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The multifaceted role of ABA in disease resistance

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Long known only for its role in abiotic stress tolerance, recent evidence shows that abscisic acid (ABA) also has a prominent role in biotic stress. Although it acts as a negative regulator of disease resistance, ABA can also promote plant defense and is involved in a complicated network of synergistic and antagonistic interactions. Its role in disease resistance depends on the type of pathogen, its specific way of entering the host and, hence, the timing of the defense response and the type of affected plant tissue. Here, we discuss the controversial evidence pointing to either a repression or a promotion of resistance by ABA. Furthermore, we propose a model in which both possibilities are integrated.

How do plants resist pathogens?

Plant defense against pathogens consists of different layers, which are either constitutively present or activated in a time-dependent manner after pathogen attack. The sequential activation of this multi-layered resistance is initiated when the plant recognizes the presence of a microbe [1]. This recognition determines the nature of the inducible defense response and varies according to the invasive strategy of the pathogen. For instance, a virus that is delivered directly into the plant by a vectoring insect will not be affected by pre-invasive mechanical barriers, such as cell walls or closed stomata. By contrast, fungal, oomycete or bacterial pathogens need to overcome these physical barriers and suppress early chemical defense barriers to infect the host successfully. Hence, the strategy by which a pathogen colonizes the plant tissue determines the stage at which the invader is recognized and defense responses are activated.

The response of the plant to pathogen attack is the result of a series of highly coordinated sequential changes at the cellular level, which are partly mediated by hormonal signals. Salicylic acid (SA) was identified early on as a central regulator of defense against (hemi)biotrophic (see Glossary) pathogens, whereas jasmonic acid (JA) and ethylene (ET) emerged as important signals in defense against necrotrophic pathogens [1]. However, the nature of the specific defense response of the plant is not determined solely by the biotrophic or necrotrophic life style of the pathogen; it also depends on additional factors, such as the timing of recognition, the activity of pathogen effectors and the type of plant tissue in which the defense is expressed. These different factors together shape the nature of the specific defense response of the plant [2]. In this context, the plant hormone abscisic acid (ABA, Box 1) has emerged as an important regulator of biotic defense responses, although its role is less straightforward than that of other defense regulatory plant hormones. ABA promotes resistance in some plant–pathogen interactions, whereas it increases susceptibility in others (reviewed in Ref. [3]). There is also evidence that it influences resistance against herbivorous insects. For example, ABA-deficient tomato (*Solanum lycopersicum*) and *Arabidopsis thaliana* mutants have been reported to be more susceptible to infestation by insects [4,5]. Indeed, transcription profiling experiments with herbivore-infested *Arabidopsis* plants revealed a modulating influence of ABA on herbivore-induced gene expression [5]. Here, we evaluate and hypothesize how different components in the ABA biosynthesis and response pathway can exert a positive or negative influence on the different layers of defense against bacterial, fungal and oomycete pathogens. We propose a model with different roles for ABA that depend on the layer

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Glossary

BABA (β-aminobutyric acid): a non-protein amino acid that primes plants for enhanced stress resistance.
Biotrophic: a mode of living of an organism that depends on a living host to survive or reproduce.
Callose: polymer of β-1,3-linked glucose residues found in phloem sieve plates, wounded tissue, pollen tubes, papillae and other cell wall reinforcements against pathogens.
Coronatine: a phytotoxin produced by several pathovars of *Pseudomonas syringae*.
Fusicoccin: a fungal toxin that leads to irreversible stomatal opening in plants.
Hemibiotrophic: an initially biotrophic mode of living of an organism that becomes necrotrophic as the interaction with its host progresses.
Hypersensitive response: apoptotic death-like reaction of one or several plant cells that prevents further growth of mainly biotrophic or hemibiotrophic pathogens.
NAC transcription factors: a large family of transcription factors that have diverse biological functions and that are present in many land plants. NAC stands for NAM (no apical meristem)–ATAF1,2 (*Arabidopsis* NAC domain containing protein 1,2)–CUC2 (cup-shaped cotyledons 2).
Necrotrophic: a mode of living of an organism that obtains its nutrients from host cells it had previously killed.
PAMP (pathogen-associated molecular pattern): a small molecular motive, such as flagellin from bacteria or chitin from fungi, that is recognized by the plant and that triggers non-self or non-cultivar specific defense.
Papilla: callose-rich cell wall apposition at the attempted point of entry of a fungus or an oomycete into a plant cell.
Pathogen effectors: pathogen molecules that manipulate host cell structure and function, thereby facilitating infection and/or triggering hypersensitive defense responses.

Box 1. Where is ABA made and what does it do?

