expressing chitinase show decreased susceptibility to infection by fungi with chitin-containing cell walls [15]. But also, in addition to a potential antifungal activity it was demonstrated that the activity of Nod factors, involved in root nodules formation, may partly be determined by action of chitinases [16].

Synergistic activity of chitinases and β-1,3-glucanases has been demonstrated in transgenic plants [17]. Some PR proteins display antimicrobial activity *in vivo* [18] but their actual role in SAR remains to be elucidated. When SAR is activated, a normally compatible plant-pathogen interaction can be converted into an incompatible one [19]. Phenotypically, systemic resistance is manifested as a protection of the plant not only against the attacking pathogen, but also against other types of pathogens. Although some specificity has recently been described, the resistance seems to be rather non-specific and long-lasting [8]. SAR is generally regarded as a widespread and conserved trait, since the phenomenon is known for species belonging to both monocotyledonous and dicotyledonous plants.

The mechanisms underlying the resistance to viruses still remain to be determined, but SAR in general is regarded as being effective against all pathogens — fungi, bacteria and viruses.

Biotic elicitors. The elicitors are recognized as signal compounds by appropriate plant perception systems displaying high sensitivity (in several cases about 10^{-9} M or even below) [20]. Oligosaccharide elicitors were among the earliest ones to be characterized in greater detail [21]. Four major classes of elicitor-active oligosaccharides have been identified: oligoglucan, oligochitin, oligochitosan of fungal origin and oligogalacturonide of plant origin. Various other substances of diverse chemical structures have been shown to possess the ability to activate plant defense responses. These include components of the cell walls as well as excreted metabolites of an oligosaccharide, (glyco)peptide and protein, or fatty acid nature. Many excellent reviews on microbial elicitors have been published [22, 23]. Evidence is emerging from the research that the final elicitor destinations in the plant cell are varied and that recognition both at the external surface and in intracellular compartments has to be anticipated. Consequently, engagement with the cognate receptors occurs at distinct cellular sites. Sufficiently pure elicitor preparations have allowed studies directed towards the identification of such putative receptors (binding proteins) in a few cases.

Elicitor recognition. The first step during induced resistance is the recognition of the signaling molecule by a specific receptor. Recent studies demonstrate that high-affinity, receptor-like binding proteins for fungal elicitors exist in the plasma membrane of several plants. Branched β-1,3-1,6-glucans are major surface and inner-wall-layer components of the mycelial walls of the genus *Phytophthora* and some other pathogens. High-affinity, reversible, and specific glucan-binding sites were found on soybean root plasma membranes and protoplasts prepared from soybean suspension cells [22]. Three β-glucan-binding proteins (75, 100, 150 kDa) have been solubilized, identified by photoaffinity labeling and highly purified by affinity chromotography [24]. The cDNAs encoding the 75 kDa binding protein have been isolated and expressed in *E. coli* and tobacco cells [25].

Investigations with elicitor-active chitin fragments have showed the existence of a single class of high-affinity binding sites for these fragments in two plant tissues, tomato and rice [26]. Chitin-binding proteins have been solubilized from a rice plasma-membrane preparation with retention of binding affinity for the chitooligosaccharide ligand by using detergents. Photoaffinity and chemical cross-linking studies with chitin oligosaccharide conjugates indicated that a 75-kDa protein carried the binding site [27]. It will be of interest to analyze the structural and functional relationships of the rice and tomato chitin-binding proteins and to compare the properties with those of the β-glucan-binding proteins from soybean.

Binding sites for glycopeptides have been also identified in wheat plasma membranes and in membranes of tomato cells. Peptide-binding studies have been performed with the Pep-13, oligopeptide derived from 42-kDa glycoprotein elicitor from *Ph. sojae*, the elicitin, cryptogenin from *P. cryptogea* [28] and the race-specific peptide elicitor AVR9 from *C. fulvum* [29]. The properties of purified binding proteins suggest their involvement in signal perception but they also give a first insight into signal transduction pathway that leads to induction of plant disease resistance.

