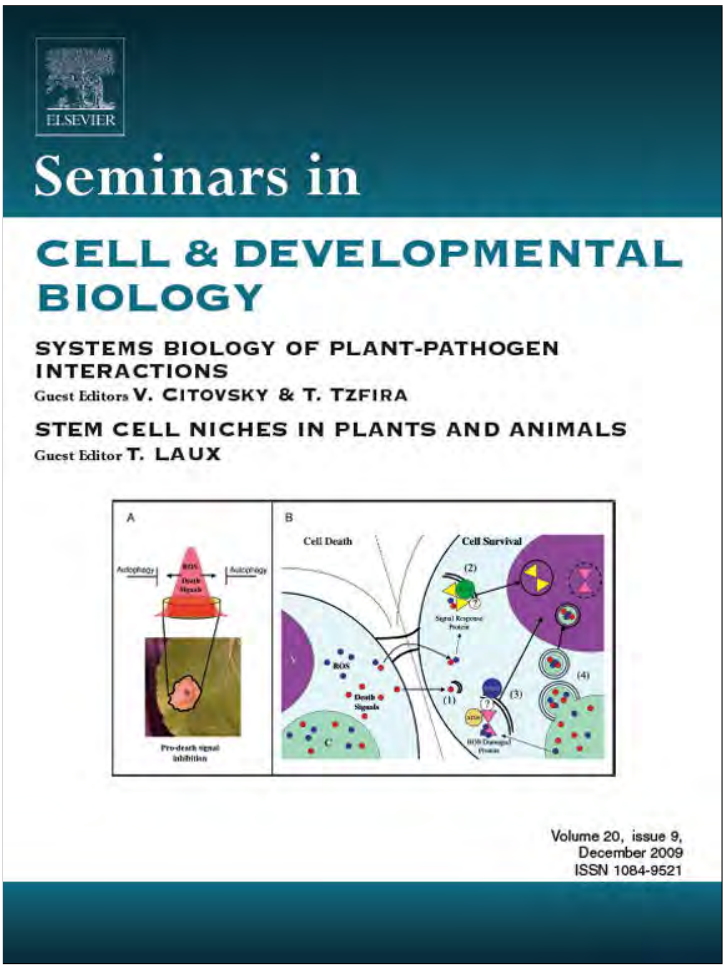

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Review

Proteasomal degradation in plant–pathogen interactions

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ABSTRACT

The ubiquitin/26S proteasome pathway is a basic biological mechanism involved in the regulation of a multitude of cellular processes. Increasing evidence indicates that plants utilize the ubiquitin/26S proteasome pathway in their immune response to pathogen invasion, emphasizing the role of this pathway during plant–pathogen interactions. The specific functions of proteasomal degradation in plant–pathogen interactions are diverse, and do not always benefit the host plant. Although in some cases, proteasomal degradation serves as an effective barrier to help plants ward off pathogens, in others, it is used by the pathogen to enhance the infection process. This review discusses the different roles of the ubiquitin/26S proteasome pathway during interactions of plants with pathogenic viruses, bacteria, and fungi.

Contents

1. Introduction

Plants are constantly exposed to pathogenic microorganisms, such as bacteria, viruses, and fungi. Like animals, they have evolved immune responses to combat infection. However, a fundamental difference between plant and animal immunity is the lack of a somatic adaptive response system and mobile responder cells in the former: instead, the plant makes use of the innate immune mechanisms of individual cells and utilizes systemic signals originating from the site of infection (reviewed in [1]). When a pathogen invades plant tissue, its components, proteins or nucleic acids, are recognized by various disease–response mechanisms, such as antiviral immunity based on small RNAs (reviewed in [2]) or a network of plant disease resistance (R) proteins (reviewed in [1,3]).

Increasing evidence implicates the ubiquitin/26S proteasome pathway (reviewed in [4])—a basic biological mechanism involved in the regulation of many of cellular processes, including animal immunity [5]—in the R-protein-mediated plant immune response [6–8]. However, the ubiquitin/26S proteasome defense mechanism does not always function for the benefit of the plant that wields it.