The name 'abscisic acid' stems from the original belief that this substance was involved in leaf abscission [57]. It is a terpenoid plant hormone derived by cleavage of C_{40} carotenoids originating from the plastidal 2-C-methyl-d-erythritol-4-phosphate pathway. The first ABA precursor is zeaxanthin (see Figure 3 in the main text), which is converted into xanthoxin by a series of enzyme-mediated epoxidation and isomerization steps and a final dioxygenation reaction that cleaves the compound from the C_{40} carotenoid. Xanthoxin is transported into the cytoplasm, where it is further oxidized to ABA (Figure I) [51].

The cellular levels of ABA are modulated by the precise balance between biosynthesis and catabolism. ABA in the form of its inactive glucose ester conjugate is highly mobile throughout the plant and is released into its active form when it has reached the target tissue. Localization studies of ABA biosynthetic enzymes indicate that the vascular bundles are the active sites of ABA synthesis in turgid, non-stressed plants [58,59]. Therefore, all vascular plant tissues have the capacity to synthesize ABA. At the subcellular level, ABA biosynthesis is predominantly confined to the plastids. The ABA response pathway entails a complex signaling network that interacts with a variety of other signal transduction pathways [60]. Much knowledge about the ABA pathway originates from genetic screens for mutants in ABA-induced seed dormancy. However, this genetic approach has never resulted in the identification of the long-sought ABA receptor. Recently, two putative ABA receptors have been identified on the basis of biochemical binding assays. One of these, a G-protein-coupled receptor, is located in the plasma membrane [61], although subsequent genetic characterization failed to confirm its role in the ABA response [62]. Another putative ABA receptor was identified as a chloroplast-located magnesium-chelatase that is involved in chlorophyll synthesis [63]. It is currently unknown how these ABA-binding proteins fit into the complex signaling network of the ABA response [64].

ABA controls numerous physiological processes in plants and is best known for its regulatory role in abiotic stress tolerance. Under conditions of drought and high salinity, it promotes tolerance of the plants to desiccation [65], enabling them to survive under adverse conditions or to colonize areas with scarse water availability. ABA also regulates developmental processes, such as seed germination, vegetative growth and bud dormancy [51]. It therefore enables plants to adapt optimally to their environment by inhibiting germination under sub-optimal conditions, partaking in developmental processes and protecting the plant against biotic and abiotic stress during its vegetative growth phase.

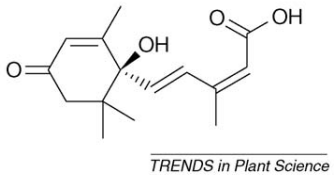

Figure I. Chemical structure of abscisic acid.

of defense involved. The model reconciles the hitherto controversial results regarding the role of this hormone in plant defense.

ABA signaling in pre-invasive penetration resistance

Pathogens need to penetrate plant tissue to infect a host plant successfully. Some fungi overcome the first cell layer by applying mechanical force onto the epidermal cell wall or by secreting cuticle- and cell-wall-degrading enzymes [6,7]. Other pathogens instead use pre-existing openings, such as stomata or wounds (Figure 1, Phase I). Plants can increase their pre-invasive penetration resistance by closing stomata rapidly upon perception of microbes, which