Signaling. Immediately downstream of the initial elicitor-receptor recognition, the activation of ion fluxes and the production of H_2O_2 are the initial responses detected in plant cells. Biochemical evidence suggests that these processes, which occur prior to the transcriptional activation of defense-related genes, appear to be mediated through the regulation of plasma membrane-bound enzymes. These include changes in Ca^{2+}-ATPase and H^+-ATPase activities [30], the activation of plasma membrane-bound ion channels [31] and the induction of a plasma membrane-bound NADPH oxidase [32, 33].

A number of signal transduction pathways have been proposed to mediate these early responses in host cells, ensuring an elicitor-induced response that is quantitatively appropriate, correctly timed and highly coordinated with other activities of the host plant cell. These pathways might comprise G proteins, changes in cytosolic Ca^{2+} concentrations and protein kinases/phosphatases, that affect the activity of key enzymes.

G proteins act as molecular signal transducers whose active or inactive states depend on the binding of GTP or GDP, respectively. The G proteins include two major subfamilies, heterotrimeric G proteins and small G proteins. Whereas the heterotrimeric G proteins contain α, β and γ subunits, the small G proteins appear to be similar to free α subunits, operating without the βγ heterodimer. Generally, it is the α subunit of the heterotrimeric G protein that has the receptor-binding region and possesses a guanosine nucleotide binding site and the GTPase activity [34]. Both classes of G proteins use the GTP/GDP cycle as a molecular switch for signal transduction. Interaction of the G protein with the activated receptor promotes the exchange of GDP, bound to the α subunit, for GTP and the subsequent dissociation of the α-GTP complex from the βγ heterodimer.

A variety of evidence suggest a role for heterotrimeric G proteins in the plant defense response pathway. Most of the research has been based on the use of non-hydrolyzable GTP analogues [35], cholera toxin [36] and mastoparan. For example, direct activation of a plasma membrane Ca^{2+} channel by a recombinant α-subunit suggests that the activation of defense responses could be mediated by G proteins [37].

Protein kinases. The phosphorylation of proteins, probably initiated by the receptor, is thought to relay the defense signal to different downstream effectors. In some cases, the receptor contains a kinase domain that may trigger the phosphorylation cascade [38], whereas in others a secondary messenger such as Ca^{2+} may trigger the protein kinases [33]. In parsley, recognition of a non-specific elicitor by the host cell also triggers a signaling pathway mediated by a mitogen-activated protein (MAP) kinase [39]. This elicitor-responsive MAP kinase is likely to be involved in transcriptional activation as the kinase translocates into the nucleus upon elicitor treatment.

Fungal elicitors induce changes in the phosporylation status of proteins in tomato cell suspension culture, and these changes correlate with an increase in cytosolic free Ca^{2+} concentrations. The dephosphorylation of the plasma membrane H^+-ATPase was evident soon after treatment with elicitors from incompatible races of *C. fulvum* [40]. Among the plant calcium-dependent protein kinases, calmodulin-like domain protein kinases (CDPKs) have attracted great attention [41]. Although CDPKs have been implicated in general

stress responses [42], specific evidence for their participation in signal transduction pathways during plant-pathogen interaction is still lacking. However, increasing evidence suggests that the elevated cytosolic calcium concentrations is a common consequence of pathogen perception [43].

Calcium homeostasis. Many of the biochemical responses associated with the defense mechanisms directly correlate with an increase in cytosolic free Ca^{2+} concentration. Measurements of external Ca^{2+} with ion-selective electrodes and of Ca^{2+} fluxes using radiometric techniques have revealed a large and transient Ca^{2+} influx. This suggests a correlation between fungal elicitor activity, hyperpolarization of the host cell plasma membrane, and Ca^{2+} influx [44]. The activation of plasma membrane Ca^{2+} channels by specific and non-specific [31] elicitors provides a direct demonstration of a pathway by which cytosolic free Ca^{2+} concentrations increase to levels that can initiate various defense responses, including production of ROS and phytoalexins [45]. Although there is increasing evidence for a role for Ca^{2+} signaling in defense responses, a fundamental question remains unanswered: how does the cell use these calcium signals to control downstream targets and the activation of a number of Ca^{2+}-dependent protein kinases (i.e. CDPKs, Ca^{2+}/calmodulin-dependent protein kinase, etc.)?

