Review

Arabidopsis defense response against *Fusarium oxysporum*

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The plant fungal pathogen *Fusarium oxysporum* (Fox) is the causal agent of root rot or wilt diseases in several plant species, including crops such as tomato (*Solanum lycopersicum*), banana (*Musa sapientum*) and asparagus (*Asparagus officinalis*). Colonization of plants by Fox leads to the necrosis of the infected tissues, a subsequent collapse of vascular vessels and decay of the plant. Plant resistance to Fox appears to be monogenic or oligogenic depending on the host. Perception of Fox by plants follows the concept of elicitor-induced immune response, which in turn activates several plant defense signaling pathways. Here, we review the Fox-derived elicitors identified so far and the interaction among the different signaling pathways mediating plant resistance to Fox.

Plant-*Fusarium oxysporum* interactions

The genus *Fusarium* comprises several fungal species widely distributed in soils and organic substrates. One of the most relevant species of this genus is *Fusarium oxysporum* (Fox), which causes vascular wilt and root rot in more than 100 species of plants [1]. Affected plants (hosts) are mostly from the tropical and subtropical areas, probably because wilt symptoms are more pronounced at elevated temperatures [2–4]. Thus, as Fox grows better in warmer condition, global warming might positively influence its incidence; this has, to date, not been reported but it should be considered. The pathogenic Fox isolates have been classified in more than 100 *formae speciales* (ff. ssp.; *forma specialis*, f. sp.), which typically names an original plant host, in recognition of the fact that a pathogenic isolate produces disease only within a particular range of host species. However, a few ff. ssp. are able to colonize a broader range of plants [1–5]. Persistence of Fox disease can be attributed to two principal factors: resistance appears to be genetically complex and thus is a difficult trait to confer by breeding. Fox can persist in affected fields for an extended period of time on plant surfaces as macroconidia or even survive on soils as dormant chlamydospores in the absence of a suitable host plant. Therefore, there is much interest in determining the molecular and genetic bases of plant innate immunity against this type of pathogens. Here, we review the underlying molecular mechanism of plant resistance to Fox, particularly in the dicot *Arabidopsis thaliana* (Figure 1).

The genetic complexity of plant resistance to Fox

Fox, like other vascular pathogens, colonizes plants through the roots [6], inducing both local and systemic plant defense responses. Depending on the specific host–Fox combination, plant resistance to Fox can be controlled by one gene (monogenic), by few genes (oligogenic) or by multiple genes (multigenic).

Perception of Fox by Arabidopsis thaliana

When examined, *Arabidopsis thaliana* resistance to different Fox races has proved to be an oligogenic trait, although qualitative resistance loci has been also described encoding canonical nucleotide binding site-leucine rich repeat (NBS-LRR) R-genes [7,8]. Different experimental approaches have been used to study the *Arabidopsis*–Fox interaction. Seedlings from thirty different *Arabidopsis* accessions inoculated with Fox f. sp. *conglutinans* showed a high variability in the severity of the disease symptoms. The quantitative phenotypic distribution on disease rating data indicated that natural resistance (determined by natural allelic variations) observed among *Arabidopsis* ecotypes appears to be dependent on several genes [8]. In a different study with soil-grown plants, six dominant resistance loci to Fox f.sp. *matthiolae* (RFO) were identified in the *Arabidopsis* Col-0 accession [7]. Among these *RFO* loci, *RFO1* was the largest contributor controlling the resistance mediated by *RFO2*, *RFO4* and *RFO6* loci [7]. Interestingly, *RFO1* confers enhanced protection to different ff. ssp. of Fox, suggesting that RFO1-mediated resistance is not race specific. *RFO1* encodes the cell wall-associated kinase-like 22 (WAK/WAKL) [9], one of 26 members of the *Arabidopsis* WAK/WAKL class, which belongs to the receptor-like kinase (RLK) protein family [10]. Furthermore, *RFO1* has been described recently to be essential for quantitative resistance to *Verticillium longisporum*, a fungus with a lifestyle and infection strategies similar to that of Fox [11]. Other RLKs, such as ERECTA, are required for resistance to several pathogens, such as the necrotroph *Plectosphaerella cucumerina*, the soil-borne bacterium *Ralstonia solanacearum* and the oomycete *Pythium irregulare*, although they are not essential for *Arabidopsis* resistance to Fox [8]. Like the perception of a bacterial PAMP by the RLKs FLS2 and EFR, ROF1 might be envisaged to play a role in the perception of a fungal PAMP. The requirement of one or several RLKs and/or additional proteins to activate *Arabidopsis* defense response against Fox remains unknown.

