Review

Activation of Defense Mechanisms against Pathogens in Mosses and Flowering Plants

Inés Ponce de León [1],* and Marcos Montesano [2]

[1] Departamento de Biología Molecular, Instituto de Investigaciones Biológicas Clemente Estable, Avenida Italia 3318, CP 11600, Montevideo, Uruguay

[2] Laboratorio de Fisiología Vegetal, Centro de Investigaciones Nucleares, Facultad de Ciencias, Mataojo 2055, CP 11400, Montevideo, Uruguay; E-Mail: montesano@cin.edu.uy

* Author to whom correspondence should be addressed; E-Mail: iponcetadeo@gmail.com; Tel.: +598-24872605; Fax: +598-24875548.

Abstract: During evolution, plants have developed mechanisms to cope with and adapt to different types of stress, including microbial infection. Once the stress is sensed, signaling pathways are activated, leading to the induced expression of genes with different roles in defense. Mosses (Bryophytes) are non-vascular plants that diverged from flowering plants more than 450 million years ago, allowing comparative studies of the evolution of defense-related genes and defensive metabolites produced after microbial infection. The ancestral position among land plants, the sequenced genome and the feasibility of generating targeted knock-out mutants by homologous recombination has made the moss *Physcomitrella patens* an attractive model to perform functional studies of plant genes involved in stress responses. This paper reviews the current knowledge of inducible defense mechanisms in *P. patens* and compares them to those activated in flowering plants after pathogen assault, including the reinforcement of the cell wall, ROS production, programmed cell death, activation of defense genes and synthesis of secondary metabolites and defense hormones. The knowledge generated in *P. patens* together with comparative studies in flowering plants will help to identify key components in plant defense responses and to design novel strategies to enhance resistance to biotic stress.

Keywords: *Physcomitrella patens*; flowering plants; defense mechanisms; ROS; cell wall; programmed cell death; defense genes; defense hormones

1. Introduction

Plants are in permanent contact with a variety of microbial pathogens, such as fungi, oomycetes, bacteria and viruses. To ward off these pathogens, plants must recognize the invaders and activate fast and effective defense mechanisms that arrest the pathogen. Perception of the pathogens is central to the activation of a successful plant defense response. Plant cells are capable of sensing evolutionarily conserved microbial molecular signatures, collectively named pathogen-associated molecular patterns (PAMPs) or microbe-associated molecular patterns (MAMPs), by plant pattern recognition receptors (PRRs) [1–3]. MAMPs are molecules that are essential for microbe fitness and survival and are conserved between different species, resulting in an efficient form to sense the presence of pathogens by the plant. Perception of PAMPs by PRRs activates an immune response, referred to as PAMP-triggered immunity (PTI), which provides protection against non-host pathogens and limits disease caused by virulent pathogens [4]. Pathogens adapted to their host plants can deliver virulence effector proteins into plant cells, which target key PTI components and inhibit plant defense [5–9]. In turn, plants have evolved resistance (R) proteins to detect directly or indirectly the effector proteins and trigger disease resistance effector-triggered immunity (ETI), which is highly specific and often accompanied by the hypersensitive response (HR) and systemic acquired resistance (SAR). An additional surveillance system for the presence of pathogens is the release or production of endogenous damage associated molecular patterns (DAMPs), including plant cell wall and cutin fragments that are released by the enzymatic action of pathogens and also trigger immune responses [3,10,11]. Thus, plant immunity can be divided in two phases: PTI triggered by PAMPs and ETI triggered by effectors, with the difference being that activated immune responses in ETI are faster and amplified compared to those in PTI [4,12]. ETI and PTI pathways result in activation of an overlapping set of downstream immune responses, suggesting that there is a continuum between PTI and ETI [13]. These downstream defense responses include the activation of multiple signaling pathways and transcription of specific genes that limit pathogen proliferation and/or disease symptom expression. In addition, antimicrobial compounds are produced, reactive oxygen species (ROS) accumulate, cell wall defense mechanisms are activated and defense hormones, such as salicylic acid (SA), ethylene and jasmonic acid (JA) accumulate [4,14–17].

During the last few years, some progress has been made on the defense mechanisms activated in mosses (Bryophytes) during pathogen assault. The moss *Physcomitrella patens* (*P. patens*) is an interesting model plant to perform functional studies of genes involved in stress responses, because its genome has been sequenced, targeted knock-out mutants can be generated by homologous recombination and it has a dominant haploid phase during its life cycle [18–20]. Mosses are non-vascular plants that diverged from flowering plants more than 450 million years ago [21]. *P. patens*, together with the sequenced vascular spikemoss *Selaginella moellendorffii* [22], provide an evolutionary link between green algae and angiosperms, allowing comparative studies of the evolution of plant defense mechanisms and gene function. In nature, mosses are infected with microbial pathogens, resulting in chlorosis and necrosis of plant tissues [23–25]. Necrotrophic pathogens are capable of infecting and colonizing *P. patens* tissues, leading to the activation of defense responses [26–32]. Most likely, *P. patens* utilizes similar mechanisms for pathogen recognition as flowering plants, since chitin (PAMP) [31] and probably cell wall fragments generated by the action of

cell wall degrading enzymes from bacterial pathogens (DAMPs) [26] are sensed by *P. patens* cells and typical PRRs and R genes homologues are present in its genome [33–35]. In addition, many of the cellular and molecular defense reactions activated in *P. patens* are similar to those reported in flowering plants. The present paper reviews the current knowledge of defense responses activated in *P. patens* and compares them to those activated in flowering plants after pathogen assault.

2. Broad Host Range Pathogens Infect both Mosses and Flowering Plants

Broad host range pathogens are capable of infecting a variety of plant species, including flowering plants and mosses. These are successful pathogens, which have adapted and developed effective invasion strategies causing disease by producing different compounds, including enzymes and toxins that interfere with metabolic targets common to many plant species. In this review, we focus on the broad host range fungus *Botrytis cinerea*, the bacterium *Pectobacterium carotovorum* subsp. *carotovorum* and the oomycetes *Pythium irregulare* and *Pythium debaryanum*. These are necrotrophic pathogens that actively kill host tissue prior to or during colonization and thrive on the contents of dead or dying cells [36].

B. cinerea is a necrotrophic fungal pathogen that attacks over 200 different plant species [37] and penetrates plant tissues by producing toxins and multiple cell wall degrading enzymes (CWDEs), including pectinolytic enzymes and cutinases that kill the host cells causing grey mould disease in many crop plants [38]. *B. cinerea* is primarily a pathogen of dicotyledonous plants, but some monocot species, including onions and lilies, are also infected [39,40]. *B. cinerea* also infect *P. patens* plants, producing maceration of the tissues and browning of stems and juvenile protonemal filaments [26,28].

P.c. carotovorum (ex *Erwinia carotovora* subsp. *carotovora*) cause soft rot in a wide range of plant species, including vegetables, potato and Arabidopsis [41]. *P.c. carotovorum* is often described as a brute-force pathogen, because its virulence strategy relies on plant CWDEs, including cellulases, proteases and pectinases, which disrupt host cell integrity and promote tissue maceration [42,43]. Cell-free culture filtrate (CF) containing CWDEs from *P.c. carotovorum* produces similar symptoms (Figure 1) and defense gene expression as those caused by *P.c. carotovorum* infection, demonstrating that CWDEs are the main virulence factors [43–48]. In addition, these CWDEs release cell wall fragments, including oligogalacturonides that act as DAMPS activating an immune response in plant cells evidenced by the activation of defense related genes and phytoalexin accumulation [44,49–51]. Recently, it was shown that two strains of *P.c. carotovorum*, SCC1, harboring the harpin-encoding *hrpN* gene, which is an elicitor of the hypersensitive response (HR) [52], and the HrpN-negative *P.c. carotovorum* strain (SCC3193) [53] infect and cause maceration in leaves of *P. patens* [26]. Green fluorescent protein (GFP) labeled- *P.c. carotovorum*, was detected in the apoplast, as well as the space of *P. patens* invaded leaf cells (Figure 2). Treatments with CFs of these strains also caused symptom development in moss tissues, evidenced by tissue maceration and browning, which was more severe with the HrpN-positive strain, suggesting that harpin may contribute to *P.c. carotovorum* virulence [26].

Figure 1. Disease symptoms evidenced by tissue maceration of plants inoculated with *Pectobacterium carotovorum* subsp. *carotovorum* (*P.c. carotovorum*) or treated with elicitors of this pathogen. (**a**) *Nicotiana tabacum* leaves inoculated with *P.c. carotovorum*$_{SCC3193}$ at 48 h post-inoculation; (**b**) *Solanum tuberosum* leaf treated during 72 h with elicitors of *P.c. carotovorum*$_{SCC3193}$; (**c**) water-treated *P. patens* colony; (**d**) *P. patens* colony treated during 48 h with elicitors of *P.c. carotovorum*$_{SCC1}$; (**e**) *Solanum tuberosum* tubers inoculated with *P.c. carotovorum*$_{SCC3193}$ (upper tuber) or treated with elicitors of this strain (lower tuber) during 24 h.
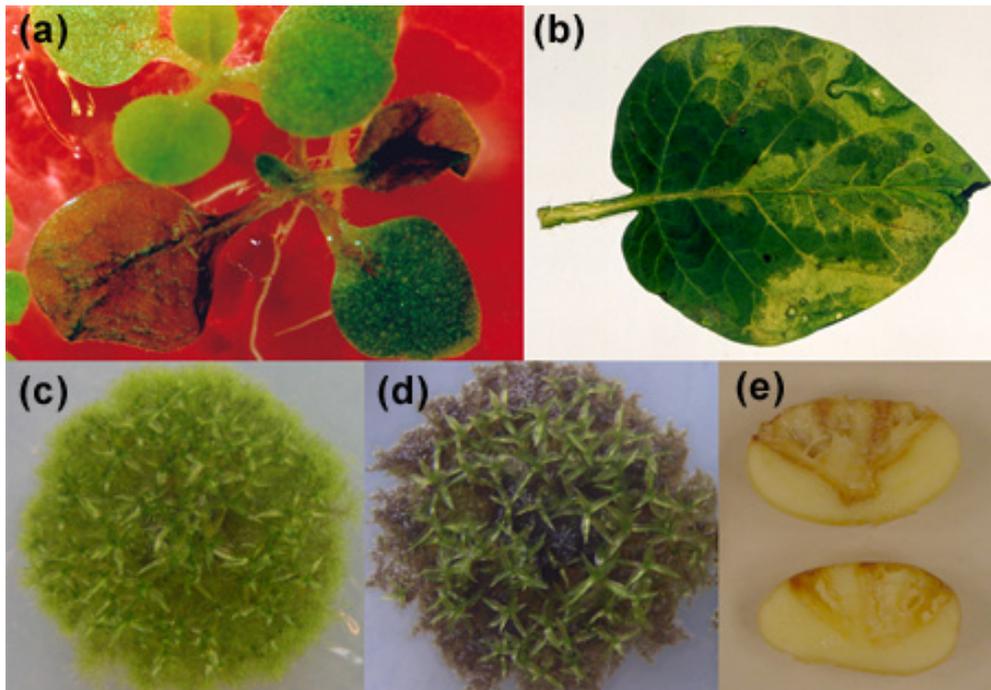
Pythium species are soil-borne vascular pathogens, which infect the plants through the root tissues and under humid conditions cause pre-/post-emergence damping-off and root and stem rots in important crop species. *Pythium* infect host young tissues, and maceration is caused by both toxins and cell wall degrading enzymes, such as pectinases, hemicellulases, cellulases and proteinases [54,55]. *P. irregulare* and *P. debaryanum* infect *P. patens*, producing tissue maceration and browning of young protonemal tissues, stems and leaves [29]. In nature, *Pythium ultimum* infect mosses, causing the formation of areas of dead moss tissues [24]. In all these moss-pathogen interactions, multiple defense reactions are activated in plant cells, although they are not sufficient to stop infection, and after a few days, moss tissues are degraded, leading to plant decay.