Recently proposed model [46] may explain the concerted action of these kinases. It was demonstrated that calmodulin KII kinases were primed by Ca^{2+} bursts of a given frequency and maintained their activity with signals of substantially lower frequency. This may allow the cells to distinguish between specific calcium signals (intracellular calcium spikes) and nonspecific changes in steady-state cytosolic Ca^{2+} concentrations. Plant cells could also reinforce intracellular calcium signals (due to the influx of Ca^{2+} from the extracellular space) by coupling these Ca^{2+} bursts with Ca^{2+} release from vacuoles [47].

Salicylic acid. After infection, endogenous levels of salicylic acid (SA) increase locally and systemically, and SA levels increase in the phloem before SAR occurs. SA is now recognized as a crucial signal for expression of SAR to many pathogens [48]. The level of resistance of plants exhibiting constitutive expression of SA is positively correlated with SA levels. This is true, for example, for natural cultivars of rice [49] and for *Arabidopsis* plants [50]. Key experiments establishing a role of SA in certain forms of SAR have utilized transgenic plants expressing the bacterial *nahG* gene encoding salicylate hydroxylase, an enzyme that catalyzes the convertion of SA to catechol. The plants containing *nahG* are not only unable to accumulate free SA, but they are incapable of mounting a SAR response to a variety of disease agents [51]. Disease resistance can be induced in plants by spray treatments with SA or its synthetic analogues [52].

However, experiments using reciprocal combinations of NahG and wild-type shoots grafted onto NahG and wild-type plants showed that SAR was elicited in the wild-type tissue even when the NahG-transformed part of the plant received the inducing infection. The data suggest that the signal emanating from the inducing tissue is not SA [53]. In cucumber, the time courses in induction and appearance of SA in the phloem combined with leaf-removal experiments were not consistent with SA being the primary systemic signal [54]. These and other experiments suggest that both SA and other systemic signals are involved in SAR signaling.

SA's role in conditioning defense responses to certain pathogens is well established. However, the mechanism by which it does so is unclear. SA and related hydroxy-benzoates interact with Fe^{2+} in heme and non-heme containing proteins, either through chelation or as an electron donor to generate a highly reactive salicylate radical [52]. For example, a SA binding protein was characterized in tobacco as a catalase [55], and allene oxide synthase [56] is a step in jasmonate synthesis that appears to be a site for SA inhibition. Both are heme proteins. However, the basis for SA's effect on SAR expression is unresolved, and it is likely that SA has multiple targets in the cell to regulate SAR. Critical for study of functional targets of SA in induced resistance is consideration of the kinetic parameters and cellular concentration of the interacting factors.

Chemical activators of SAR. SAR was first described as response to pathogen infection. Subsequently, it has been found that treatment of plants with low-molecular-weight compounds can also induce SAR. The use of chemicals to activate SAR provides novel alternatives for disease control in agronomic systems as well as tools for the elucidation of the SAR signal transduction cascade [9, 57]. To be considered an activator of SAR, a chemical

should exhibit three characteristics [58]: first, the compound or its significant metabolites should not exhibit direct antimicrobial activity; second, it should induce resistance against the same spectrum of pathogens as in biologically activated SAR; and third, it should induce the expression of the same marker genes as evident in pathogen-activated SAR.

Several chemicals, including inorganic compounds (phosphate salts, powdered silicium) have been reported to induce resistance in cucumber, bean and maize [59], but have failed to fulfill the above criteria. Natural organic compounds, such as polyunsaturated fatty acids (arachidonic, linolenic, linolic) could induce SAR in potato against *Ph. infestans* [8]. This effect is not accompanied by enhanced SA levels or by SAR-gene expression in the systemically protected parts of the plant [59]. Oligomers of chitosan (poly-N-glucosamine), which are likely to be released from walls of invading fungi, can protect tomato roots from fungal infection. Other compounds, such as DL-3-aminobutanolic acid or propenazole, have been shown to induce PR-1 gene expression and effective against rice blast. Local treatments with DL-3-aminobutyric acid (BABA) protect tomato, potato, and tobacco systemically against *Ph. infestans* and *Peronospora tabacina*, respectively.

