Genes controlling expression of defense responses in Arabidopsis — 2001 status
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In the past two years, the focus of studies of the genes controlling expression of defense responses in Arabidopsis has shifted from the identification of mutants to gene isolation and the ordering of genes within branches of the signal transduction networks. It is now clear that gene-for-gene resistance can be mediated through at least three genetically distinguishable pathways. Additional genes affecting salicylic-acid-dependent signaling have been identified, and double-mutant analyses have begun to reveal the order in which they act. Genes required for jasmonic-acid-dependent signaling and for induced systemic resistance have also been identified.

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Abbreviations
ACD2 ACCELERATED CELL DEATH 2
avr avirulence
coi1 coronatine insensitive 1
cpr1 constitutive PR 1
dnd1 defense no death 1
dtb9 detachment 9
EDS1 ENHANCED DISEASE SUSCEPTIBILITY 1
ein2 ethylene insensitive2
ET ethylene
HR hypersensitive response
ISR induced systemic resistance
JA jasmonic acid
jar1 jasmonic acid resistant 1
LRR leucine-rich repeat
LZ leucine-zipper
MPK4 MITOGEN-ACTIVATED PROTEIN KINASE 4
nahG salicylate hydroxylase
NBS nucleotide-binding site
NDR1 NON-RACE-SPECIFIC DISEASE RESISTANCE 1
NPR1 NON-EXPRESSOR OF PR 1
PAD4 PHYTOALEXIN DEFICIENT 4
PBS1 avrPphB Susceptible 1
PDF1.2 PLANT DEFENSIN 1.2
PR-1 PATHOGENESIS-RELATED PROTEIN-1
R resistance
RPP7 RESISTANCE TO PEROSONOSPORA PARASITICA 7
RP55 RESISTANCE TO PSEUDOMONAS SYRINGAE 5
RPW8 RESISTANCE TO POWDERY MILDEW 8
SA salicylic acid
SAR systemic acquired resistance
SID1 SA INDUCTION DEFICIENT 1
snl1 suppressor of npr1-1 inducible
TIR toll-interleukin 2 receptor

Introduction
Plants defend themselves from attack by microbial pathogens by activating a battery of defense responses after infection. Provided that they are activated with sufficient speed, these responses are generally quite effective in preventing disease. Consequently, there is considerable interest in understanding the signal transduction networks that control the activation of defense responses in plants. One approach to this problem is to use the powerful Arabidopsis genetic system to identify plant genes that have crucial roles in regulating the activation of defense responses. This article summarizes progress made using this system since the previous review of this topic was written [1]. A model describing the circuitry of the signal transduction network is presented in Figure 1.

Gene-for-gene resistance is a particularly strong form of plant disease resistance. Plants carry specific resistance (R) genes that are able to recognize pathogens carrying corresponding avirulence (avr) genes. This reaction triggers a rapid defense response that generally includes the programmed cell death of plant cells that are in contact with the pathogen, a phenomenon called the hypersensitive response (HR). Widespread difficulties in detecting direct interactions between R and avr proteins have led to the hypothesis that R proteins guard plant proteins (i.e. ‘guardees’) that are the targets of pathogen avr proteins, triggering the HR and other responses when avr-guardee interactions are detected [2].

Activation of the HR triggers a systemic resistance response known as systemic acquired resistance (SAR). This response includes the accumulation of the signal molecule salicylic acid (SA) throughout the plant and the consequent expression of a characteristic set of defense genes, including PR-1. Plants expressing SAR are more resistant to subsequent attack by a variety of otherwise virulent pathogens. Many defense responses that are characteristic of SAR also contribute to local resistance that is mediated by some R genes, and to the local growth limitation of moderately virulent pathogens. In a large expression profiling experiment, at 48 hours after infection, the spectra of plant genes expressed in response to a virulent Peronospora parasitica isolate and an isolate that triggers gene-for-gene resistance were similar [4**]. Responses triggered by R genes generally occur much faster than responses to virulent pathogens; this presumably explains why R-gene-mediated resistance is so effective.