Figure 2. Colonization of *P. patens* leaves by *B. cinerea*, *P. debaryanum* and *P.c. carotovorum*. Stained hyphae are visualized with the fluorescent dye solophenyl flavine 7GFE 500 after 24 h of *B. cinerea* inoculation (**a**) and (**b**) 48 h of *P. debaryanum* inoculation. (**c**) Leaves of *P. patens* inoculated with *P.c. carotovorum*$_{SCC3193}$ carrying a GFP-expressing plasmid at 48 h post-inoculation. The scale bar represents 20 μm.
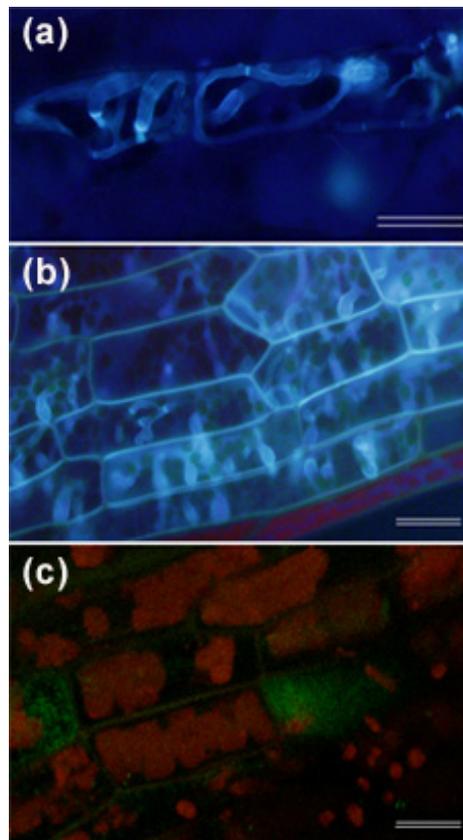
3. Activation of Cell Wall Associated Defense Responses

Pathogens are capable of penetrating the plant cell wall and gain access to cellular nutrients. Plant cells have developed pre-invasive structural defenses, including the cuticle and modifications of the cell wall that serve as barriers for the advance of potential pathogens [38,56]. Modification of the plant cell wall is an important defense mechanism operating in the defense response of flowering plants against necrotrophs [57,58]. Reinforcement of the cell wall involves accumulation of phenolic compounds, ROS and callose deposition at attempted penetration sites, making the cell wall less vulnerable to degradation by CWDEs. Callose is a high–molecular weight β-(1,3)-glucan polymer that is usually associated, together with phenolic compounds, polysaccharides and antimicrobial proteins, with cell wall appositions, called papillae, which are proposed to be effective barriers that are induced at the sites of pathogen attack [59,60]. Callose depositions are formed during early stages of pathogen invasion to inhibit pathogen penetration and are sites of accumulation of antimicrobial secondary metabolites [61]. Callose deposition plays a role in the defense response of *Arabidopsis thaliana* against *P. irregulare*, since the callose synthase mutant *pmr4* is more susceptible to this oomycete compared with wild-type plants [62]. Phenolic compounds are also incorporated in cell walls of *Pythium*-infected tissues of flowering plants [63]. Similarly, the *P. patens* defense response against

P. irregulare and *P. debaryanum* involves the accumulation of phenolic compounds, which were observed in the entire cell wall of infected cells (Figure 3) [29]. In contrast to *P. irregulare*-infected *Arabidopsis* plants [62], callose-containing wall appositions were usually not detected in *Pythium*-infected moss tissues [29]. However, callose depositions were observed when an old *Pythium* inoculum was used and colonization was not extensive, showing that these cell wall appositions can be formed at attempted infection sites, halting the progress of the invading pathogen [29].

Figure 3. Reactive oxygen species (ROS) production and cell wall reinforcement in pathogen-infected plant tissues. Generation of intracellular ROS was observed using 2′,7′-dichlorodihydrofluorescein diacetate in *P. patens* leaves inoculated with *P. irregulare* (**a**) and *B. cinerea* (**b**) at 24 hpi. Hydrogen peroxide accumulation was detected by cerium chloride staining and transmission electron microscopy in *Solanum tuberosum* leaves treated with water (**c**) and treated with elicitors of *P.c. carotovorum* (**d**). Arrows indicate examples of electron-dense deposits of cerium perhydroxides in chloroplasts. Cell wall associated defenses were detected with toluidine blue staining of a *B. cinerea*-infected leaf (**e**) and safranin-*O* staining of a *P. irregulare* infected leaf (**f**) showing incorporation of phenolic compounds into the cell walls. The scale bar in a, b, e and f represents 20 μm, while in c and d, the scale bar represents 200 nm.
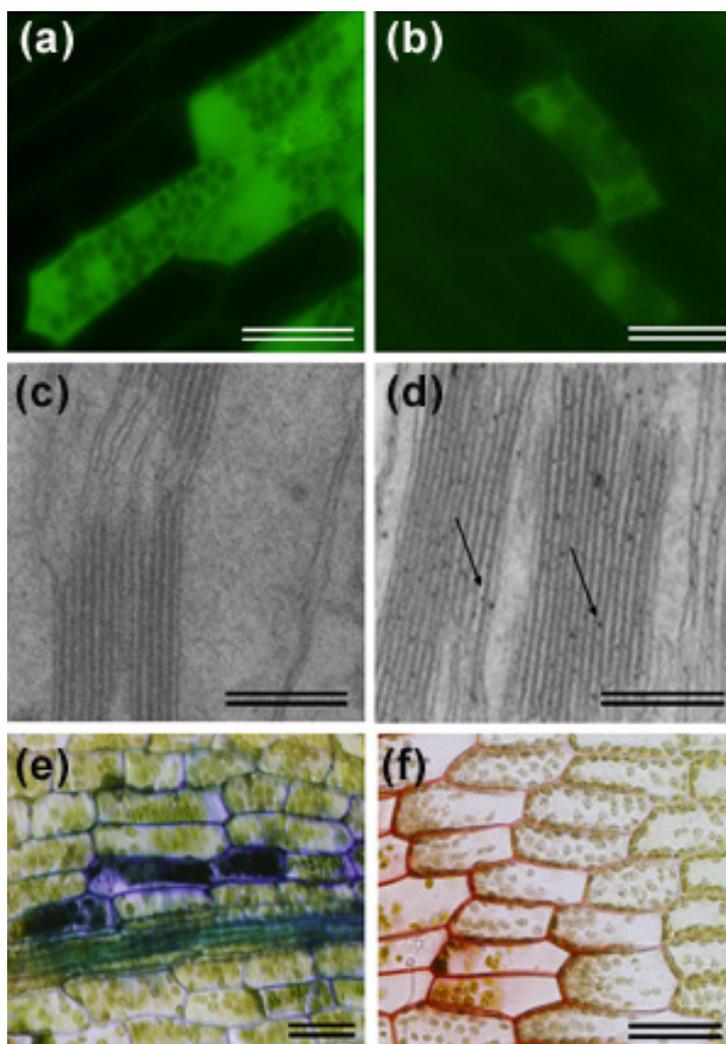
Modification of the plant cell wall by the incorporation of phenolic compounds is also an important defense mechanism in the response of flowering plants against *B. cinerea* [57,58]. Increased activity of type III cell wall peroxidases, which probably influence the degree of crosslinking, resulted in enhanced resistance to *B. cinerea* [64]. Upon *B. cinerea* infection, *P. patens* incorporates phenolic compounds in the cell wall and increases expression of dirigent (DIR) encoding gene(s) [28]. DIR proteins are thought to mediate the coupling of monolignol plant phenols to yield lignans and lignins [65], and it is suggested that they participate in the defense response against pathogens [66,67]. Consistently, enzymes involved in monolignol biosynthesis, including putative cinnamoyl-CoA reductases, increase in *Arabidopsis* plants inoculated with *B. cinerea* [68].

The genome of *P. patens* contains orthologs of all the core lignin biosynthetic enzymes with the exception of ferulate 5-hydroxylase (F5H), which converts G (guaiacyl) monolignol to S (syringyl) monolignol [69]. The occurrence of lignins in bryophytes is still controversial, and instead, mosses may have wall-bound phenolics that resemble lignin [70,71]. The lack of genuine lignin together with the absence of S monolignols in *P. patens* could contribute to the high susceptibility observed in *Pythium* and *B. cinerea* infected moss tissues [28,29]. Recently, Lloyd and coworkers suggested that syringyl-type lignols in particular are important for successful defense of flowering plants against *B. cinerea* [72].

4. ROS Accumulation and Programmed Cell Death in Pathogen-Infected and Elicitor-Treated Plant Tissues

The production of ROS is one of the earliest plant cell responses following pathogen recognition and is involved in cell wall strengthening via cross-linking of glycoproteins, defense signaling and induction of the hypersensitive response [73]. Plant cells produce ROS after *B. cinerea* attack, which assist fungal colonization, since treatments with antioxidants suppress fungal infection [57]. Aggressiveness of different *B. cinerea* isolates correlates with the amount of H_2O_2 and hydroxyl radicals present in leaf tissues during infection [74]. In addition to increased ROS production generated by the host plant as part of a defense mechanism, *B. cinerea* itself produces ROS, including hydrogen peroxide, which accumulates in germinating conidia during the early steps of tissue infection [75,76]. Inactivation of the major *B. cinerea* H_2O_2-generating superoxide dismutase (SOD) retarded development of disease lesions, indicating that this enzyme is a virulence factor leading to the accumulation of phytotoxic levels of hydrogen peroxide in plant tissues [77]. Thus, ROS production is an important component of *B. cinerea* virulence, and increased levels of ROS in plant cells contributes to host cell death and favors fungal infection [78]. ROS production also increased in moss tissues after *B. cinerea*, *P. irregulare* and *P. debaryanum* infection (Figure 3) [28,29]. Single cells respond rapidly to *B. cinerea* hyphae contact by generating ROS, suggesting that, like vascular plants [78,79], the oxidative burst is probably induced before and during *B. cinerea* invasion.

