Review

Strangers in the matrix: plant cell walls and pathogen susceptibility

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Early in infection, pathogens encounter the outer wall of plant cells. Because pathogen hydrolases targeting the plant cell wall are well-known components of virulence, it has been assumed that wall disassembly by the plant itself also contributes to susceptibility, and now this has been established experimentally. Understanding how plant morphological and developmental remodeling and pathogen cell wall targeted virulence influence infections provides new perspectives about plant–pathogen interactions. The plant cell wall can be an effective physical barrier to pathogens, but also it is a matrix where many proteins involved in pathogen perception are delivered. By breaching the wall, a pathogen potentially reveals itself to the plant and activates responses, setting off events that might halt or limit its advance.

The plant cell wall, a dynamic matrix

The shape, architecture and biomechanical properties of plants and their organs are determined by the cell wall matrix surrounding each cell [1–3]. The primary cell wall is composed largely of complex and interacting polysaccharides with associated proteins, phenolic compounds and ions. The plant cell wall is not a static structure; it is subtly remodeled during cell growth, rearranged during organ development and disassembled during terminal processes such as organ abscission and fruit softening. The plant wall also is the interface for some of the earliest interactions between plants and a wide range of other organisms, including insects, pathogens and symbionts [4–7].

From the pathogen point of view, the plant cell wall is a nutrient source and a barrier that limits access to the cellular contents. Pathogenesis can involve discrete or extensive breakdown of the host extracellular wall matrix. Enzymes produced by pathogens target wall polysaccharides [4,8,9]. However, at times, plants also reduce the integrity of their own walls and this correlates, in many cases, with increased susceptibility. Fruit ripening is a clear example of a developmental transition in which endogenous wall disassembly is coincident with increased pathogen susceptibility. It has been speculated that wall disassembly by the plant contributes to pathogen susceptibility but, as reviewed here, only recently has this been established experimentally. These experiments demonstrated that plant cell wall degrading proteins (CWDPs), which cooperatively remodel, rearrange and disassemble plant wall polysaccharides (Table 1), influence pathogen susceptibility [4,5,10–13] (Figure 1).

But do alterations of the plant wall polysaccharide integrity *per se* limit or facilitate pathogenesis? Many proteins produced by plants in response to pathogens or involved in pathogen perception are extracellular, that is, they are secreted and located, at least partially, in the cell wall [14]. Alterations to the wall matrix during pathogenesis or normal plant developmental processes might influence the function, expression or localization of these proteins, affecting the outcome of plant–pathogen interactions. This review synthesizes current information about how plant and pathogen CWDPs modify the plant wall and affect its functions as a barrier, food source and matrix for extracellular pathogen-perceiving proteins and thus influence interactions between plants and their pathogens.

Pathogen cell-wall-degrading agents as virulence factors

Because much of the plant primary wall matrix consists of complex polysaccharides, these carbon-rich macromolecules might be catabolized as energy sources by pathogens [15]. Nevertheless, cell walls are physical barriers. Pathogen CWDPs are the primary means by which pathogens confront the cell wall and are important virulence factors [16–19]. Plant pathogens are traditionally divided into three classes: biotrophs that live at the expense of viable cells, necrotrophs that feed on dead biomass and hemibiotrophs that have a mixed lifestyle, behaving as biotrophs early and as necrotrophs later in their life cycles [20]. Although extensive plant tissue maceration typically is a feature of necrotrophic infections, plant wall disassembly is not limited to these pathogens, and both biotrophs and necrotrophs secrete diverse CWDPs. Understanding how pathogen CWDPs impact host wall integrity might suggest how these broadly used but specifically deployed virulence functions influence plant–pathogen interactions.

Biotrophic pathogens and plant cell wall degradation

Maintaining the viability of infected host cells is crucial for the survival of biotrophic organisms and so relatively little host wall lysis typically accompanies their establishment

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Table 1. Plant cell-wall-metabolism-associated genes that influence plant susceptibility to pathogens

