Plant pathogens have evolved diverse strategies to manipulate and co-opt host cellular function to enable infection. One strategy commonly employed by plant-parasitic cyst and root-knot nematodes is molecular mimicry of host proteins and small-molecule ligands. In an important new example of this phenomenon, Kim et al. (2018) have now identified a putatively secreted peptide from the root-knot nematode Meloidogyne incognita that mimics the Arabidopsis INFLORESCENCE DEFICIENT IN ABSCISSION (IDA) signaling peptide, which controls floral organ abscission and lateral root emergence.

Phytopathogens have evolved sophisticated mechanisms to enhance their ability to infect host plants. These include the molecular mimicry of cellular activities and functions, the ability to encode factors that mirror host proteins in function or structure to manipulate cellular functions for the pathogen’s benefit. Such mimicry may enable the pathogen to establish infection while escaping the host’s immune detection system. Although molecular mimicry is a common strategy employed by bacterial and viral pathogens in various animal systems (Stebbins and Galán, 2001; Elde and Malik, 2009), information about this phenomenon in phytopathogens is relatively limited.

The plant-parasitic cyst and root-knot nematodes, unlike other plant pathogens, appear to rely heavily on molecular mimicry to parasitize host plants (Hewezi, 2015). An example of cyst nematode mimicry is the secretion of effector proteins containing a conserved 12-amino acid C-terminal motif sharing strong sequence similarity with plant CLAVATA3/ESR (CLE) ligand peptides (Mitchum et al., 2012). Similarly, multiple tandemly arrayed CLE-like motifs have been identified in various members of the secreted Meloidogyne Avirulence Protein (MAP) family (Rutter et al., 2014). Thus, plant CLE ligands represent weak common targets for mimicry by two evolutionarily diverse species of plant-parasitic nematodes.

Other widely distributed mimics produced by plant-parasitic nematodes are the secreted chorismate mutases (Doyle and Lambert, 2003; Huang et al., 2005; Vanholme et al., 2009). Because of the absence of its substrate in animals, it is anticipated that parasitic nematodes mimic host chorismate mutase to alter secondary metabolic pathways, presumably to interfere with defense-related functions. Another effector that may mimic a host protein to subvert the defense response is the annexin-like effector from cyst nematodes (Patel et al., 2010). It can complement the Arabidopsis annexin1 mutant despite low amino acid sequence identity between the two proteins (Patel et al., 2010). The identification of a number of effectors with putative mimicry functions from plant-parasitic nematodes suggests that these parasites use molecular mimicry to interfere with and/or exploit essential cellular functions required for parasitism.

The origin of nematode-encoded mimics

Horizontal gene transfer (HGT) seems to be the most plausible source for nematode mimics, with several potential such events having been reported in plant-parasitic nematodes (Scholl et al., 2003; Danchin et al., 2010; Haegeman et al., 2011). This type of mimicry can be detected through sequence similarity and phylogeny. However, it is reasonable to expect that in some cases, because of the rapid evolution of parasitic nematodes, the nematode-encoded mimics may have little or no similarity to host factors that they imitate. Also, in nematode-encoded mimics generated through convergent evolution, parasitic...
nematodes independently evolve to acquire functions or structures that mirror those of host plants with limited sequence similarity.

Plant-parasitic nematodes can also use structural mimicry to co-opt host post-translational modification mechanisms to the nematode’s advantage. One example is the cyst nematode effector 10A07, which appears to structurally mimic a plant kinase substrate in order to become phosphorylated inside plant cells (Hewezi et al., 2015). Phosphorylation of the 10A07 effector is required for its translocation and function in the nucleus. Since pathogen-encoded structural mimics have little or no sequence similarity to the host factors that they model, their identification remains challenging and mainly relies on functional and structural analyses.

**Meloidogyne incognita IDA-like peptide and mimicry of INFLORESCENCE DEFICIENT IN ABSCISSION**

Kim et al. (2018) provide another intriguing example of how root-knot nematodes may hijack signaling pathways to promote parasitism. Two putatively secreted peptides with sequence similarity to Arabidopsis INFLORESCENCE DEFICIENT IN ABSCISSION (IDA) have been identified from the root-knot nematode Meloidogyne incognita (Kim et al., 2018). The *M. incognita* IDA-like genes, MiIDL1 and MiIDL2, encode a small protein with N-terminal signal peptide for secretion. Several studies have demonstrated the function of the IDA signaling peptide in cell separation that mediates floral organ abscission and lateral root emergence (Butenko et al., 2003; Cho et al., 2008; Santiago et al., 2016), presumably through the regulation of various cell wall-modifying enzymes (Kumpf et al., 2013). The IDA peptide functions as a ligand of two functionally redundant plasma membrane-localized receptor-like kinases known as HAE and HSL2. IDA binding to the receptors initiates a signaling pathway leading to gene expression changes through the activity of a set of KNOX transcription factors (Liljegren, 2012; Niederhuth et al., 2013; Meng et al., 2016).