Some defense responses are activated by signal transduction networks that require jasmonic acid (JA) and ethylene (ET)
A model describing the positions of Arabidopsis genes in signal transduction networks that control the activation of defense responses. This figure is meant to provide a rough outline of the sites of action of various gene products in disease resistance signaling. It does not account for all of the described phenotypes of the various signaling mutants. Boxes containing the word ‘resistance’ represent the numerous effectors of resistance, whose effectiveness may vary greatly according to the pathogen eliciting the response. There are certainly interconnections among the pathways shown in (a), (b), (c), and (d), but many of these are not sufficiently clear to allow them to be easily drawn.

(a) Three R-gene dependent pathways are shown, one that requires NDR1 and PBS2, a second that requires EDS1 and PAD4, and a third for which the required genes have not been reported. (b) In SA-dependent signaling, CPR1, EDR1, and CPR5 tend to repress pathway activation, and act upstream of PAD4. The cpr6 mutation exerts a positive effect upstream of PAD4, but it is difficult to predict the function of the wild-type gene as cpr6 is dominant. PAD4 and EDS1 promote SA accumulation, as do SII2 and EDS5. SA also promotes expression of PAD4 and EDS1. PAD4 promotes expression of resistance responses in an SA-independent manner. Formation of lesions promotes SA accumulation in a manner that is independent of PAD4 and EDS1, but may require EDS5. Downstream of SA, NPR1 mediates the activation of expression of genes such as PR-1, acting together with TGA transcription factors in a manner that is inhibited by SN11. DTH9 also acts downstream of SA to activate resistance responses. (c) JA and ET act together to activate expression of genes such as PDF1.2. This activation is promoted by lesion formation and by cpr6. MPK4, COI1 and JAR1 are required to transduce the JA signal, while EIN2 is required to transduce the ET signal. Camalexin production requires both PAD4 and COI1, and some lesion-mimic mutations cause camalexin accumulation in lesions. (d) ISR activation requires JA, followed by ET. ISR1 affects sensitivity to ET. NPR1 is required downstream of JA and ET to activate resistance. The model does not show the complicated interactions between SA and JA signaling. For example, MPK4 inhibits SA signaling, possibly by promoting JA signaling, but the nature of the relationship between the promotion of JA signaling and the inhibition of SA signaling is not understood.

R-gene signal transduction

Mutations in PBS1, NDR1, EDS1, PAD4, and PBS2 block gene-for-gene resistance that is mediated by some R genes. The only R gene known to be affected by PBS1 mutations is RPS5 [5]. This observation raises the intriguing possibility that PBS1 encodes the ‘guardian’ monitored by RPS5. As RPS5 and the corresponding avr gene, avrPphB, have both been isolated, it should be possible to test this hypothesis in the near future when PBS1 has been isolated.

R genes known to require NDR1 belong to the leucine zipper (LZ) subclass of nucleotide-binding site (NBS)-leucine-rich repeat (LRR) genes. R proteins known to require EDS1 belong to the subset of the NBS-LRR class of R proteins with an amino-terminal domain similar to the Drosophila Toll and mammalian interleukin 2 receptors (TIR-NBS-LRR) [6]. Although the effect of pad4 mutations on R-gene function has not been studied in great detail, it seems that R genes that require EDS1 also require PAD4 [7], an idea that is consistent with the extensive phenotypic similarities between pad4 and eds1 mutants [8,9,10,11]. Similarly, R genes that require NDR1 also require PBS2, although some R genes with an absolute requirement for NDR1 are not completely blocked by mutations in PBS2 and vice versa [5]. All of this evidence is consistent with the hypothesis of Aarts et al. [6], who suggested that there may be two downstream pathways triggered by R genes, with the structure of the R protein determining which downstream factors are required.