2,6-dichloroisonicotinic acid (INA) and its methyl ester (both reffered to as INA) were the first synthetic compounds shown to activate SAR in dicotyledonous as well as in monocotyledonous plant species against a wide spectrum of pathogens, ranging from viruses, bacteria to fungi [53]. INA was weakly antifungal in vitro and induced the expression of SAR genes prior to challenge inoculation [9, 60]. Two INA-related molecules were reported to protect rice against *M. grisea* by inducing SAR. Like INA, both compounds have almost no antifungal activity in vitro and enhance lipoxygenase and peroxidase enzyme activities in treated plants after pathogen inoculation. Thus, INA provides a very important research tool to probe into pathways leading to SAR.

However, both SA and INA were unsufficiently tolerated by some crop plants to warrant practical use as plant protection compounds. Recently, the synthetic chemical benzo(1,2,3)thiadiazole-7-carbothioic acid S-methyl ester (BTH) was demonstrated to be a potent SAR activator. Like INA, BTH has practically no antifungal effect and protects a number of plants including wheat, rice, sunflower and tobacco [59, 60]. The resistance observed in the plants after treatment with INA or BTH is not due to a direct action of the compounds on the pathogen, because neither the compounds nor their significant metabolites exhibit *in vitro* antibiotic activity. Moreover, in tobacco, *Arabidopsis* and wheat, INA and BTH induce the same set of SAR genes that is induced by SA [61].

Neither INA nor BTH treatment causes elevated levels of SA in the plant, and both compounds activate SAR when applied to NahG plants, suggesting that both INA and BTH act independently or downstream of SA in SAR signaling [62]. Work with *nim1* (noninducible immunity) mutants of *Arabidopsis* indicated that INA, BTH and SA activate the SAR signal transduction pathway through the same signaling cascade [9]. Furthermore, the structural similarities of the three compounds [61] suggest that they may all bind to the same receptor, although direct evidence for this is lacking.

Genetic analysis of SAR. Genetic engineering for pathogen resistance has mainly been focussed on the construction of plants that constitutively express individual defensive genes, such as PR genes, to reduce pathogen growth and symptom expression, consistent with a role of PRs in the expression of SAR [12]. Although in specific cases this approach has been proven successful, increased resistance as a result of overexpression of PR genes is not general. Novel insights in plant defense signaling have been instrumental in developing of new approaches to engineer plants with increased resistance by manipulating master switches of inducible plant defense pathways. Several genes that appear to be key to the regulation of systemic resistance were identified and cloned. A series of mutants that express constitutive resistance in a susceptible host background have been described in *Arabidopsis*. These include both mutants that express spontaneous lesions (e.g. *lsd* mutants [63] as well as one class that expresses resistance without spontaneous lesions (e.g. *cpr* mutants) [64]. Another class of mutants isolated from *Arabidopsis* was found by screening for lack of resistance expression in response to SA or synthetic resistance activators. This screen resulted in the isolation of the npr1 or *sai1* mutant [65]. This is an important finding as this gene is key in the expression of salicylic acid-

mediated resistance. Use of transgenic technology has further allowed evaluation of SA [51] and catalases [66] in the signaling pathway that leads to resistance. Several approaches involve activating the SAR pathway to confer constitutive, broad-spectrum resistance against microbial pathogens. Tobacco plants were transformed with two bacterial genes (*ics* and *ipl*) coding for enzymes that convert chorismate into SA by a two-step process [67]. When the two enzymes were targeted to the chloroplasts, the transgenic CSA (constitutive SA biosynthesis) plants showed a 500- to 1000-fold increased accumulation of SA and SA glucoside compared to control plants. Defense genes, particularly those encoding acidic PR proteins were constitutively expressed in CSA plants. This expression did not affect the plant phenotype, but the CSA plants showed enhanced resistance to infection by tobacco mosaic virus (TMV) and the fungal pathogen *Oidium lycopersici* resembling SAR in non-transgenic plants. A similar approach was undertaken [50] when a novel hybrid enzyme with SA synthase activity was engineered by fusing an isochorismate synthase gene and isochorismate-pyruvate gene from the bacterium *Pseudomonas aeruginosa*. The fusion gene was overexpressed in *Arabidopsis* and with the protein targeted to the chloroplasts, transgenic plants showed increased levels of free and conjugated SA and enhanced disease resistance towards the oomycete pathogen *P. parasitica*. Cao et al. [68] investigated the possibility of generating broad-spectrum disease resistance through overexpression of the SAR regulatory protein NPR1. Indeed, NPR1-overexpressing *Arabidopsis* plants showed enhanced resistance towards the bacterial pathogen *P. syringae* pv. *maculicola* and the oomycete *P. parasitica*. Thus, engineered activation of key steps of the SAR pathway provides an attractive tool for controlling plant diseases.