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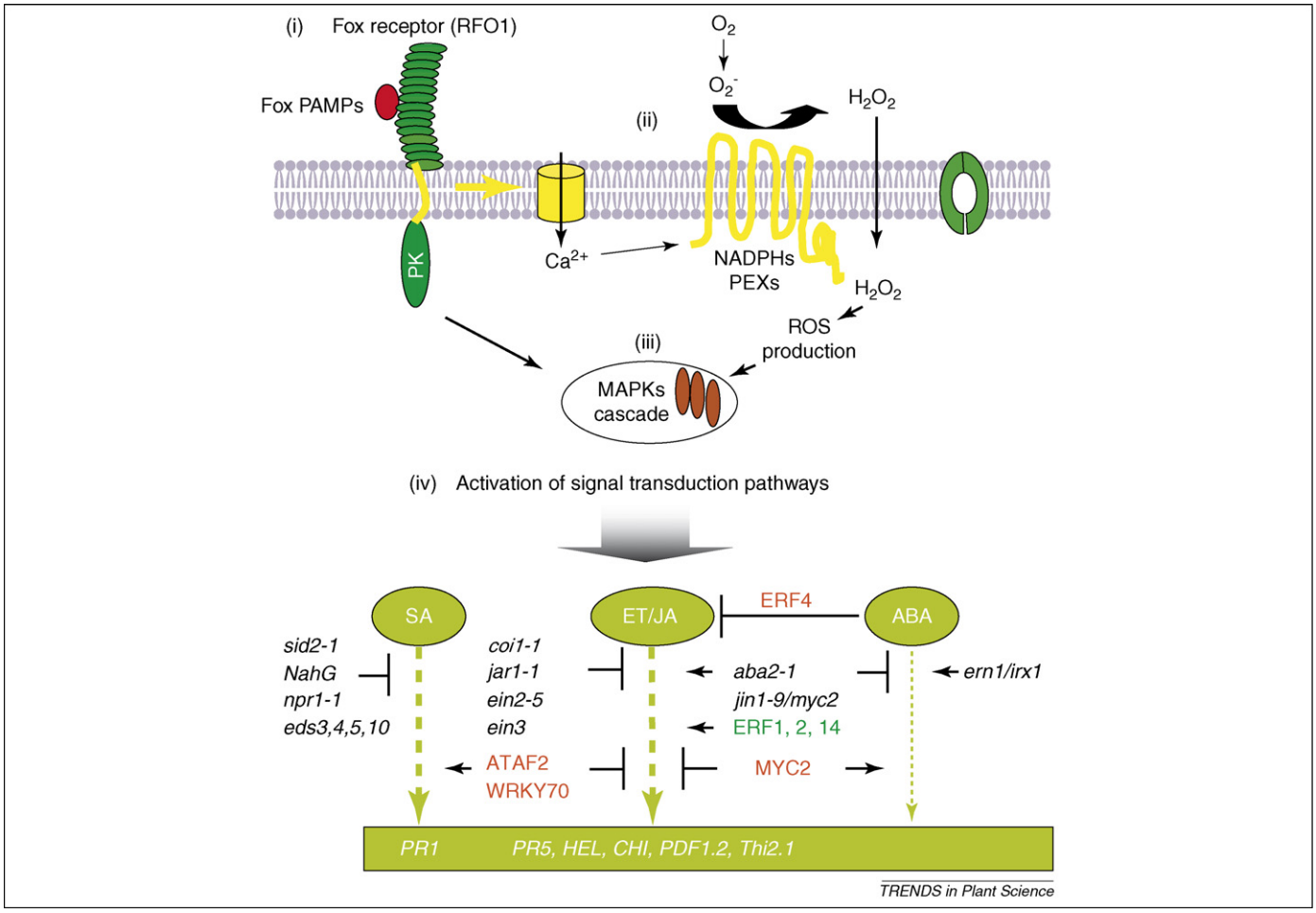

Figure 1. Signal transduction network controlling *Arabidopsis thaliana* resistance to *Fusarium oxysporum* sp. (Fox). **(i)** Recognition of fungal elicitors/PAMPs (pathogen-associated molecular patterns) by membrane-anchored Fox receptor proteins, such as RFO1 [22,74], induce downstream signaling. **(ii)** Both activation of calcium channels and the increase of cytoplasmic calcium trigger the activation of NADPH oxidases and/or peroxidases (PEXs) [20,28,46], resulting in hydrogen peroxide (H_2O_2) production and oxidative burst (ROS). **(iii)** Subsequently, a MAP-kinase cascade (red circles) actives downstream defensive pathways (marked in green circles), such as those mediated by the plant hormones salicylic acid (SA), ethylene (ET), jasmonic acid (JA) and abscisic acid (ABA). **(iv)** These signal transduction pathways control the expression of defensive genes against Fox, such as *PR1, PR5, PDF1.2* and *Thi2.1* [7,40,43] through different subsets of transcription factors (TFs). TFs such as ERF4, WRKY70 [36], ATAF2 [62], and JIN1/AtMYC2 [33,75,76], which are described as negative regulators of *Arabidopsis* defense response, are indicated in red, whereas the positive regulators ERF1, ERF2 and ERF14 [36,40,65] are showed in green. The relative position between these TFs for each pathway has not been confirmed yet; ERF14 and JIN1/AtMYC2 have been suggested to act upstream from ERF1 [33,65]. T-bars indicate *Arabidopsis* signaling mutants impaired in resistance to Fox, whereas arrows indicate mutants showing an enhanced resistance to Fox.

Perception of Fox by tomato (Solanum lycopersicon)

Plant–Fox interaction has been studied profusely in tomato. Interaction between Fox f. sp. *lycopersici* (Fol) and tomato is race–cultivar specific. Six *I* loci (*I* for '*immunity to Fusarium wilt*') conferring resistance to different Fol races have been described and some of them have been found to encode resistance proteins of the NBS-LRR subclass [12–14]. The locus *I-2* confers complete plant resistance to specific races of Fox [12,15], whereas other *I* loci give only partial resistance to the pathogen [16]. Similarly, some effector proteins (e.g. SIX1) required for Fol virulence in tomato have been identified. The Fox gene *SIX1* encodes a small, cysteine-rich protein secreted during colonization of the xylem [13]. The resistance mediated by the *I-3* gene [14] seems to rely on the recognition of SIX1, further indicating that SIX1 could be the corresponding Avr protein, [17]. The results obtained in the analysis of the interaction between tomato, *Arabidopsis* and Fox illustrate the genetic complexity and variability of plant resistance to Fox that can be mediated either by recognition of elicitor/PAMP or effector/Avr proteins.

