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At the molecular plant–nematode interface: New players and emerging paradigms

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Abstract

Plant-parasitic nematodes (PPNs) secrete an array of molecules that can lead to their detection by or promote infection of their hosts. However, the function of these molecules in plant cells is often unknown or limited to phenotypic observations. Similarly, how plant cells detect and/or respond to these molecules is still poorly understood. Here, we highlight recent advances in mechanistic insights into the molecular dialogue between PPNs and plants at the cellular level. New discoveries reveal a) the essential roles of extra- and intracellular plant receptors in PPN perception and the manipulation of host immune- or developmental pathways during infection and b) how PPNs target such receptors to manipulate their hosts. Finally, the plant secretory pathway has emerged as a critical player in PPN peptide delivery, feeding site formation and non-canonical resistance.

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Cell–surface receptor, Cyst nematode, Nematode effector, NLR immune receptor, Parasite, Peptide mimic, Plant–nematode interaction, Root–knot nematode, Secretory pathway.

Introduction

Plants have evolved a multilayered immune system consisting of extra- and intracellular immune receptors to protect themselves from invading organisms, including plant-parasitic nematodes (PPNs). In return, PPNs have evolved a range of molecular tools to evade and modulate host immunity, similar to animal parasitic nematodes [1]. This is particularly true for obligatory sedentary endoparasitic PPNs with a biotrophic lifestyle like cyst (CNs) and root-knot nematodes (RKNs), which fully depend on their hosts for development and reproduction. To complete their life cycle, CNs and RKNs spend 4–8 weeks inside host roots where they induce the formation of a highly metabolically active feeding site for nutrient uptake [2]. In this review, we explore recent advances (last 1–3 years) in the field of molecular plant–nematode interactions with an emphasis on mechanistic studies that contribute to novel insights at the host–parasite interface. Here, we define interface as the biochemical, molecular–genetic, or functional interaction between nematode-derived compounds and extra- and intracellular plant receptors involved in development and immunity. Moreover, we investigate to which extent novel concepts in the broader field of host–pathogen interactions apply to plant–nematode interactions to provide a new perspective on not only how plants detect and respond to PPNs, but also how PPNs cope with and adapt to their hosts. Specific examples of CNs and RKNs are highlighted to identify emerging topics that can aid in building new research hypotheses and directions in—but not limited to—the field of molecular plant nematology.

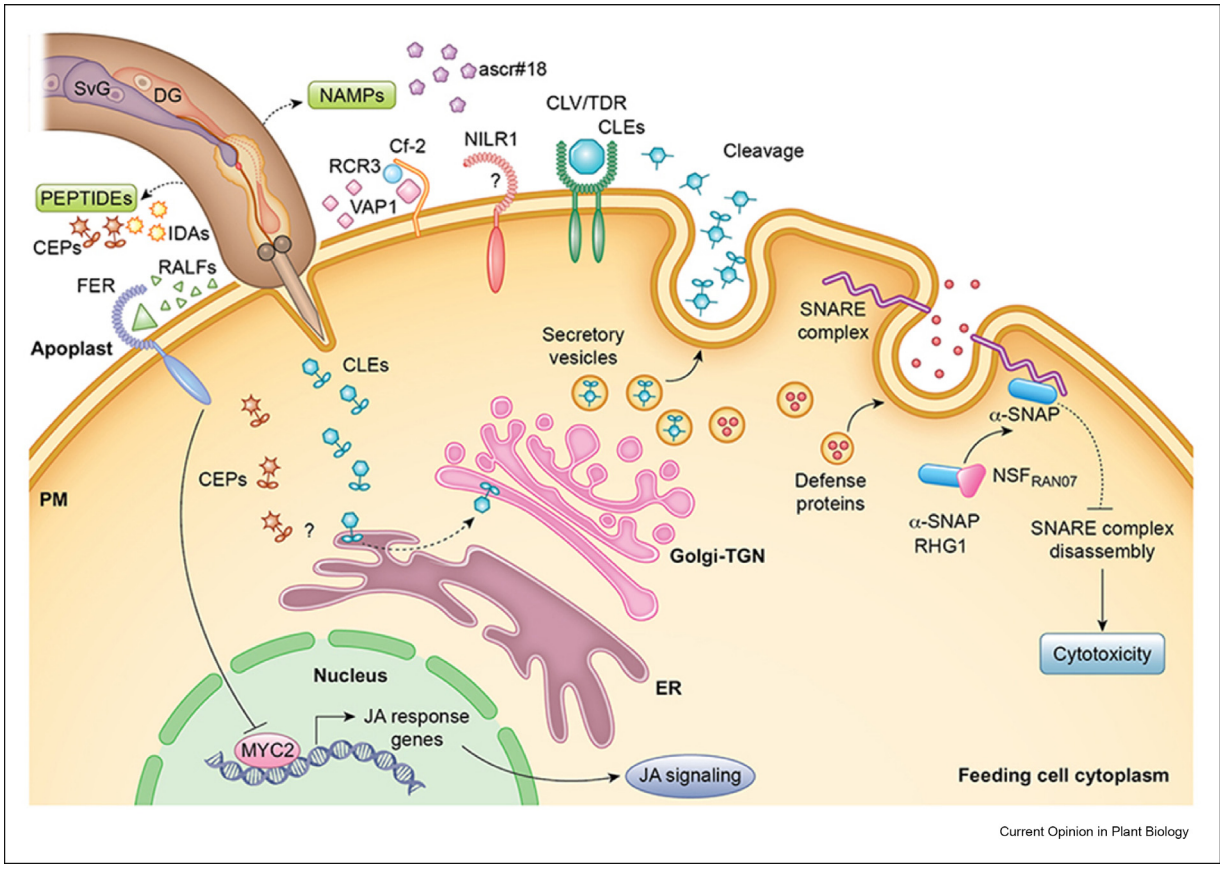
Scratching the surface: Extracellular receptors shaping the host–parasite interface