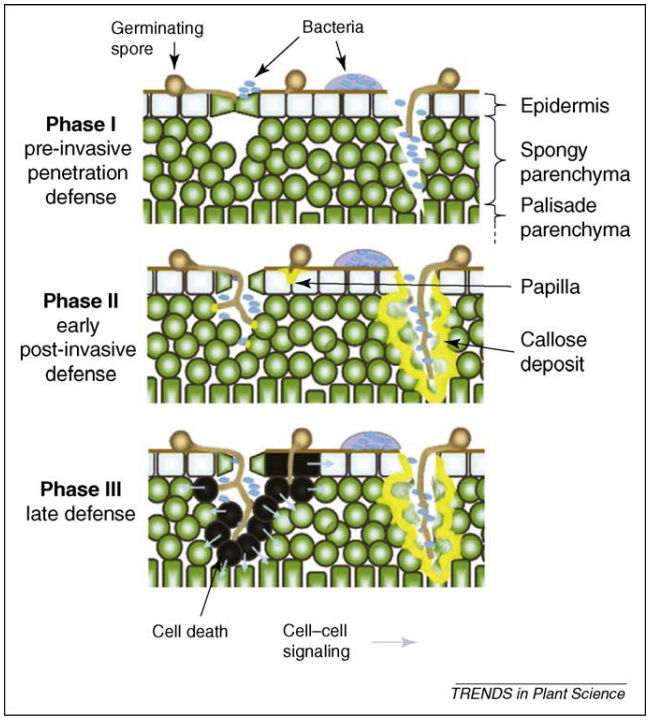

Figure 1. Phases of plant defense. At first contact with their host, pathogens face the first pre-invasive defense barrier of the plant (Phase I). Some fungal and oomycete pathogens can penetrate the cell wall directly, whereas others enter the tissue through natural openings, such as stomata or wounds [6,7]. Bacteria depend largely on these openings, because most are unable to penetrate directly through the cuticle and cell wall. Plants can enhance their pre-invasive defense barrier by rapid stomatal closure upon recognition of the pathogen [8]. After successful penetration, pathogens face the second barrier of early post-invasive defense (Phase II). This includes early cellular responses at the infection sites, such as formation of papillae and rapid accumulation of ROS (not shown) [20]. Early post-invasive penetration defense is followed by transcriptomic and metabolomic reprogramming, which can result from a hypersensitive response. This late defense barrier (Phase III) is associated with the production of intra- and intercellular signals, including defense hormones and vascular long-distance signals, which regulate a broad spectrum of defensive compounds to halt further invasion by the pathogen [1].

occurs within 1 h after inoculation with pathogenic and non-pathogenic bacteria [8]. This defense response can be mimicked by application of pathogen-associated molecular patterns (PAMPs), such as the flagellin derivative flg22 and lipopolysacharides. ABA-deficient *aba3-1* plants fail to express rapid stomatal closure, indicating that ABA has an important role in this defense response. The ABA-dependent control of PAMP-induced stomatal closure requires nitric oxide (NO), the protein kinase OPEN STOMATA (OST) and a functional SA signaling pathway [8].

Some virulent pathogens can counteract stomatal closure. For example, *Pseudomonas syringae* pv. *tomato* DC3000 can re-open stomata by using the effector molecule coronatine [8], whereas other effectors are responsible for stomatal re-opening in other plant–pathogen combinations [9]. For instance, the bacterial citrus pathogen *Xanthomonas axonopodis* pv. *citri* mimics a plant natriuretic peptide to antagonize ABA-dependent stomatal closure [10]. These peptides are produced in response to biotic and abiotic stress, during which they regulate cell water homeostasis and stomatal aperture through cyclic GMP-dependent signaling [11]. Fungal virulence factors, such as fusicoccin and oxalate, can also antagonize stomatal closure [12,13].

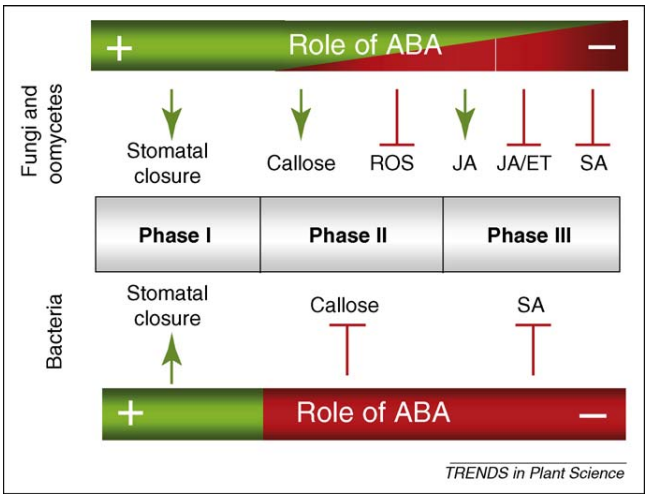

Figure 2. Contribution of ABA to disease resistance or susceptibility. ABA has a multifaceted role throughout different phases of plant defense, and its role varies according to the timing and invasive strategy of the challenging pathogen (Figure 1, main text). During Phase I, ABA stimulates resistance against fungi and oomycetes by mediating stomatal closure [8,9,12,13]. Throughout Phase II, it promotes callose deposition in response to infection by fungi and oomycetes. However, in certain cases, ABA production can suppress early ROS production and cause increased susceptibility, as observed during the interaction between tomato and *Botrytis cinerea* [20]. By contrast, components in the ABA response pathway can suppress bacteria-induced callose deposition and, therefore, contribute negatively to resistance [14,16]. During Phase III, ABA interacts with SA-, JA- and ET-dependent defense pathways. It inhibits SA-dependent resistance [38,39] and modulates JA-dependent resistance by suppressing JA responses that are synergistically regulated by ET [40] but can promote a branch of the JA response that acts antagonistically with ET [43].

Hence, ABA-dependent stomatal closure is likely to function as a pre-invasive defense barrier against which some virulent pathogens have evolved counteractive mechanisms.

ABA signaling in post-invasive penetration resistance

After successful penetration, microbes face a second layer of defense (Figure 1, Phase II), which is characterized by rapid deposition of callose-rich cell wall enforcements and generation of reactive oxygen species (ROS). During expression of this early post-invasive penetration resistance, the role of ABA is controversial and seems to vary among different plant–pathogen interactions (Figure 2).