Early events of plant infection by Fox

The role of ROS in Arabidopsis–Fox interaction

Necrotrophic fungi are able to produce hydrolytic enzymes and induce plant reactive oxygen species (ROS) and cell death. This cell death would allow the fungus to access the nutrients and contribute to survival and disease development. Recent works have described that cell death induced by some necrotrophic fungi might have opposite effects on disease development. In case of Botrytis *cinerea* and its elicitors, death tissue has been described to facilitate growth of the pathogen [18,19]. In addition, in the *Arabidopsis cpr5/hys1* mutant, which shows spontaneous cell death lesions and higher expression levels of the *SEN1* (senescence associated protein 1) gene, the production of ROS contributes to Fox infection [20]. However, in *Asparagus*, a rapid induction of root epidermal cell death and activation of phenyl-ammonia lyase and peroxidase proteins was associated with restriction of *Fusarium oxysporum* f. sp. *asparagi* growth [21]. These contradictory results seem to indicate that ROS and cell death might have different effects depending on the interaction, or that

there are different kinds of cell death and/or ROS that might have opposing roles on the growth of necrotrophic fungus.

ROS that might mediate the necrosis induced by Fox might have different origins. Several Fox elicitor molecules might induce this necrosis, such as the so-called NLPs (Nep1-like proteins) [22] or some recently described phytotoxins [23]. Nep-1 has been found to be present in bacteria, fungi and oomycetes and induces the expression of the *AtrbohD* gene, which encodes a NADPH oxidase involved in ROS production [22]. Recent works are in line with the idea that both peroxidase and NADPH oxidase are sources for production of ROS and might be involved in plant response to pathogens. Interestingly, ROS production in *Arabidopsis* cell suspension cultures in response to Fox elicitor was dependent on peroxidases [24,25]. Moreover, transgenic *Arabidopsis* plants expressing antisense French bean (*Vicia faba*) peroxidase exhibit impaired oxidative burst [26] and increased susceptibility to other pathogens [27]. ROS produced by the Atrboh NADPH oxidases has been described to act sometimes as negative regulators of cell death [28]. Peroxidases would act both as basal defense components as well as activators of NADPH oxidases, whereas NADPH oxidases would have a dual role in both responses [25]. Still, it is controversial whether this initial production of ROS facilitates or restricts the progression of the infection. ROS function might depend on the specific *Arabidopsis*-pathogen recognition and its action might by modulated by the interaction with other signals [29]. In case of Fox–*Arabidopsis* interaction, cell death mediated by ROS production might contribute to disease development although whether it is ROS or the cell death itself that contributes to the infection remains unclear.

Signal transduction networks in *Arabidopsis*-Fox resistance

Upon pathogen recognition by plants, several signal transduction pathways are activated. The role of the signaling pathways mediated by salicylic acid (SA), jasmonic acid (JA) and ethylene (ET) in the *Arabidopsis* innate immune response is well established [30]. Furthermore it is known that cooperative or antagonistic interactions between the different pathways mediated by SA, JA and ET exist. More recently, the abscisic acid (ABA) pathway has also been implicated in defense response through interaction with other pathways and the fine-tuned regulation of the crosstalk between these pathways seems to determine the output of plant defensive responses to Fox [31–37]. Analysis of the *Arabidopsis*–Fox interaction has lead to the identification of signaling pathways required for plant resistance to Fox, as well as key regulators of innate immunity against this type of vascular pathogens.

Fox was shown to induce systemic acquired resistance (SAR) and pathogenesis-related proteins (PRs) in *Arabidopsis*, indicating that the SA pathway plays a role in plant resistance to Fox [38]. Moreover, treatment of plant leaves with SA before Fox inoculation reduced disease symptoms on the plant [39].

Subsequently, several groups have explored the signal transduction network controlling *Arabidopsis* resistance to Fox f. sp. *conglutinans* and Fox f. sp. *lycopersici* has been explored by analyzing the pathogen susceptibility, at different stages, of mutants defective in the ET (*ein2–5*), JA (*co1–1* and *jar1–1*) and SA (*NahG*, *sid2–1*, *eds5–1*, *npr1–1*, *pad4–1* and *eds1–1*) pathways. These analyses revealed that SA, ET and JA pathways influence the Fox-disease outcome in *Arabidopsis*. By contrast, the function in *Arabidopsis* resistance to Fox of the *PAD4* and *EDS1* genes, which regulate different R-gene signaling pathways [40], and *NPR1*, an essential component in SA-mediated defense response in *Arabidopsis* [32], needs additional clarification based on the contradictory results obtained. Further analyses of the susceptibility of *eds-3*, *eds-4* and *eds-10* mutants to other Fox isolates corroborated the function of the SA pathway in *Arabidopsis* resistance to Fox [7]. These data indicate that SA, ET and JA signaling pathways interact in a positive way in the activation of *Arabidopsis* resistance to Fox. Similar cooperative effects have been described for *Arabidopsis* resistance to other pathogens, such as the necrotrophs *B. cinerea* and *P. cucumerina* or the vascular oomycete *P. irregulare* [41]. Despite the cooperative function of these pathways in regulating *Arabidopsis* resistance to Fox, it has been found that constitutive expression of some transcriptional regulators of these pathways is sufficient to confer enhanced resistance to Fox [40], and also to other necrotrophic and vascular pathogens [42]. For example, the overexpression of *Arabidopsis NPR1* in tomato and wheat (*Triticum aestivum*) conferred increased resistance to Fox f. sp. *lycopersici* [43] and *Fusarium graminacearum* [44], respectively.