Abbreviations: PCD, programmed cell death; TMV, *Tobacco mosaic virus*; VIGS, virus-induced gene silencing; SCF complex, Skp1/Cullin/F-box protein complex; R protein, resistance protein; RISC, RNA-induced silencing complex.

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Some pathogens have evolved the ability to subvert the host's proteasomal degradation pathway to enhance their infection. Here, we discuss different aspects of the involvement of the ubiquitin/26S proteasome pathway in interactions of plants with pathogenic viruses, bacteria, and fungi.

2. Overview of the ubiquitin/26S proteasome pathway

Cellular processes require the removal of proteins that are misfolded or foreign, or whose function is no longer required. These proteins are targeted to proteolytic degradation by tagging them with polymeric chains of ubiquitin. Ubiquitin is a small protein composed of 76 amino acids, which is highly conserved among eukaryotes. Its name reflects its ubiquitous expression in essentially all eukaryotic cells. Ubiquitin tagging and polymerization occur at lysine residues. The first ubiquitin monomer in the polyubiquitin chain attaches to a lysine residue on the target protein, followed by attachment of additional ubiquitin subunits to lysine 48 of the previously attached monomer. While attachment of ubiquitin monomers through lysine residues 29 and 63 during the process of polyubiquitination has been reported, it is believed that this alternative polyubiquitin chain structure is intended for cellular processes other than protein degradation [9]. Polyubiquinated proteins are recognized and degraded by the 26S proteasome, consisting of the 19S regulatory particle that recognizes, selects and binds the polyubiquitinated proteins, cleaves the polyubiquitin chains and forwards the targeted polypeptide into the lumen of the 20S core particle, where proteolytic degradation takes place [10,11].

Polyubiquitination of a target protein requires ubiquitin-activating (E1) and ubiquitin-conjugating (E2) enzymes, as well as ubiquitin ligase (E3) (reviewed in [12]). E1 activates ubiquitin monomers and transfers them to the conjugating enzyme E2, which either attaches them to the target protein by itself or is directed to do so by the E3 ligase. E3 ligases represent the largest and most diverse group of ubiquitinating enzymes. This diversity makes biological sense. E3 ligases have evolved to target a wide spectrum of cellular as well as foreign, e.g., pathogen-derived, proteins destined for degradation by the 26S proteasome. This diversity of targets requires a comparable diversity of the E3 ligases that recognize them. Presently, there are four known E3 ligase families: HECT, SCF, APC, and RING/U-box, classified based on their subunit composition and mechanism of action (reviewed in [12,13]), which include hundreds of protein species. The *Arabidopsis* genome, for example, encodes over 1200 different components of the E3 ligase complexes [13,14]. The base function of E2 enzymes is to carry the activated ubiquitin moiety to the target polypeptide, and they are therefore frequently referred to as ubiquitin-carrier (UBC) proteins. Because E2 enzymes are often targeted to their substrates by the E3 ligases, they need not be significantly diversified, and only a few dozen of them are found in the genome of *Arabidopsis* [13,14]. Finally, only two genes coding for the E1 enzymes, which catalyze ATP-mediated ubiquitin activation, are found in the *Arabidopsis* genome [13,14], placing the ubiquitin-activating E1 enzymes at the apex of the E-enzyme hierarchy of diversity, followed by more diverse E2 enzymes and the highly diverse components of the E3 ligase complex.

One of the better studied E3 ligases (reviewed in [12]) is the Skp1/Cullin/F-box protein (SCF) complex [15,16]. Yeast SCF complexes have been extensively characterized, and they consist of a scaffold protein, Cdc53 or Cullin, a ubiquitin-conjugating enzyme Cdc34, Rbx1 which helps recruit and activate Cdc34, and Skp1 which recruits the F-box protein (reviewed in [16,17]). F-box proteins—a highly diversified type of polypeptide with almost 700 predicted members in the *Arabidopsis* proteome [18]—are responsible for substrate recognition of the SCF complex. The F-box motif is typically located in the protein's N-terminal region, and it mediates interaction with the rest of the SCF complex via Skp1, while the highly variable C terminus of F-box proteins mediates interaction with the target protein. Thus, by associating with different F-box proteins, SCF complexes can be targeted to different and specific substrate proteins [17].