Early post-invasive penetration resistance against bacteria

Although ABA exerts a positive role in pre-invasive defense against bacteria, its role in post-invasive defense against bacteria seems to be mostly negative. Experiments with *Arabidopsis* mutants in the ABA signaling gene *ABI2* (*ABSCISIC ACID INSENSITIVE 2*) provided evidence that ABA can repress bacterial induction of callose [14]. Both *ABI1* and *ABI2* encode structurally related homologues of protein phosphatase 2C (PP2C) that act as negative regulators in the ABA response [15]. Consequently, loss-of-function mutations in *ABI1* and *ABI2* induce hyper-responsiveness to ABA, whereas dominant gain-of-function mutations, such as *abi1-1* and *abi2-2*, cause ABA insensitivity [14–16]. ABA hyper-responsive *abi2* mutants deposit less callose upon infection with *P. syringae*, whereas ABA-insensitive *abi2-1* mutants deposit augmented levels of callose [14]. In agreement with this, ABA was recently found to suppress callose deposition in *Arabidopsis* cotyledons upon treatment with the bacterial PAMP flagellin. Hence, ABA can suppress bacteria-induced callose in *Arabidopsis* (Figure 2) [16].

An additional role for ABA in defense against bacteria comes from the finding that the early ABA-responsive gene

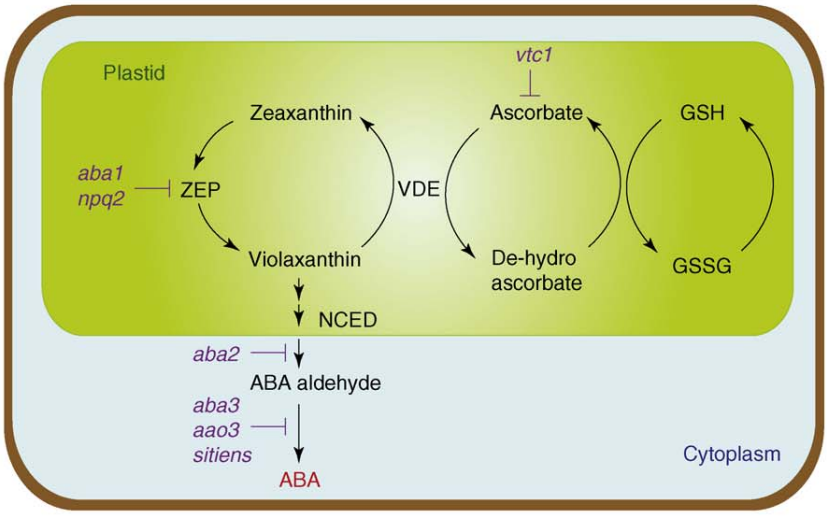

Figure 3. The ABA biosynthetic pathway and its interaction with the ascorbate–glutathione cycle. The biosynthesis of ABA involves multiple redox-dependent reactions that occur in the plastid and the cytoplasm [51]. The enzyme zeaxanthin epoxidase (ZEP) converts zeaxanthin into violaxanthin through an epoxidation reaction that occurs under low light and relatively alkaline conditions. The *Arabidopsis* mutants *aba1* (*abscisic acid deficient 1*) and *npq2* (*non-photochemical quenching 2*) are both affected in this step. The conversion of violaxanthin into zeaxanthin is catalyzed by violaxanthin de-epoxidase (VDE) and requires oxidation of ascorbate into de-hydro ascorbate. As a result, reduced levels of ascorbate in the *vtc1* (*vitamin C1*) mutant stimulate ABA biosynthesis [21]. By contrast, enhanced VDE activity antagonizes ABA production, reduces ascorbate levels and promotes conversion of reduced glutathione (GSH) into oxydized glutathione (GSSG). This leads to a reduction of the redox-buffering capacity in the cell and enables augmented ROS accumulation. Violaxanthin is converted into xanthoxin through a series of isomerization reactions and a dioxygenation step by 9-*cis*-epoxycarotenoid di-oxygenase (NCED) [21], which cleaves xanthoxin from the C_{40} carotenoid. The final steps in ABA biosynthesis, the conversion of xanthoxin into ABA, occur in the cytoplasm and involve a dehydrogenase (xanthoxin:NAD^+ oxidoreductase) (mutated in *aba2*) and the ABA aldehyde oxidase (affected in the *Arabidopsis* mutants *aba3, aao3* [*Arabidopsis aldehyde oxidase 3*] and the *sitiens* mutant of tomato [52–54]).

ERD15 (*EARLY RESPONSIVE TO DEHYDRATION 15*) stimulates resistance against the bacterium *Erwinia carotovora* but suppresses ABA-dependent tolerance to osmotic stress [17]. Although the exact nature of ERD15-dependent resistance is unknown, it seems evident that ERD15 has a role in crosstalk between biotic and abiotic stress resistance.