Additionally, other signaling pathways, such as glutathione biosynthesis, might be activated for *Arabidopsis* resistance to Fox. The *Arabidopsis pad2–1* mutant, impaired in a glutathione synthase [45], was found to be more susceptible to Fox f. sp. *conglutinans* and Fox f. sp. *lycopersici* [40]. Furthermore, *esa1* mutant plants, which are defective in the activation of ROS production, are more susceptible than *Arabidopsis* wild-type plants to virulent isolates Fox f. sp. *matthiolae*, *Fusarium solani* and *Fusarium culmorum*, as well as the non virulent isolate Fox f. sp. *cubense* [46]. These data indicate that, in addition to the SA, ET and JA pathways, other signals, such as ROS, might influence in the disease outcome.

The ABA signaling in *Arabidopsis* resistance to Fox

Several recent papers have proposed that ABA signaling, in addition to regulating plant development and response to abiotic stress, also plays a role in the regulation of innate immunity [37,41,47–49]. Meta-analysis of pathogen-inducible genes in *Arabidopsis* reveals that a significant subset of ABA-regulated genes are activated upon pathogen infection [41]. In some plant–pathogen interactions, such as that between *Arabidopsis* and the vascular bacterium *Ralstonia solanacearum*, ABA signaling plays a direct function in the activation of the defensive response. This is evidenced by mutants impaired in ABA biosynthesis (*aba*) or signaling (*abi*) that exhibit enhanced susceptibility to this pathogen [50]. This positive regulatory function of ABA signaling in *Arabidopsis* innate immunity is also supported by the enhanced resistance to several pathogens (e.g. *R. solanacearum* and necrotrophic pathogens) of the secondary cell wall mutant *ern1/irx1*, which shows higher

levels of endogenous ABA than wild-type plants and a constitutive expression of ABA-regulated defense-related genes [50]. However, in other plant–pathogen interactions, ABA seems to play a negative regulatory function by inactivating other defense signaling pathways, such as those mediated by SA or JA/ET [33,34,36,37,41]. Specific examples for this negative function have been observed in plant–pathogen interaction between tomato and *B. cinerea*, or *Arabidopsis* and any of the following pathogens: the necrotrophic fungi *B. cinerea*, *P. cucumerina* [51], the vascular oomycete *Pythium irregulare* [41], the necrotrophic bacteria *Erwinia carotovora* or the hemibiotroph bacteria *Pseudomonas syringae* pv tomato DC3000 [49].

This negative function of ABA has been proposed to be a mechanism used by some pathogens to suppress plant basal resistance [49]. In the *Arabidopsis*–Fox interaction, the *aba2–1* mutant, which is impaired in ABA biosynthesis, shows an increased resistance to Fox; moreover, the *jin1–9*/*myc2* mutants, which are impaired in the MYC2 transcriptional factor, a positive regulator of ABA signaling and a negative regulator of JA response, showed an increased resistance to Fox [31,33]. These data suggest a negative function of ABA in *Arabidopsis* resistance to Fox. However, the *ern1*/*irx1* mutant that shows a constitutive activation of ABA pathway displays an increased resistance to Fox ([50]; A. Sanchez-Vallet and A. Molina, unpublished). These contradictory results reflect the complexity of the function of ABA signaling in plant resistance to pathogens, in particular in the *Arabidopsis*–Fox interaction. Transcriptomic analysis of *Arabidopsis* response to Fox would contribute to clarify the putative function of ABA signaling in this interaction.

Role of heterotrimeric G-proteins in plant resistance to Fox

Heterotrimeric G proteins are GTPases composed of α, β and γ subunits that function as signal mediators in the transduction of diverse external signals in plants, mammals and yeast [52]. In plants heterotrimeric G proteins also regulate several signaling pathways, such as those mediated by auxin, gibberellin and ABA [52–56].

Recently, the *Arabidopsis* heterotrimeric G protein has been described to be required for resistance to Fox. Based on the analysis of the complete genome sequence of *Arabidopsis*, there is only one gene for each of the Gα and Gβ subunits (*GPA1* and *AGB1*, respectively) and two genes encoding Gγ subunit (*AGG1* and *AGG2*; [52]). *Arabidopsis* mutants defective in Gα and Gβ subunits (*gpa1* and *agb1*, respectively) have been found to be more resistant and susceptible, respectively, to different Fox isolates than wild-type plants [8,57]. Moreover, mutants in the γ2 (*agg2*), but not in γ1 subunit (*agg*1), also showed an increased susceptibility to Fox [57,58]. Interestingly, similar results on susceptibility were observed with the *gpa1* and *agb1* mutants when these plants were inoculated with the necrotrophic fungi *P. cucumerina* and *B. cinerea*. These data support a function of these heterotrimeric G proteins in *Arabidopsis* resistance to Fox and other necrotrophic fungi. The molecular base of the heterotrimeric G protein-mediated resistance is unknown, but seems to be independent of the SA, ET and JA pathways. However, the Gβ-deficient mutant has been described to be more sensitive to JA treatment than wild type, suggesting a function of heterotrimeric G protein in JA-mediated signaling [57]. Furthermore, the implication of heterotrimeric G proteins in ROS production and defense responses has been confirmed in rice (*Oryza sativa*) and *Arabidopsis* [54,59].