In plants, F-box proteins have been shown to play a key role in a variety of cellular functions and developmental processes [15,19–22], and they are also beginning to emerge as a crucial factor in plant immunity and defense mechanisms [23,24]. A number of ubiquitin/26S proteasome pathway-related genes are now known to be involved in plant–pathogen interactions. Below, we focus on specific examples of how proteasomal degradation is involved in plant defense responses to pathogens and how some plant pathogens can take over this component of the host defense system (summarized in Fig. 1).

3. Proteasomal degradation and plant viral infection

3.1. Proteasomal degradation and R-protein-mediated defense

The plant response to pathogens often relies on the conserved network of R-proteins (reviewed in [1,3]). Most R-proteins fall into five distinct classes based on their structural motifs. The *N* gene of tobacco (*Nicotiana tabacum*), mediating the innate plant response to *Tobacco mosaic virus* (TMV) [6,25,26], encodes a class 3 R-protein, defined by leucine-rich repeats, a putative nucleotide-binding site and an N-terminal region with similarity to the Toll-Interleukin 1 Receptor (TIR) proteins [3,27]. The *N* gene confers resistance to TMV by inducing a hypersensitive response and necrosis, which confines the virus to the local site of infection [26].

One of the key components acting downstream of multiple R-proteins, including the tobacco *N* gene product, and upstream of peroxide-induced cell death, is RAR1, implicated in defense mechanisms in a variety of plant species [28–30]. The *RAR1* gene of *Nicotiana benthamiana* is required for functionality of the *N*-gene-mediated defenses [6]. RAR1 interacts with SGT1, a conserved component of the SCF complex, which binds to Skp1 [31,32]. All three proteins, RAR1, SGT1 and SKP1, are also present in a single complex *in planta* [6]. Both RAR1 and SGT1 interact *in vivo* with CSN4, one of the components of the COP9 signalosome, a complex involved in protein degradation via the ubiquitin/26S proteasome pathway [33]. SCF and COP9 complexes act in concert, and COP9 has been shown to play a key role in mediating the E3 ubiquitin ligase activity of SCF [34]. Suppression of either SGT1, SKP1—and thus the entire SCF complex—or the COP9 signalosome using virus-induced gene silencing (VIGS) in transgenic *N. benthamiana* plants carrying the tobacco *N* gene abolished the normal *N*-gene-mediated response to viral infection. Since the SCF and COP9 complexes are directly involved in the ubiquitin/26S proteasome pathway, it is likely that the resistance mediated by the *N* gene is based on SCF/COP9 targeting of specific cellular proteins, such as negative regulators of defense response and/or apoptosis inhibitors, directing them to proteasomal degradation and allowing initiation of the anti-pathogen response and programmed cell death (PCD) of the infected cells. Notably, the *N*-gene-mediated resistance mechanism may be conserved among different plant species, as overexpression of *Arabidopsis SGT1* was able to rescue *N*-gene responses in *SGT1*-suppressed *N. benthamiana* plants [6].

3.2. Proteasomal degradation of viral movement proteins

Plant viruses spread from cell to cell via the plasmodesmata, the plant's intercellular connection. Viral movement through plasmodesmata is facilitated by virus-encoded movement proteins (MPs) (reviewed in [35–37]). While MP sequences are not significantly