Gene/mutant	Role	Phenotype	Refs
Pectin methyl esterase inhibitor (*AtPMEI-1, AtPMEI-2, CaPMEI1*)	Regulation of the activity of plant PMEs	Overexpression of *PMEI* in *Arabidopsis* reduces Infection by *Botrytis cinerea.* Virus-induced gene silencing of *CaPMEI1* in pepper increases susceptibility to *Xanthomonas campestris* pv. vesicatoria and resistance to *Pseudomonas syringae* pv. tomato	[10,11]
Extensin (*EXT1*)	Hyp-rich cell wall structural glycoprotein	Overexpression of *EXT1* in *Arabidopsis* reduces invasiveness of *Pseudomonas syringae*	[79]
Endo-β-1,4 glucanase (*Cel1, Cel2*)	Cell wall hydrolase	Suppression of the endo-β-1,4-glucanases Cel1 and Cel2 reduces susceptibility to *Botrytis cinerea* in tomato	[5]
Pectate lyase-like gene (*PMR6*)	Catalyzes the β-elimination cleavage of homogalacturonan pectins	Mutations in the *Arabidopsis PMR6* gene confer resistance to powdery mildew (*Erysiphe cichoracearum*)	[13]
Polygalacturonase (*PG*)	Catalyzes hydrolysis of the α-1,4-galacturonide links in homogalacturonan	Fruit with reduced PG were more resistant to *Geotrichum candidum* and *Rhizopus stolonifer* but were as susceptible to *Colletotrichum gloeosporoides* as wild type	[49,50]
Polygalacturonase-inhibiting protein (*PGIP*)	Inhibitor of pathogen polygalacturonases	Transgenic expression of pear PGIP in tomato and grape limits fungal colonization. Overexpression of *AtPGIP1* and *AtPGIP2*, confers resistance against *Botrytis cinerea* infection, and antisense suppression of the *Arabidopsis thaliana AtPGIP1* gene enhances susceptibility to *Botrytis cinerea*	[33–35]
Polygalacturonase and expansin (*PG+Exp1*)	Proteins participating in fruit ripening associated cell wall breakdown	The simultaneous suppression of polygalacturonase and expansin reduces susceptibility of tomato fruit to *Botrytis cinerea*	[4]
Cellulose synthase (*CESA4/IRREGULAR XYLEM5* [*IRX5*], *CESA7/IRX3, CESA8/IRX1*)	Synthesis of the β-1,4-glucans of cellulose microfibrils	Mutations in these proteins confer enhanced resistance to *Ralstonia solanacearum* and *Plectosphaerella cucumerina*	[81]
Pectin methylesterase (*FaPE1*)	Catalyzes the hydrolysis of methyl esters of homogalacturonan carboxyl groups	Trangenic wild strawberry (*Fragaria vesca)* fruits overexpressing *FaPE1* show increased resistance to *Botrytis cinerea*	[12]

[21]. The biotrophic smut fungus, *Ustilago maydis,* has relatively few CWDP-encoding genes: 33 in contrast to 138 in the hemibiotrophic *Magnaporthe grisea* and 103 in the necrotrophic *Fusarium graminearum* genomes [22]. Nonetheless, establishment of the haustorium, a specialized feeding structure, requires a local and precise breaching of the host cell wall (Figure 2a). A large opening through the host wall surrounds the haustorial neck (e.g. *Puccinia graminis*: external diameter ~600 nm [23]), suggesting that pathogen CWDPs have a crucial role in the establishment of biotrophic pathogen infections. This suggestion is supported in the case of the biotrophic ergot fungus, *Claviceps purpurea*; it produces two endo-polygalacturonases (endo-PGs) and both are required for virulence and growth between cells [17].

Necrotrophic pathogens and plant cell wall targets

Unlike most biotrophic pathogens, necrotrophic organisms secrete a substantial array of CWDPs targeting multiple plant cell wall polysaccharides and causing extensive tissue destruction (Figure 2b). Often, many pathogen CWDP isozymes with different substrate preferences and inde-