Key regulators of *Arabidopsis* resistance to Fox

Different sets of transcription factors (TFs) have been implicated in the regulation of *Arabidopsis* resistance to Fox, as previously described for other plant–pathogen interactions [60]. One of these TFs is *ATAF2*, a member of the NAC (no apical meristem) protein family, which is induced by wounding in leaves and also responds to JA and SA treatment, but not to ABA [61]. Overexpression of *ATAF2* in *Arabidopsis* increased susceptibility to Fox and blocked the expression of Fox-inducible defense genes, such as *PDF1.2* and *PR1*. *ATAF2* has been proposed to function as a repressor of Fox-inducible defense responses in *Arabidopsis* [62]. This function might be independent of ABA, because wound induction of *ATAF2* is not altered in *abi* mutants, which are ABA insensitive [62].

Ethylene response factor (ERF) proteins belong to a family of TFs composed of 122 members in *Arabidopsis* [63]. Several ERFs TFs have been implicated directly in the activation or inhibition of *Arabidopsis* defense response against Fox. Thus, overexpression of *ERF1*, an integrator of ET and JA responses [64], enhanced resistance to Fox in *Arabidopsis* and also to necrotrophic fungi, such as *B. cinerea* and *P. cucumerina* [40]. *ERF1* induction upon pathogen challenge is blocked in the *coi1* and *ein3* mutants, which are defective in the JA and ET signaling pathways, respectively. These results further corroborate the relevant function of these pathways in *Arabidopsis* resistance to Fox [31]. In the *coi1* or *ein3* mutants, the expression of *ERF2* TF upon pathogen infection was also abolished. Likewise with *ERF1*, plants overexpressing the *ERF2* gene were more resistant to Fox than wild-type plants [36]. A similar function in resistance to Fox has been described for *ERF14*, as loss-of-function mutants in this gene showed increased susceptibility to Fox. This result is in line with the fact that induction of *ERF1* and *ERF2* by ethylene depends on *ERF14* [65]. By contrast, *ERF4*, which does not respond to ET, JA or ABA [65,66], mediates antagonistic interactions between SA, JA [32] and ABA [33,66]. *ERF4* has been proposed to act downstream of *NPR1* and the TF *WRKY70* in SA-mediated suppression of JA-inducible *PDF1.2* expression [36]. The inactivation of the *Arabidopsis* ERF4 and AtMYC2 leads to increased resistance to Fox, probably by enhancing JA plant defense response [33,36]. The molecular mechanism controlling induction of specific *Arabidopsis ERFs* in response to Fox infection remains unclear, although it seems to be similar to that operating in the ethylene control of plant growth [60].

Resistance response mediated by these TFs depends on the regulation of expression of overlapping downstream defensive genes. Some of these ERF-regulated genes encode antimicrobial proteins or enzymes involved in the synthesis of secondary metabolites. Thus, transgenic *ERF1*-overexpressing plants show a constitutive expres-

sion of the antimicrobial defensin PDF1.2 and other PR proteins, which can explain the enhanced resistance of these plants to Fox. Similarly, it has been found that overexpression of certain antimicrobial proteins, such as thionins, is sufficient to confer enhanced resistance to Fox in *Arabidopsis* [67] and tomato [68]. The rapid changes in the level of expression of these TFs upon *Arabidopsis* infection by Fox, as well as the resistance phenotype of TFs mutants indicate a relevant role of these TFs as positive or negative key regulators on the production of antimicrobial compounds.

Concluding remarks

The current, most relevant knowledge of the signal transduction network controlling *Arabidopsis* resistance to Fox is presented in Figure 1 [32,33,36,62,66]. The mechanism of Fox perception by plants is not clear, although some potential plant receptors, such as RFO1, and some Fox PAMPs (e.g. Nep-1) have been identified. Upon fungal infection, production of ROS mediated by NADPH oxidases and peroxidases occurs and several defensive pathways are activated [21,26,28,36,40]. Among them, those mediated by SA, JA, ET and ABA seem to play an essential function in the modulation and networking of *Arabidopsis* innate immune response. The molecular mechanism controlling the mutually antagonistic or cooperative interactions between ABA and SA, JA and ET signaling pathways are still unknown. *Arabidopsis* resistance to Fox is positively or negatively regulated by different families of TFs (Figure 1). However, additional studies will be necessary to determine other molecular components that are mediating this plant–fungal interaction. It has to be noted that plant defense responses are interconnected with other developmental mechanisms, such as stomatal closing [48], senescence [69], flowering [70], cell wall synthesis [8], gibberellin metabolism [71], shade avoidance [72] and abiotic stress. It has been suggested that, depending on the kind of plant stress, some signaling pathways might be dominant over others, adding yet another level of complexity to our model of antagonistic interactions [33]. In this review, we have highlighted the complexity and potential variability of resistance to Fox among different plant species [73] by comparing tomato and *Arabidopsis* defense mechanisms. Thus careful interpretation is called for when considering similar mechanisms in other species or crops.