Other recent results have shown that the situation cannot be this simple. Two R genes, RPP7 and RPP8, require neither EDS1 nor NDR1 (although resistance is weakly suppressed...
in an edsl ndrl double mutant), suggesting that there is at least a third pathway for the transduction of R-gene signals [12••]. RPP13-mediated resistance does not require EDS1, PAD4, PBS2, or NDR1, is completely unaffected in an edsl ndrl double mutant, and is not blocked by nahG [13•]. RPP7 has not been cloned, but RPP8 and RPP13 are LZ-NBS-LRR proteins that are similar to each other [14,15]. Hence, these genes are exceptions to the rule that LZ-NBS-LRR proteins require NDR1. Taken together, the data support a model including at least three signal transduction cascades acting downstream of R genes, one that is NDR1-dependent, a second that is EDS1-dependent, and a third for which no genetic components have yet been defined. This conclusion rests on the assumption that the mutant ndrl, edsl, pad4, and pbs2 alleles that were tested are all null. Otherwise, the observed differences in genetic requirements could reflect quantitative differences in the signaling activities of the various alleles, rather than action of different signaling pathways. The commonly-used ndrl, pad4, and edsl alleles are likely null, as they are deletions or nonsense mutations that destabilize the mRNAs. The nature of the pbs2 alleles will not be known until PBS2 is isolated.

What determines which pathway is used by a particular R gene is not clear. For example, the R gene HRT is more than 90% identical to RPP8 [16], yet HRT-mediated resistance is blocked by the transgene nahG [17], which encodes an SA-degrading enzyme, whereas resistance mediated by RPP8 or RPP13 is unaffected by nahG [12••,13•]. Unfortunately, the effects of mutations in NDR1, EDS1, PAD4, or PBS2 on HRT-mediated resistance were not tested [17]. In another example, the resistance mediated by the broad-spectrum R gene RWP8 requires EDS1 and is blocked by nahG. The protein encoded by RWP8 includes a coiled-coil domain but otherwise bears little similarity to the LZ-NBS-LRR genes [18•]. Although the pathway used by a particular R gene may be determined by the structural features of the R gene, factors in addition to whether the R gene is of the LZ-NBS-LRR or the TIR-NBS-LRR type are clearly important.

A few of the genes that mediate R-gene signal transduction have been isolated. NDR1 encodes a protein with two predicted transmembrane domains [19]. It is possible that part of the function of NDR1 is to hold R proteins close to the membrane. EDS1 and PAD4 encode proteins with similarity to triacyl glycerol lipases [8,9]. The significance of this is not known, but it is tempting to speculate that EDS1 and PAD4 are involved in the synthesis or degradation of a signal molecule. Mutations in either gene can cause a defect in SA accumulation and expression of both genes can be induced by SA or pathogen infection, suggesting that they act in the SA pathway upstream of SA, possibly as part of a signal amplification loop [8,9].

**SA-dependent signaling**

SA-dependent signaling is important for some gene-for-gene resistance responses, for local responses that limit the growth of virulent pathogens, and for SAR. SAR is a resistance response that is activated throughout the plant in response to local infection by necrotizing pathogens. As described above, EDS1 and PAD4 act upstream of SA to promote SA accumulation. The ankyrin-repeat protein NPR1 (also known as NIM1 [NON-INDUCIBLE IMMUNITY 1] and SA11 [SALICYLIC ACID INSENSITIVE 1]) acts downstream of SA to promote the expression of the SAR-associated genes PR-1, BGL2, and PR-5.