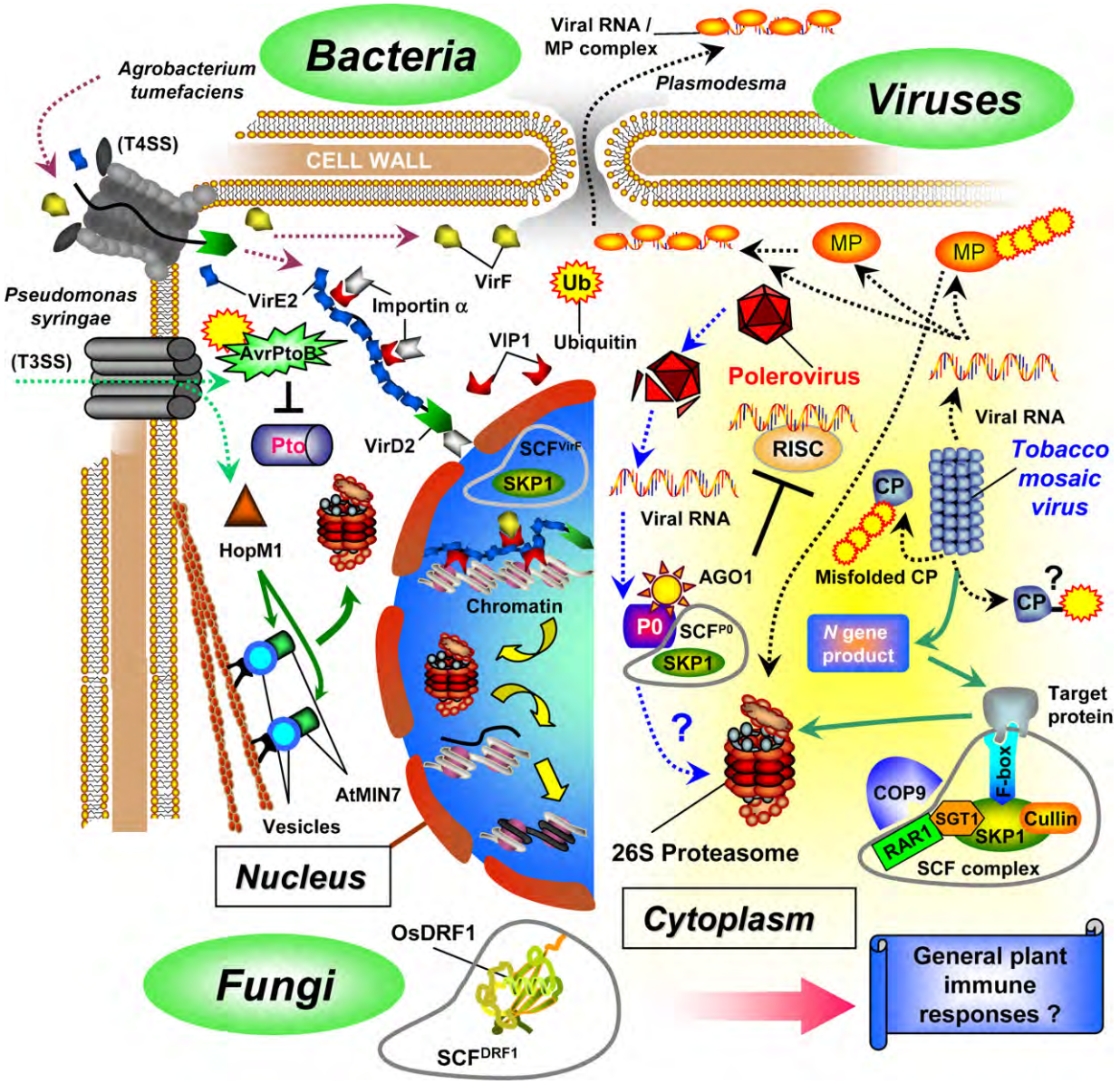

Fig. 1. Summary of the key processes involving proteasomal degradation in plant–pathogen interactions. Viruses: *Tobacco mosaic virus* (TMV) intrusion activates the *N* gene-mediated response, which involves the SCF complex. The TMV movement protein (MP) and misfolded coat protein (CP) are polyubiquitinated and degraded by the proteasome. The TMV coat protein (CP) is also monoubiquitinated, but the role of this monoubiquitination remains obscure. Poleroviral RNA silencing suppressor P0 is an F-box protein that targets AGO1, a key component of the RISC complex, and destabilizes via the SCF^{P0} pathway, thereby inhibiting silencing of the viral RNA by the host. Bacteria: uncoating of the *Agrobacterium* T-complex prior to T-DNA integration and/or expression is promoted by the bacterial F-box protein VirF, exported into the host cell with via the type IV secretion system (T4SS). VirF binds the host VIP1 protein which, in turn, associates with the T-complex packaging protein VirE2, these interactions direct VIP1 and VirE2 to degradation by the 26S proteasome via the SCF^{VirF} pathway. *Pseudomonas syringae* AvrPtoB effector protein, exported into the host cell via the type III secretion system (T3SS), is detected by the plant cell Pto resistance protein, conferring resistance. In susceptible plants which lack Pto, AvrPtoB interacts with ubiquitin and, presumably, the host proteasomal degradation machinery to inhibit PCD response and promote disease progression. An additional P. syringae effector protein, HopM1, destabilizes a vesicle trafficking-related protein AtMIN7, contributing to suppression of host responses to the infection. Fungal pathogens are counteracted by a general immune defense F-box protein OsDRF1, which likely functions in the SCF^{DRF1} complex. For further details, see text.

conserved among different viral families [38], many MPs possess a set of common properties, including the ability to bind single-stranded nucleic acids, interact with the cytoskeleton and increase the size-exclusion limit of plasmodesmata to allow transport of MP-viral genomic RNA complexes through these intercellular connections (reviewed in [35–37]). One of the models for MP function involves binding to the viral genome, docking it to plasmodesmata, and then facilitating its transport into the neighboring cell by increasing the plasmodesmal size-exclusion limit (reviewed in [35–37]).