P.c. carotovorum elicitor treatment also increases ROS production in *P. patens* tissues (Ponce de León *et al.*, unpublished results), similarly to flowering plants [80]. In addition, the fungal elicitor chitin and chitosan caused an oxidative burst in *P. patens* cells [30,32]. The importance of ROS production as a defense mechanism against microbial pathogen in mosses was demonstrated in the *P. patens* class III peroxidase knock-out mutant *Prx34*, which showed enhanced susceptibility to

fungal pathogens compared to wild-type *P. patens* plants [30]. This mutant is unable to generate an oxidative burst after elicitor treatment. While a saprophytic fungal isolate of genus *Irpex* and a pathogenic isolate of *Fusarium* sp. caused only mild symptom development in wild-type plants, hyphal growth was abundant and symptoms were severe in *Prx34* knock-out plants, leading to moss decay [30]. Class III peroxidases from flowering plants are known to have antifungal activity [81], and recently, it was shown that the secreted effector Pep1 from the fungus *Ustilago maydis* directly interacts with a class III peroxidase from maize, suppressing the plant defense response by interfering with ROS production [82]. The functional relevance of the Pep1-peroxidase (POX12) interaction was demonstrated with POX12 silenced plants, which were infected by the *pep1* deletion mutant, indicating that inhibition of this peroxidase by Pep1 is crucial for *U. maydis* infection [82]. In addition, PpTSPO1 moss knock-out mutants, which are impaired in mitochondrial protoporphyrin IX uptake and produce elevated levels of intracellular ROS [83], exhibited increased susceptibility to a fungal necrotrophic pathogen, including *Irpex* sp. and *Fusarium avenaceum*, suggesting that PpTSPO1 controls redox homeostasis, which is necessary for efficient resistance against pathogens [32].

Cell death plays a different role in plant response to biotrophs and necrotrophs. The hypersensitive response (HR) is a type of programmed cell death (PCD) with features of two types of cell death recently described, vacuolar cell death and necrotic cell death [84]. HR cell death contributes to resistance to biotrophic pathogens by confining the pathogen and limiting its growth [4]. Biotrophic pathogens actively suppress the HR by using effectors. *Pseudomonas syringae* and *Xanthomonas campestris* deliver 15 to 30 effectors into host cells using type III secretion systems to suppress PTI and ETI, including the HR [85]. In contrast, necrotrophic pathogens actively stimulate the HR, which enhances tissues colonization and host susceptibility. Plant mutants with enhanced cell death have increased resistance to biotrophic pathogens, but higher susceptibility to necrotrophic fungi [86,87]. *B. cinerea* produces nonspecific phytotoxic metabolites, which contribute to cell death on different plant hosts [76]. As part of its invasion strategy, *B. cinerea* promotes PCD in plant cells [78], and studies in flowering plants suggest that *B. cinerea* needs HR to achieve full pathogenicity [78,88]. *Arabidopsis* mutants with an accelerated cell death response are more susceptible to *B. cinerea*, while mutants with reduced or delayed cell death are generally more resistant [89]. *P. patens* also activate an HR-like response after *B. cinerea* colonization, evidenced by protoplast shrinkage, accumulation of ROS and autofluorescent compounds, chloroplasts breakdown and TUNEL (terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling) positive nuclei of infected cells [26,28]. Pathogen-infected *P. patens* tissues also showed other characteristics of PCD, including nucleus condensation and DNA fragmentation, presence of nuclease activities and formation of cytoplasmic vacuoles [31]. Treatments with elicitors, such as CFs of *P.c. carotovorum* and chitosan, also provoked cell death in *P. patens* tissues [26,31]. Harpin proteins from *Pectobacterium* sp. [90,91], *Xanthomonas axonopodis* [92] or *Pseudomonas syringae* [93] elicit HR in flowering plants. Consistently, moss cells treated with the CF of the *P.c. carotovorum* harpin-positive strain SCC1 showed hallmarks of PCD, including protoplast shrinkage, accumulation of autofluorescent compounds and chloroplasts breakdown, while none of these features were detectable in CF treatments with the *P.c. carotovorum* harpin-negative strain SCC3193 [26]. Chitosan induces ROS production and cell death with hallmarks of PCD in young protonemal tissues and gametophores [31]. Interestingly, genes involved in plant PCD, such as those encoding proteases, deoxiribonucleases and

ribonucleases and the antiapoptotic Bax Inhibitor-1 (BI-1) are induced after pathogen or elicitor treatment of *P. patens* [31]. The most convincing evidence indicating that genetically programmed cell death occurs in moss cells in response to some pathogens, comes from studies showing that transgenic *P. patens* plants overexpressing BI-1 are more resistance to necrotrophic fungal pathogens [31].

5. Induced Expression of Defense-Related Genes and Synthesis of Metabolites

Perception of a pathogen by a plant triggers rapid defense responses via multiple signaling pathways that lead to the induced expression of genes with different roles in defense. These include genes encoding functionally diverse pathogenesis-related (PR) proteins, transcription factors and enzymes involved in the production of metabolites (e.g., phenylpropanoids) and hormones [15,94,95]. Transcriptional reprogramming occurs rapidly after pathogen infection, and in the case of *Arabidopsis-B cinerea* interaction, a high-resolution temporal analysis demonstrated that approximately one-third of the *Arabidopsis* genome is differentially expressed during the initial stages of infection [96]. As expected, *P. patens* also sense the presence of pathogens and elicitors and respond rapidly by activating defense gene expression. *B. cinerea*, *P. irregulare* and *P. debaryanum* induce the expression of *PAL* (phenylalanine ammonia-lyase), *CHS* (chalcone synthase) and *LOX1* (lipoxygenase) in *P. patens* tissues [26,28,29]. PAL is a key enzyme in the synthesis of phenylpropanoids, including lignin monomers, phytoalexin antibiotics and the production of SA and CHS is the first enzyme in the synthesis of flavonoids [95]. LOXs are enzymes involved in the synthesis of oxygenated fatty acids (oxylipins), including JA and aldehydes, which play important functions in plant defense against microbial infection and insects [97]. Elicitors of *P.c. carotovorum* also induce *PpPAL*, *PpCHS*, *PpLOX1* and the pathogenesis-related gene *PpPR-1* [26]. ROS-responsive genes encoding alternative oxidase (PpAOX), NADPH-oxidase (PpNOX) and LOX (PpLOX7) are induced by chitosan [32], while *B. cinerea* and *P.c. carotovorum* elicitors induce the expression of *P. patens* genes encoding glutathione S-transferases and ascorbate peroxidases (Ponce de León *et al.*, unpublished data).

Mosses are known to contain a whole range of secondary metabolites, which are not present in flowering plants. The *P. patens* genome has been duplicated 30 and 60 million years ago, and metabolic genes seem to have been retained in excess following duplication, leading probably, in part, to the high versatility of moss metabolism [98]. Some of these metabolites, such as flavonoids, have played important roles in the adaptation of plants to land, to cope with a variety of stresses, including ultraviolet-B (UV-B) radiation, desiccation stress and co-evolving herbivores and pathogens. For example, *P. patens* has a higher number of members composing PAL and CHS multigene families as compared to flowering plants [99,100], and some specific genes could contribute to host defense. Consistently, several genes of the phenylpropanoid pathway leading to flavonoids synthesis, including 4-coumarate:coenzyme A ligase, several CHS and chalcone isomerase are induced in *P. patens* tissues after *P.c. carotovorum* elicitor treatments (Navarrete and Ponce de León *et al.*, unpublished results). Moreover, recent studies showed that *P. patens* accumulated quercetin derivatives in response to UV-B radiation [99]. These flavonoids could also be involved in moss defense responses, since quercetin induces a resistance mechanism in *Arabidopsis* tissues in response to *Pseudomonas syringae* pv. *tomato* DC3000 infection, evidenced by an oxidative burst, callose deposition, and induced expression of *PR-1* and *PAL* [101]. In addition, the *Pythium* and *B. cinerea* inducible PpLOX1 [26,28] can use

arachidonic acid as a substrate leading to the production of oxylipins, which are not present in flowering plants [102–104] and could contribute to the *P. patens* defense response. PpLOX1 and PpLOX2 can produce 12-hydroperoxy eicosatetraenoic acid (12-HPETE) from arachidonate, which in turn serves as substrate for a hydroperoxide lyase (HPL) [102,105] or PpLOX1 and PpLOX2, which posses hydroperoxide cleaving activity [102,103], leading to the production of different C8- and C9-oxylipins. *P. patens* HPL can also use 9-hydroperoxides of C18-fatty acids as substrate, producing (2E)-nonenal and C8-volatiles [105]. The aldehyde (2E)-nonenal could contribute to the defense of *P. patens*, since it has antimicrobial activity against certain pathogens, including *Pseudomonas syringae* pv. *tomato* and *Phytophthora infestans* [106].

Chitosan induces the production of secondary metabolites in *P. patens*, such as cyclic diterpenes, and increases transcript levels of genes encoding key biosynthetic enzymes of this metabolic pathway [31,107]. Inducible ent-kaurane–related diterpenoids play important roles in protecting vascular plants against microbial pathogens, as is the case for the causal agent of rice blast disease, *Magnaporthe grisea* [108], and *Rhizopus microsporus* and *Colletotrichum graminicola*, which cause stalk rot in maize [109].

6. Defense Hormones

Plant hormones, including SA, JA, ethylene, abscisic acid (ABA) and auxins, are involved in the defense response of flowering plants against pathogens, and the role played by these hormones is related to the particular host-pathogen interaction [110]. In general, SA is effective in mediating plant resistance against biotrophs, whereas JA and ethylene are effective in mediating resistance against necrotrophs [111–114]. The interplay between these defense hormones, both agonistic and antagonistic, will determine the outcome of the interaction and minimizes fitness costs, generating a flexible signaling network that allows fine tuning of the inducible defense mechanisms [110,115,116].