Recently, additional genes that act in the SA signaling pathway have been identified, double-mutant analyses have placed some negative regulators in the pathway, and NPR1-interacting factors have been identified. Mutations in EDS1 (also known as SID1) and SID2 (also known as EDS16 [20]) abolish the increase in SA levels observed in infected plants. In fact, SA levels in these mutants are as low as they are in plants carrying the nahG transgene, which encodes an enzyme that degrades SA to catechol. Hence, EDS5 and SID2 are suggested to function upstream of SA accumulation [21]. A mutation in EDS4 causes reduced SA accumulation and reduced sensitivity to SA, so EDS4 seems to function in SA signaling [22]. Interestingly, although eds5, sid2, edsl, eds4, and pad4 mutations (as well as the transgene nahG) reduce SA levels and expression of PR-1, only pad4 and nahG reduce production of the phytoalexin camalexin [21–23]. It appears, therefore, that low SA production does not cause the camalexin defect in these plants, and that pad4 and nahG may affect signaling pathways in addition to the SA-dependent pathway.

Double-mutant analyses have been used to place some of the regulatory factors in the SA signaling network in order. A probable null mutation in EDR1 enhances resistance to *Pseudomonas syringae* and *Ershiphe cichoracearum*, and causes more rapid expression of defense-related genes, such as PR-1, after infection [24,25••]. The resistance is blocked by nahG and by eds1, pad4, or nim1 (allelic to npr1) mutations, indicating that the effect of the npr1 mutation requires SA-dependent signaling [25••]. Presumably, the mitogen-activated protein kinase (MAPK) kinase kinase (MAPK KK) encoded by EDR1 is involved in the negative regulation of SA signaling, acting upstream of pad4 and eds3 [25••]. A mutation in the MAPK gene MPK4 causes constitutively high SA accumulation, PR-1 expression and resistance to *P. syringae* [26•]. These phenotypes are blocked by nahG but not by the npr1 mutation [26•]. The effects of other mutations were not tested. It does not seem likely that MPK4 is a component of the EDR1 kinase cascade, as the phenotypes of mpk4 are considerably more severe than those of edrl and are NPR1-independent. Rather, MPK4 may impact SA signaling upstream of SA by affecting the balance between SA-dependent and jasmonic acid (JA)-dependent signaling, as discussed further below [26•]. The mutations cpr1 and cpr6 cause constitutively high SA levels, PR-1 expression, and enhanced disease resistance. These phenotypes are blocked by mutations in eds5 [27••], eds1 [10•], or pad4 [11•], placing the effects of
the *cpr* mutations on SA signaling upstream of *PAD4*. Reminiscent of the situation with *MPK4*, however, the disease resistance phenotypes of *cpr1* and *cpr6* are only partially blocked by mutations in *npr1*, demonstrating that there must be SA-dependent, NPR1-independent resistance mechanisms [27••]. In *dnd1* *pad4* or *dnd2* *pad4* double mutants, the high SA and PR-1 expression levels that are characteristic of *dnd* plants are retained but susceptibility to *P. syringae* is as high as it is in *pad4* plants, suggesting that there is also a *PAD4*-dependent, SA-independent component of resistance [11*].

Many mutants with constitutively high SA levels, defense-gene expression, and disease resistance also display a lesion-mimic phenotype. That is, they undergo spontaneous cell death in the absence of pathogen attack. Some of the genes defined by these mutations may function as negative regulators of hypersensitive cell death, whereas others may merely perturb cellular metabolism in a way that leads to cell death, which then triggers the SAR signal transduction cascade. Indeed, some transgenes that perturb cellular metabolism, including the bacterio-opsin proton pump [28] and antisense protoporphyrinogen oxidase [29], cause a lesion-mimic phenotype. The identities of recently isolated lesion-mimic genes are consistent with the idea that many lesion-mimic mutations disrupt cellular metabolism. *ACD2* encodes a protein that is similar to red chlorophyll catabolite reductase, an enzyme responsible for the proper catabolism of the porphyrin component of chlorophyll [30]. Presumably, loss of this enzyme in *acd2* mutants results in the accumulation of toxic catabolites that trigger the lesions. This enzyme may also play a role in coping with pathogen damage as overexpression of *ACD2* attenuates disease symptoms [30]. *DND1* encodes a cyclic nucleotide-gated ion channel [31]. This channel could be involved in the regulation of ion flows that are related to programmed cell death. Alternatively, the loss of this function could simply perturb cellular homeostasis in a manner that promotes cell death. (Recently, it has been recognized that both *dnd1* and *dnd2* mutants are lesion-mimics under certain growth conditions [11*,32,*].)