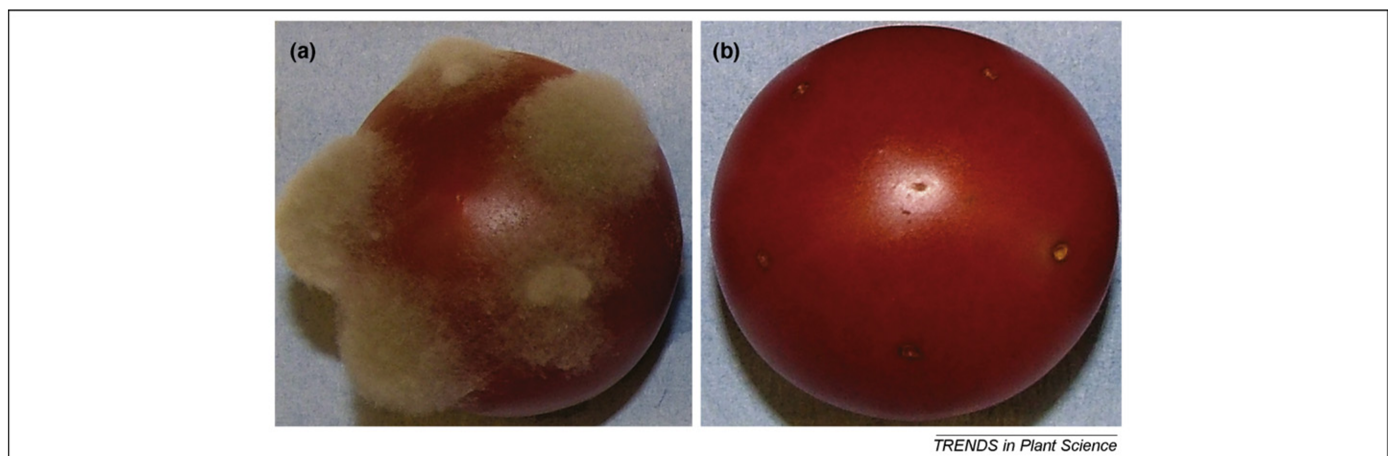

Figure 1. Endogenous plant cell wall metabolism influences plant susceptibility to pathogens. The simultaneous suppression of the cooperative plant cell-wall-modifying proteins polygalacturonase (PG) and expansin (LeExp1) reduced dramatically the susceptibility of ripe tomato fruit to the fungus *B. cinerea* [4]. **(a)** Wild-type Ailsa Craig tomato fruit and **(b)** fruit simultaneously suppressed for *LeExp1* and *PG* five days after inoculation. Fruit from both genotypes were harvested at the red ripe stage and inoculated with *B. cinerea* conidia on the day of harvest.

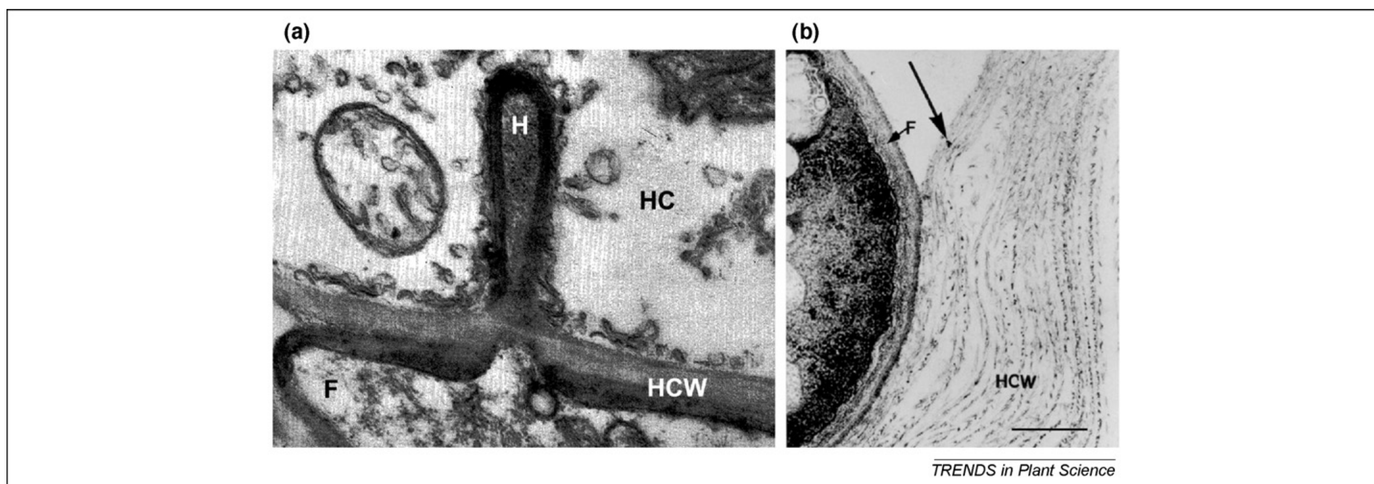

Figure 2. Images of the plant cell wall matrix during establishment of biotrophic and necrotropic pathogen infections. **(a)** The biotrophic fungus *Puccinia graminis* f. sp. *tritici* (F) penetrates the plant host cell (HC) with a haustorium (H). The developing haustorium protrudes through a conical opening with a ca. 600 nm diameter extending through the host cell wall (HCW). HCW penetration by the growing haustorium appears to be primarily chemical rather than physical. It should be appreciated how the cell wall breaching is precise and localized to allow viable host cell penetration by the fungus. The magnification is ×42 800. Reproduced, with permission, from Ref. [23]. **(b)** The colonization of plant host tissue by the necrotrophic fungus *B. cinerea* (F) is associated with extensive disassembly of the HCW. HCW shredding is evident and extensive HCW pectin digestion is suggested by the poor labeling of pectic substances with colloidal gold (arrow). The scale bar represents 500 nm. Reproduced, with permission, from Ref. [90].