Early post-invasive penetration resistance against oomycetes and fungi

Although it has been known for two decades that ABA has a negative role in disease resistance against oomycetes [18], first indications for a regulatory role of ABA in fungal disease resistance came from the discovery that the ABA-deficient tomato mutant *sitiens* is resistant to the necrotrophic fungus *Botrytis cinerea* [19]. Recently, it was demonstrated that this resistance is based on increased accumulation of ROS during the early stages of tissue penetration [20]. Pre-treatment with the callose synthesis blocker 2-deoxy-D-glucose has no influence on the *sitiens*-induced resistance but reduces the basal resistance of wild-type plants. Hence, increased ROS production in *sitiens* precedes callose-mediated defense against *B. cinerea*. Based on the finding that application of the antioxidant ascorbate can restore susceptibility to *B. cinerea* [20], it is tempting to speculate that *sitiens*-induced resistance is caused by an interaction between the xanthophyll cycle and the ROS-buffering ascorbate–gluthatione cycle (Figure 3). In support of this, a mechanistic link between ABA biosynthesis and ascorbate has been demonstrated [21], which showed that low ascorbate in the *Arabidopsis vtc1* (*vitamin C1*) mutant stimulates ABA production. The *sitiens* mutation in tomato blocks the last step in ABA biosynthesis. If this mutation results in enhanced accumulation of ABA precursors, it would disturb the balance of the xanthophyll cycle and cause enhanced activity of violaxanthin de-epoxidase (VDE; Figure 3). VDE converts violaxanthin into zeaxanthin and, by doing so, oxydizes ascorbate into de-hydro ascorbate (Figure 3). The resulting decrease in ascorbate could account for the augmented capacity of *sitiens* plants to produce ROS.

In contrast to the results described above (Figure 4), it has recently been demonstrated that the ABA-inducible MYB transcription factor AIM1 (ABSCISIC ACID-INDUCED MYB1) controls ABA sensitivity, abiotic stress tolerance and basal resistance against *B. cinerea* in tomato [22]. AIM1 RNA interference (RNAi) plants display increased accumulation of root Na^+ ions, suggesting a positive role of ABA-regulated ion fluxes in early defense against *B. cinerea* [22]. Hence, ABA exerts a multifaceted influence on resistance of tomato against *B. cinerea*. It seems likely that its impact depends on the interaction with other, yet unknown, defense signals.

In *Arabidopsis*, ABA has a positive role in papillae-mediated defense against *Leptosphaeria maculans* [23]. When exposed to this necrotroph, both the ABA biosynthetic mutant *aba1-3* and the ABA-response mutant *abi1-1* display enhanced disease susceptibility that coincides with reduced callose deposition. Interestingly, not all components in the ABA response contribute to post-invasive penetration resistance against *L. maculans*. For instance, the *abi2-1* mutation, unlike the *abi1-1* mutation, fails to confer enhanced susceptibility to *L. maculans*, indicating that ABI1 and ABI2 act differentially on callose-mediated defense against *L. maculans*. Because *abi2-1* plants have been reported to deposit more callose than do wild-type plants upon infection with *P. syringae* [14], it is possible that the two PP2C proteins act antagonistically on pathogen-induced callose production, thereby providing extra regulatory potential to this defense response (Figure 4).

Another link between ABA and post-invasive penetration defense in *Arabidopsis* has recently been found [24]. Mutations in the ABA-inducible NAC transcription factor ATAF1 (*Arabidopsis* NAC domain containing protein 1) were reported to reduce penetration resistance against the non-host fungus *Blumeria graminis* f.sp. *hordei* (*Bgh)* and concomitantly compromise ABA-induced seed dormancy and root growth inhibition. Transcriptomic analysis of *Bgh*-infected *ataf1* plants revealed hyperinduction of ABA-inducible genes that are associated with abiotic stress tolerance. Hence, ATAF1 promotes ABA-dependent biotic stress resistance but suppresses ABA-dependent abiotic stress resistance. A similar antagonistic function has been described for ERD15 [13]. This suggests that early-acting ABA-inducible signaling components, such as ATAF1 and ERD15, represent a branching point in the global switch between ABA-dependent penetration resistance and ABA-dependent abiotic defense [3] (Figure 4).

Priming of early post-invasive penetration resistance

The plant innate immune system harbors a regulatory system that can adjust the inducible defense arsenal to the prevailing environmental conditions. Upon perception of specific environmental cues, plants develop an enhanced defensive capacity that is effective against a broad spectrum of pathogens. This induced resistance is often based on a priming of the inducible defense arsenal, which results in a faster and stronger defense activation at the moment that the plant is attacked [25]. Much knowledge about the molecular regulation of priming comes from research on chemically induced priming responses in *Arabidopsis*. The chemical priming agent β-aminobutyric acid (BABA) has been demonstrated to boost different defense mechanisms, including post-invasive penetration mechanisms, such as the deposition of callose-rich papillae [26,27].