Double-mutant experiments involving some lesion-mimic mutants have revealed interesting features of SA-dependent signal transduction. In *cpr5* mutants, SA level and PR-1 expression and disease resistance are partially reduced by *eds1* and *pad4* mutations, and are completely blocked by the *eds5* mutation [10*,11*,27••]. This finding shows that activation of SA accumulation does not absolutely require *EDS1* and *PAD4*, but that *EDS5* may be required. The SA and PR-1 expression phenotypes of *dnd1* and *dnd2* mutants are unaffected by *PAD4*, confirming the observations that suggested that there is a *PAD4*-independent pathway to SA accumulation [11*,23,*]. However, *pad4* blocks the enhanced resistance phenotypes of *dnd1* and *dnd2*, suggesting that there are resistance responses whose expression requires a function of *PAD4* other than its activation of SA accumulation [11*]. The numerous lesion-mimic mutants that have been isolated over the years may prove to be useful in devising genetic screens to identify components of the *PAD4*/EDS1-independent route to SA accumulation. It would also be interesting to survey lesion-mimic mutants to see if any of them activate SA accumulation in ways that are independent of *EDS5* or *SID2*.

*NPR1* is required downstream of SA to activate the expression of *PR-1*. Recent results suggest that *NPR1* may directly participate in the transcriptional control of defense-gene expression. NPR1 concentrates in the nucleus in response to SA, and nuclear localization is required for the activation of *PR-1* expression by NPR1 [33]. NPR1 also interacts with TGA-type transcription factors in yeast two-hybrid assays [34–36] and promotes the binding of TGA2 to its binding site [36]. As yet, no role for TGA factors in activating defense-gene expression has been detected, so the significance of the NPR1–TGA-factor interaction is not certain. SA-inducible *PR-1* expression is restored in *npr1 sni1* plants [37]. SNI1 is also a nuclear-localized protein [37]. A reasonable model to explain these results is that the activation of *PR-1* expression requires that repression of *PR-1* must be released by SNI1, allowing *NPR1* to interact with transcription factors to activate gene expression [37].

The existence of SA-dependent, NPR1-independent resistance mechanisms was suggested by the observation that responses that are blocked by *nahG* are not necessarily blocked by *npr1*. This logic is now somewhat questionable as gene expression and camalexin accumulation are less severely affected in the low-SA mutants *eds5* and *sid2* than in plants containing *nahG* [21,38]. Nevertheless, the existence of an SA-dependent, NPR1-independent resistance mechanism is still supported by the observation that *eds5* completely blocks the enhanced disease resistance of *cpr1*, *cpr5*, and *cpr6* mutants, whereas *npr1* blocks it only partially [27••]. The *dth9* mutation may define a component of this pathway. Plants carrying the *dth9* mutation express PR genes normally in response to SA treatment but they fail to develop resistance, demonstrating that *DTH9* is required for SAR but not for the gene expression changes known to be characteristic of SAR [39••]. The *dth9* mutant could now be used as a tool to identify other factors that are required for SA-dependent resistance.

**Jasmonic acid/ethylene-dependent signaling**

The role of JA and ET in the activation of disease resistance mechanisms was demonstrated by the observation that expression of the *PDF1.2* gene and other genes was prevented by mutations that block JA signaling (i.e. *coi1*) or ethylene signaling (i.e. *ein2*). JA and ET seem to be required simultaneously, as *PDF1.2* expression is not activated by either ET treatment of *coi1* plants or JA treatment of *ein2* plants [40]. Furthermore, resistance to the fungal pathogen *Alternaria brassicicola* is compromised in *coi1* plants, and pretreatment with JA enhances resistance to
This pathogen [41], whereas ein2 plants display enhanced susceptibility to the fungal pathogen Botrytis cinerea [42]. Mutations in OPR3 (12-OXOPHYTODIENOIC ACID REDUCTASE 3), a gene encoding an enzyme that is required for JA synthesis, were identified as a consequence of their male-sterility phenotypes [43,44]. The opr3 mutants could be used to determine the effect of blocking JA synthesis on defense responses. The coi1 mutation is commonly considered to reflect the loss of JA signaling, but COI1 encodes an F-box protein that presumably functions in targeting proteins for ubiquitin-dependent degradation [45]. It is possible, therefore, that COI1 has pleiotropic effects beyond its effect on JA signaling.