P. patens is capable of producing ABA, auxin and cytokinin [117–119], and during the last few years, most studies on moss hormones have been focused on ABA-dependent abiotic stress responses and the regulation of development processes by auxin and cytokinin [120–124]. Until present, only a few studies have been focused on moss hormones in plant-pathogen interactions. The role of ABA in defense responses depends on the infection stage, the type of tissue infected and the specific host pathogen interaction [125]. Evidence indicates that ABA plays a role in the resistance of flowering plants, including stomatal closure, defense gene expression and ROS production/scavenging [57,125–128]. In flowering plants, ABA antagonizes resistance to *B. cinerea*, since ABA-deficient mutants are more resistant to infection [58,62,129]. Consistently, increased ABA levels contribute to the development of grey mould in tomato [57,125]. *B. cinerea*-infected *P. patens* plants showed a small increase in ABA content when mycelium growth was extensive, suggesting that ABA could be produced by *B. cinerea* itself [130] to promote susceptibility by interfering with defense signaling, like the SA pathway, as has been reported previously for flowering plants [131,132].

Bryophytes produce ethylene [133,134] and the *P. patens* genome encodes proteins homologous to ethylene signaling components [18,135]. There are seven putative ethylene receptor proteins in *P. patens* [135] and genes encoding EIN3, EIL and ERF-type components, although the existence of a CTR1 component of ethylene signaling is less clear [136]. A mutation of the presumed ethylene

binding site of PpETR7 inhibits the *P. patens* ethylene response, indicating that *P. patens* perceives ethylene using PpETR7 [136]. Ethylene induces defense mechanisms in flowering plants, including the production of phytoalexins, PR proteins, the induction of the phenylpropanoid pathway and cell wall modifications [137]. Resistance against *B. cinerea* is thought to be influenced by ethylene [138–140]. *B. cinerea* produces ethylene itself and can interfere in this way with plant defense signaling [141]. Ethylene production increases in Arabidopsis after *B. cinerea* infection [142], and pretreatment of tomato plants with ethylene results in increased resistance against *B. cinerea*, evidenced by decreased disease symptoms and fungal biomass [137]. In addition, ethylene influenced phenylpropanoid metabolism, leading to accumulation of hydroxycinnamates and monolignols at the plant cell wall, is linked to ethylene-mediated resistance against *B. cinerea* [72]. Although studies on the effect of ethylene on the *P. patens* defense system has not been addressed, the ethylene precursor, 1-aminocyclopropane-1-carboxylic acid (ACC), induces the expression of some defense genes in *P. patens* (Ponce de León *et al.*, unpublished results), suggesting that, like flowering plants, ethylene participates in the moss defense response. The use of the candidate ethylene receptors mutant *Ppetr7-1* will contribute to understanding the role played by ethylene in the defense of *P. patens* against pathogen infection.

Until very recently, it was unknown if bryophytes produce SA and JA. The *P. patens* genome has 14 putative genes encoding PALs [99] and several putative homologues of isochorismate synthases, supporting the synthesis of SA in this moss. In addition, *P. patens* synthesizes at least seven LOXs [104], two allene oxide synthase (AOS) [143,144], three allene oxide cyclase (AOC) [145,146] and several putative 12-oxo-phytodienoic acid (OPDA) reductases genes [147,148], which encodes enzymes leading to the production of JA. Until present, enzymatic activity has been confirmed for LOXs, AOSs and AOC [104,143–146], although OPR3 activity, which is the only enzyme capable of converting cis-(+)-OPDA to JA, is still missing [147]. Like flowering plants, *P. patens* responds to *B. cinerea* and *P. irregulare* infection by increasing endogenous levels of the precursor of JA, OPDA [28,29,62,149]. Transcript levels of genes encoding enzymes involved in OPDA biosynthesis, including LOX and AOS, are induced in *B. cinerea* infected tissues [28]. OPDA reductase transcript levels also increase in *P. patens* tissues in response to *B. cinerea* inoculation [28]. However, JA could not be detected in healthy, pathogen-infected, elicitor-treated or wounded *P. patens* tissues, suggesting that oxylipins are not further metabolized to JA [28,145,150]. Thus, cis-(+)-OPDA might function as a signaling molecule in *P. patens* instead of JA. Studies with the *Arabidopsis opr3* mutant have shown that OPDA is active as a defense signal against pathogens and regulates defense gene expression [150–152]. Interestingly, moss tissues respond to the presence of OPDA and JA by decreasing rhizoid length and moss colony size [28], similarly to the reduced growth of seedlings and roots observed in OPDA and Methyl Jasmonate (MeJA) treated *Arabidopsis* [153–156]. Moreover, JA, MeJA and OPDA induced the expression of *PAL* in *P. patens*, showing that the presence of these oxylipins is sensed by this moss and signal transduction events are activated, leading to increased levels of defense-related transcripts [29]. The *P. patens* genome has six putative genes encoding the JA-isoleucine receptor COI (coronatine insensitive) and six encoding the repressor JAZ (jasmonate ZIM-domain) [157]. *P. patens* COI-like receptors could bind other oxylipins instead of JA-isoleucine, including cis-(+)-OPDA and/or cis-(+)-OPDA-isoleucine. Thus, the JA signaling pathway could have evolved after divergence of bryophytes and vascular plants. In addition, the similarities between the

auxin receptor (TIR1) and COI1 suggest that COI-1 could have evolved from a TIR1 ancestor by gene duplication, leading to perception of JA-isoleucine by successive mutations [157].

Salicylic acid levels increase in response to *B. cinerea* infection in flowering plants [158,159] and in *P. patens* [28]. Like flowering plants, SA seems to play an important role in the defense of *P. patens* against microbial pathogens. SA treatment of moss tissues induces the expression of the defense gene *PAL* [28], and SA application induced defense mechanisms and increased resistance to *P.c. carotovorum* in *P. patens* colonies [160]. SA-mediated resistance could be due to activation of similar defense mechanisms in mosses and flowering plants, since exogenous SA application to tobacco plants also increase resistance against *P.c. carotovorum* [161]. In flowering plants, SA plays a key role in the activation of defense mechanisms associated with the HR and participates in a feedback amplification loop, both upstream and downstream of cell death [162,163]. The generation of SA-deficient NahG transgenic moss plants will help to elucidate SA involvement in moss defense, including the HR-like response.

7. Conclusions

During land colonization, plants gradually evolved defense strategies to cope with radiation, desiccation stress and airborne pathogens by newly acquired specialized metabolic pathways, such as the phenylpropanoid metabolism. Recently, significant progress has been made on sequencing genomes of plants that occupy interesting positions within the evolutionary history of plants, including the non-vascular moss *P. patens* and the vascular spikemoss *S. moellendorffii* [18,22]. *P. patens* occupies a key position halfway between green algae and flowering plants, allowing evolutionary and comparative studies of defense mechanisms across the green plant lineage. Interestingly, it was recently shown that *P. patens* has acquired genes related directly or indirectly with defense mechanisms by means of horizontal gene transfer from fungi and viruses [164]. The possible uptake of foreign DNA from fungi associated with early land plants could have facilitated the transition to a hostile land environment [164,165]. *P. patens* respond to pathogen infection or elicitor treatment by inducing defense-related gene expression and producing metabolites and hormones that could play different roles in defense. Several defense mechanisms are shared between *P. patens* and flowering plants, and functional conservation of some signaling pathways probably indicate common ancestral defense strategies [28–30,32,136]. While the JA signaling pathway may have evolved after the divergence of bryophytes and vascular plants, ethylene, ABA and SA likely have their origins in the early stages of land colonization. The use of *P. patens* mutants in key components of these signaling pathways will help to determine the role played by these hormones in moss defense. *P. patens* also offers the possibility to identify novel metabolites, some of which are not present in flowering plants, including arachidonic acid-derived oxylipins that could play a role in defense responses. In addition, experimentation with *P. patens* could help to unravel defense pathways and gene functions in plants through the generation of knock-out mutants and single point mutations of genes involved in disease resistance and to identify clear mutant phenotypes due to the presence of a dominant gametophytic haploid phase [19]. Large-scale analyses of transcripts from pathogen-infected or elicitor-treated moss plants together with functional genomic and comparative studies with flowering plants will help to identify key components in the plant defense response and to design strategies to enhance plant resistance to biotic stress.

Acknowledgments

Conflict of Interest

The authors declare no conflict of interest.

References

1. Ausubel, F.M. Are innate immune signaling pathways in plants and animals conserved? *Nat. Immunol.* **2005**, *6*, 973–979.
2. Bittel, P.; Robatzek, S. Microbe-associated molecular patterns (MAMPs) probe plant immunity. *Curr. Opin. Plant Biol.* **2007**, *10*, 335–341.
3. Boller, T.; Felix, G. A renaissance of elicitors: perception of microbe-associated molecular patterns and danger signals by pattern-recognition receptors. *Annu. Rev. Plant Biol.* **2009**, *60*, 379–406.
4. Jones, J.D.; Dangl, J.L. The plant immune system. *Nature* **2006**, *444*, 323–329.
5. Abramovitch, R.B.; Janjusevic, R.; Stebbins, C.E.; Martin, G.B. Type III effector AvrPtoB requires intrinsic E3 ubiquitin ligase activity to suppress plant cell death and immunity. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 2851–2856.
6. Boller, T.; He, S.Y. Innate immunity in plants: An arms race between pattern recognition receptors in plants and effectors in microbial pathogens. *Science* **2009**, *324*, 742–744.
7. Cui, H.; Wang, Y.; Xue, L.; Chu, J.; Yan, C.; Fu, J.; Chen, M.; Innes, R.W.; Zhou, J.M. *Pseudomonas syringae* effector protein AvrB perturbs *Arabidopsis* hormone signaling by activating MAP kinase 4. *Cell Host Microbe* **2010**, *7*, 164–175.
8. Grant, S.R.; Fisher, E.J.; Chang, J.H.; Mole, B.M.; Dangl, J.L. Subterfuge and manipulation: Type III effector proteins of phytopathogenic bacteria. *Annu. Rev. Microbiol.* **2006**, *60*, 425–449.
9. Zhou, J.M.; Chai, J.J. Plant pathogenic bacterial type III effectors subdue host responses. *Curr. Opin. Microbiol.* **2008**, *11*, 179–185.
10. Denoux, C.; Galletti, R.; Mammarella, N.; Gopalan, S.; Werck, D.; De Lorenzo, G.; Ferrari, S.; Ausubel, F.M.; Dewdney, J. Activation of defense response pathways by OGs and flg22 elicitors in Arabidopsis seedlings. *Mol. Plant* **2008**, *1*, 423–445.
11. Lotze, M.T.; Zeh, H.J.; Rubartelli, A.; Sparvero, L.J.; Amoscato, A.A.; Washburn, N.R.; Devera, M.E.; Liang, X.; Tör, M.; Billiar, T. The grateful dead: damage associated molecular pattern molecules and reduction/oxidation regulate immunity. *Immunol. Rev.* **2007**, *220*, 60–81.
12. Tsuda, K.; Katagiri, F. Comparing signaling mechanisms engaged in pattern-triggered and effector-triggered immunity. *Curr. Opin. Plant Biol.* **2010**, *13*, 459–465.
13. Thomma, BP.; Nurnberger, T.; Joosten, MH. Of PAMPs and effectors: the blurred PTI-ETI dichotomy. *Plant Cell* **2011**, *23*, 4–15.
14. Nicaise, V.; Roux, M.; Zipfel, C. Recent advances in PAMP-triggered immunity against bacteria: Pattern recognition receptors watch over and raise the alarm. *Plant Physiol.* **2009**, *150*, 1638–1647.