pendent regulation but with similar catalytic mechanisms are produced, effectively targeting diverse structural wall polysaccharides [18,24–27]. As might be expected, mutagenesis of one or a few CWDPs does not necessarily lead to reduced virulence, implying enzyme redundancy [28–31]. For example, the gray mold, *Botrytis cinerea,* has at least six PGs (BcPGs) that are expected to hydrolyze partially de-esterified homogalacturonans, a major wall pectin [27]. The broad host range or specific pathogenic functions of this necrotroph might be associated with individual BcPGs because mutations in two of the six *BcPG*s result in reduced virulence [18,25]. Sequencing *BcPG1, BcPG2* and *BcPG3* from 34 *B. cinerea* isolates provided little evidence of host-mediated genetic subdivision among BcPGs [32]. *In vitro*, most of the BcPGs produced distinct pectin-degradation products [25]. Additional characterization of the preferred substrates for each BcPG might identify motifs that determine substrate specificity. The importance of necrotrophic pathogen PGs to virulence also has been demonstrated with plant-encoded proteins that selectively inhibit microbial PGs and reduce susceptibility [33–35].

Other pectin-modifying enzymes required by necrotrophic pathogens for full virulence include pectate lyases (PELs) and pectin methylesterases (PMEs). *Pseudomonas viridiflava* virulence has been attributed to a secreted PEL [16]. Decay of avocado (*Persea gratissima*) fruit by *Colletotrichum gloeosporioides* is reduced by disruption of *pelB* alone [19], whereas *Nectria haematococca* virulence on pea is dramatically reduced only when both of its PELs are suppressed [36]. Maceration of apple (*Pyrus malus*) fruit by *B. cinerea,* strain Bd90, is reduced in PME (*Bcpme1*) mutants [37], although virulence of the B05.10 strain on tomato (*Solanum lycopersicon*) and grape (*Vitis vinifera*) leaves is unaffected when both *Bcpme1* and *Bcpme2* are disrupted [38].

In general, most virulence-associated CWDPs are involved in pectin digestion, but recent work has shown that CWDPs that degrade the wall cellulose-hemicellulose network, specifically the xylans and xyloglucans, contribute to the success of some pathogens. A xylanase is associated with virulence of the bacterial leaf blight (*Xanthomonas oryzae* pv. oryzae) on rice (*Oryza sativa*) [39]. Disrupting the *B. cinerea* endo-β-1,4-xylanase, *xyn11A,* decreases macerating lesions on grape berries and tomato leaves, although the total endo-xylanase activity is only reduced by 30% [40].

Translocation through the plant cell wall

Pathogenic bacteria, such as *Pseudomonas syringae* and *Agrobacterium tumefaciens*, that employ a type III or type IV secretion system translocate effector proteins through plant cell walls via long, thin, flexible extracellular filaments or pili [41–43]. Pili penetrate the host plant's cell wall and thus might be expected to reduce the pathogen's dependency on CWDPs [44]. However, an *A. tumefaciens* PG mutant was unable to induce root decay and was less tumorigenic than wild-type strains [45], suggesting that the lack of PG might reduce the capacity of the bacteria to access nutrient sources in the host or limit transfer of the T-DNA through the host cell wall. Pili generally have an external diameter about as large as the largest plant cell wall pores (6–10 nm [46]). Mild exogenous pectinase treatments enlarge wall pores without compromising plant cell viability, and these treatments improve transformation of sunflower (*Helianthus annuus*) by *Agrobacterium* [46,47]. Thus, although it is not known how or whether the plant wall matrix affects the delivery of bacterial effectors, plant or microbial CWDPs and plant wall porosity probably have important roles.

All plant pathogens must, in some way, confront host cell walls. Necrotrophs target several parts of the cell wall polysaccharide matrix, causing extensive damage, but other pathogens transit the wall more subtly, using limited decomposition and physical structures and thereby preserving plant cell viability.