Cell–surface receptors involved in the perception of nematode-derived compounds

Infectious juveniles of CNs and RKNs invade the root system of host plants upon hatching and migration through the soil. A cocktail of nematode-derived compounds mainly produced in the salivary gland cells is passively or actively released in both the rhizosphere prior to invasion and inside the root upon host entry and feeding site initiation [3]. This allows the plant's surveillance system to detect the presence and activity of PPNs, resulting in the activation of defense responses [4]. Cell–surface receptors (CSRs) are thought to play a key role in this process. However, little is known about the contribution of CSRs at the host–parasite interface. Although the conserved

nematode ascaroside pheromone ascr#18 was identified as a nematode-associated molecular pattern (NAMP) [5], it is unknown how this compound is perceived by plant cells, although it most likely involves receptor(s) located at the cell surface. The first identified nematode CSR conferring basal immunity to PPNs is nematode-induced LRR-RLK 1 (NILR1), but the active component(s) in so called NemaWater (water collected after incubation with infective juveniles) that acts as a NAMP are not yet identified to our knowledge. The active compound(s) is likely of peptide origin due to its reported heat lability and protease-sensitive nature [6]. CSRs also play a role in effector-triggered immunity (ETI) as demonstrated for the *Cladosporium fulvum* resistance (*R*) gene Cf-2, which encodes a tomato receptor-like protein (RLP). Cf-2 confers not only apoplastic immunity to a fungus, but also to the CN *Globodera rostochiensis* through perturbation of the secreted papain-like Cys protease (PLCP) RCR3 by the CN effector venom–allergen protein 1 (VAP1) [7]. This remains the only PPN effector-CSR pair known to trigger host-specific defense responses. Given the rich blend of nematode-derived compounds released at the host–parasite interface, it is expected that plants have evolved a spectrum of CSRs to detect PPNs or their activities in the apoplast (Figure 1). Their potential as novel sources of resistance to counteract PPNs in plants is yet underexplored. It will be interesting to see if the perception of unrelated

Figure 1



Emerging roles for plant cell surface receptors and the host secretory machinery in nematode parasitism and host defense. Distinct nematode-derived compounds, spanning NAMPs (ascaroside #18 (ascr#18) [5]) and effectors, are released into the apoplast or cytoplasm, which can be perceived by multiple known cell–surface receptors (CSRs; nematode-induced LRR-RLK 1 (NILR1) [6], *Cladosporium fulvum* 2 (Cf-2) [7], CLAVATA (CLV) [14], TDIF receptor (TDR) [15], FERONIA (FER) [8**]) and others yet to be identified, resulting in the downstream activation/suppression of host immune or developmental pathways. PPNs exploit CSRs to counteract apoplastic immunity or to promote parasitism by the release of peptide effectors, including CLAVATA3/embryo surrounding region (CLEs) [11], rapid alkalinization factor (RALFs) [8**], inflorescence deficient in abscission (IDAs) [47], and C-terminally encoded peptide (CEPs) [48], some of which may be directly delivered to the apoplast and others to the cytoplasm of host cells. Two critical roles for the host secretory machinery has emerged: first, to allow nematode CLE (and possibly CEP) peptide effectors to reach the apoplast for hijacking CSRs to mediate feeding site formation [13**] and second, to prevent the host plant cell from forming a feeding site by the induction of a non-canonical cytotoxic defense response [19,20**]. DG, dorsal gland cell; ER, endoplasmic reticulum; JA, jasmonic acid; MYC2, basic-helix-loop-helix (bHLH) transcription factor; NAMP, nematode-associated molecular pattern; PM, plasma membrane; α-SNAP, α-soluble NSF attachment protein; NSF$_{RAN07}$, *Rhg1*-associated NSF on chromosome 07; RCR3, papain-like Cys protease; RHG1, resistance to *Heterodera glycines* 1; SNARE, soluble NSF attachment protein receptor; SvG, subventral gland cell; TGN, trans-Golgi network; VAP1, venom-allergen protein 1.

nematode-derived compounds by different CSRs ultimately converges on conserved downstream defense pathways to prevent host invasion.

Exploiting the host secretory machinery to target cell–surface receptors in the apoplast

PPN peptide mimics are a class of secreted effectors that trigger developmental pathways through CSRs ([10]). In contrast to what is likely to be direct apoplastic delivery of peptides such as rapid alkalinization factor (RALF) peptide mimics by RKN [8**], CNs deliver CLAVATA3/embryo surrounding region (CLE)-like peptide mimics into the host cell cytoplasm ([11]; Figure 1]. To reach their intended apoplastic destination and garner plant-specific glycosylation patterns [12], these peptide mimics exploit the host cell secretory machinery. A recent study shows how CLEs utilize a conserved translocation motif (VD-T) within their "pro" (variable) domains to facilitate post-translational trafficking through the endoplasmic reticulum secretory pathway to their apoplastic destination ([13**]; Figure 1). In the apoplast, CLEs target one or more CSRs involved in stem cell signaling pathways as a means to co-opt host developmental programs for feeding site formation [14,15]. While the mechanisms of CLE peptide effector processing by host proteases and the recognition of these processed peptides by their respective receptor/s remains mostly unknown, it is increasingly evident that CN CLEs display signatures of adaptation to the hosts they selectively parasitize. Outside the conserved VD-T domain, there is considerable sequence divergence across CN CLEs both within and among species that is known to contribute to host-specific recognition [11,13**]. The recognition of plant CLE peptides by CSRs relies on host post-translational modification (PTM) including proteolytic cleavage to release one or more bioactive peptides [16], as well as conserved and differential binding specificities of the peptide itself [17]. Therefore, CN CLE effector sequence diversification at the proteolytic cleavage sites and/or within the peptide domain may underly host-range restriction and expansion events. This possibility was highlighted in a recent study linking CN *Heterodera sacchari* CLE peptide effectors with adaptation to their monocot hosts. In a comparative sequence analysis, the authors reveal a greater degree of sequence and functional conservation of *H. sacchari* CLEs with host versus non-host plant CLEs [18*] in support of a role for CLEs in shaping host-range in CNs. Moreover, secretion of diverse peptides may expand the nematodes' peptide effector repertoires for simultaneous perception by multiple CSRs as a means to modulate the growth-defense balance of the host for feeding site formation. Recently, RALFs were discovered from PPN for the first time [8**]. So far unique to RKN, these peptide mimics target CSRs for host immune suppression. RKN RALFs were shown to suppress basal immunity by targeting the CSR FERONIA (FER) in Arabidopsis and rice roots [8**], and the FER homolog LMM1 (lesion mimic mutant 1) in soybean [9].