15. van Loon, L.C.; Rep, M.; Pieterse, C.M.J. Significance of inducible defense-related proteins in infected plants. *Annu. Rev. Phytopathol.* **2006**, *44*, 135–162.

16. Bent, A.F.; Mackey, D. Elicitors, effectors, and R genes: The new paradigm and a lifetime supply of questions. *Annu. Rev. Phytopathol.* **2007**, *45*, 399–436.

17. Zipfel, C. Early molecular events in PAMP-triggered immunity. *Curr. Opin. Plant Biol.* **2009**, *12*, 414–420.

18. Rensing, S.A.; Lang, D.; Zimmer, A.D.; Terry, A.; Salamov, A.; Shapiro, H.; Nishiyama, T.; Perroud, P.F.; Lindquist, E.A.; Kamisugi, Y.; *et al.* The *Physcomitrella* genome reveals evolutionary insights into the conquest of land by plants. *Science* **2008**, *319*, 64–69.

19. Schaefer, D.G. A new moss genetics: targeted mutagenesis in *Physcomitrella patens*. *Annu. Rev. Plant Biol.* **2002**, *53*, 477–501.

20. Cove, D. The moss Physcomitrella patens. Annu. Rev. Genet. **2005**, 39, 339–358.

21. Lewis, L.A.; McCourt, R.M. Green algae and the origin of land plants. *Am. J. Bot.* **2004**, *91*, 1535–1556.

22. Banks, J.A.; Nishiyama, T.; Hasebe, M.; Bowman, J.L.; Gribskov, M.; dePamphilis, C.; Albert, V.A.; Aono, N.; Aoyama, T.; Ambrose, B.A.; *et al.* The *Selaginella* genome identifies genetic changes associated with the evolution of vascular plants. *Science* **2011**, *332*, 960–963.

23. Döbbeler, P. Biodiversity of bryophilous ascomycetes, *Biodivers. Conserv.* **1997**, *6*, 721–738.

24. Davey, M.L.; Currah, R.S. Interactions between mosses (Bryophyta) and fungi. *Can. J. Bot.* **2006**, *84*, 1509–1519.

25. Davey, M.L.; Tsuneda, A.; Currah, R.S. Pathogenesis of bryophyte hosts by the ascomycete *Atradidymella muscivora*. *Am. J. Bot*. **2009**, *96*, 1274–1280.

26. Ponce de León, I.; Oliver, J.P.; Castro, A.; Gaggero, C.; Bentancor, M.; Vidal, S. *Erwinia carotovora* elicitors and *Botrytis cinerea* activate defense responses in *Physcomitrella patens*. *BMC Plant Biol.* **2007**, *7*, 52.

27. Ponce de León, I. The moss *Physcomitrella patens* as a model system to study interactions between plants and phytopathogenic fungi and oomycetes. *J. Pathog.* **2011**, doi:10.4061/2011/719873.

28. Ponce De León, I.; Schmelz, E.A.; Gaggero, C.; Castro, A.; Álvarez, A.; Montesano, M. *Physcomitrella patens* activates reinforcement of the cell wall, programmed cell death and accumulation of evolutionary conserved defence signals, such as salicylic acid and 12-oxo-phytodienoic acid, but not jasmonic acid, upon *Botrytis cinerea* infection. *Mol. Plant Pathol.* **2012**, *13*, 960–974.

29. Oliver, J.P.; Castro, A.; Gaggero, C.; Cascón, T.; Schmelz, E.A.; Castresana, C.; Ponce de León, I. *Pythium* infection activates conserved plant defense responses in mosses. *Planta* **2009**, *230*, 569–579.

30. Lehtonen, M.T.; Akita, M.; Kalkkinen, N.; Ahola-Iivarinen, E.; Rönnholm, G.; Somervuo, P.; Thelander, M.; Valkonen, J.P. Quickly-released peroxidase of moss in defense against fungal invaders. *New Phytol.* **2009**, *183*, 432–443.

31. Lawton, M.; Saidasan, H. Pathogenesis in mosses. *Annu. Plant Rev.* **2009**, *36*, 298–339.

32. Lehtonen, M.T.; Akita, M.; Frank, W.; Reski, R.; Valkonen, J.P. Involvement of a class III peroxidase and the mitochondrial protein TSPO in oxidative burst upon treatment of moss plants with a fungal elicitor. *Mol. Plant-Microbe Interact.* **2012**, *25*, 363–371.

33. Schwessinger, B.; Ronald, P.C. Plant innate immunity: Perception of conserved microbial signatures. *Annu. Rev. Plant Biol.* **2012**, *63*, 451–482.

34. Akita, M.; Valkonen, J.P.T. A novel gene family in moss (*Physcomitrella patens*) shows sequence homology and a phylogenetic relationship with the TIR-NBS class of plant disease resistance genes. *J. Mol. Evol.* **2002**, *55*, 595–605.

35. Xue, J.Y.; Wang, Y.; Wu, P.; Wang, Q.; Yang, L.T.; Pan, X.H.; Wang, B.; Chen, J.Q. A primary survey on bryophyte species reveals two novel classes of nucleotide-binding site (NBS) genes. *PLoS One* **2012**, *7*, e36700.

36. Stone, J.K. Necrotroph. In *Encyclopedia of Plant Pathology*; Maloy, O.C., Murray, T.D., Eds.; Wiley: New York, NY, USA, 2001; Volume 2, pp. 676–677.

37. Elad, Y.; Williamson, B.; Tudzynski, P.; Delen, N. *Botrytis: Biology, Pathology and Control*; Kluwer Academic Publishers: Dordrecht, The Netherlands, 2004.

38. van Kan, J.A. Licensed to kill: The lifestyle of a necrotrophic plant pathogen. *Trends Plant Sci.* **2006**, *11*, 247–253.

39. Prins, T.W.; Tudzynski, P.; Tiedemann, A.V.; Tudzynski, B.; ten Have, A.; Hansen, M.E.; Tenberge, K.; van Kan, J.A.L. Infection strategies of *Botrytis cinerea* and related necrotrophic pathogens. In *Fungal Pathology*; Kronstad, J.W., Ed.; Kluwer Academic Publishers: Dordrecht, The Netherlands, 2000; pp. 33–64.

40. Staats, M.; van Baarlen, P.; van Kan, J.A. Molecular phylogeny of the plant pathogenic genus *Botrytis* and the evolution of host specificity. *Mol. Biol. Evol.* **2005**, *22*, 333–346.

41. Perombelon, M.C.M.; Kelman, A. Ecology of the Soft Rot *Erwinias*. *Annu Rev. Phytopathol.* **1980**, *18*, 361–387.

42. Toth, I.K.; Birch, P.R. Rotting softly and stealthily. *Curr. Opin. Plant Biol.* **2005**, *8*, 424–429.

43. Palva, T.K.; Holmström, K.O.; Heino, P.; Palva, E.T. Induction of plant defense response by exoenzymes of *Erwinia carotovora* ssp. *carotovora*. *Mol. Plant-Microbe Interact.* **1993**, *6*, 190–196.

44. Norman, C.; Vidal, S.; Palva, E.T. Oligogalacturonide-mediated induction of a gene involved in jasmonic acid synthesis in response to the cell-wall-degrading enzymes of the plant pathogen *Erwinia carotovora*. *Mol. Plant-Microbe Interact.* **1999**, *12*, 640–644.

45. Norman-Setterblad, C.; Vidal, S.; Palva, E.T. Interacting signal pathways control defense gene expression in *Arabidopsis* in response to cell wall-degrading enzymes from *Erwinia carotovora*. *Mol. Plant-Microbe Interact.* **2000**, *13*, 430–438.

46. Vidal, S.; Ponce de León, I.; Denecke, J.; Palva, E.T. Salicylic acid and the plant pathogen *Erwinia carotovora* induce defense genes via antagonistic pathways. *Plant J.* **1997**, *11*, 115–123.

47. Vidal, S.; Eriksson, A.R.B.; Montesano, M.; Denecke, J.; Palva, E.T.; Cell wall degrading enzymes from *Erwinia carotovora* cooperate in the salicylic acid-independent induction of a plant defense response. *Mol. Plant-Microbe Interact.* **1998**, *11*, 23–32.

48. Montesano, M.; Brader, G.; Ponce de Leon, I.; Palva, ET. Multiple defense signals induced by *Erwinia carotovora* ssp. *carotovora* in potato. *Mol. Plant Pathol.* **2005**, *6*, 541–549.

49. Montesano, M.; Kõiv, V.; Mäe, A.; Palva, E.T. Novel receptor-like protein kinases induced by *Erwinia carotovora* and short oligogalacturonides in potato. *Mol. Plant Pathol.* **2001**, *2*, 339–346.

50. Davis, K.R.; Lyon, G.D.; Darvill, A.G.; Albersheim, P. Host-pathogen interactions: XXV. Endopolygalacturonic acid lyase from *Erwinia carotovora* elicits phytoalexin accumulation by releasing plant cell wall fragments. *Plant Physiol.* **1984**, *74*, 52–60.

51. Nothnagel, E.A.; McNeil, M.; Albersheim, P.; Dell, A. Host-pathogen interactions: XXII. A galacturonic acid oligosaccharide from plant cell walls elicits phytoalexins. *Plant Physiol.* **1983**, *71*, 916–926.

52. Rantakari, A.; Virtaharju, O.; Vähämiko, S.; Taira, S.; Palva, E.T.; Saarilahti, H.T.; Romantschuk, M. Type III secretion contributes to the pathogenesis of the soft-rot pathogen *Erwinia carotovora* partial characterization of the hrp gene cluster. *Mol. Plant-Microbe Interact.* **2001**, *14*, 962–968.

53. Mattinen, L.; Tshuikina, M.; Mäe, A.; Pirhonen, M. Identification and characterization of Nip, necrosis-inducing virulence protein of *Erwinia carotovora* subsp. *carotovora*. *Mol. Plant-Microbe Interact.* **2004**, *17*, 1366–1375.