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References

1 Agrios, G.N., ed. (2005) *Plant Pathology* (5th edn), Elsevier Academic Press
2 Okubara, P. and Paulitz, T. (2005) Root defense responses to fungal pathogens: A molecular perspective. *Plant Soil* 274, 215–226
3 Di Pietro, A. *et al.* (2003) *Fusarium oxysporum*: exploring the molecular arsenal of a vascular wilt fungus. *Mol. Plant Pathol.* 4, 315–325
4 Roncero, M.I.G. *et al.* (2003) *Fusarium* as a model for studying virulence in soilborne plant pathogens. *Physiol. Mol. Plant Pathol.* 62, 87–98
5 Forsyth, L.M. *et al.* (2006) Identification and characterization of non-pathogenic *Fusarium oxysporum* capable of increasing and decreasing *Fusarium* wilt severity. *Mycol. Res.* 110, 929–935
6 Czymmek, K.J. *et al.* (2007) *In vivo* time-lapse documentation using confocal and multi-photon microscopy reveals the mechanisms of invasion into the *Arabidopsis* root vascular system by *Fusarium oxysporum*. *Fungal. Genet. Biol.* 44, 1011–1023
7 Diener, A.C. and Ausubel, F.M. (2005) *RESISTANCE TO FUSARIUM OXYSPORUM 1*, a dominant *Arabidopsis* disease-resistance gene, is not race specific. *Genetics* 171, 305–321
8 Llorente, F. *et al.* (2005) ERECTA receptor-like kinase and heterotrimeric G protein from *Arabidopsis* are required for resistance to the necrotrophic fungus *Plectosphaerella cucumerina*. *Plant J.* 43, 165–180
9 Verica, J.A. and He, Z.H. (2002) The cell wall-associated kinase (WAK) and WAK-like kinase gene family. *Plant Physiol.* 129, 455–459
10 Johnson, K.L. and Ingram, G.C. (2005) Sending the right signals: regulating receptor kinase activity. *Curr. Opin. Plant Biol.* 8, 648–656
11 Johansson, A. *et al.* (2006) Early responses in the *Arabidopsis–Verticillium longisporum* pathosystem are dependent on *NDR1*, JA- and ET-associated signals via cytosolic NPR1 and *RFO1*. *Mol. Plant Microbe Interact.* 19, 958–969
12 Simons, G. *et al.* (1998) Dissection of the *Fusarium I2* gene cluster in tomato reveals six homologs and one active gene copy. *Plant Cell* 10, 1055–1068
13 Hemming, M.N. *et al.* (2004) Fine mapping of the tomato *I-3* gene for *Fusarium* wilt resistance and elimination of a co-segregating resistance gene analogue as a candidate for I-3. *Theor. Appl. Genet.* 109, 409–418
14 Lim, G.T. *et al.* (2006) Mapping the *I-3* gene for resistance to *Fusarium* wilt in tomato: application of an *I-3* marker in tomato improvement and progress towards the cloning of *I-3*. *Australas. Plant Pathol.* 35, 671–680
15 Ori, N. *et al.* (1997) The *I2C* family from the wilt disease resistance locus *I2* belongs to the nucleotide binding, leucine-rich repeat superfamily of plant resistance genes. *Plant Cell* 9, 521–532
16 Sela-Buurlage, M.B. *et al.* (2001) Genome-wide dissection of *Fusarium* resistance in tomato reveals multiple complex loci. *Mol. Genet. Genomics* 265, 1104–1111
17 Rep, M. *et al.* (2005) *Fusarium oxysporum* evades *I-3*-mediated resistance without altering the matching avirulence gene. *Mol. Plant Microbe Interact.* 18, 15–23
18 Govrin, E.M. and Levine, A. (2000) The hypersensitive response facilitates plant infection by the necrotrophic pathogen *Botrytis cinerea*. *Curr. Biol.* 10, 751–757
19 Govrin, E.M. *et al.* (2006) An elicitor from *Botrytis cinerea* induces the hypersensitive response in *Arabidopsis thaliana* and other plants and promotes the gray mold disease. *Phytopathology* 96, 299–307
20 Schenk, P.M. *et al.* (2005) The *SEN1* gene of *Arabidopsis* is regulated by signals that link plant defence responses and senescence. *Plant Physiol. Biochem.* 43, 997–1005
21 He, C. *et al.* (2001) Activation of defense responses to *Fusarium* infection in *Asparagus densiflorus*. *Eur. J. Plant Pathol.* 107, 473–483
22 Bae, H. *et al.* (2006) Necrosis- and ethylene-inducing peptide from *Fusarium oxysporum* induces a complex cascade of transcripts associated with signal transduction and cell death in *Arabidopsis*. *Plant Physiol.* 141, 1056–1067
23 Nishiuchi, T. *et al.* (2006) *Fusarium* phytotoxin trichothecenes have an elicitor-like activity in *Arabidopsis thaliana*, but the activity differed significantly among their molecular species. *Mol. Plant Microbe Interact.* 19, 512–520
24 Davies, D.R. *et al.* (2006) Production of reactive oxygen species in *Arabidopsis thaliana* cell suspension cultures in response to an elicitor from *Fusarium oxysporum*: implications for basal resistance. *J. Exp. Bot.* 57, 1817–1827
25 Bindschedler, L.V. *et al.* (2006) Peroxidase-dependent apoplastic oxidative burst in *Arabidopsis* required for pathogen resistance. *Plant J.* 47, 851–863
26 Blee, K.A. *et al.* (2001) Molecular identification and expression of the peroxidase responsible for the oxidative burst in French bean (*Phaseolus vulgaris* L.) and related members of the gene family. *Plant Mol. Biol.* 47, 607–620
27 Bolwell, G.P. *et al.* (2002) The apoplastic oxidative burst in response to biotic stress in plants: a three-component system. *J. Exp. Bot.* 53, 1367–1376