MPs of several plant viruses may be targeted by the proteasomal degradation machinery of the host cell. For example, treatment of virus-infected tobacco protoplasts with proteasomal inhibitors MG115 or *clasto*-lactacystin-β-lactone resulted in the accumulation of polyubiquitinated forms of MP, indicating involvement of the 26S proteasome in MP turnover [39]. Similarly, MP of *Turnip yellow mosaic virus* (TYMV) has been shown to be a substrate for polyubiquitination [40].

What remains unclear, however, is whether it is the plant defense response or the virus itself that triggers proteasomal degradation of MPs. On the one hand, the MP is central for the spread of viral infection, which makes it an obvious target for the host defense machinery. On the other hand, MP accumulation is detrimental to the host, for example, due to its deposition in and interference

with plasmodesmata [41] and/or disruption of the cell endoplasmic reticulum [42]. Removal of excess MP, therefore, is important to maintain host viability, which is required for persistent viral infection. In this case, targeting of excess MP to the ubiquitin/26S proteasome pathway may represent an example of exploitation of the host cellular pathway by the virus for effective invasion. Interestingly, suppression of the host ubiquitination machinery leads to increased plant resistance to TMV infection, supporting the notion that MP-targeted proteolysis is beneficial to the pathogen. Perturbation of the plant ubiquitin system by expression of a ubiquitin variant with a lysine-to-arginine substitution at position 48 inhibited TMV infection [43], suggesting that the host ubiquitin/26S proteasome pathway may, in fact, assist viral attack.

While plant viruses move locally from cell to cell via plasmodesmata in non-vascular tissues, systemic, long-distance viral transport occurs though the phloem (reviewed in [35,44]). This systemic movement is impaired by inhibition of the 26S proteasome. Specifically, VIGS-mediated silencing of RPN9, one of the 26S proteasome subunits, has been shown to inhibit the systemic spread of two taxonomically distinct viruses, TMV and *Turnip mosaic virus* (TuMV), in *N. benthamiana* [45]. RNP9 is involved in auxin transport and brassinosteroid signaling, two processes that are crucial for vascular tissue formation. Thus, the effect of the ubiquitin/26S proteasome on viral systemic movement may be indirect, via developmental disruption of the viral spread conduit, the host vasculature [45].