JA signaling is also involved in control of the formation of lesions that are induced by ozone treatment. This observation is interesting in the context of disease resistance signaling because ozone-induced cell death may be similar to hypersensitive cell death. The red1 (radical-induced cell death1) mutant develops spreading lesions after ozone treatments that do not induce lesions in wild-type plants [46]. In this mutant, the HR lesions induced by infection with a bacterial pathogen that triggers gene-for-gene resistance are larger than those in wild-type plants [46]. The ozone-triggered cell death in red1 plants is inhibited by JA and promoted by ethylene. Thus, JA and ET act in opposition to each other during the formation of ozone-induced lesions, whereas they both promote PDF1.2 expression [46]. In a related study, nahG plants showed increased tolerance to ozone, JA treatment decreased SA levels and increased ozone tolerance, and mutants blocked in JA signaling (i.e. jar1) or synthesis (i.e. the fatty-acid deficient 3 [fad3]fad7 fad8 triple mutant) showed decreased tolerance [47].

There are many other examples of cross talk between SA and JA/ET signaling. Many lesion-mimic mutants, including cpr5, cpr6, acd2, dud1, dud2, and ssi1 (suppressor of SA insensitivity 1), display constitutively high expression of both PR-1 and PDF1.2, suggesting that the SA and JA signaling pathways may share common activating signals. Expression of the JA-dependent gene PDF1.2 is, however, strongly inhibited by SA, as demonstrated by observations including increased rose-bengal-induced PDF1.2 expression in pad4 mutants [22], increased cpr6-dependent PDF1.2 expression in cpr6 eds5, cpr6 pad4, and cpr6 eds1 double mutants [10,11,27], enhanced PDF1.2 expression in sid2 plants infected with Erisyphe orontii [20], and enhanced PDF1.2 expression in npr1 or nahG plants treated with rose bengal or infected with Alternaria brassicicola [48,49]. JA can also repress the expression of SA-induced genes. For example, treatment with JA repressed the ozone-induced accumulation of SA and expression of PR-1 [47]. The mpk4 mutation blocks the JA-inducible expression of PDF1.2 and causes the constitutive activation of SA-dependent signaling, suggesting either that the block in JA signaling relieves the suppression of SA signaling or that the activation of SA signaling blocks JA signaling. The former explanation is supported by the observation that the activation of PDF1.2 expression is also blocked in nahG mpk4 double mutants [26]. Consistent with the idea that JA and SA may sometimes act together rather than in opposition to each other, some genes can be activated by either JA or SA treatment [50].

**Induced systemic resistance**

Colonization of roots by certain rhizosphere bacteria confers a form of disease resistance called induced systemic resistance (ISR). ISR occurs in nahG plants, so it is not an SA-dependent phenomenon. No significant changes in plant gene expression have been associated with ISR. Nonetheless, progress has been made in the genetic dissection of this phenomenon. Several years ago, it was found that ISR requires NPR1. This is interesting as it implies that NPR1 is involved in perception of more than one signal (i.e. SA and the ISR signal), and may respond in one of two ways (by activating PR-1 expression or by activating ISR). If NPR1 acts as an adaptor molecule that brings the components of signaling complexes together, this sort of dual role might be expected. ISR is blocked by mutations that interfere with either ET or JA signaling. As ethylene can induce ISR in jar1 mutants, it is thought that the requirement for JA lies upstream of the requirement for ET in ISR signaling (for review, see [51]).