28 Torres, M.A. *et al.* (2005) Pathogen-induced, NADPH oxidase-derived reactive oxygen intermediates suppress spread of cell death in *Arabidopsis thaliana*. *Nat. Genet.* 37, 1130–1134
29 Torres, M.A. *et al.* (2006) Reactive oxygen species signaling in response to pathogens. *Plant Physiol.* 141, 373–378
30 Glazebrook, J. (2005) Contrasting mechanisms of defense against biotrophic and necrotrophic pathogens. *Annu. Rev. Phytopathol.* 43, 205–227
31 Lorenzo, O. *et al.* (2003) ETHYLENE RESPONSE FACTOR1 integrates signals from ethylene and jasmonate pathways in plant defense. *Plant Cell* 15, 165–178
32 Spoel, S.H. *et al.* (2003) NPR1 modulates cross-talk between salicylate- and jasmonate-dependent defense pathways through a novel function in the cytosol. *Plant Cell* 15, 760–770
33 Anderson, J.P. *et al.* (2004) Antagonistic interaction between abscisic acid and jasmonate-ethylene signaling pathways modulates defense gene expression and disease resistance in *Arabidopsis*. *Plant Cell* 16, 3460–3479
34 Takahashi, H. *et al.* (2004) Antagonistic interactions between the SA and JA signaling pathways in *Arabidopsis* modulate expression of defense genes and gene-for-gene resistance to cucumber mosaic virus. *Plant Cell Physiol.* 45, 803–809
35 Kariola, T. *et al.* (2005) Chlorophyllase 1, a damage control enzyme, affects the balance between defense pathways in plants. *Plant Cell* 17, 282–294
36 McGrath, K.C. *et al.* (2005) Repressor- and activator-type ethylene response factors functioning in jasmonate signaling and disease resistance identified via a genome-wide screen of *Arabidopsis* transcription factor gene expression. *Plant Physiol.* 139, 949–959
37 Kariola, T.B. *et al.* (2006) Early response to dehydration 15. A negative regulator of ABA-responses in *Arabidopsis*. *Plant Physiol.* DOI: 10.1104/pp.106.086223
38 Mauchmani, B. *et al.* (1994) Systemic acquired resistance in *Arabidopsis thaliana* induced by a predisposing infection with a pathogenic isolate of *Fusarium oxysporum*. *Mol. Plant Microbe Interact.* 7, 378–383
39 Edgar, C.I. *et al.* (2006) Salicylic acid mediates resistance to the vascular wilt pathogen *Fusarium oxysporum* in the model host *Arabidopsis thaliana*. *Australas. Plant Pathol.* 35, 581–591
40 Berrocal-Lobo, M. and Molina, A. (2004) Ethylene response factor 1 mediates *Arabidopsis* resistance to the soilborne fungus *Fusarium oxysporum*. *Mol. Plant Microbe Interact.* 17, 763–770
41 Adie, B.A.T. and Perez-Perez, J. (2007) ABA is an essential signal for plant resistance to pathogens affecting JA biosynthesis and the activation of defenses in *Arabidopsis*. *Plant Cell* 19, 1665–1681
42 Berrocal-Lobo, M. *et al.* (2002) Constitutive expression of *ETHYLENE-RESPONSE-FACTOR1* in *Arabidopsis* confers resistance to several necrotrophic fungi. *Plant J.* 29, 23–32
43 Lin, W.C. *et al.* (2004) Transgenic tomato plants expressing the *Arabidopsis NPR1* gene display enhanced resistance to a spectrum of fungal and bacterial diseases. *Transgenic Res.* 13, 567–581
44 Makandar, R. *et al.* (2006) Genetically engineered resistance to *Fusarium* head blight in wheat by expression of *Arabidopsis NPR1*. *Mol. Plant Microbe Interact.* 19, 123–129
45 Parisy, V. *et al.* (2007) Identification of *PAD2* as a γ-glutamylcysteine synthetase highlights the importance of glutathione in disease resistance of *Arabidopsis*. *Plant J.* 49, 159–172
46 Hemelrijck, W.V. *et al.* (2006) The *Arabidopsis* defense response mutant esa1 as a model to discover novel resistance traits against *Fusarium* diseases. *Plant Sci.* 171, 585–595
47 Mauch-Mani, B. and Mauch, F. (2005) The role of abscisic acid in plant-pathogen interactions. *Curr. Opin. Plant Biol.* 8, 409–414
48 Melotto, M. *et al.* (2006) Plant stomata function in innate immunity against bacterial invasion. *Cell* 126, 969–980
49 de Torres-Zabala, M. *et al.* () *Pseudomonas syringae pv. tomato hijacks the Arabidopsis abscisic acid signalling pathway to cause disease.* 26200714341443
50 Hernandez-Blanco, C. *et al.* (2007) Impairment of cellulose synthases required for *Arabidopsis* secondary cell wall formation enhances disease resistance. *Plant Cell* 19, 890–903
51 AbuQamar, S. *et al.* (2006) Expression profiling and mutant analysis reveals complex regulatory networks involved in *Arabidopsis* response to *Botrytis* infection. *Plant J.* 48, 28–44