The signaling pathway underlying BABA-induced priming of callose requires intact ABA signaling. The *Arabidopsis ZEP* (*ZEAXANTHIN EPOXIDASE*) mutant *aba1-5*, for instance, fails to deposit augmented levels of papillae upon BABA treatment after infection by nectrotrophic fungi [23]. A genetic screen for mutants impaired in BABA-induced sterility (*ibs*) has identified a mutation that affects the transcriptional regulation of *ZEP*. This *ibs3* mutant is concomitantly affected in BABA-induced priming of callose [28]. It might be that the inability of *ZEP* mutants to express an augmented callose response is related to the antioxidant properties of zeaxanthin and the above-mentioned interaction between the xanthophyll cycle and ascorbate. Mutations in *ZEP* block violaxanthin production and can be expected to oxydize less ascorbate through the xanthophyll pathway (Figure 2). The resulting

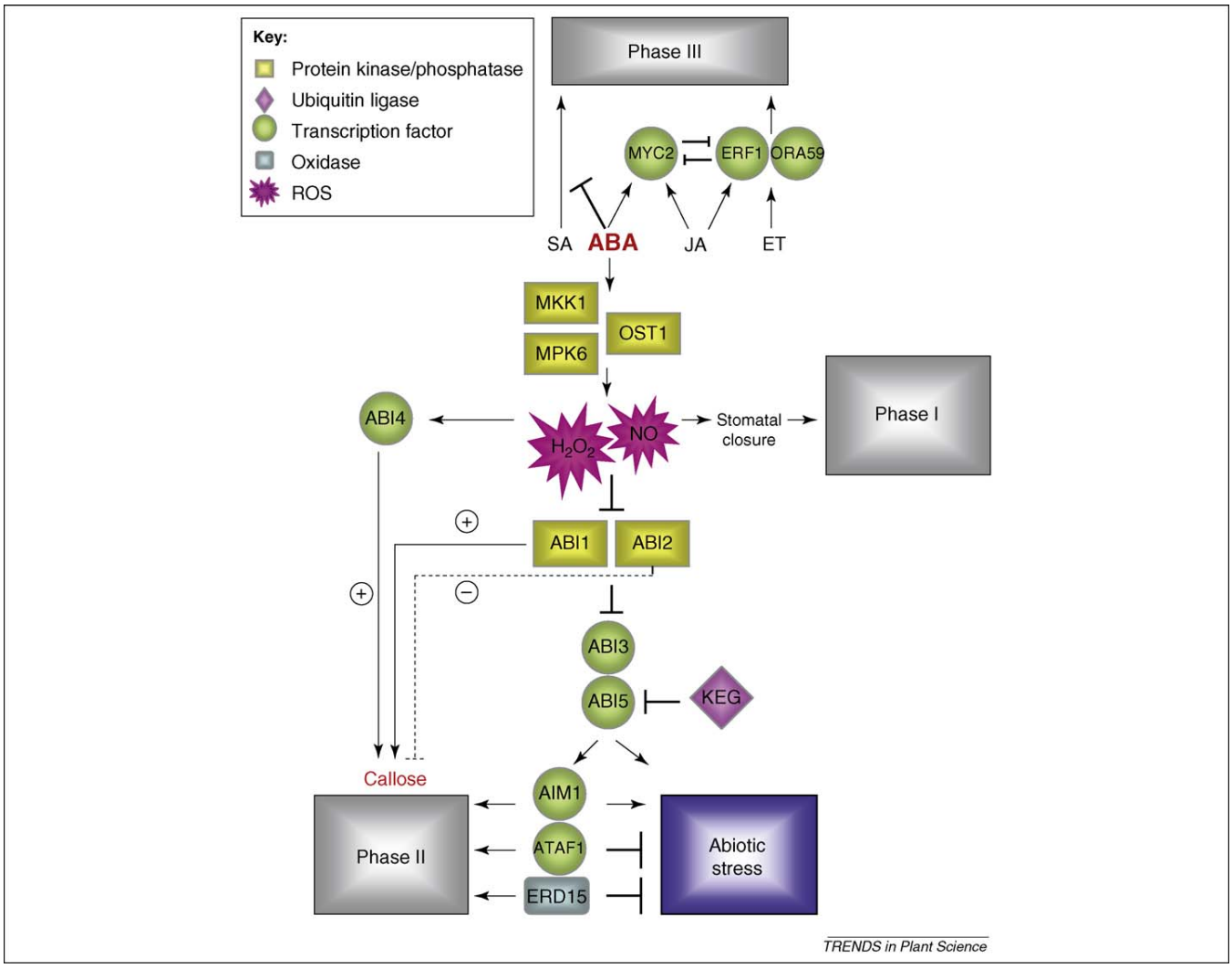

Figure 4. Effects of the ABA signaling web on early and late defense barriers. ABA boosts pre-invasive penetration resistance (Phase I) by stimulating PAMP-induced stomatal closure [6]. A pathway that involves the mitogen-activated protein kinase kinase 1 (MKK1)–mitogen-activated protein kinase 6 (MPK6) signaling cascade [55] and the protein kinase OST1 (OPEN STOMATA 1) [56] regulates ABA-induced ROS production, which consecutively regulates stomatal closure and other downstream signaling events. After tissue penetration by pathogens, ABA can either promote or suppress early post-invasive defenses (Phase II). The ABI4 (ABSCISIC ACID INSENSITIVE 4) transcription factor [23], which integrates light-dependent ROS, sucrose and ABA signaling, acts as a positive regulator of ABA-dependent callose deposition against fungal pathogens [25]. Two closely related protein phosphatase 2C homologues, ABI1 and ABI2, function as negative regulators of the ABA pathway [11]. The activity of ABI1 and ABI2 is repressed by ABA-induced ROS [15], thereby stimulating the downstream pathway. Interestingly, ABI1 and ABI2 seem to regulate callose deposition antagonistically through as yet unknown mechanisms [14,23]. Downstream of ABI1 and ABI2, the ABA response is channeled through a variety of transcription factors and other signaling components. Levels of the ABI5 transcription factor are controlled by the RING-type E3 ligase KEG (KEEP ON GOING) [36], which represses abiotic stress responses [36] and early post-invasive defense in *Arabidopsis* [35]. Furthermore, the early-acting transcription factor AIM1 (ABSCISIC ACID-INDUCED MYB1) has recently been shown to control positively abiotic stress tolerance and early post-invasive defense in tomato [22]. Other early-acting signaling components, such as the transcription factors ATAF1 (*Arabidopsis* NAC domain containing protein 1) [24] and the proline oxidase ERD15 (EARLY RESPONSIVE TO DEHYDRATION 15) [17] stimulate