54. Martin, F. Pythium. In *Pathogenesis and Host Specificity in Plant Diseases: Histopathological, Biochemical, Genetic and Molecular Bases*; Komoto, K., Singh, U.S., Singh, R.P., Eds.; Pergamon Press: Oxford, UK, 1994; pp. 17–36.

55. Campion, C.; Massiot, P.; Rouxel, F. Aggressiveness and production of cell-wall degrading enzymes by *Pythium violae*, *Pythium sulcatum* and *Pythium ultimum*, responsible for cavity spot on carrots. *Eur. J. Plant Pathol.* **1997**, *103*, 725–735.

56. Mendgen, K.; Hahn, M.; Deising, H. Morphogenesis and mechanisms of penetration by plant pathogenic fungi. *Annu. Rev. Phytopathol.* **1996**, *34*, 367–386.

57. Asselbergh, B.; Curvers, K.; Franca, S.C.; Audenaert, K.; Vuylsteke, M.; Van Breusegem, F.; Höfte, M. Resistance to *Botrytis cinerea* in sitiens, an abscisic acid-deficient tomato mutant, involves timely production of hydrogen peroxide and cell wall modifications in the epidermis. *Plant Physiol.* **2007**, *144*, 1863–1877.

58. Curvers, K.; Seifi, H.; Mouille, G.; de Rycke, R.; Asselbergh, B.; Van Hecke, A.; Vanderschaeghe, D.; Höfte, H.; Callewaert, N.; van Breusegem, F.; Höfte, M. Abscisic acid deficiency causes changes in cuticle permeability and pectin composition that influence tomato resistance to *Botrytis cinerea*. *Plant Physiol.* **2010**, *154*, 847–860.

59. Jacobs, A.K.; Lipka, V.; Burton, R.A.; Panstruga, R.; Strizhov, N.; Schulze-Lefert, P.; Fincher, G.B. An *Arabidopsis* callose synthase, GSL5, is required for wound and papillary callose formation. *Plant Cell* **2003**, *15*, 2503–2513.

60. Ton, J.; Mauch-Mani, B. Beta-amino-butyric acid-induced resistance against necrotrophic pathogens is based on ABA-dependent priming for callose. *Plant J.* **2004**, *38*, 119–130.

61. Luna, E.; Pastor, V.; Robert, J.; Flors, V.; Mauch-Mani, B.; Ton, J. Callose deposition: A multifaceted plant defense response. *Mol. Plant-Microbe Interact.* **2011**, *24*, 183–193.

62. Adie, B.A.; Pérez-Pérez, J.; Pérez-Pérez, M.M.; Godoy, M.; Sánchez-Serrano, J.J.; Schmelz, E.A.; Solano, R. ABA is an essential signal for plant resistance to pathogens affecting JA biosynthesis and the activation of defenses in *Arabidopsis*. *Plant Cell* **2007**, *19*, 1665–1681.

63. Benhamou, N.; Bélanger, R. Induction of systemic resistance to *Pythium* damping-off in cucumber plants by benzothiadiazole: ultrastructure and cytochemistry of the host response. *Plant J.* **1998**, *14*, 13–21.

64. Ramírez, V.; Agorio, A.; Coego, A.; García-Andrade, J.; Hernández, M.J.; Balaguer, B.; Ouwerkerk, P.B.; Zarra, I.; Vera, P. MYB46 modulates disease susceptibility to *Botrytis cinerea* in *Arabidopsis. Plant Physiol.* **2011**, *155*, 1920–1935.

65. Davin, L.B.; Lewis, N.G. Dirigent proteins and dirigent sites explain the mystery of specificity of radical precursor coupling in lignan and lignin biosynthesis. *Plant Physiol.* **2000**, *123*, 453–462.

66. Coram, T.E.; Wang, M.; Chen, X. Transcriptome analysis of the wheat–*Puccinia striiformis* f. sp. *tritici* interaction. *Mol. Plant Pathol.* **2008**, *9*, 157–169.

67. Chakravarthy, S.; Velásquez, A.C.; Ekengren, S.K.; Collmer, A.; Martin, G.B. Identification of *Nicotiana benthamiana* genes involved in pathogen associated molecular pattern-triggered immunity. *Mol. Plant-Microbe Interact.* **2010**, *23*, 715–726.

68. Ferrari, S.; Gallettim, R.; Denoux, C.; De Lorenzo, G.; Ausubel, F.M.; Dewdney, J. Resistance to *Botrytis cinerea* induced in *Arabidopsis* by elicitors is independent of salicylic acid, ethylene or jasmonate signaling but requires PAD3. *Plant Physiol.* **2007**, *144*, 367–379.

69. Xu, Z.; Zhang, D.; Hu, J.; Zhou, X.; Ye, X.; Reichel, K.L.; Stewart, N.R.; Syrenne, R.D.; Yang, X.; *et al.* Comparative genome analysis of lignin biosynthesis gene families across the plant kingdom. *BMC Bioinformatics* **2009**, *10*, S3.

70. Popper, Z.A. Evolution and diversity of green plant cell walls. *Curr. Opin. Plant Biol.* **2008**, *11*, 286–292.

71. Weng, J.K.; Chapple, C. The origin and evolution of lignin biosynthesis. *New Phytol.* **2010**, *187*, 273–285.

72. Lloyd, A.J.; William Allwood, J.; Winder, C.L.; Dunn, W.B.; Heald, J.K.; Cristescu S.M.; Sivakumaran, A.; Harren, F.J.; Mulema, J.; Denby, K.; *et al.* Metabolomic approaches reveal that cell wall modifications play a major role in ethylene-mediated resistance against *Botrytis cinerea. Plant J.* **2011**, *67*, 852–868.

73. Torres, M.A.; Jones, J.D.; Dangl, J.L. Reactive oxygen species signaling in response to pathogens. *Plant Physiol.* **2006**, *141*, 373–378.

74. Tiedemann, A.V. Evidence for a primary role of active oxygen species in induction of host cell death during infection of bean leaves with *Botrytis cinerea. Physiol. Mol. Plant Pathol.* **1997**, *50*, 151–166.

75. Schouten, A.; Tenberge, K.B.; Vermeer, J.; Stewart, J.; Wagemakers, L.; Williamson, B.; van Kan, J.A. Functional analysis of an extracellular catalase of *Botrytis cinerea. Mol. Plant Pathol.* **2002**, *3*, 227–238.

76. Choquer, M.; Fournier, E.; Kunz, C.; Levis, C.; Pradier, J.M.; Simon, A.; Viaud, M. *Botrytis cinerea* virulence factors: New insights into a necrotrophic and polyphageous pathogen. *FEMS Microbiol. Lett.* **2007**, *277*, 1–10.

77. Rolke, Y.; Liu, S.; Quidde, T.; Williamson, B.; Schouten, A.; Weltring, K.M.; Siewers, V.; Tenberge, K B.; Tudzynski, B.; Tudzynski, P. Functional analysis of H_2O_2-generating systems in *Botrytis cinerea*: The major Cu-Zn-superoxide dismutase (BCSOD1) contributes to virulence on French bean, whereas a glucose oxidase (BCGOD1) is dispensable. *Mol. Plant Pathol.* **2004**, *5*, 17–27.

78. Govrin, E.M.; Levine, A. The hypersensitive response facilitates plant infection by the necrotrophic pathogen *Botrytis cinerea. Curr. Biol.* **2000**, *10*, 751–757.

79. Asai, S.; Yoshioka, H. Nitric oxide as a partner of reactive oxygen species participates in disease resistance to necrotrophic pathogen *Botrytis cinerea* in *Nicotiana benthamiana*. *Mol. Plant-Microbe Interact.* **2009**, *22*, 619–629.

80. Montesano, M.; Scheller, H.V.; Wettstein, R.; Palva, E.T. Down-regulation of photosystem I by *Erwinia carotovora*-derived elicitors correlates with H_2O_2 accumulation in chloroplasts of potato. *Mol. Plant Pathol.* **2004**, *5*, 115–123.

81. Ghosh, M. Antifungal properties of haem peroxidase from *Acorus calamus*. *Ann. Bot.* **2006**, *98*, 1145–1153.

82. Hemetsberger, C.; Herrberger, C.; Zechmann, B.; Hillmer, M.; Doehlemann, G. The *Ustilago maydis* effector Pep1 suppresses plant immunity by inhibition of host peroxidase activity. *PLoS Pathog.* **2012**, *8*, e1002684.

83. Frank, W.; Baar, K.; Qudeimat, E.; Woriedh, M.; Alawady, A.; Ratnadewi, D.; Gremillon, L.; Grimm, B.; Reski, R. A mitochondrial protein homologous to the mammalian peripheral-type benzodiazepine receptor is essential for stress adaptation in plants. *Plant J.* **2007**, *51*, 1004–1018.

84. van Doorn, W.G.; Beers, E.P.; Dangl, J.L.; Franklin-Tong, V.E.; Gallois, P.; Hara-Nishimura, I.; Jones, A.M.; Kawai-Yamada, M.; Lam, E.; Mundy, J.; *et al.* Morphological classification of plant cell deaths. *Cell Death Differ.* **2011**, *18*, 1241–1246.

85. Kjemtrup, S.; Nimchuk, Z.; Dangl, J.L. Effector proteins of phytopathogenic bacteria: Bifunctional signals in virulence and host recognition. *Curr. Opin. Microbiol.* **2000**, *3*, 73–78.

86. Kachroo, P.; Shanklin, J.; Shah, J.; Whittle, E.J.; Klessig, D.F. A fatty acid desaturase modulates the activation of defense signaling pathways in plants. *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 9448–9453.

87. Veronese, P.; Chen, X.; Bluhm, B.; Salmeron, J.; Dietrich, R.; Mengiste, T. The BOS loci of *Arabidopsis* are required for resistance to *Botrytis cinerea* infection. *Plant J.* **2004**, *40*, 558–574.

88. Dickman, M.B.; Park, Y.K.; Oltersdorf, T.; Li, W.; Clemente, T.; French, R. Abrogation of disease development in plants expressing animal antiapoptotic genes. *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 6957–6962.

89. van Baarlen, P.; Woltering, E.J.; Staats, M.; van Kan, J.A.L. Histochemical and genetic analysis of host and non-host interactions of Arabidopsis with three *Botrytis* species: an important role for cell death control. *Mol. Plant Pathol.* **2007**, *8*, 41–54.

90. Wei, Z.M.; Laby, R.J.; Zumoff, C.H.; Bauer, D.W.; He, S.Y.; Collmer, A.; Beer, S.V. Harpin, elicitor of the hypersensitive response produced by the plant pathogen *Erwinia amylovora*. *Science* **1992**, *257*, 85–88.

