Plant Proteins and Processes Targeted by Parasitic Nematode Effectors

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Sedentary endoparasitic nematodes, such as root-knot nematodes (RKN; Meloidogyne spp.) and cyst nematodes (CN; Heterodera spp. and Globodera spp.) cause considerable damage to agricultural crops. RKN and CN spend most of their life cycle in plant roots, in which they induce the formation of multinucleate hypertrophied feeding cells, called “giant cells” and “syncytia,” respectively. The giant cells result from nuclear divisions of vascular cells without cytokinesis. They are surrounded by small dividing cells and they form a new organ within the root known as a root knot or gall. CN infection leads to the fusion of several root cells into a unique syncytium. These dramatically modified host cells act as metabolic sinks from which the nematode withdraws nutrients throughout its life, and they are thus essential for nematode development. Both RKN and CN secrete effector proteins that are synthesized in the oesophageal glands and delivered to the appropriate cell in the host plant via a syringe-like stylet, triggering the ontogenesis of the feeding structures. Within the plant cell or in the apoplast, effectors associate with specific host proteins, enabling them to hijack important processes for cell morphogenesis and physiology or immunity. Here, we review recent findings on the identification and functional characterization of plant targets of RKN and CN effectors. A better understanding of the molecular determinants of these biotrophic relationships would enable us to improve the yields of crops infected with parasitic nematodes and to expand our comprehension of root development.

Keywords: root-knot nematodes, cyst nematodes, galls, syncytium, effectors

INTRODUCTION

Plant-parasitic nematodes (PPN) are microscopic worms that withdraw nutrients from the cytoplasm of cells in the aerial or below-ground parts of plants. Root-knot nematodes (RKN) and cyst nematodes (CN) are the most widely studied PPN, as these two groups are the most damaging to crop plants (Singh et al., 2013). RKN from the Meloidogyne genus are found throughout the world and are extremely polyphagous, infecting thousands of plant species, including both monocotyledons and eudicotyledons (Blok et al., 2008). By contrast, CN tend to specialize on a particular crop and form two common genera: Globodera spp. (potato CN) and Heterodera spp. (sugar beet, soybean, or cereal CN), each of which causes huge yield losses on its host.

Both CN and RKN are sedentary endoparasites and obligate biotrophs. Mobile preparasitic juveniles (J2) penetrate the host root, traveling toward the vascular cylinder, where they become...
sedentary, triggering the formation of an unusual feeding site. The RKN feeding site consists of so-called “giant cells” (Figure 1A). These cells are produced from about half a dozen vascular root cells, which undergo repeated nuclear divisions without cell division. These cells become polynucleate and may be more than 300 times larger than normal cells. Giant cells are surrounded by dividing cells, the hyperplasia and hypertrophy of which lead to the formation of a novel organ called a gall (Kyndt et al., 2013; Favery et al., 2016; Palomares-Rius et al., 2017). By contrast, CN induce the formation of a different type of feeding site called a syncytium. Syncytium formation involves partial dissolution of the root cell wall and protoplast fusion, leading to an iterative process of fusion of the first CN-infested vascular cell with its neighbors (Figure 1B; Sobczak and Golinowski, 2011; Palomares-Rius et al., 2017). Some mature syncytia are the result of fusions of more than 200 cells. Giant cells and syncytia have a number of features in common, including a fully expanded endoplasmic reticulum, a fragmented vacuole, a reorganized cytoskeleton, thickened cell walls with local ingrowths, a large mitochondrial network and endoreduplicated nuclei (Kyndt et al., 2013; Rodiuc et al., 2014). These specialized feeding cells supply the nematodes with nutrients throughout the sedentary part of their life cycle. Female RKN lay their eggs in a gelatinous matrix generally on the root surface, whereas the cyst of CN consists of a dead and hardened female containing eggs.

Root-knot nematodes and CN secrete molecules called “effectors,” to facilitate invasion of the host root, avoid plant defense responses and reprogram root cells to form specialized feeding cells. These effectors are produced principally in three oesophageal salivary glands and are then injected into plant cells via the syringe-like stylet. The activity of the oesophageal glands is developmentally regulated. The two subventral glands (SvG) secrete effectors allowing J2 penetration and migration in the root while proteins secreted during parasitism are produced by SvG and particularly by the dorsal gland (DG) (Nguyen et al., 2018). Some effectors may also be produced in other secretory organs, such as chemosensory amphids, or directly secreted through the PPN cuticle. Molecular dialog studies have focused mostly on secreted proteinaceous effectors (Hewezi and Baum, 2013; Mitchum et al., 2013; Quentin et al., 2013; Hewezi, 2015; Ali et al., 2017; Vieira and Gleason, 2019) even though other secreted molecules, such as phytohormones, have been shown to favor these interactions (Siddique and Grundler, 2018).