Similar to its Arabidopsis counterpart, MiIDL1 is assumed to be processed to a 22-amino acid bioactive peptide. Interestingly, exogenous application of synthetic MiIDL1 peptide meaningfully rescued the abscission phenotype of the Arabidopsis *ida* mutant, providing the first indication of a mimicry function of MiIDL1 in host cells. In addition, genetic complementation of the Arabidopsis *ida* mutant with the full-length MiIDL1 gene containing the N-terminal signal peptide sequence produced the wild-type floral organ abscission phenotype (Kim et al., 2018). The importance of MiIDL1 for nematode pathogenesis was demonstrated by data showing that silencing *MiIDL1* transcripts in the nematode through a host-induced RNAi approach significantly reduced the number and size of nematode-induced galls. It seems most likely that during nematode infection MiIDL1 peptide mimics IDA function in particular root cell types that are not usually subjected to an IDA-mediated signaling pathway. However, it remains to be determined whether MiIDL1 peptide exploits host HAE/HSL2 receptors during infection or utilizes different receptors with similar functions, taking into consideration the low sequence similarity between IDA and MiIDL1.

**The power of being imperfect**

The sequence identity between MiIDL1 and the mimicked plant IDA is low and limited to the conserved C-terminal motif. This situation is characteristic of convergent evolution, although the possibility that the mimicry function of MiIDL1 was acquired via divergent evolution cannot be ruled out. Regardless of evolutionary origin, the ability of *MiIDL1* to complement the Arabidopsis *ida* mutant, despite strong sequence divergence, is fascinating. The low sequence similarity between MiIDL1 and IDA may enable the nematode to mirror the function of IDA sufficiently without falling completely under the control of host cellular regulatory mechanisms.

In this context, pathogen mimics that show perfect or near-perfect sequence similarity to host factors (such as cyst nematode CLE-like peptides) may be speculated to be less advantageous to the pathogens because of their limited ability to disrupt cellular activity to the benefit of the pathogen while falling under host cellular control. Conversely, being too divergent may enable the plant immune system to identify pathogen mimics. Thus, co-opting or subverting host cellular functions to the pathogen’s benefit without being recognized appears to be the most advantageous tactic for the pathogen, though this has yet to be determined experimentally.

**New targets for generating nematode resistance**

IDA genes are highly conserved in plants and the encoded peptides may represent vulnerable hotspots for the nematode to hijack IDA-mediated signaling pathways and establish infection. Highly conserved genes nevertheless often undergo a small amount of ‘evolutionary flexibility’ and this may limit the plant’s ability to escape mimicry. Nevertheless, even with this level of sequence variation, the host plants may acquire substitutions in certain IDA-peptide residues that enable them to evade mimicry without affecting their binding affinity to HAE or HSL2. In this context, complementation of the Arabidopsis *ida1* mutant with IDA transgenes containing point mutations in various conserved amino acids may lead to the identification of residues that enable the plants to evade mimicry without compromising the interaction ability of IDA with HAE or HSL2. These conserved residues would provide excellent targets for generating nematode resistance through non-GMO genome editing approaches.

The use of mimicry by parasitic nematodes to recognize and gain entry to host plants is intriguing and well worth additional exploration since interference of host-pathogen recognition may lead to innovative nematode control strategies. With the rapid development of sequencing technologies
the genome sequences of a significant number of phytopathogens and their host plants have now become available, and so it is possible to explore the function of molecular mimicry in other plant pathosystems. This should lead to the identification of attractive targets for disease resistance.

**Keywords:** Abscission, IDA, ligand peptide, *Meloidogyne incognita*, MiIDL1, molecular mimicry.

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**References**

Butenko MA, Patterson SE, Grini PE, Stenvik GE, Amundsen SS, Mandal A, Aalen RB. 2003. Inflorescence deficient in abscission controls floral organ abscission in Arabidopsis and identifies a novel family of putative ligands in plants. The Plant Cell **15**, 2296–2307.