Plant-cell-wall-modifying proteins as susceptibility factors

Plant CWDPs modify the composition and structure of the wall polysaccharides as part of normal plant developmental programs. What has not been recognized previously is that plant CWDPs contribute to susceptibility to pathogens. Endogenous wall metabolism might facilitate pathogen infection, either because wall substrates are made more physically accessible to pathogen CWDPs or because the plant enzymes convert wall polymers into appropriate nutritional substrates for the invading microorganism. Observations suggest that plant CWDPs influence susceptibility, but given the complexity of interactions within the cell wall matrix, how does this disassembly facilitate pathogen infection? Is it by making nutrients more accessible or are other aspects of the plant–pathogen interaction altered?

Cell wall polysaccharide degradation by plant CWDPs and susceptibility to pathogens

Evidence that reduced wall integrity facilitates pathogen success comes from observations of mutant plants arrested in developmentally regulated fruit cell wall disassembly. Fruit from the tomato mutants, *Never ripe* (*Nr*) and *non-ripening* (*nor*), do not execute normal ripening-associated extensive wall disassembly and do not soften; they are also less susceptible to necrotrophic pathogens [48]. However, wall metabolism is just one of the many ripening-related changes that are affected by these mutations. This complexity leaves open the possibility that other differences unrelated to wall metabolism, such as altered levels of preformed antimicrobial compounds or perturbed induction of defense responses, are responsible for the reduced susceptibility. Fruit from another ripening-inhibited tomato mutant, *rin*, transgenically overexpressing *Cel2*, a putative cellulose- or hemicellulose-targeting β-1,4-endoglucanase, are more susceptible than normal nontransgenic *rin* fruit to gray mold, suggesting that this fruit CWDP contributes to susceptibility [5].

Plant CWDPs and pathogen susceptibility have been analyzed also in normally ripening fruit. Early work showed that tomato fruit with reduced PG were less susceptible to the necrotrophs *Rhizopus stolonifer* and *Geotrichum candidum* than unmodified fruit [49]. However, additional studies found that fruit with reduced PG expression were as susceptible to *Colletotrichum gloeosporoides* and *B. cinerea* as control fruit [4,50]. Suppressed expression of the tomato fruit ripening related expansin, *LeExp1,* increased firmness because expansins probably alter cellulose–hemicellulose interactions and influence the pectin depolymerization that normally accompanies ripening [51,52], but no differences in resistance to the necrophs *B. cinerea* and *Alternaria alternata* were observed [53]. By contrast, tomato fruit susceptibility to *B. cinerea* is dramatically reduced by the simultaneous suppression of expression of both *LePG* and *LeExp1* during ripening, an alteration that substantially increased firmness [4]. Because *B. cinerea* grew less well on walls isolated from uninfected PG- and expansin-suppressed fruit than on control fruit walls, a direct role for wall polysaccharide structure and composition in pathogen susceptibility was proposed. The wall swelling and pectin depolymerization that normally accompany tomato ripening are substantially reduced in the PG- and expansin-suppressed fruits, suggesting that these CWDPs, which cooperate in wall remodeling during ripening, influence the access of other fruit and fungal CWDPs to their polysaccharide substrates *in muro,* thus contributing to subsequent ripening-associated changes in texture and pathogen susceptibility. However, the induction of other pathogen responses as a result of the suppressed PG and expansin expression has not been ruled out as an explanation for the decreased susceptibility.

Pectate lyases are another class of pectin-modifying enzymes. At least one of the 29 *Arabidopsis* PEL-like genes, *PMR6,* is required for *Erisiphe cichoracearum* infection of vegetative tissues [13]. The phenotype of the *pmr6* mutant is not dependant on known inducible defense pathways, although *pmr6* leaves have increased wall pectins, suggesting that resistance is associated with modifications of the wall.

Pathogens also have mechanisms that hijack or induce plant cell wall disassembly functions. Parasitic nematodes stimulate *Arabidopsis* pectin acetylesterase (PAE) expression during feeding site establishment, thereby facilitating pectin degradation by other nematode CWDPs [54]. As the nematode *Heterodera schachtii* forms large multinucleate syncytial feeding structures in host roots, multiple *Arabidopsis* endo-1,4-β-glucanases and expansins are upregulated [55,56]. During the interaction between sweet clover and the bacterial symbiont *Sinorhizobium meliloti* [57], host cell expansion and nodule formation are accompanied by expansin expression, which probably promotes cell expansion as it does in elongating hypocotyl cells [58].