Various approaches have been used to characterize nematode effector repertoires. Proteomic analysis has directly identified about 500 proteins secreted by M. incognita parasitic J2s or females (Bellafiore et al., 2008; Wang et al., 2012). Effector identification has greatly benefited from advances in sequencing technologies. Complete genome sequences are now available for four RKN – M. incognita, M. hapla, M. javanica, and M. arenaria (Abad et al., 2008; Opperman et al., 2008; Blanc-Mathieu et al., 2017) – and three CN: G. pallida, G. rostochiensis, and H. glycines (Cotton et al., 2014; Eves-van den Akker et al., 2016; Masonbrink et al., 2019). Bioinformatic methods for identifying genes encoding putative secreted proteins, which are based on the presence of a signal peptide for secretion but absence of transmembrane domains, remain the most convenient approach to identify candidate effector genes. cis-regulatory sequences called “DOG boxes” were recently identified within the promoters of G. rostochiensis and H. glycines genes encoding effectors specifically expressed within the DG of the CN (Eves-van den Akker et al., 2016; Masonbrink et al., 2019). This discovery opens up new possibilities for effector prediction and implies that effector production in the DG is synchronized by master regulators, such as key transcription factors (Eves-van den Akker and Birch, 2016). Finally, transcriptomics has made it possible to compare different stages of nematode development and to identify RKN (Li et al., 2016; Petiot et al., 2016; Nguyen et al., 2018; Shukla et al., 2018) and CN (Cotton et al., 2014; Kumar et al., 2014; Yang et al., 2017; Gardner et al., 2018) genes upregulated in plants. In situ hybridisation (ISH) has generally been used for the initial validation of candidate effector gene expression within secretory organs (Figure 1C and Table 1). Remarkably, the secretion of a few effectors has been demonstrated in planta, by immunolocalisation (Table 1).

Delivery to the host apoplast has been demonstrated for several effectors (Jaubert et al., 2005; Vieira et al., 2011; Iberkleid et al., 2013; Eves-van den Akker et al., 2014; Zhuo et al., 2019), but few demonstrations of translocation into the host feeding cell have been reported (Jaouannet et al., 2012; Lin et al., 2012; Chen et al., 2017; Lilley et al., 2018; Naalden et al., 2018). These studies have expanded the repertoire of putative effectors considerably, with hundreds of ISH-validated effectors now known (Truong et al., 2015; Gardner et al., 2016). However, the vast majority of these proteins are pioneer proteins with no known functional domains. As a result, the functions of only a few RKN and CN effectors have been deciphered. Cell wall-degrading effectors have been reported to help nematodes to penetrate and migrate within the root, and effectors suppressing plant defenses have been described (Quentin et al., 2013; Goverse and Smant, 2014), but only a few effectors have been shown to contribute to the de novo organogenesis and maintenance of feeding sites. Functional analyses of PPN effectors have clearly benefited from the identification of the host targets of these molecules, mostly through yeast two-hybrid approaches (Table 1). We review here the most recent advances in our understanding of RKN and CN effector functions, focusing on those for which the plant processes targeted have been identified.