Disruption of host cell vesicular trafficking as a new paradigm in driving non-canonical resistance to PPN

Non-canonical plant resistance mechanisms that counteract PPN infection by blocking some housekeeping pathways also exploited by PPN for parasitism, is an emerging paradigm in molecular plant-nematode interactions. This is highlighted by recent studies in soybean showing how resistant plants locally disrupt their own secretory pathway to prevent CN feeding site formation. A picture has emerged (Figure 1) in which atypical α-soluble N-ethylmaleimide sensitive factor (NSF) attachment proteins (α-SNAPs) from the resistance locus to *Heterodera glycines* 1 (*RHG1*) are unable to bind NSF and accumulate locally within host cells selected by the nematode for feeding site establishment. . Hyperaccumulation of atypical α-SNAPs prevents SNARE complex disassembly, which disrupts cellular vesicular trafficking leading to feeding site toxicity [19]. In uninfected resistant plants, the RHG1 α-SNAP is stabilized against the cytotoxic effects of dysfunctional vesicular trafficking by its atypical NSF binding partner (RAN07) to maintain plant viability [20**]. Recent studies have also highlighted a new and unknown role of a γ-SNAP [21], and α-SNAP - t-SNARE (syntaxin) interactions have unveiled a potential linkage between vesicular trafficking and the mitochondrial apoptotic pathway [22,23]. Thus, it is clear that scientific research to date has only scratched the surface of understanding non-canonical resistance pathways. Moreover, newly discovered epistatic interactions between these atypical *R* genes and pleiotropic effects against more than one PPN add additional layers of complexity [24*,25]. Whether these forms of resistance or components thereof are unique to soybean or extend to other plant species awaits further study.

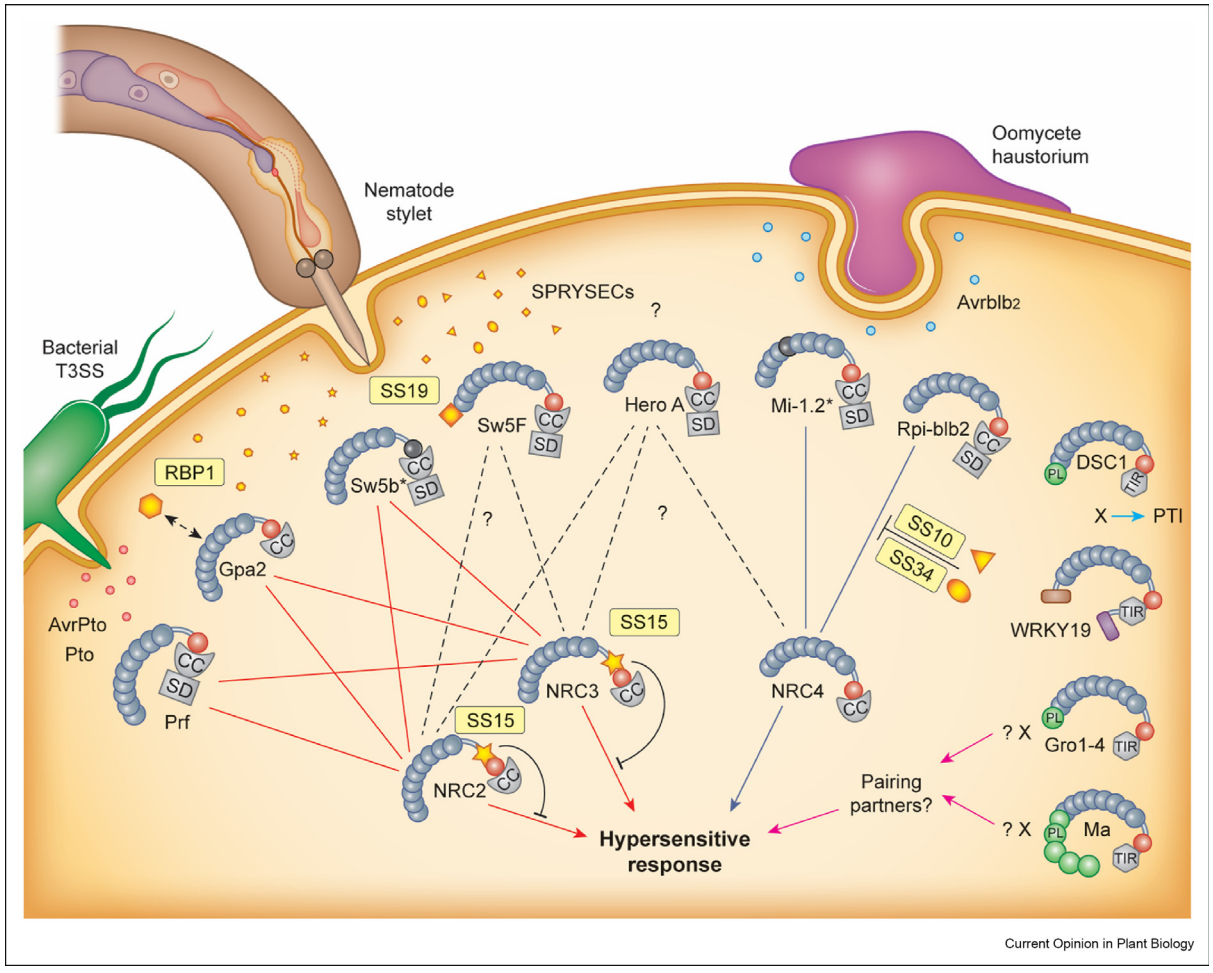
Insights inside: Concerted actions of intracellular NLR immune receptors in plant resistance against PPNs