Cell wall modification by plant CWDPs and susceptibility to pathogens

Pectin methylesterase (PME) removes methyl esters from pectic polyuronides and consequently produces free carboxyl groups, modifies the pH and charge of the wall and allows the formation of calcium bridges, which might increase wall strength [59]. In addition, the major wall pectin, homogalacturonan, is cleaved more readily by PG and PEL after de-esterification [60]. *In vitro*, *B. cinerea* prefers unesterified polyuronides as a carbon source, and hosts with greater pectin esterification have reduced pathogen susceptibility [11]. Plant PME-inhibiting proteins (PMEIs) regulate polyuronide esterification and influence pathogen susceptibility [61,62]. Overexpression of *AtPMEI-1* or *AtPMEI-2* in *Arabidopsis* increased pectin methyl esterification and reduced susceptibility to *B. cinerea* without inducing defense responses [11]. In pepper (*Capsicum annuum*), overexpression of *CaPMEI1* increased resistance to *Pseudomonas syringae*, whereas silencing of *CaPMEI1* increased susceptibility to *Xanthomonas campestris* [10]. However, *Arabidopsis* plants overexpressing *PMEI* are susceptible to the biotroph *Hyaloperonospora parasitica* [11]. An *Arabidopsis pmr5* mutant with reduced pectin methyl- and acetyl-esterification and higher pectin content is more resistant to the powdery mildews *Erysiphe cichoracearum* and *E. orontii* [63].

In tomato, PME activity increases during early fruit development, declines late in ripening [64] and is associated with decreased pectin esterification [65]. Initial reports indicated that *PME* suppression had little effect on tomato fruit softening but drastically reduced tissue integrity only when the fruit are overripe [64]. However, recently Phan *et al.* [66] reported that suppressed *Pme1* expression resulted in fruit that softened faster than controls. Pathogen susceptibility has not been evaluated in *PME*-suppressed fruit.

In addition to the total overall pectin esterification, the distribution of esters (randomly along the homogalacturonan pectin backbone versus clustered in blocks) also influences susceptibility. Blockwise distribution of homogalacturonan methyl esters is associated with susceptibility to wheat stem rust (*Puccinia graminis* f. sp. *tritici*), whereas more random distribution of esterification sites is observed in resistant wheat genotypes [67], perhaps reflecting the substrate specificities of pathogen CWDPs.

Thus, although depolymerization of plant wall matrix polysaccharides by endogenous plant CWDPs facilitates susceptibility, other alterations to the polysaccharides might also influence susceptibility. Whether wall polysaccharide disassembly and modification *per se* influence susceptibility or lead to other changes in responses awaits a more complete dissection of wall polymer structures and new information about how changes in those structures are perceived.

Pathogen perception and plant response deployment

Plant and pathogen CWDPs directly affect wall structure and composition and thus increase pathogen susceptibility; however, degradation of the plant wall matrix also might reveal intruder presence and signal for responses, including timely wall reinforcement or plant responses that limit infections by pathogens [68]. What are the possible consequences of wall modifications that lead to altered pathogen perception and signaling?

Cell wall degradation and signaling

In addition to their role as a physical barrier, plant walls are a repository of extracellular pathogen-responsive proteins and a potential source of response-activating oligosaccharides. Cell wall pectin-derived oligosaccharides (PDOs), generated by microbial or plant CWPDs, apparently act as signaling molecules [69]. PDOs contribute to fruit-ripening regulation [70] and when applied exogenously can trigger defense responses [71]. The responses depend on the structure, size, esterification and concentration of the PDOs, and these characteristics are determined by plant and pathogen CWDPs acting either independently or simultaneously and cooperatively, as when a ripening fruit is infected [1,8,9,12,25,60,70,72–74].

Although previous research has focused on responses to exogenously applied, *in vitro*-produced PDOs [75,76], PDO generation and defense activation have been evaluated using transgenic plants with modified wall metabolism [12,77]. Overexpression of a strawberry (*Fragaria vesca*) fruit-specific PME reduced the methyl esterification of pectins and therefore the size of endogenous PDOs, presumably by exposing more pectin sites to cleavage by strawberry PGs and PELs [12]. This altered PDO population and constitutive activation of defenses might underlie the observed decreased susceptibility to *B. cinerea*.

Wall fortifications limit pathogen activities

Localized cell wall fortification has been shown to be part of plant defenses [68]. Deposition of phenolic compounds and crosslinkage of wall structural proteins are apparently responsible for the increased resistance to *B. cinerea* of abscisic-acid-deficient *sitiens* tomato leaves [78].