**PARASITISM REQUIRES THE MANIPULATION OF DIVERSE HOST FUNCTIONS**

Nematode effectors target the apoplast and different subcellular compartments, including the nuclei, reflecting the diversity of host cell processes manipulated to promote infection and feeding site formation (Table 1). Many of the members of the PPN effector repertoire have been shown to suppress plant immunity (Goverse and Smant, 2014; Favery et al., 2016; Ali et al., 2017). However, their precise mode of action remains largely unknown and only a few of their direct targets in plants...
have been identified. PPN effectors may interact with host proteins to scavenge reactive oxygen species (ROS) accumulating during the oxidative burst following the induction of pathogen-associated molecular pattern (PAMP)-triggered immunity (PTI). *M. javanica* MjTTLS scavenges ROS by interacting with a thioredoxin reductase catalytic subunit (AtFTRc) in the plant (Lin et al., 2016). *H. schachtii* Hs10A06 has been shown to interact with a spermindine synthase (AtSPDS2), thereby enhancing spermindine production and inducing ROS-scavenging activity when the spermindine is oxidized by polyamine oxidase (Hewezi et al., 2010). Various pathogenesis-related (PR) proteins involved in the production of antimicrobial proteins by plants in response to pathogen attack have also been identified as direct targets of nematode effectors. *H. glycines* Hg30C02 targets a beta-1,3-endoglucanase (AtPR2), the inactivation of which in a mutant *Arabidopsis* line increases susceptibility to cyst nematode infection (Hamamouch et al., 2012). *M. graminicola* MgMO237 has been shown to suppress PTI by interacting with multiple host PR proteins, a 1,3-beta-glucan synthase (OsGSC), the cysteine-rich repeat secretory protein 55 (OsCRRSP55) and a pathogenesis-related Bet v I family protein (OsBetvI) (Chen et al., 2018). The GrVAP-1 effector from *G. rostochiensis* targets an apoplastic papain-like cysteine protein (PLCP) called RCR3Prm, to subvert immunity. GrVAP-1 is also recognized by a plant immune receptor called Cf-2 that can trigger effector-triggered immunity (ETI) followed by a hypersensitive response (Lozano-Torres et al., 2012).

Like other classes of plant pathogens that have to overcome host defenses, PPNs produce effectors that converge on evolutionarily conserved host targets called “hubs” (Carella et al., 2018). The *M. incognita* “Passe-Muraille” peptide effector, for example, interacts with subunit 5 of the COP9 signalosome (CSN5) (Bournaud et al., 2018), a hub targeted by bacterial, fungal and viral effectors (Mukhtar et al., 2011; Wefling et al., 2014). The function of CSN5 in RKN parasitism remains unknown, but this target protein is known to be involved in plant salicylic acid-mediated defense (Kazan and Lyons, 2014). Similarly, the *H. schachtii* Hs25A01 effector interacts with eIF-2bs, a member of the eIFs family of translation initiation factors including known host targets of fungi, bacteria and viruses, and a role for this target in parasitism was demonstrated by the observation of changes in susceptibility to nematodes in eIF-2bs knockout mutants (Pogorelko et al., 2016). A third striking example is provided by PLCPs, which constitute key hubs in plant immunity (Misas-Villamil et al., 2016). PLCPs are targeted by *M. chitwoodi* Mc01194 (Davies et al., 2015) and...
| **Nematode effectors** | **Plant targets** | **References** |
|-------------------------|-----------------|---------------|
| **Nematode effectors** | **Plant species, annotation, and name** | **Y2H**<sup>(c)</sup> | **Co-IP or other**<sup>(c)</sup> | **BiFC**<sup>(c)</sup> | **Evidence for a role in parasitism** |
| Name | Annotation | In planta localisation<sup>(a)</sup> | Plant species, annotation, and name | | | |
| Mi8D05 | Unknown | nd | Tomato aquaporin tonoplast intrinsic protein 2 (STIP2) | ✓ | | |
| Mi16D10 | CLE-like peptide | nd | Tomato and Arabidopsis SCARECROW-like transcription factors (SCL) | ✓ | ✓ | nd |
| MPFN3 | Profilin | Actin filaments (TE) | Actin monomers | ✓ | | nd |
| MPM | Nucleus (TE) | Soybean fifth subunit of the COP9 signalosome (GmCSN5) | ✓ | | | |
| Mi8D10 | Macrophage migration inhibitory Factor | Cytoplasmic (IL) | Arabidopsis annexin 1 and 4 (AnnAt1 and AnnAt4) | ✓ | ✓ | nd |
| Mi16D10 | Transthyretin-like protein | Cytoplasmic and nuclear (TE) | Rice 1,3-beta-glucan synthase (OsGSSQ), cysteine–rich repeat secretory protein 55 (OsGRRPS55), pathogenesis–related BetvI family protein (OsBetvI) | ✓ | ✓ | nd |
| Mj16820 | Unknown | Cytoplasmic and nuclear (TE) | Rice dehydration-stress inducible protein 1 (OsDIP1) | ✓ | ✓ | nd |
| MC01194 | Unknown | nd | Arabidopsis papain-like cysteine protease responsive to dehydration (RD21A) | ✓ | ✓ | nd |
| HgCLE1 | CLE-like peptide | Syncytia cytoplasm (IL) | Soybean OLAVATA (OLV1A, OLV2A, and OLV2B), LRR-RLP proteins (RPK2A and RPK2B) | ✓ | | |
| HgCLE2 | | | | | | |
| Hg30002 | Unknown | nd | Arabidopsis beta-1,3-endoglucanase (AtPR2) | ✓ | ✓ | nd |
| HgSLP1 | SNARE-Like Protein | nd | Soybean resistance protein α-SNAP (RHG1) | ✓ | | Soybean resistance protein |
| HgGLAND4 | Gr-3E10-like | Nucleus (TE) | Arabidopsis DNA<sup>(5)</sup>: repressor of two lipid transfer protein (LTP) gene expression | ✓ | | LTP At OE lines less susceptible to Hs and Pst |
| HsCLE2 | CLE-like peptide | nd | Soybean OLAVATA (OLV1A, OLV2A, and OLV2B), LRR-RLP proteins (RPK2A and RPK2B) | ✓ | | clv1, clv2 and rpk2 At KO less susceptible to Hs |
| Hs10A06 | Unknown | Cytoplasmic (TE) | Arabidopsis spermidine synthase 2 (AISPDS2) | ✓ | ✓ | SDPS2 At OE lines more susceptible to Hs, KO lines susceptibility to Hs unchanged |