Unlike TMV MP, TMV coat protein (CP) is only monoubiquitinated [46]. Because just a minute portion of the total TMV CP that accumulates in the infected cells undergoes monoubiquitination [46], and poly-, rather than monoubiquitination, is required for protein targeting to proteasomal degradation, CP monoubiquitination may not be important for CP turnover. Instead, it may play a regulatory role in an as-yet undetermined event during the TMV–host interaction. At the same time, misfolded TMV CP is massively polyubiquitinated in tobacco cells, apparently directing it to the conventional proteasomal degradation pathway [47].

3.3. Involvement of proteasomal degradation in the activity of viral RNA-silencing suppressors

In addition to R-protein-mediated immunity, plants have evolved another innate immune response to invading viruses, which is based on post-transcriptional RNA silencing [48–51]. In most cases, this response is induced by viral genomic or transcript RNA molecules, and it involves conversion of single-stranded RNA into double-stranded RNA by RDR6 (reviewed in [52–54]). Double-stranded RNAs are then processed by the cellular machinery to produce small interfering (si) RNAs that are incorporated into RNA-induced silencing complexes (RISCs), within which siRNAs direct the cleavage of the complementary viral transcripts [55,56].

To counteract the plant's antiviral response, many viruses encode suppressor proteins that block host RNA silencing by targeting different steps of the silencing pathway [57–60]. One of these viral RNA-silencing suppressors, the P0 protein of poleroviruses, is an F-box protein that interacts with the host cell's SKP1 protein. This interaction occurs via the P0 F-box domain, and it is required for the biological activity of P0 [61], indicating that this viral silencing suppressor may function within an SCF^{P0} complex. P0 also interacts directly with the key component of the RISC, ARGONAUTE1 (AGO1), destabilizing it [62,63]. Surprisingly, however, the P0-induced degradation of AGO1 is not affected by the proteasomal inhibitor MG132 [62], leaving the question of the 26S proteasome's involvement in P0 activity unresolved. Nevertheless, the fact that a plant virus has evolved an F-box protein to hijack the host SCF complexes for suppression of antiviral defense suggests that the cellular SCF pathway not only acts to protect the plant against viruses (as in the case of the *N* gene), but is also exploited by the invading virus to facilitate infection.

4. Proteasomal degradation in fungal and bacterial infection

4.1. Proteasomal degradation in antifungal defense

Recently, the rice (*Oryza sativa*) defense-related F-box 1 (OsDRF1) protein has been identified and shown to participate in plant antifungal defenses [64]. Expression of OsDRF1 is induced by treatment with benzothiadiazole, a general inducer of the plant defense response [65–67], as well as by inoculation with the rice blast fungus *Magnaporthe grisea* [64]. Importantly, when the *OsDRF1* gene was introduced into the genome of a heterologous plant species, tobacco the resulting transgenic plants exhibited enhanced resistance to viral (*Tomato mosaic virus*, ToMV) and bacterial (*Pseudomonas syringae*) pathogens, indicating the general nature of OsDRF1's function in plant defense [64]. OsDRF1 could potentially represent one of the key regulators of plant immunity, for example, by destabilizing a conserved inhibitor(s) of the defense response. This idea gains support from the observations that, in response to salicylic acid treatment or ToMV inoculation, the expression levels of two general defense-related genes, *PR-1a* and *Sar8.2b* [68], were elevated to a higher degree in *OsDRF1*-transgenic tobacco than in the wild-type plants, suggesting that OsDRF1 enhances the overall responsiveness of plant defense [64]. However, because expression of OsDRF1 was not induced by general stress factors, this F-box protein is most likely specific to the plant's immune, rather than general, stress responses [64].

4.2. Proteasomal uncoating of Agrobacterium T-DNA

Both animal and plant bacterial pathogens use type III and/or type IV secretion systems to inject host cells with effector proteins, which often mimic the functions of the eukaryotic factors that are required for infection and provided by the host cells (reviewed in [69]). One of *Agrobacterium tumefaciens*' effector proteins is an F-box protein that insinuates itself into the host ubiquitin/26S proteasome pathway and subverts it to enhance infection (reviewed in [5,69]).