post-invasive defense but suppress ABA-dependent abiotic stress tolerance, thereby acting as a branching point in the crosstalk between biotic and abiotic stress. The role of ABA in late defense (Phase III) is mostly negative. ABA antagonizes SA-dependent defenses and JA-dependent defenses that are regulated by the ET-dependent transcription factors ERF1 (ETHYLENE RESPONSIVE FACTOR 1) and ORA59 (APETALA2/ETHYLENE RESPONSE FACTOR domain transcription factor 59) [41,42]. However, ABA acts positively on JA-inducible defenses that are controlled by the MYC2 transcription factor [40,43–45].

increase in antioxidative capacity is expected to lower lipid oxidation and, accordingly, reduce membrane recycling and vesicle trafficking. Because early post-invasive resistance depends on vesicle-mediated transport of antimicrobial molecules and secretion of defense proteins [16,29], a limitation in the capacity of cellular vesicle trafficking would hamper augmented deposition of papillae.

Another ABA signaling compound in the pathway controlling BABA-induced priming of callose is the activator protein 2 (AP2) transcription factor ABI4 [28], which also has a role in light- and sugar-inducible stress responses [30]. It binds to the CCAC core motif in promoters of light- and ABA-responsive genes [31] and mutations in this motif affect ABA-, high light- and H_2O_2-dependent gene regulation [32]. Hence, ABI4 integrates ROS and ABA signaling at the transcriptional level. This function of ABI4 might also have a role in primed expression of post-invasive cell wall defense.

Further evidence for a functional link between ABA and priming is based on the *Arabidopsis edr1-1* (*enhanced disease resistance 1-1*) mutant, which shows enhanced resistance to infection by biotrophic pathogens [33]. The

finding that *edr1-1* deposits augmented amounts of callose in response to *Hyaloperonospora arabidopsidis* infection [34], indicates that *edr1-1* is constitutively primed to express early post-invasive defense. Recently, *edr1-1* was shown to be more responsive to ABA [35]. Furthermore, a genetic suppressor screen for mutations that block *edr1*-mediated disease resistance lead to the identification of the *keg-4* (*keep on going-4*) mutant, which concomitantly blocked ABA hyper-responsiveness in *edr1-1* [35]. *KEG* encodes an ubiquitin ligase that functions as a negative regulator in ABA signaling by targeting the ABI5 transcription factor for degradation [36]. Unlike other mutations in KEG, the *keg-4* mutation is thought to enhance ubiquitin ligase activity, causing lower ABI5 levels and decreased ABA sensitivity [35]. This finding not only implicates ABI5 as a positive regulator in early post-invasive resistance but also illustrates that ubiquination-mediated breakdown of ABA signaling components represents an additional regulatory mechanism in ABA-dependent control of disease resistance.