Typical and atypical toll-interleukin resistance (TIR)-like receptors (TNLs) involved in plant resistance against PPN: Partners in crime?

In addition to CSR, plants contain intracellular nucleotide binding leucine-rich repeat receptors (NLRs) to detect pathogen-derived effectors or their activities inside the cell [26]. Although PPN are no exception to this rule, only a few NLR immune receptors have been identified and characterized in the last two decades. However, it is expected that their numbers will increase, as PPN resistance loci often map in genomic regions containing *R* gene clusters encoding NLR immune receptors. NLRs can be subdivided into TNLs or coiled-coil (CC) receptors (CNLs) depending on their N-

terminal domain [26]. Currently, two TNLs involved in PPN resistance are known: Gro1-4 conferring host-specific resistance to the CN *G. rostochiensis* in potato [27] and Ma conferring complete-spectrum resistance to RKN in Prunus [28]. Ma contains an atypical, expanded C-terminal region with five duplicated exons each corresponding to a post-LRR (PL) domain. This domain, with an unknown role and structure, is often present as a single domain in other TNLs, including Gro1-4 [29,30*]. TNLs often show a strict pairing with a helper/sensor NLR for proper functioning [31]. Mutation in a conserved motif of a PL-domain of RPS4 (Resistance to *Pseudomonas syringae*) impaired the resistance mediated by the RPS4/RRS1 (Resistance to

Figure 2



An emerging picture of two branches of the concerted action of intracellular NLR immune receptors in plant immunity to PPN. The first branch consists of the two genetically linked TIR-NB-LRR genes (TNLs) DSC1 and WRKY19, which co-regulate basal defense to RKN in Arabidopsis [33*]. TNLs encoded by the known *R* genes *Gro1-4* from potato [27] and *Ma* from Prunus [28] may also act as NLR pairs in concert with a yet unknown TNL pairing partner to confer host-specific resistance to CNs and RKNs, respectively (pink lines). The second branch consists of known CN and RKN *R* genes encoding the CC-NB-LRR (CNLs) immune receptors Gpa2 [35], Hero A [36] and Mi-1.2 [37], which are part of a large redundant NLR signaling network in Solanaceae where they group together with other sensor NLRs encoded by *R* genes like *Sw5b* conferring resistance to tospoviruses, *Prf* conferring bacterial resistance upon Pto-mediated detection of AvrPto and *Rpi-blb2* conferring resistance to late blight upon Avrblb2 detection [42]. Whereas Gpa2 depends on the helper NLRs NRC2 and NRC3 like Sw5b and Prf (red lines), Mi-1.2 depends on the helper NRC4 similar to Rpi-blb2 (blue lines) [42]. CN SPRYSEC (SS; orange icons) effector variants SS10 (triangle), SS15 (star), SS19 (square), and SS34 (oval) target different nodes of this NLR signaling network upon secretion by the nematode into the cytoplasm. SS10 and SS34 block effector-dependent Rpi-blb2 activity upstream of NRC4, whereas SS15 binds to the NB-ARC domain (red subunit) of the helpers NRC2 and NRC3 to block downstream activity of Gpa2, Prf and Sw5b* [43**]. SS19 binds specifically to the LRR domain (grey subunits) of Sw5F, but the functional implications are unknown [43**]. Still, SS19 can suppress RBP-1 (hexagonal) induced Gpa2 and Sw5b* cell death activity, but not Mi-1.2* auto activity [49]. This suggests that NRC2/NRC3 dependent defense pathways are targeted, but this needs to be proven. Also, the role of NRC helpers in HeroA and Sw5F functioning requires further testing (dashed lines). SD, Solanaceae Domain; CC, coiled-coil domain; TIR, toll-interleukin-resistance domain; PL, Post-LRR domain; T3SS, type III secretion system; Mi-1.2* and Sw5b*, autoactive mutants Mi-1.2^{T557S} and Sw5b^{D857V} (position of the mutations indicated in black subunits); PTI, PAMP-triggered immunity.

Ralstonia solanacearum) pair, suggesting a role for this domain in immune signaling and/or pairing [32]. Whether this is also the case for the PL domain in Gro1-4 and Ma needs further investigation and requires the identification of a corresponding (genetically-linked) partner similar to RRS1 to demonstrate the formation of a functional immune complex involved in CN and RKN resistance (Figure 2). Interestingly, the first evidence for a role of NLR gene pairs in plant defense to PPN was obtained for the TNL immune receptor DOMINANT SUPPRESSOR OF Camta 3 NUMBER 1 (DSC1) and the atypical TNL-WRKY-MAPx protein WRKY19, which co-regulate susceptibility of Arabidopsis to RKN [33*]. Their head-to-head orientation in the Arabidopsis genome shows remarkable similarity with that of RRS1 and RPS4 [34], suggesting they may function as a TNL immune receptor pair. However, no molecular or biochemical evidence has been provided yet to support this idea. Unlike other TNL pairs involved in dominant disease resistance in plants, DSC1/WRKY19 seem to regulate basal levels of immunity to RKN. This implies that the role of TNLs may extend beyond their typical role in *R* gene-mediated nematode resistance.