91. Kariola, T.; Palomäki, T.A.; Brader, G.; Palva, E.T. *Erwinia carotovora* subsp. *carotovora* and *Erwinia* -derived elicitors HrpN and PehA trigger distinct but interacting defense responses and cell death in Arabidopsis. *Mol. Plant-Microbe Interact.* **2003**, *16*, 179–187.

92. Kim, J.G.; Jeon, E.; Oh, J.; Moon, J.S.; Hwang, I. Mutational analysis of *Xanthomonas* harpin HpaG identifies a key functional region that elicits the hypersensitive response in nonhost plants. *J. Bacteriol.* **2004**, *186*, 6239–6247.

93. Alfano, J.R.; Bauer, D.W.; Milos, T.M.; Collmer, A. Analysis of the role of the *Pseudomonas syringae* pv. *syringae* HrpZ harpin in elicitation of the hypersensitive response in tobacco using

functionally non-polar hrpZ deletion mutations, truncated HrpZ fragments, and hrmA mutations. *Mol. Microbiol.* **1996**, *19*, 715–728.

94. Zhu, Q.; Dröge-Laser, W.; Dixon, R.A.; Lamb, C. Transcriptional activation of plant defense genes. *Curr. Opin. Genet. Dev.* **1996**, *6*, 624–630.

95. Dixon, R.A.; Paiva, N.L. Stress-induced phenylpropanoid metabolism. *Plant Cell* **1995**, *7*, 1085–1097.

96. Windram, O.; Madhou, P.; McHattie, S.; Hill, C.; Hickman, R.; Cooke, E.; Jenkins, D.J.; Penfold, C.A.; Baxter, L.; Breeze, E.; *et al*. Arabidopsis Defense against Botrytis cinerea: Chronology and Regulation Deciphered by High-Resolution Temporal Transcriptomic Analysis. *Plant Cell* **2012**, *24*, 3530–3557.

97. Feussner, I.; Wasternack, C. The lipoxygenase pathway. *Annu. Rev. Plant Biol.* **2002**, *53*, 275–297.

98. Rensing, S.A.; Ick, J.; Fawcett, J.A.; Lang, D.; Zimmer, A.; Van de Peer, Y.; Reski, R. An ancient genome duplication contributed to the abundance of metabolic genes in the moss *Physcomitrella patens*. *BMC Evol. Biol.* **2007**, *7*, 130.

99. Wolf, L.; Rizzini, L.; Stracke, R.; Ulm, R.; Rensing, S.A. The molecular and physiological responses of *Physcomitrella patens* to ultraviolet-B radiation. *Plant Physiol.* **2010**, *153*, 1123–1134.

100. Koduri, P.K.; Gordon, G.S.; Barker, E.I.; Colpitts, C.C.; Ashton, N.W.; Suh, D.Y. Genome-wide analysis of the chalcone synthase superfamily genes of *Physcomitrella patens*. *Plant Mol. Biol.* **2010**, *72*, 247–263.

101. Jia, Z.; Zou, B.; Wang, X.; Qiu, J.; Ma, H.; Gou, Z.; Song, S.; Dong, H. Quercetin-induced H(2)O(2) mediates the pathogen resistance against Pseudomonas syringae pv. Tomato DC3000 in *Arabidopsis thaliana*. *Biochem. Biophys. Res. Commun.* **2010**, *28*, 522–527.

102. Wichard, T.; Göbel, C.; Feussner, I.; Pohnert, V. Unprecedented lipoxygenase/hydroperoxide lyase pathways in the moss *Physcomitrella patens*. *Angew. Chem. Int. Edit.* **2004**, *44*, 158–161.

103. Senger, T.; Wichard, T.; Kunze, S.; Gobel, C.; Lerchl, J.; Pohnert, G.; Feussner, I. A multifunctional lipoxygenase with fatty acid hydroperoxide cleaving activity from the moss *Physcomitrella patens*. *J. Biol. Chem.* **2005**, *280*, 7588–7596.

104. Anterola, A.; Göbel, C.; Hornung, E.; Sellhorn, G.; Feussner, I.; Grimes, H. *Physcomitrella patens* has lipoxygenases for both eicosanoid and octadecanoid pathways. *Phytochemistry* **2009**, *70*, 40–52.

105. Stumpe, M.; Bode, J.; Gobel, C.; Wichard, T.; Schaaf, A.; Frank, W.; Frank, M.; Reski, R.; Pohnert, G.; Feussner, I. Biosynthesis of C9-aldehydes in the moss *Physcomitrella patens*. *Biochim. Biophys. Acta* **2006**, *1761*, 301–312.

106. Prost, I.; Dhondt, S.; Rothe, G.; Vicente, J.; Rodriguez, M.J.; Kift, N.; Carbonne, F.; Griffiths, G.; Esquerré-Tugayé, M.T.; Rosahl, S.; *et al*. Evaluation of the antimicrobial activities of plant oxylipins supports their involvement in defense against pathogens. *Plant Physiol.* **2005**, *139*, 1902–1913.

107. Von Schwartzenberg, K.; Schultze, W.; Kassner, H. The moss *Physcomitrella patens* releases a tetracyclic diterpene. *Plant Cell Rep.* **2004**, *22*, 780–786.

108. Peters, R.J. Uncovering the complex metabolic network underlying diterpenoid phytoalexin biosynthesis in rice and other cereal crop plants. *Phytochemistry* **2006**, *67*, 2307–2317.

109. Schmelz, E.A.; Kaplan, F.; Huffaker, A.; Dafoe, N.J.; Vaughan, M.M.; Ni, X.; Rocca, J.R.; Alborn, H.T.; Teal, P.E. Identity, regulation, and activity of inducible diterpenoid phytoalexins in maize. *Proc. Natl. Acad. Sci. USA* **2011**, *108*, 5455–5460.

110. López, M.A.; Bannenberg, G.; Castresana, C. Controlling hormone signaling is a plant and pathogen challenge for growth and survival. *Curr. Opin. Plant Biol*. **2008**, *11*, 420–427.

111. Feys, B.J.; Parker, J.E. Interplay of signaling pathways in plant disease resistance. *Trends Genet.* **2000**, *16*, 449–455.

112. Lund, S.T.; Stall, R.E.; Klee, H.J. Ethylene regulates the susceptible response to pathogen infection in tomato. *Plant Cell* **1998**, *10*, 371–382.

113. Greenberg, J.T.; Silverman, F.P.; Liang, H. Uncoupling salicylic acid-dependent cell death and defense-related responses from disease resistance in the Arabidopsis mutant acd5. *Genetics* **2000**, *156*, 341–350.

114. Pilloff, R.K.; Devadas, S.K.; Enyedi, A.; Raina, R. The *Arabidopsis* gain-of-function mutant Dll1 spontaneously develops lesions mimicking cell death associated with disease. *Plant J*. **2002**, *30*, 61–70.

115. Mur, L.A.; Kenton, P.; Atzorn, R.; Miersch, O.; Wasternack, C. The outcomes of concentration-specific interactions between salicylate and jasmonate signaling include synergy, antagonism, and oxidative stress leading to cell death. *Plant Physiol.* **2006**, *140*, 249–262.

116. Koornneef, A.; Pieterse, C.M. Cross talk in defense signaling. *Plant Physiol.* **2008**, *146*, 839–844.

117. Komatsu, K.; Nishikawa, Y.; Ohtsuka, T.; Taji, T.; Quatrano, R.S.; Tanaka, S.; Sakata, Y. Functional analyses of the ABI1-related protein phosphatase type 2C reveal evolutionarily conserved regulation of abscisic acid signaling between Arabidopsis and the moss *Physcomitrella patens*. *Plant Mol. Biol.* **2009**, *70*, 327–340.

118. Bierfreund, N.M.; Reski, R.; Decker, E.L. Use of an inducible reporter gene system for the analysis of auxin distribution in the moss *Physcomitrella patens*. *Plant Cell Rep.* **2003**, *21*, 1143–1152.

119. Schwartzenberg, K.V.; Nunez, M.F.; Blaschke, H.; Dobrev, P.I.; Novak, D.O.; Motyka, V.; Strnad, M. Cytokinins in the bryophyte *Physcomitrella patens*: analyses of activity, distribution, and cytokinin oxidase/dehydrogenase overexpression reveal the role of extracellular cytokinins. *Plant Physiol.* **2007**, *145*, 786–800.

120. Khandelwal, A.; Cho, S.H.; Marella, H.; Sakata, Y.; Perroud, P.F.; Pan, A.; Quatrano, R.S. Role of ABA and ABI3 in desiccation tolerance. *Science* **2010**, *327*, 546.

121. Bhyan, S.B.; Minami, A.; Kaneko, Y.; Suzuki, S.; Arakawa, K.; Sakata, Y.; Takezawa, D. Cold acclimation in the moss *Physcomitrella patens* involves abscisic acid-dependent signaling. *J. Plant Physiol.* **2012**, *169*, 137–145.

122. Prigge, M.J.; Bezanilla, M. Evolutionary crossroads in developmental biology: *Physcomitrella patens*. *Development* **2010**, *137*, 3535–3543.

123. Jang, G.; Dolan, L. Auxin promotes the transition from chloronema to caulonema in moss protonema by positively regulating PpRSL1and PpRSL2 in *Physcomitrella patens*. *New Phytol.* **2011**, *192*, 319–327.

124. Saleh, O.; Issman, N.; Seumel, G.I.; Stav, R.; Samach, A.; Reski, R.; Frank, W.; Arazi, T. MicroRNA534a control of BLADE-ON-PETIOLE 1 and 2 mediates juvenile-to-adult gametophyte transition in *Physcomitrella patens*. *Plant J.* **2011**, *65*, 661–674.

125. Ton, J.; Flors, V.; Mauch-Mani, B. The multifaceted role of ABA in disease resistance. *Trends Plant Sci.* **2009**, *14*, 310–317.

126. Mauch-Mani, B.; Mauch, F. The role of abscisic acid in plant-pathogen interactions. *Curr. Opin. Plant Biol.* **2005**, *8*, 409–414.

127. Bari, R.; Jones, J.D. Role of plant hormones in plant defence responses. *Plant Mol. Biol.* **2009**, *69*, 473–488.

128. Grant, M.R.; Jones, J.D. Hormone (dis)harmony moulds plant health and disease. *Science* **2009**, *324*, 750–752.

129. AbuQamar, S.; Chen, X.; Dhawan, R.; Bluhm, B.; Salmeron, J.; Lam, S.; Dietrich, R.A.; Mengiste, T. Expression profiling and mutant analysis reveals complex regulatory networks involved in Arabidopsis response to *Botrytis* infection. *Plant J.* **2006**, *48*, 28–44.