ABA signaling in late disease resistance

The onset of late disease resistance is characterized by events such as the hypersensitive response, an oxidative burst and expression of defense-related genes. These events lead to the generation of local and systemic signal(s), which inform other plant parts that pathogen attack is imminent [37] (Figure 1, Phase III). ABA also exerts different effects at this stage of disease resistance by either suppressing resistance [38,39] or promoting susceptibility [40].

Antagonism of late SA-dependent resistance by ABA

Using two chemicals that stimulate the SA-dependent defense response, it was demonstrated that ABA suppresses SA-dependent disease resistance [38], confirming earlier results showing that application of ABA suppresses SA-inducible defense activation by *P. syringae* DC3000 [39]. Hence, ABA functions as an inhibitor of SA-dependent defenses. Virulent bacteria, such as *P. syringae* DC3000, exploit this signaling crosstalk after successful penetration of the plant tissue [14] and benefit at this stage of infection from the ABA-induced suppression of SA-dependent defenses.

Interplay between ABA and JA during late penetration resistance

Investigation of the interplay among JA-, ET- and ABA-dependent defense signals in *Arabidopsis* revealed that ABA promotes susceptibility to *Fusarium oxysporum* and suppresses JA- and ET-dependent induction of defense-related genes, such as *PDF1.2* (*PLANT DEFENSIN 1.2*), *CHI* (*CHITINASE*), *PR4* (*PATHOGENESIS RELATED PROTEIN 4*) and *LEC* (*LEAFY COTYLEDON*) [40]. Expression of these genes is regulated by the transcription factors ORA59 (APETALA2/ETHYLENE RESPONSE FACTOR domain transcription factor 59) and ERF1 (ETHYLENE RESPONSIVE FACTOR 1), which integrate JA- and ET-dependent defense signals [41,42]. Conversely, expression of other JA-inducible genes, such as *VSP2* (*VEGETATIVE STORAGE PROTEIN 2*), are regulated by the MYC2 transcription factor that integrates ABA- and JA-dependent signals [40,43–45]. These two branches of the JA response pathway act antagonistically on each other [43]. Interestingly, a recent transcriptome analysis of *Arabidopsis* during infection by *Pythium irregulare* estimated that ABA regulates the expression of approximately one-third of the genes that are induced by this pathogen [46]. Because basal resistance against *P. irregulare* depends on intact JA signaling [47], it is likely that ABA exerts this positive effect via the MYC2-dependent branch of the JA pathway. By contrast, the enhanced susceptibility to *F. oxysporum* can be explained by the fact that this pathogen is resisted through the ORA59, ERF1-dependent branch of the JA response, which is antagonized by ABA [40]. Both examples highlight the delicate role that ABA has in the fine-tuning of JA-dependent defenses.

Conclusions and outlook

The role of ABA in disease resistance remains complex owing to its multifaceted function in different tissues and developmental stages of the plant. Current knowledge about its physiological impact on plant resistance is insufficient to provide solid explanations for the recent burst of sometimes contradictory reports. However, amidst this apparent controversy, we discern a general pattern that suggests a stimulatory role of ABA in plant defense during early stages of pathogen invasion but a mostly suppressive influence at later colonization stages (Figure 2).

Early defense through ABA-dependent stomatal closure and callose deposition is sufficient to halt most potentially harmful microbes. However, strong stimulation by PAMPs can lead to activation of SA- and JA-dependent defense mechanisms [48]. Given that SA- and JA-dependent defenses are predominantly active during the later stages of pathogen infection (Phase III; Figure 1), they will be unnecessary as long as the early defense barrier is sufficient to stop pathogen invasion. This multifaceted function of ABA points to a cost-efficient strategy by which plants regulate their defense: ABA promotes early defense barriers to halt pathogens in the initial stage of colonization and simultaneously prevents unnecessary activation of costly SA- and JA-dependent defenses.

The proposed model does not provide explanations for all observations regarding ABA and plant disease resistance. Perhaps the most controversial function of ABA comes from its role in pathogen-induced callose deposition. A recent study [16] showed that ABA suppresses callose deposition in *Arabidopsis* cotyledons upon treatment with the bacterial PAMP flagellin. Earlier findings demonstrated that *P. syringae*-induced callose deposition is suppressed by ABA [14]. However, multiple studies from different groups have demonstrated that ABA exerts a positive influence on callose deposition after infection by fungi [23,28,49,50]. Moreover, it was recently demonstrated [50] that the fungal PAMP chitosan promotes ABA synthesis and that chitosan-induced callose is inhibited by pre-treatment with an ABA inhibitor. We therefore conclude that bacteria and fungi activate different pathways to trigger callose. Future research efforts need to include different attackers, such as bacteria, fungi and

oomycetes, to further elucidate the exact role of ABA in post-invasive cell wall defense.

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