In *Arabidopsis*, overexpression of the hydroxyproline-rich glycoprotein extensin is involved in wall reinforcement that limits pathogen invasion [79]. Because defense response marker expression was not altered, extensive protein crosslinking in the wall *per se* might be sufficient for susceptibility differences. The simultaneous suppression of two putative endo-β-glucanases, *Cel1 and Cel2,* reduced tomato leaf susceptibility to *B. cinerea*, potentially due to the reduced glucanase activity; however, the timely deposition of callose, a potential defense-related wall reinforcement, was also observed [5].

Plant cell wall modifications influence response functions to pathogens

Modifications to the plant wall might indirectly determine resistance by constitutively activating pathogen responses. For example, the jasmonic acid pathway is activated in the *Arabidopsis* cellulose synthase mutant *cev1* [80]. Other cellulose synthase mutants have increased resistance to *Ralstonia solanacearum* and *Plectosphaerella cucumerina* as a result of the activation of salicylic acid-, ethylene- and jasmonic acid-independent signaling pathways and the expression of antimicrobial peptides and enzymes involved in the synthesis of antipathogen secondary metabolites [81].

Plant proteins that inhibit pathogen CWDPs reduce susceptibility to pathogens (reviewed in [82]). As in *B. cinerea*, *Xylella fastidiosa* PGs are virulence factors [18,83], and expression of the pear fruit PG-inhibiting protein (PGIP) in tomato [35] and grape [33] reduces susceptibility to *B. cinerea* and *X. fastidiosa*, respectively. *Vitis vinifera* PGIP expression reduces BcPG2-dependent maceration of *Nicotiana benthamiana*, even though no inhibition or interaction between the *B. cinerea* BcPG2 and the grape VvPGIP is observed *in vitro* [84], suggesting that some pathogen PG–plant PGIP interactions only occur *in muro*. PGIPs bind to pectins [85,86], and the ability of PGIPs to contribute to defenses might depend on the architecture of the wall. However, impacts of cell wall structure and development- and pathogen-related modifications on the placement of PGIPs and other apoplastic defense- and pathogen-related proteins have not been explored.

Although PGIPs selectively inhibit many pathogen and insect PGs [87], they do not inhibit ripening fruit PGs, and these PGIPs are expressed in fruit without pathogen challenge [88,89]. During fruit ripening, the fruit PG hydrolyzes pectins and thus reduces the association between PGIP and the wall (M. Egli and J. Labavitch, unpublished), potentially compromising PGIP's contribution to defenses.