Sensor NLRs involved in PPN detection depend on NRC helper NLRs for their activity

Currently, three CNLs encoded by major *R* genes to PPN are known: *Gpa2* conferring pathotype-specific resistance to *Globodera pallida* in potato [35] and *Hero A* and *Mi-1.2* conferring broad-spectrum resistance to either CN (*G. pallida* and *G. rostochiensis*) [36] or RKN [37] in tomato, respectively. How NLRs confer immunity to PPN is largely unknown, since their molecular and functional characterization is hampered by the paucity of matching nematode effectors. Only for Gpa2 the corresponding CN effector Ran-binding protein-like-1 (RBP-1) is known [38], providing a unique molecular tool set to study the mechanisms underlying NLR-mediated immunity to nematodes in plant cells, including effector detection and immune receptor functioning [39]. As an alternative, autoactive NLR mutants can be generated to study their molecular function until a matching effector is identified as was shown for Mi-1.2 [40,41]. Using this approach, it was recently discovered that these NLRs do not act on their own but with the help of other NLRs within a larger immune signaling network. In Solanaceae, this network consists of helper NLRs of the NLR required for HR-associated cell death (NRC) family that form functionally redundant pairs with different sensor NLRs encoded by known *R* genes to confer intracellular immunity to oomycetes, bacteria, viruses, insects, and nematodes [42]. In the context of this NLR network, known nematode *R* genes from potato and tomato, encoding intracellular NLR immune receptors, are considered to act as sensors in nematode detection upstream of NRC helper proteins (Figure 2). Mi-1.2 depends on NRC4 for its function, as silencing of NRC4 compromised the plant's ability to elicit a hypersensitive cell death response mediated by the autoactive mutant Mi-1.2^{T557S}. In contrast, Gpa2 depends on NRC2 and NRC3, as silencing of these helper NLRs prevented a cell death response upon detection of the matching effector RBP-1 [43**]. Hero A also belongs to the superclade of sensor NLRs [42] and is thus expected to depend on NRC helper(s) as well. It is yet unknown if and how NRC helpers contribute to PPN resistance in plant roots, since only the effect on effector-dependent (Gpa2) and effector independent (Mi-1.2 ^{T557S}) cell death was tested.

PPN effector variants target different nodes of the NLR signaling network in Solanaceae

In return, PPN have evolved effectors to counteract NLR immunity [44]. The SPRY domain containing secreted (SPRYSEC) effector family constitutes by far the most diversified effector family in CNs with more than 30 variants in the genome of the potato cyst nematode *G. pallida*. These effectors, which range between 23 and 30 kDa in size, are secreted into the cytoplasm during early infection and for several members an immune suppression phenotype is reported [45,46]. However, the underlying molecular mechanisms were unknown until the recent discovery that specific SPRYSEC (SS) family members target different nodes of the NLR immune network in Solanaceous plant species [43**] (Figure 2). Whereas SS10 and SS34 were able to suppress the activity of the sensor NLR Rpi-blb2 from potato conferring resistance to the oomycete *Phytophthora infestans*, they were unable to suppress cell death triggered by the autoactive NRC4 helper NLRs indicating that they act upstream in the NLR immune network. For SS15, however, immune suppression of different sensor NLRs was shown to be dependent on the specific downstream targeting of the helper NLRs NRC2 and NRC3 *in planta*. SS15 interacts directly with the nucleotide binding-Apaf1-resistance-CED4 (NB-ARC) domain of NRC2 *in vitro* and binds both autoactive and inactive NRC mutants, indicating that this nematode effector can form a complex with specific helper NRCs pre- and post-activation. From this, a model was proposed in which SS15 can block the function of helper NRCs either by preventing conformational changes or complex formation with up- or downstream components or PTM of the NRC helper proteins. While targeting different central nodes in the NLR network by SPRYSECs may be highly beneficial for CNs to evade immunity, this is likely counterbalanced by the development of novel sensor NLRs in the host to detect the presence or activity of the effectors. It is expected that selection pressure imposed by sensor NLR detection on SPRYSEC effectors then

drives further diversification to escape host recognition. If so, SPRYSEC diversity may reflect the complexity of the NLR signaling network in Solanaceous hosts and could explain the remarkable expansion of the SPRYSEC effector family in CNs during host adaptation.

Conclusions

Studies focused on the host−parasite interface have led to exciting discoveries in our understanding of the molecular mechanisms underlying plant nematode parasitism. Similar to other pathogens, CSRs play key roles in the perception of PPN effectors, including peptide mimics. In addition to the direct release of such compounds into the apoplast, the host secretory machinery is hijacked in a yet unprecedented fashion to deliver mimics of endogenous peptide signals - both locally and at a distance—to the cell surface to promote feeding site expansion. It will be interesting to see if similar strategies for peptide or effector delivery have been adopted by other pathogens as well. In return, plants evolved to modify their secretory machinery to evoke a cytotoxic response leading to feeding site collapse. Fascinating discoveries await as to how the non-canonical resistance protein complex detects nematodes and how nematodes evolve novel virulence activities around it. Similarly, the exciting discovery of effector variants targeting nodes of the NLR immune network will not only aid in understanding how PPNs evolve virulence activities to evade host recognition and defense activation, but also shows the potential of PPNs to suppress core components of the plant immune system. The wider implications of immunosuppression by PPNs on the immunity of plants to other pathogens in a multitrophic context also warrants further study. The answers to these questions will be critical for scientists to bioengineer more durable disease resistance while maintaining crop yield.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest
** of outstanding interest

1. Bobardt SD, Dillman AR, Nair MG: **The two faces of nematode infection: virulence and immunomodulatory molecules from nematode parasites of mammals, insects and plants**. *Front Microbiol* 2020, **11**:577846, https://doi.org/10.3389/fmicb.2020.577846.