Some ecotypes fail to develop ISR, a trait that maps to a single locus dubbed ISR1 [52]. The dominant ISR1 allele confers the ability to develop ISR [52]. Interestingly, the ISR trait cosegregates with high basal resistance to a virulent strain of *P. syringae*, suggesting that ISR and general resistance responses are intimately related [52]. ISR1 also cosegregates with sensitivity to ethylene, with the ISR1 allele correlating with increased sensitivity to ethylene [53]. Simultaneous induction of SAR and ISR resulted in enhanced resistance relative to the induction of SAR alone, suggesting that ISR is an example of a JA-dependent response that is not inhibited by SA [54].

**Genes not yet placed into pathways**

Several interesting mutants have been described that probably affect disease resistance signaling but that are not yet characterized in sufficient detail to allow them to be placed in particular positions in the network. Two genes, HXC2 (Hypersensitivity to Xanthomonas campestris pv. campesris 2) and RXC5 (Resistance to Xanthomonas campestris 5), are required for resistance to a particular isolate of *Xanthomonas campestris*, implying that they may be part of a gene-for-gene resistance mechanism [18]. FLS2 (FLAGELLIN SENSITIVE 2) encodes a receptor-like kinase that is required for responses to bacterial flagellin, but the effects of fls2 mutations on resistance to bacterial pathogens have not yet been reported [55,56]. Many other mutants with enhanced disease resistance [57–60] or enhanced susceptibility to various pathogens [5,20,61] have also been described recently.
Conclusions and future prospects

A major area of progress in the past year has been in elucidating the relative sites of action of signaling components in signal transduction cascades. On the basis of the different requirements of various R genes for other genes to mediate resistance, R-gene-dependent signaling has been resolved into at least three different pathways. New genes have been identified in the SA signaling pathway, and constitutive mutants have been useful in ordering components of the pathway.

There is still much work to be done to define genes that are required for resistance. Although progress has been made in defining the signal transduction cascades that control the expression of certain defense-related genes, there is no clear correlation between gene expression patterns and disease resistance (see [11*, 27**] for examples). In the future, the application of genome-wide expression profiling to various mutants with defects in disease resistance signaling should greatly facilitate both the elucidation of signaling networks and the identification of genes with roles in the regulation and execution of disease resistance responses. The work of Maleck et al. [4**] demonstrates the power of this sort of analysis. In the next year or two, many more reports of genome-wide expression analysis can be expected, as well as the isolation of many of the genes that correspond to the interesting mutations described in this review.

Acknowledgements

I apologize to scientists whose work I overlooked or was not able to include because of length limitations.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as: **of special interest** and *of outstanding interest*


The double-mutant analysis reported in this paper placed CPR1 and CPR6 upstream of EDS1 in SA-dependent signaling.


The double-mutant analysis placed CPR1 and CPR6 upstream of PAD4 in SA-dependent signaling.


The genes RPP7 and RPP8 were shown to function independently of NDR1, EDS1, and NPR1, thus defining a possible third pathway for R-gene function.


The r gene RPP13 was found to act independently of EDS1 and NDR1, confirming the existence of at least three alternative pathways for R-gene function.


The isolation of the broad-spectrum R gene RPW8 is reported. RPW8 is structurally very different from known R genes, yet it requires EDS1 function.


EDR1 is isolated and found to encode a MAPKKK. Double-mutant analysis revealed that EDR1 acts upstream of EDS1 to suppress the activation of SA signaling.


A mutation in MF4 was found to block JA signaling and activate SA signaling. These results demonstrate a role for a MAP kinase in defense signaling, and illustrate cross-talk between JA-dependent and SA-dependent signaling pathways.


A detailed analysis of double and triple mutants reveals that CPR1 and CPR6 act upstream of EDS5, and detects complex interactions among SA, ET, and JA signaling that affect disease resistance.