Jasmonic acid. The jasmonates, derived from peroxidized linolenic acid, are members of a large class of oxygenated lipids (oxylipins) generated by the action of lipoxygenases on polyunsaturated fatty acids. In various plants, a rapid accumulation of jasmonic acid (JA) and its volatile ester methyl jasmonate were observed in response to their treatment with elicitors of defense responses.

A classic example of SAR is a systemic accumulation of proteinase inhibitor proteins in tomato plants after the attack of insects. These proteins inhibit digestive serine proteinases of herbivorous insects and reduce further insect feeding [69]. As a result of wounding, an 18-amino acid peptide, systemin, is generated through cleavage from a larger protein, pro-systemin. This peptide is translocated via the phloem and its perception in distant leaves leads to phospholipid hydrolysis and the release of the JA precursor linolenic acid. Then linolenic acid is rapidly metabolized via the octadecanoid pathway into JA, which in turn activates genes encoding proteinase inhibitors [70, 71]. Direct experimental evidence with transgenic supression of proteinase inhibitors [72] strongly supports most of the elements of this model. In addition, mutants that are insensitive to jasmonic acid or cannot synthesize this signal molecule have been valuable in understanding the regulation of jasmonate-dependent type of induced resistance [73].

It is unknown if systemin-like molecules with similar function are present in other plant species. The capacity for jasmonate and related oxylipin synthesis is highly conserved among plants, but the molecular triggers for oxylipin production in the context of SAR, except perhaps in the case of systemin in tomato, are not characterized.

Interestingly, ethylene has been shown to be co-required in the process of JA-dependent induced resistance [74].

Ethylene. A role for ethylene (ET), a well-known product of wounded plant tissue, has been suggested in SAR through experiments in which its synthesis or action has been modified. Plant treatment with ethephon, an unstable compound releasing ET, resulted in the accumulation of mRNA for PR proteins [9]. ET can positively regulate jasmonate levels in the plant [74], and jasmonate and ET appear to be required together to induce a defensin gene in *Arabidopsis* [75]. Defensins are small cystein-rich peptides with antimicrobial activity. Expression of the alfalfa defensin in transgenic potato plants provides fungal resistance in the greenhouse and under field conditions [76]. The ET-signaling pathway has been used to improve resistance against microbial pathogens. ET is perceived by a family of ET receptors, which, when mutated, give rise to dominant ET insensitivity, indicating that the ET response is negatively regulated [77]. Several genes encoding ET receptors have been isolated from *Arabidopsis* and tomato. The ET-insensitive Nr (Never ripe) mutant of to-

mato contains a mutation in the ET receptor gene NR, which is homologous the *Arabidopsis* ET receptor gene *ers1*. Interestingly, the Nr mutant showed increased tolerance to the fungal pathogen *Fusarium oxysporum* and the bacterial pathogen [78]. Overexpression of the wildtype NR gene in tomato, resulting in a stronger negative regulation of the ET response and reduced ET sensitivity, conferred increased tolerance to *Xanthomonas campestris* as well [79]. However, the effect of ET insensitivity varies greatly in different plant-pathogen interactions. For example, transformation of tobacco plants with the mutant *Arabidopsis etr1* gene, conferring dominant ET insensitivity, resulted in the loss of non-host resistance against the normally non-pathogenic soil-born oomycete *Pythium sylvaticum* [80].