2. Siddique S, Grundler F: **Parasitic nematodes manipulate plant development to establish feeding sites**. *Curr Opin Microbiol* 2018, **46**:102−108, https://doi.org/10.1016/j.mib.2018.09.004.

3. Eves-van den Akker S: **Plant-nematode interactions**. *Curr Opin Plant Biol* 2021, **62**:102035, https://doi.org/10.1016/j.pbi.2021.102035.

4. Sato K, Kadota Y, Shirasu K: **Plant immune responses to parasitic nematodes**. *Front Plant Sci* 2019, **10**:1165, https://doi.org/10.3389/fpls.2019.01165.

5. Manosalva P, Manohar M, Von Reuss SH, Chen S, Koch A, Kaplan F, Choe A, Micikas RJ, Wang X, Kogel K-H: **Conserved nematode signalling molecules elicit plant defenses and pathogen resistance**. *Nat Commun* 2015, **6**:1−8.

6. Mendy B, Wang'ombe MW, Radakovic ZS, Holbein J, Ilyas M, Chopra D, Holton N, Zipfel C, Grundler FM, Siddique S: **Arabidopsis leucine-rich repeat receptor−like kinase NILR1 is required for induction of innate immunity to parasitic nematodes**. *PLoS Pathog* 2017, **13**, e1006284.

7. Lozano-Torres JL, Wilbers RHP, Gawronski P, Boshoven JC, Finkers-Tomczak A, Cordewener JHG, America AHP, Overmars HA, Klooster JWV, Baranowski L, Sobczak M, Illyas M, Renier ALH, Schots A, de Wit PJGM, Bakker J, Goverse A, Smant G: **Dual disease resistance mediated by the immune receptor Cf-2 in tomato requires a common virulence target of a fungus and a nematode**. *Proc Natl Acad Sci Unit States Am* 2012, **109**:10119−10124.

8. ** Zhang X, Peng H, Zhu S, Xing J, Li X, Zhu Z, Zheng J, Wang L, Wang B, Chen J, *et al.*: **Nematode-encoded RALF peptide mimics facilitate parasitism of plants through the FERONIA receptor kinase**. *Mol Plant* 2020, **13**:1434−1454.
First report of putatively secreted RALF peptide mimics in phytonematodes and a role for peptide mimicry in host immune modulation.

9. Zhang X, Wang D, Chen J, Wu D, Feng X, Yu F: **Nematode RALF-like 1 targets soybean malectin-like receptor kinase to facilitate parasitism**. *Front Plant Sci* 2021, **12**:775508.

10. Ronald P, Joe A: **Molecular mimicry modulates plant host responses to pathogens**. *Ann Bot* 2018, **121**:17−23.

11. Wang J, Lee C, Replogle A, Joshi S, Korkin D, Hussey R, Baum TJ, Davis EL, Wang X, Mitchum MG: **Dual roles for the variable domain in protein trafficking and host-specific recognition of *Heterodera glycines* CLE effector proteins**. *New Phytol* 2010, **187**:1003−1017.

12. Chen S, Lang P, Chronis D, Zhang S, De Jong WS, Mitchum MG, Wang X: ***In planta* processing and glycosylation of a nematode CLAVATA3/endosperm surrounding region-like effector and its interaction with a host CLAVATA2-like receptor to promote parasitism**. *Plant Physiol* 2015, **167**:262−272.

13. ** Wang J, Dhroso A, Liu X, Baum TJ, Hussey RS, Davis EL, Wang X, Korkin D, Mitchum MG: **Phytonematode peptide effectors exploit a host post-translational trafficking mechanism to the ER secretory pathway using a novel translocation signal**. *New Phytol* 2021, **229**:563−574.
Sheds new light on the sophisticated strategy used by CN to exploit the host's secretory pathway for parasitism and points to an undescribed post-translational trafficking pathway in plants.

14. Replogle A, Wang J, Bleckmann A, Hussey RS, Baum TJ, Wang X, Davis EL, Mitchum MG: **Nematode CLE signaling in Arabidopsis requires *CLAVATA2* and *CORYNE***. *Plant J* 2011, **65**:430−440.

15. Guo X, Wang J, Gardner M, Fukuda H, Kondo Y, Etchells P, Wang X, Mitchum MG: **Identification of cyst nematode B-type CLE peptides and modulation of the vascular stem cell pathway for feeding cell formation**. *PLoS Pathog* 2017, **13**, e1006142.

16. Stührwohldt N, Schaller A: **Regulation of plant peptide hormones and growth factors by post-translational modification**. *Plant Biol* 2019, **21**:49–63.

17. Li Z, Chakraborty S, Xu G: **Differential CLE peptide perception by plant receptors implicated from structural and functional analyses of TDIF-TDR interactions**. *PLoS One* 2017, **12**, e0175317.

18. * Pokhare SS, Thorpe P, Hedley P, Morris J, Habash SS, Elashry A, Eves-van den Akker S, Grundler FMW, Jones JT: **Signatures of adaptation to a monocot host in the plant-parasitic cyst nematode *Heterodera sacchari***. *Plant J* 2020, **103**:1263–1274.
Provides supportive evidence of a role for peptide mimicry underlying host specialization in PPN.