Cho SK, Larue CT, Chevalier D, Wang H, Jinn TL, Zhang S, Walker JC. 2008. Regulation of floral organ abscission in *Arabidopsis thaliana*. Proceedings of the National Academy of Sciences, USA **105**, 15629–15634.

Danchin EG, Rosso MN, Vieira P, de Almeida-Engler J, Coutinho PM, Henriissat B, Abad P. 2010. Multiple lateral gene transfers and duplications have promoted plant parasitism ability in nematodes. Proceedings of the National Academy of Sciences, USA **107**, 17651–17656.

Doyle EA, Lambert KN. 2003. *Meloidogyne javanica* chorismate mutase 1 alters plant cell development. Molecular Plant-Microbe Interactions **16**, 123–131.

Elde NC, Malik HS. 2009. The evolutionary conundrum of pathogen mimicry. Nature Reviews. Microbiology **7**, 787–797.

Haegeman A, Jones JT, Danchin EG. 2011. Horizontal gene transfer in nematodes: a catalyst for plant parasitism? Molecular Plant-Microbe Interactions **24**, 879–887.

Hewezi T, Juvala PS, Piya S, Maier TR, Rambani A, Rice JH, Mitchum MG, Davis EL, Hussey RS, Baum TJ. 2015. The cyst nematode effector protein 10A07 targets and recruits host posttranslational machinery to mediate its nuclear trafficking and to promote parasitism in Arabidopsis. The Plant Cell **27**, 891–907.

Hewezi T. 2015. Cellular signaling pathways and posttranslational modifications mediated by nematode effector proteins. Plant Physiology **169**, 1018–1026.

Huang G, Dong R, Allen R, Davis EL, Baum TJ, Hussey RS. 2005. Two chorismate mutase genes from the root-knot nematode *Meloidogyne incognita*. Molecular Plant Pathology **6**, 23–30.

Kim J, Yang R, Chang C, Park Y, Tucker ML. 2018. The root-knot nematode (*Meloidogyne incognita*) produces a functional mimic of the Arabidopsis IDA signaling peptide. Journal of Experimental Botany **69**, 3009–3021.

Kumpf RP, Shi CL, Larrieu A, Sto IM, Butenko MA, Peret B, Riiser ES, Bennett MJ, Aalen RB. 2013. Floral organ abscission peptide IDA and its HAE/HSL2 receptors control cell separation during lateral root emergence. Proceedings of the National Academy of Sciences, USA **110**, 5235–5240.

Liljegren SJ. 2012. Organ abscission: exit strategies require signals and moving traffic. Current Opinion in Plant Biology **15**, 670–676.

Meng X, Zhou J, Tang J, Li B, de Oliveira MVV, Chai J, He P, Shan L. 2016. Ligand-induced receptor-like kinase complex regulates floral organ abscission in Arabidopsis. Cell Reports **14**, 1330–1338.

Mitchum MG, Wang X, Wang J, Davis EL. 2012. Role of nematode peptides and other small molecules in plant parasitism. Annual Review of Phytopathology **50**, 175–195.

Niederhuth CE, Cho SK, Seitz K, Walker JC. 2013. Letting go is never easy: abscission and receptor-like protein kinases. Journal of Integrative Plant Biology **55**, 1251–1283.

Patel N, Hamamouch N, Li C, Hewezi T, Hussey RS, Baum TJ, Mitchum MG, Davis EL. 2010. A nematode effector protein similar to annexins in host plants. Journal of Experimental Botany **61**, 235–248.

Rutter WB, Hewezi T, Maier TR, Mitchum MG, Davis EL, Hussey RS, Baum TJ. 2014. Members of the *Meloidogyne* avirulence protein family contain multiple plant ligand-like motifs. Phytopathology **104**, 879–885.

Santiago J, Brandt B, Wildhagen M, Hohmann U, Hothorn LA, Butenko MA, Hothorn M. 2016. Mechanistic insight into a peptide hormone signaling complex mediating floral organ abscission. Elife **5**, e15075.

Scholl EH, Thorne JL, McCarter JP, Bird DM. 2003. Horizontally transferred genes in plant-parasite nematodes: a high-throughput genomic approach. Genome Biology **4**, R39.

Stebbins CE, Galán JE. 2001. Structural mimicry in bacterial virulence. Nature **412**, 701–705.

Vanholme B, Kast P, Haegeman A, Jacob J, Grunewald W, Gheysen G. 2009. Structural and functional investigation of a secreted chorismate mutase from the plant-parasitic nematode *Heterodera schachtii* in the context of related enzymes from diverse origins. Molecular Plant Pathology **10**, 189–200.