Cross-talk between signaling pathways. The previous sections have illustrated that SA, JA and ET play important roles in the regulation of defense responses and that genetic engineering of the corresponding signaling pathways can effectively enhance resistance. However, evidence is accumulating that components from the SA-, JA- and ET-dependent defense pathways can affect each other's signaling [81]. For example, SA and its functional analogs, isonicotinic acid and benzothiobiasol, suppressed the JA-dependent expression of the defense genes in *Arabidopsis* [82], most probably through the inhibition of JA biosynthesis and action. Other researchers [83] demonstrated that tobacco plants inoculated with TMV could not develop SAR because of the inhibition of JA activity by SA, which accumulated after viral infection. Thus, SA accumulation, which confers plant resistance against a wide range of pathogens, can suppress the ET-JA-dependent signaling pathways, and these latter pathways provide for the resistance against insects and certain groups of pathogens. JA and ET usually exert an additive action. However, in some cases JA and ET have been shown to stimulate the signal function of SA leading to enhanced *PR* gene expression [84].

In experiments performed on *Arabidopsis* mutants differing in their sensitivity towards JA and in their capacity for SA formation, it was shown that different mechanisms activated SA-dependent and ET-JA-dependent signaling pathways [85]. It turned out that ET-JA-dependent defense responses were activated by necrotrophic pathogens, which used dead plant cells for their nutrition. In contrast, SA-dependent responses are mainly induced by biotrophs, which use alive plant tissues for their nutrition. The possible conclusion is that the plants switch on different defense mechanisms depending on the nutrition type of the invading pathogen.

Experiments thoroughly exploring signaling conflicts and synergies in plant-pathogen interactions will be essential to realize fully the potential of SAR in plant protection against biotic stress.

Conclusion. In the past decade, growing concern about the harmful impact of repeated fungicide applications has encouraged a search for strategies that could provide alternative, ecologically safe means for improving disease control. Increasing knowledge of the mechanisms underlying plant defense responses against pathogen attack has strengthened the idea that sensitizing a plant to respond more rapidly to infection could confer increased protection against virulent pathogens.

More than 3000 articles on induced pathogen resistance have been published since 1995 [57]. However, many questions are still unanswered and require further investigation. It is clear that plants can express induced resistance to pathogens after a prior infection or other resistance activating treatment. Significant advances have been made in understanding the genes that are involved in regulating the resistant state as well as the chemical signals that modulate the induced response. SAR can be an alternative mechanism to antagonism for achieving biological control of plant disease. Most bacterial control agents of plant pathogens function partially or completely through antagonism [86]. There are several advantages of SAR. First, it is ecologically safe, because based on activated plant innate defenses, while antagonism relies on direct inhibition of pathogens with antibiotics and hydrogen cyanide. Second, SAR, once expressed, activates multiple defense responses, i.e. mechanical strengthening of cell walls (lignin, callose, suberin, etc.), phytoalexin synthesis, PR-proteins accumulation. Third, the wide spectrum of pathogens that can be controlled (ten and more) with a single inducing agent, while antagonism is generally not active against diverse pathogens. And, finally, by definition, SAR protects the plant systemically following induction with an inducing agent to a single part of the plant, while other mechanisms of biological control are generally not systemic.

The use of biotic and synthetic inducers to activate SAR provides novel alternatives for plant protection and detailed understanding of this pathway is important for both practical and theoretical reasons.

РЕЗЮМЕ. Растение-хозяин после распознавания патогена включает серию своих защитных реакций. Одни реакции индуцируются в месте проникновения патогена и являются «локальными». Другие — это «системные» защитные реакции, которые проявляются в неинфицированных частях растения. Недавно были обнаружены гены, которые участвуют в передаче сигнала для индуцирования системной устойчивости. Клонирование этих генов и анализ функций соответствующих белков позволили приблизиться к пониманию процессов, регулирующих активацию защитных реакций у растений. Получены доказательства важной роли системной защиты в проявлении устойчивости растений к биотическому стрессу. Когда у трансгенных растений или мутантов блокированы пути трансдукции сигнала для включения системных защитных реакций, устойчивость снижается. И, напротив, при стимуляции путей трансдукции этого сигнала происходит повышение устойчивости. Выяснение механизмов формирования системной устойчивости у растений представляет интерес как с теоретической, так и с практической точки зрения.

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Received 10.03.04