19. Bayless AM, Smith JM, Song J, McMinn PH, Teillet A, August BK, Bent AF: **Disease resistance through impairment of SNAP-NSF interaction and vesicular trafficking by soybean Rhg1**. *Proc Natl Acad Sci Unit States Am* 2016, **113**:E7375. E7372.

20. ** Bayless AM, Zapotocny RW, Grunwald DJ, Amundson KK, Diers BW, Bent AF: **An atypical N-ethylmaleimide sensitive factor enables the viability of nematode-resistant Rhg1 soybeans**. *Proc Natl Acad Sci Unit States Am* 2018, **115**: E4512–E4521.
Demonstrates how NSF_{RAN07} protects against the cytotoxic effects of the soybean cyst nematode resistance-conferring Rhg1 α-SNAP protein in the absence of nematode infection. A finding critically important for any efforts to engineer this type of resistance in crop plants.

21. Butler KJ, Fliege C, Zapotocny R, Diers B, Hudson M, Bent AF: **Soybean cyst nematode resistance QTL cqSCN-006 alters the expression of a γ-SNAP protein**. *Mol Plant Microbe Interact* 2021, https://doi.org/10.1094/MPMI-07-21-0163-R.

22. Dong J, Zielinski RE, Hudson ME: **t-SNAREs bind Rhg1 α-SNAP and mediate soybean cyst nematode resistance**. *Plant J* 2020, **104**:318–331.

23. Wang R, Deng M, Yang C, Yu Q, Zhang L, Zhu Q, Guo X: **A Qa-SNARE complex contributes to soybean cyst nematode resistance via regulation of mitochondria-mediated cell death**. *J Exp Bot* 2021, https://doi.org/10.1093/jxb/erab301.

24. * Usovsky M, Lakhssassi N, Patil GB, Vuong TD, Piya S, Hewezi T, Robbins RT, Stupar RM, Meksem K, Nguyen HT: **Dissecting nematode resistance regions in soybean revealed pleiotropic effect of soybean cyst and reniform resistance genes**. *Plant Genome* 2021, e20083, https://doi.org/10.1002/tpg2.20083.
Reveals the same combination of α-SNAP genes in soybean confers resistance to two different genera of syncytium-forming PPN. Moreover, this is intriguing in light of the fact that RN also secretes CLEs and CEPs, potentially exploiting the host secretory pathway similar to CN CLEs.

25. Basnet P, Meinhardt CG, Usovsky M, Gillman JD, Joshi T, Song Q, Diers B, Mitchum MG, Scaboo A: **Epistatic interaction between *Rhg1-a* and *Rhg2* in PI 90763 confers resistance to virulent soybean cyst nematode populations**. *Theor Appl Genet* 2021, https://doi.org/10.1007/s00122-022-04091-2.

26. Lolle S, Stevens D, Coaker G: **Plant NLR-triggered immunity: from receptor activation to downstream signaling**. *Curr Opin Immunol* 2020, **62**:99–105.

27. Paal J, Henselewski H, Muth J, Meksem K, Menéndez CM, Salamini F, Ballvora A, Gebhardt C: **Molecular cloning of the potato *Gro1-4* gene conferring resistance to pathotype Ro1 of the root cyst nematode *Globodera rostochiensis*, based on a candidate gene approach**. *Plant J* 2004, **38**:285–297, https://doi.org/10.1111/j.1365-313X.2004.02047.x.

28. Claverie M, Dirlewanger E, Bosselut N, Van Ghelder C, Voisin R, Kleinhentz M, Lafargue B, Abad P, Rosso MN, Chalhoub B, *et al.*: **The *Ma* gene for complete-spectrum resistance to *Meloidogyne* species in *Prunus* is a TNL with a huge repeated C-terminal post-LRR region**. *Plant Physiol* 2011, **156**:779–792.

29. Van Ghelder C, Esmenjaud D: **TNL genes in peach: insights into the post-LRR domain**. *BMC Genom* 2016, **17**, https://doi.org/10.1186/s12864-016-2635-0.

30. * Van Ghelder C, Esmenjaud D, Callot C, Dubois E, Mazier M, Duval H: **Ma orthologous genes in *Prunus* spp. shed light on a noteworthy NBS-LRR cluster conferring differential resistance to root-knot nematodes**. *Front Plant Sci* 2018, **11**, https://doi.org/10.3389/fpls.2018.01269.
Shows how PL exon duplications and losses shape TNL structure by giving rise to atypical PL domain repeats with polymorphisms that may underlie differential resistance spectra to RKNs and an original immune mechanism in woody perennials.

31. Feehan JM, Castel B, Bentham AR, Jones JDG: **Plant NLRs get by with a little help from their friends**. *Curr Opin Plant Biol* 2020, **56**:99–108.

32. Ma Y, Guo H, Hu L, Martinez PP, Moschou PN, Cevik V, Ding P, Duxbury Z, Sarris PF, Jones JDG: **Distinct modes of derepression of an Arabidopsis immune receptor complex by two different bacterial effectors**. *Proc Natl Acad Sci USA* 2018, **115**: 10218–10227.

33. * Warmerdam S, Sterken MG, Sukarta OCA, van Schaik CC, Oortwijn MEP, Lozano-Torres JL, Bakker J, Smant G, Goverse A: **The TIR-NB-LRR pair DSC1 and WRKY19 contributes to basal immunity of Arabidopsis to the root-knot nematode *Meloidogyne incognita***. *BMC Plant Biol* 2020, **20**:73.
First report on the role of two TNLs (DSC1 and WRKY19), of which the encoding genes are genetically linked in a head-to-head orientation. DSC1 and WRKY19 seem to co-regulate host susceptibility to RKN in Arabidopsis probably as a TIR-NB-LRR immune receptor pair.