Agrobacterium is a phytopathogenic gram-negative soil bacterium that causes crown-gall disease in plants, manifested by neoplastic growths resulting from integration of transferred DNA (T-DNA), derived from the bacterial tumor-inducing (Ti) plasmid, into the plant nuclear genome (reviewed in [70–72]). Besides being a natural phytopathogen, *Agrobacterium* is perhaps the most commonly used vector for gene transfer into plants, in both research and biotechnology applications [73], representing a unique example of natural trans-kingdom DNA transfer. Furthermore, under laboratory conditions, *Agrobacterium* has the capacity to genetically transform virtually any eukaryotic cell [74].

Agrobacterium T-DNA transfer is induced by plant-specific signals, usually wound-released phenolic compounds, that activate the virulence (*vir*) gene region on the Ti plasmid. The T-DNA is then mobilized from the Ti plasmid as a single-stranded DNA molecule (T-strand) by the VirD1/VirD2 helicase/endonuclease protein complex. The effectors of the T-strand, with a single molecule of VirD2 covalently attached to its 5′ end as well as several Vir proteins, are introduced into the plant cell via the type IV secretion system. In the host-cell cytoplasm, the T-strand is packaged by the bacterial single-stranded DNA-binding protein VirE2. The resulting transfer (T) nucleoprotein complex is imported into the host-cell nucleus via the cellular importin α pathway. The T-complex is then targeted to the host chromatin and stripped of its protein components, and the T-strand integrates into the host genome

(reviewed in [71–73,75,76–79]). The native *Agrobacterium* T-DNA encodes a set of plant oncogenes [80] which promote uncontrolled division of the transformed cells, as well as genes specifying the production of opines—amino acid and sugar phosphate derivatives secreted by the transformed cells and utilized almost exclusively by the *Agrobacterium* as a carbon and nitrogen source [81]. Different *Agrobacterium* strains are classified as octopine or nopaline types, according to the class of opines encoded by their T-DNA [81].

Nuclear import of the T-complex and its chromatin targeting are facilitated by the host VirE2 Interacting Protein 1 (VIP1), which binds to VirE2, importin α and nucleosomes, acting as a molecular adaptor between the T-complex and, first, the nuclear import machinery and then, the chromatin [82–86]. Whereas the protein components of the T-complex, such VirE2 and its associated VIP1, are critical for its intracellular movement, they become a liability before integration as they physically mask the DNA molecule. Thus, once the T-complex reaches the host chromatin, its proteins must be removed. Recent evidence suggests that another exported *Agrobacterium* effector, VirF, may promote this uncoating. VirF is an F-box protein that interacts with the plant SKP1 proteins [87,88]. VirF also binds VIP1 and destabilizes it in plant and yeast cells [88], which are known to be genetically transformed by *Agrobacterium* [89,90]. Furthermore, VirF, which does not recognize VirE2, can promote VirE2 destabilization in the presence of VIP1 [88], suggesting that VirF can destabilize the entire VIP1–VirE2 complex. In yeast, VIP1 and VirE2 destabilization by VirF is Skp1-dependent as it does not occur in a s*kp1-4* mutant [91], indicating that this destabilization occurs via the SCF^{VirF} pathway [88]. That VirF may help to uncoat the T-complex docked at the host chromatin is supported by the ability of VirF to associate simultaneously with purified VIP1, VirE2, single-stranded DNA and nucleosomes *in vitro* [82]. The involvement of the 26S proteasome in *Agrobacterium* infection is consistent with the inhibitory effect of the proteasomal inhibitor MG132 on the transformation process [88].

Historically, VirF, which is encoded by the octopine-type, but not nopaline-type *Agrobacterium* strains, has been considered a bacterial host-range factor [92–94]. For example, VirF enhances *Agrobacterium* infectivity in tomato and tree tobacco (*Nicotiana glauca*) [94], but it is not required for infection of tobacco or *Arabidopsis*. Thus, plant species whose infection does not require VirF may encode F-box protein functions that can substitute for VirF during transformation. Our recent experiments (AZ, AK, VC, unpublished) have identified such an *Arabidopsis* F-box protein, which is induced by *Agrobacterium* infection and promotes proteasomal destabilization of VIP1 and VirE2 in yeast and *in planta*. Collectively, these data suggest that *Agrobacterium* has evolved to utilize the host ubiquitin/26S proteasome system for enhancement of its infectivity and expansion of its host range.