130. Siewers, V.; Smedsgaard, J.; Tudzynski, P. The P450 monooxygenase BcABA1 is essential for abscisic acid biosynthesis in *Botrytis cinerea*. *Appl. Environ. Microbiol.* **2004**, *70*, 3868–3876.

131. Audenaert, K.; De Meyer, G.B.; Höfte, M.M. Abscisic acid determines basal susceptibility of tomato to *Botrytis cinerea* and suppresses salicylic acid dependent signaling mechanisms. *Plant Physiol.* **2002**, *128*, 491–501.

132. Yasuda, M.; Ishikawa, A.; Jikumaru, Y.; Seki, M.; Umezawa, T.; Asami, T.; Maruyama-Nakashita, A.; Kudo, T.; Shinozaki, K.; Yoshida, S.; *et al.* Antagonistic interaction between systemic acquired resistance and the abscisic acid-mediated abiotic stress response in *Arabidopsis*. *Plant Cell* **2008**, *20*, 1678–1692.

133. Rohwer, F.; Bopp, M. Ethylene Synthesis in Moss Protonema. *J. Plant Physiol.* **1985**, *117*, 331–338.

134. Osborne, D.J.; Walters, J.; Milborrow, B.V.; Norville, A.; Stange, L.M.C. Evidence for a non-ACC ethylene biosynthesis pathway in lower plants. *Phytochemistry* **1995**, *42*, 51–60.

135. Ishida, K.; Yamashino, T.; Nakanishi, H.; Mizuno, T. Classification of the genes involved in the two-component system of the moss *Physcomitrella patens*. *Biosci. Biotechnol. Biochem.* **2010**, *74*, 2542–2545.

136. Yasumura, Y.; Pierik, R.; Fricker, M.D.; Voesenek, L.A.; Harberd, N.P. Studies of *Physcomitrella patens* reveal that ethylene-mediated submergence responses arose relatively early in land-plant evolution. *Plant J.* **2012**, *72*, 947–959.

137. Díaz, J.; ten Have, A.; van Kan, J.A. The role of ethylene and wound signaling in resistance of tomato to *Botrytis cinerea*. *Plant Physiol.* **2002**, *129*, 1341–1351.

138. Penninckx, I.A.M.A.; Eggermont, K.; Terras, F.R.G.; Thomma, B.P.H.J.; De Samblanx, G.W.; Buchala, A.; Métraux, J.P.; Manners, J.M.; Broekaert, W.F. Pathogen-induced systemic activation of a plant defensin gene in Arabidopsis follows a salicylic acid-independent pathway. *Plant Cell* **1996**, *8*, 2309–2323.

139. Thomma, B.P.H.J.; Eggermont, K.; Tierens, K.F.M.J.; Broekaert, W.F. Requirement of functional ethylene-insensitive 2 gene for efficient resistance of Arabidopsis to infection by *Botrytis cinerea*. *Plant Physiol.* **1999**, *121*, 1093–1101.

140. Berrocal-Lobo, M.; Molina, A.; Solano, R. Constitutive expression of ETHYLENE-RESPONSE-FACTOR1 in Arabidopsis confers resistance to several necrotrophic fungi. *Plant J.* **2002**, *29*, 23–32.

141. Chague, V.; Elad, Y.; Barakat, R.; Tudzynski, P.; Sharon, A. Ethylene biosynthesis in *Botrytis cinere*a. *FEMS Microbiol. Ecol.* **2002**, *40*, 143–149.

142. Han, L.; Li, G.J.; Yang, K.Y.; Mao, G.; Wang, R.; Liu, Y.; Zhang, S. Mitogen-activated protein kinase 3 and 6 regulate *Botrytis cinerea*-induced ethylene production in Arabidopsis. *Plant J.* **2010**, *64*, 114–127.

143. Bandara, P.K.; Takahashi, K.; Sato, M.; Matsuura, H.; Nabeta, K. Cloning and functional analysis of an allene oxide synthase in *Physcomitrella patens*. *Biosci. Biotechnol. Biochem.* **2009**, *73*, 2356–2359.

144. Scholz, J.; Dickmanns, A.; Feussner, I.; Ficner, R. Crystal Structures of *Physcomitrella patens* AOC1 and AOC2: Insights into the Enzyme Mechanism and Differences in Substrate Specificity. *Plant Physiol.* **2012**, *160*, 1251–1266.

145. Stumpe, M.; Göbel, C.; Faltin, B.; Beike, A.K.; Hause, B.; Himmelsbach, K.; Bode, J.; Kramell, R.; Wasternack, C.; Frank, W.; *et al*. The moss *Physcomitrella patens* contains cyclopentenones but no jasmonates: mutations in allene oxide cyclase lead to reduced fertility and altered sporophyte morphology. *New Phytol.* **2010**, *188*, 740–749.

146. Hashimoto, T.; Takahashi, K.; Sato, M.; Bandara, P.K.G.S.S.; Nabeta, K. Cloning and characterization of an allene oxide cyclase, PpAOC3, in *Physcomitrella patens*. *Plant Growth Regul.* **2011**, *65*, 239–245.

147. Breithaupt, C.; Kurzbauer, R.; Schaller, F.; Stintzi, A.; Schaller, A.; Huber, R.; Macheroux, P.; Clausen, T. Structural basis of substrate specificity of plant 12-oxophytodienoate reductases. *J. Mol. Biol.* **2009**, *392*, 1266–1277.

148. Li, W.; Liu, B.; Yu, L.; Feng, D.; Wang, H.; Wang, J. Phylogenetic analysis, structural evolution and functional divergence of the 12-oxophytodienoate acid reductase gene family in plants. *BMC Evol. Biol.* **2009**, *9*, 90.

149. Vicedo, B.; Flors, V.; de la O Leyva, M.; Finiti, I.; Kravchuk, Z.; Real, M.D.; García-Agustín, P.; González-Bosch, C. Hexanoic acid-induced resistance against *Botrytis cinerea* in tomato plants. *Mol. Plant-Microbe Interact.* **2009**, *22*, 1455–1465.

150. Browse, J. Jasmonate passes muster: A receptor and targets for the defense hormone. *Annu. Rev. Plant Biol.* **2009**, *60*, 183–205.

151. Stintzi, A.; Weber, H.; Reymond, P.; Browse, J.; Farmer, E.E. Plant defense in the absence of jasmonic acid: The role of cyclopentenones. *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 12837–12842.

152. Taki, N.; Sasaki-Sekimoto, Y.; Obayashi, T.; Kikuta, A.; Kobayashi, K.; Ainai, T.; Yagi, K.; Sakurai, N.; Suzuki, H.; Masuda, T.; *et al*. 12-Oxo-phytodienoic acid triggers expression of a distinct set of genes and plays a role in wound-induced gene expression in Arabidopsis. *Plant Physiol.* **2005**, *139*, 1268–1283.

153. Mueller, S.; Hilbert, B.; Dueckershoff, K.; Roitsch, T.; Krischke, M.; Mueller, M.J.; Berger, S. General detoxification and stress responses are mediated by oxidized lipids through TGA transcription factors in Arabidopsis. *Plant Cell* **2008**, *20*, 768–785.

154. Staswick, P.E.; Su, W.P.; Howell, S.H. Methyl jasmonate inhibition of root-growth and induction of a leaf protein are decreased in an *Arabidopsis thaliana* mutant. *Proc. Natl. Acad. Sci. USA* **1992**, *89*, 6837–6840.

155. Vellosillo, T.; Martinez, M.; Lopez, M.A.; Vicente, J.; Cascon, T.; Dolan, L.; Hamberg, M.; Castresana, C. Oxylipins produced by the 9-lipoxygenase pathway in Arabidopsis regulate lateral root development and defense responses through a specific signaling cascade. *Plant Cell* **2007**, *19*, 831–846.

156. Yan, Y.; Stolz, S.; Chételat, A.; Reymond, P.; Pagni, M.; Dubugnon, L.; Farmer, E.E. A downstream mediator in the growth repression limb of the jasmonate pathway. *Plant Cell* **2007**, *19*, 2470–2483.

157. Chico, J.M.; Chini, A.; Fonseca, S.; Solano, R. JAZ repressors set the rhythm in jasmonate signaling. *Curr. Opin. Plant Biol.* **2008**, *11*, 486–494.

158. El Oirdi, M.; El Rahman, T.A.; Rigano, L.; El Hadrami, A.; Rodriguez, M.C.; Daayf, F.; Vojnov, A.; Bouarab, K. *Botrytis cinerea* manipulates the antagonistic effects between immune pathways to promote disease development in tomato. *Plant Cell* **2011**, *23*, 2405–2421.

159. Veronese, P.; Nakagami, H.; Bluhm, B.; Abuqamar, S.; Chen, X.; Salmeron, J.; Dietrich, R.A.; Hirt, H.; Mengiste, T. The membrane-anchored *Botrytis* induced kinase1 plays distinct roles in *Arabidopsis* resistance to necrotrophic and biotrophic pathogens. *Plant Cell* **2006**, *18*, 257–273.

160. Andersson, R.A.; Akita, M.; Pirhonen, M.; Gammelgård, E.; Valkonen, J.P.T. Moss-*Erwinia* pathosystem reveals possible similarities in pathogenesis and pathogen defense in vascular and nonvascular plants. *J. Gen. Plant Pathol.* **2005**, *71*, 23–28.

161. Palva, TK.; Hurtig, M.; Saindrenan, P.; Palva, ET. Salicylic Acid Induced Resistance to *Erwinia carotovora* subsp, *carotovora* in tobacco. *Mol. Plant-Microbe Interact.* **1994**, *7*, 356–363.

162. Dangl, J.L.; Dietrich, R.A.; Richberg, M.H. Death Don't Have No Mercy: Cell Death Programs in Plant-Microbe Interactions. *Plant Cell.* **1996**, *8*, 1793–1807.

163. Alvarez, M.E. Salicylic acid in the machinery of hypersensitive cell death and disease resistance. *Plant Mol. Biol.* **2000**, *44*, 429–442.

164. Yue, J.; Hu, X.; Sun, H.; Yang, Y.; Huang, J. Widespread impact of horizontal gene transfer on plant colonization of land. *Nat. Commun.* **2012**, *3*, doi:10.1038/ncomms2148.

165. Wang, B.; Yeun, L.H.; Xue, J.Y.; Liu, Y.; Ané, J.M.; Qiu, Y.L. Presence of three mycorrhizal genes in the common ancestor of land plants suggests a key role of mycorrhizas in the colonization of land by plants. *New Phytol.* **2010**, *186*, 514–525.