34. Narusaka M, Shirasu K, Noutoshi Y, Kubo Y, Shiraishi T, Iwabuchi M, Narusaka Y: ***RRS1* and *RPS4* provide a dual resistance-gene system against fungal and bacterial pathogens**. *Plant J* 2009, **60**:218–226, https://doi.org/10.1111/j.1365-313X.2009.03949.x.

35. Van der Vossen EA, van der Voort JN, Kanyuka K, Bendahmane A, Sandbrink H, Baulcombe DC, *et al.*: **Homologues of a single resistance-gene cluster in potato confer resistance to distinct pathogens: a virus and a nematode**. *Plant J* 2000, **23**:567–576, https://doi.org/10.1046/j.1365-313x.2000.00814.x.

36. Ernst K, Kumar A, Kriseleit D, Kloos D-U, Phillips MS, Ganal MW: **The broad-spectrum potato cyst nematode resistance gene (*Hero*) from tomato is the only member of a large gene family of NBS-LRR genes with an unusual amino acid repeat in the LRR region**. *Plant J* 2002, **31**:127–136, https://doi.org/10.1046/j.1365-313x.2002.01341.x.

37. Milligan SB, Bodeau J, J Yaghoobi J, Kaloshian I, Zabel P, Williamson VM: **The root knot nematode resistance gene *Mi* from tomato is a member of the leucine zipper, nucleotide binding, leucine-rich repeat family of plant genes**. *Plant Cell* 1998, **10**:1307–1319.

38. Sacco MA, Koropacka K, Grenier E, Jaubert MJ, Blanchard A, *et al.*: **The cyst nematode SPRYSEC protein RBP-1 elicits Gpa2- and RanGAP2- dependent plant cell death**. *PLoS Pathog* 2009, **5**, e1000564, https://doi.org/10.1371/journal.ppat.1000564.

39. Zheng Q, Putker V, Goverse A: **Molecular and cellular mechanisms involved in host-specific resistance to cyst nematodes in crops**. *Front Plant Sci* 2021, **12**:641582, https://doi.org/10.3389/fpls.2021.641582. Published 2021 Mar 9.

40. Hwang CF, Williamson VM: **Leucine-rich repeat-mediated intramolecular interactions in nematode recognition and cell death signaling by the tomato resistance protein Mi**. *Plant J* 2003, **34**:585–593.

41. Lukasik-Shreepaathy E, Slootweg E, Richter H, Goverse A, Cornelissen BJC, Takken FLW: **Dual regulatory roles of the extended N-terminus for activation of the tomato Mi-1.2 resistance protein**. *Mol Plant Microbe Interact* 2012, **25**: 1045–1057, https://doi.org/10.1094/MPMI-11-11-0302.

42. Wu C-HA, Abd-El-Haliem A, Bozkurt TA, Belhaj K, Terauchi R, Vossen JH, Kamoun S: **NLR network mediates immunity to diverse pathogens**. *Proc Natl Acad Sci Unit States Am* 2017, **114**:8113–8118, https://doi.org/10.1073/pnas.1702041114.

43. ** Derevnina L, Contreras MP, Adachi H, Upson J, Vergara Cruces A, Xie R, *et al.*: **Plant pathogens convergently evolved to counteract redundant nodes of an NLR immune receptor network**. *PLoS Biol* 2021, **19**, e3001136, https://doi.org/10.1371/journal.pbio.3001136.
Uncovers molecular mechanisms underlying host immune suppression by CN SPRYSEC effectors by demonstrating that they target different nodes of the NLR signaling network, including the direct binding to the NB-ARC domain of NRC helper proteins.

44. Goverse A, Smant G: **The activation and suppression of plant innate immunity by parasitic nematodes**. *Annu Rev Phytopathol* 2014, **52**:243–265, https://doi.org/10.1146/annurev-phyto-102313-050118.

45. Diaz-Granados A, Petrescu A-J, Goverse A, Smant G: **SPRYSEC effectors: a versatile protein-binding platform to disrupt plant innate immunity**. *Front Plant Sci* 2016, **7**:1575, https://doi.org/10.3389/fpls.2016.01575.

46. Mei Y, Wright KM, Haegeman A, Bauters L, Diaz-Granados A, Goverse A, Gheysen G, Jones JT, Mantelin S: **The *Globodera pallida* SPRYSEC effector GpSPRY-414-2 that suppresses plant defenses targets a regulatory component of the dynamic microtubule network**. *Front Plant Sci* 2018, **9**:1019, https://doi.org/10.3389/fpls.2018.01019.

47. Kim J, Yang R, Chang C, Park Y, Tucker ML: **The root-knot nematode *Meloidogyne incognita* produces a functional mimic of the Arabidopsis inflorescence deficient in abscission signaling peptide**. *J Exp Bot* 2018, **69**:3009–3021.

48. Eves-Van Den Akker S, Lilley CJ, Yusup HB, Jones JT, Urwin PE: **Functional C-terminally encoded peptide (CEP) plant hormone domains evolved *de novo* in the plant parasite *Rotylenchulus reniformis***. *Mol Plant Pathol* 2016, **17**:1265–1275.

49. Postma WJ, Slootweg EJ, Rehman S, Finkers-Tomczak A, Tytgat TO, van Gelderen K, Lozano-Torres JL, Roosien J, Pomp R, van Schaik C, *et al.*: **The effector SPRYSEC-19 of Globodera rostochiensis suppresses CC-NB-LRR-mediated disease resistance in plants**. *Plant Physiol* 2012, **160**:944–954, https://doi.org/10.1104/pp.112.200188.