52 Perfus-Barbeoch, L. *et al.* (2004) Plant heterotrimeric G protein function: insights from *Arabidopsis* and rice mutants. *Curr. Opin. Plant Biol.* 7, 719–731
53 Beffa, R. *et al.* (1995) Cholera-toxin elevates pathogen resistance and induces pathogenesis-related gene-expression in tobacco. *EMBO J.* 14, 5753–5761
54 Joo, J.H. *et al.* (2005) Different signaling and cell death roles of heterotrimeric G protein α and β subunits in the *Arabidopsis* oxidative stress response to ozone. *Plant Cell* 17, 957–970
55 Komatsu, S. *et al.* (2004) Alterations by a defect in a rice G protein α subunit in probenazole and pathogen-induced responses. *Plant Cell Environ.* 27, 947–957
56 Suharsono, U. *et al.* (2002) The heterotrimeric G protein alpha subunit acts upstream of the small GTPase Rac in disease resistance of rice. *Proc. Natl. Acad. Sci. U. S. A.* 99, 13307–13312
57 Trusov, Y. *et al.* (2006) Heterotrimeric G proteins facilitate *Arabidopsis* resistance to necrotrophic pathogens and are involved in jasmonate signaling. *Plant Physiol.* 140, 210–220
58 Trusov, Y. *et al.* (2007) Heterotrimeric G protein γ subunits provide functional selectivity in G βγ dimer signaling in *Arabidopsis*. *Plant Cell* 19, 1235–1250
59 Suharsono, U. *et al.* (2002) The heterotrimeric G protein α subunit acts upstream of the small GTPase Rac in disease resistance of rice. *Proc. Natl. Acad. Sci. U. S. A.* 99, 13307–13312
60 Pierik, R. *et al.* (2006) The Janus face of ethylene: growth inhibition and stimulation. *Trends Plant Sci.* 11, 176–183
61 Olsen, A.N. *et al.* (2005) NAC transcription factors: structurally distinct, functionally diverse. *Trends Plant Sci.* 10, 79–87
62 Delessert, C. *et al.* (2005) The transcription factor ATAF2 represses the expression of pathogenesis-related genes in *Arabidopsis*. *Plant J.* 43, 745–757
63 Nakano, T. *et al.* (2006) Genome-wide analysis of the *ERF* gene family in *Arabidopsis* and rice. *Plant Physiol.* 140, 411–432
64 Nakano, T. *et al.* (2006) Identification of genes of the plant-specific transcription-factor families cooperatively regulated by ethylene and jasmonate in *Arabidopsis thaliana*. *J. Plant Res.* 119, 407–413
65 Onate-Sanchez, L. *et al.* (2007) AtERF14, a member of the ERF family of transcription factors, plays a nonredundant role in plant defense. *Plant Physiol.* 143, 400–409
66 Yang, Z. *et al.* (2005) *Arabidopsis* ERF4 is a transcriptional repressor capable of modulating ethylene and abscisic acid responses. *Plant Mol. Biol.* 58, 585–596
67 Epple, P. *et al.* (1997) Overexpression of an endogenous thionin enhances resistance of *Arabidopsis* against *Fusarium oxysporum*. *Plant Cell* 9, 509–520
68 Chan, Y.L.P. *et al.* (2005) Transgenic tomato plants expressing an *Arabidopsis* thionin (*Thi2.1*) driven by fruit-inactive promoter battle against phytopathogenic attack. *Planta* 221, 386–393
69 Takemoto, D. *et al.* (2006) A p67Phox-like regulator is recruited to control hyphal branching in a fungal-grass mutualistic symbiosis. *Plant Cell* 18, 2807–2821
70 Schwachtje, J. *et al.* (2006) SNF1-related kinases allow plants to tolerate herbivory by allocating carbon to roots. *Proc. Natl. Acad. Sci. U. S. A.* 103, 12935–12940
71 Day, R.B. *et al.* (2004) Two rice *GRAS* family genes responsive to *N*-acetylchitooligosaccharide elicitor are induced by phytoactive gibberellins: evidence for cross-talk between elicitor and gibberellin signaling in rice cells. *Plant Mol. Biol.* 54, 261–272
72 Izaguirre, M.M. *et al.* (2006) Remote sensing of future competitors: impacts on plant defenses. *Proc. Natl. Acad. Sci. U. S. A.* 103, 7170–7174
73 Anderson, J.P. *et al.* (2005) Plant defence responses: conservation between models and crops. *Funct. Plant Biol.* 32, 21–34
74 Ramonell, K. *et al.* (2005) Loss-of-function mutations in chitin responsive genes show increased susceptibility to the powdery mildew pathogen *Erysiphe cichoracearum*. *Plant Physiol.* 138, 1027–1036
75 Lorenzo, O. *et al.* (2004) *JASMONATE-INSENSITIVE1* encodes a MYC transcription factor essential to discriminate between different jasmonate-regulated defense responses in *Arabidopsis*. *Plant Cell* 16, 1938–1950
76 Megraw, M. *et al.* (2006) MicroRNA promoter element discovery in *Arabidopsis*. *RNA* 12, 1612–1619