4.3. 26S proteasome in R-protein-mediated response to *Pseudomonas syringae*

Another case of a bacterial effector that is delivered to the host plant cell and likely participates in proteasomal degradation is AvrPtoB of *P. syringae*. This protein is exported from the bacterium via the type III secretion system and functions to prevent the host PCD response to infection (reviewed in [95]). To counteract AvrPtoB, tomato plants resistant to *P. syringae* express a native R-protein, Pto, which recognizes AvrPtoB and elicits a hypersensitive response, leading to rapid localized PCD which limits the infection. In the susceptible tomato plants, which lack Pto, AvrPtoB suppresses PCD, allowing efficient infection and development of the disease [96,97]. The C-terminal domain of AvrPtoB shares homology with the RING/U-box family of E3 ubiquitin ligases. It possesses E3 ligase activity *in vitro* [7], and interacts specifically with the tomato ubiquitin [8]. Inactivation of the E3 ligase activity of AvrPtoB leads to its loss of function, and transient expression of such a mutated AvrPtoB in tomato leaves was unable to suppress PCD. Furthermore, *P. syringae* expressing the mutant AvrPtoB lost its anti-apoptotic ability and exhibited significantly suppressed virulence in tomato [7].

Yet another *P. syringae* effector protein exported into the host cell, HopM1 [98], has been shown to interact with *Arabidopsis* immunity-associated (AtMIN) proteins [99]. Transient expression of HopM1 in *N. benthamiana* leaves or bacterial infection of *Arabidopsis* resulted in reduced levels of the AtMIN7 protein. Importantly, HopM1 did not affect *AtMIN7* transcription, while the proteasomal inhibitors MG132 and epoxomicin completely blocked the HopM1-mediated reduction in AtMIN7 protein level [99]. Thus, HopM1 likely binds and destabilizes AtMIN7 via the ubiquitin/26S proteasome pathway. Because HopM1 does not share homology with the E3 ligases, it most probably serves as a molecular linker between AtMIN7 and the bona fide proteasomal degradation machinery of the host cell. Interestingly, AtMIN7 may be involved in the vesicle trafficking system which is linked to the polarized cell-wall-associated defense in plants [100,101]. Destabilization of AtMIN7 promoted by HopM1, which also localizes to the host-cell endomembrane system [99], may therefore disable vesicular trafficking in the host cell, thereby suppressing cellular defenses.

5. Concluding remarks

Plant cell proteasomal degradation pathways may play a dual role in the infection process (summarized in Fig. 1): they may represent the host's defense against the pathogen, as in the case of tobacco *N*-gene-mediated resistance, or they may present the pathogen with an opportunity to enhance its infectivity, as in the case of proteasomal uncoating of the *Agrobacterium* T-complex. In other cases, the beneficiary is less clear: does TMV, the host, or both benefit from reduced levels of TMV MP following proteasomal degradation?

This ambivalent role of proteasomal degradation in the plant defense response may result from the close co-evolution of plants and their pathogens. It is likely that some 26S proteasome-based immune responses, initially employed by plants to ward off invaders, have been subverted by pathogens in the course of evolution. Interestingly, similar "hijacking" of the ubiquitin/26S proteasome pathway to circumvent host immune responses is employed by animal pathogens. Examples of such pathogens include the human cytomegalovirus (HCMV), whose US11 protein contributes to proteasomal degradation of major histocompatibility complex class I molecules, thus evading recognition by the host immune system [102], or the human papillomavirus (HPV) oncoprotein E6, which promotes proteasomal degradation of the cellular tumor suppressor protein p53 [103]. So is the 26S proteasome friend or foe in the plant's encounter with pathogens? The answer may be: both.

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