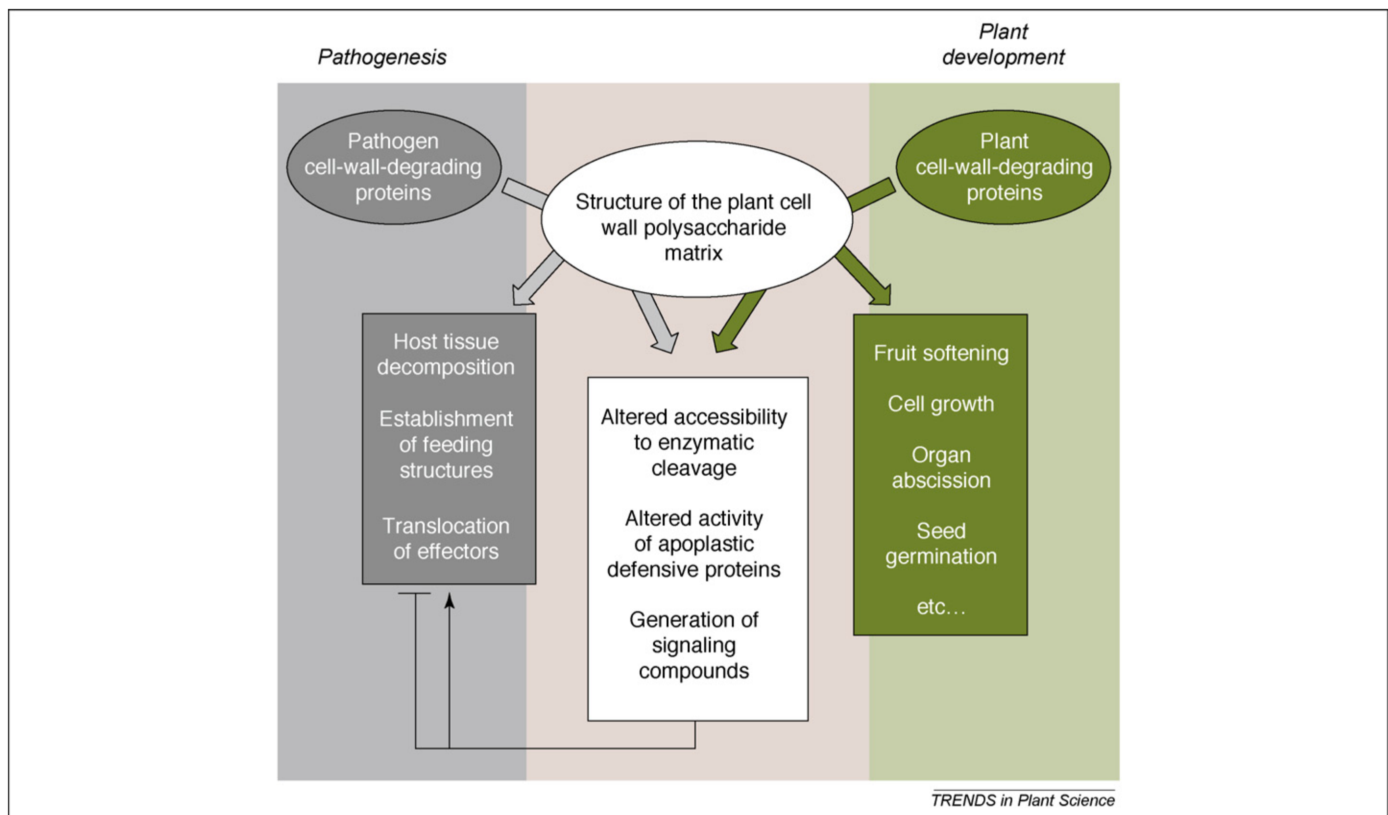

Figure 3. Schematic depiction of the outcomes of plant and pathogen cell-wall-degrading proteins (CWDPs) targeting polysaccharide structures within the plant cell wall matrix. The plant cell wall is a barrier to pathogens, but the plant wall polysaccharide matrix also can be a scaffold for pathogen sensing and responsive proteins and a source of pathogen-signaling molecules. In pathogenesis, the plant wall is the site of the earliest interactions between plants and pathogens and is the target of pathogen CWDPs that disassemble the wall polysaccharide matrix, facilitating infections by both necrotrophs and biotrophs. In plant development, the plant wall matrix is disassembled by plant CWDPs, and this apparently eases pathogen infection processes. As a barrier, a repository of signals and a nutrient source for pathogens, the plant cell wall polysaccharide matrix has a role in plant–pathogen interactions that is determined by the interplay between plant development, which involves modifications and disassembly of the wall, and pathogen virulence, which targets the polysaccharides within the plant wall.

The fact that the PG- and Exp-suppressed fruit do not display the normal ripening-associated increase in pathogen susceptibility [4] might result from the retention of PGIP in fruit walls because pectin disassembly is limited.

Box 1. Questions to be answered

On the plant side

- Do plant CWDPs or inhibitors of pathogen CWDPs cooperate in determining susceptibility or resistance, and how is this cooperation executed?
- How do apoplastic and membrane-anchored proteins that extend into the apoplast interact with the cell wall matrix, and how do modifications to wall architecture influence the position, retention and activity of pathogen responsive/sensing proteins?
- What are the chemical structures and the *in muro* activities of PDOs, and do they contribute to information sharing between plants and pathogens?

On the pathogen side

- What are the *in planta* functions of multiple, independently regulated pathogen CWDPs?
- Are the pathogen CWDP isoforms redundant in function, thus insuring against the loss of key functions, or does each have a particular role, thus ensuring the pathogen's success?

Concluding remarks and perspectives

Because the plant cell wall is the matrix where pathogens and plants initiate their interaction, *in muro* events have a substantial impact on the outcome. The wall is a barrier to pathogens, but it is also a source of pathogen-signaling molecules and can be a scaffold for plant proteins involved in sensing and responding to pathogens. The wall is the target of pathogen CWDPs, and disassembly of the wall polysaccharides facilitates infections by necrotrophs and biotrophs. Wall disassembly by plant CWDPs also enables infection processes. The extent to which the plant cell wall can serve as a barrier, a source of signals or a reservoir of nutrients for pathogens is determined by the interplay between plant developmental processes that involve wall modification and disassembly and pathogen virulence processes that affect wall polysaccharide integrity (Figure 3). However, important questions remain unanswered (Box 1). Understanding the interactions between plants and pathogens when they meet within the plant cell wall matrix provides an opportunity to listen in on molecular conversations between members of different kingdoms and, potentially, learn new ways to enhance plant protection.

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