(Continued)
### TABLE 1 | Continued

| Nematode effectors | Plant targets | References |
|--------------------|--------------|------------|
| **Name** | **Annotation** | **In planta localisation** | **Plant species, annotation, and name** | **Y2H**(c) | **Co-IP or other**(c) | **BiFC**(c) | **Evidence for a role in parasitism** |
| Hs10A07 | Unknown | Cytoplasmic and nuclear (TE) | Arabidopsis plant kinase (IPK) and transcription factor (IAA16) | ✓ | ✓ | ✓ | IPK or IAA16 At OE lines more susceptible to Hs, At KO lines are less susceptible to Hs | Hewzi et al., 2015 |
| Hs19C07 | Unknown | Cytoplasmic (TE) | Arabidopsis auxin influx transporter (LAX3) | ✓ | ✓ | | AUX/LAX double and quadruple mutants less susceptible to Hs | Lee et al., 2011 |
| Hs25A10 | Unknown | Cytoplasmic (TE) | Arabidopsis F-box containing protein (ATAUF1), chalcone synthase (ACCHS), translation initiation factor (AtEF-2bs) | ✓ | ✓ | ✓ | elf-2bs At KO more susceptible to Hs, csh and auff1 KO susceptibility to Hs unchanged | Pogorelko et al., 2016 |
| Hs30D08 | Unknown | Nucleus (TE) | Arabidopsis suppressor of mec-8 and unc-52 spliceosomal protein homolog 2 (SMU2) | ✓ | ✓ | | smu2-1 At KO are less susceptible to Hs | Verma et al., 2018 |
| Hs32E03 | Unknown | Nucleus (TE) | Arabidopsis histone deacetylase (HDT1) and histone Chaperone (FKBP53) | ✓ | ✓ | | hdt KO susceptibility to Hs unchanged | Vijayapalani et al., 2018 |
| HsGBP | Cellulose-binding protein | Cytoplasmic (TE) | Arabidopsis pectin methylesterase (PME3) | ✓ | ✓ | ✓ | PME3 At OE lines more susceptible to Hs, At KO less susceptible to Hs | Hewzi et al., 2008 |
| Hs4E02 | Unknown | Nucleus (TE) | Arabidopsis papain-like cysteine protease responsive to dehydration (RD21A) | ✓ | ✓ | | nd | Pogorelko et al., 2019 |
| Hs4F01 | Annexin-like | nd | Arabidopsis 2OG-Fe (II) oxygenase/oxidoreductase family (JOX2) | ✓ | | | nd | Patel et al., 2010 |
| HsVAP2 | Venom allergen-like protein | Nucleus (TE) | barley CYP404-like protein (HvOLP) | ✓ | ✓ | | nd | Luo et al., 2019 |
| HsGLAND5 | Unknown | Cytoplasm and nucleoplasm (TE) | Arabidopsis PYRUVATE DEHYDROGENASE SUBUNIT (AEMB3003) | ✓ | ✓ | | nd | Yang et al., 2019 |

**Cyst Nematodes, Globodera pallida (Gp) and G. rostochiensis (Gr)**

| Name | Annotation | In planta localisation | Plant species, annotation, and name | Y2H**(c)** | Co-IP or other**(c)** | BiFC**(c)** | Evidence for a role in parasitism |
|------|------------|------------------------|-------------------------------------|-----------|---------------------|---------|-----------------------------|
| GpRBP1 | SPRYSEC | Cytoplasmic (TE) | Potato CC-NB-LRR resistance protein (GPA-2) | ✓ | | | Potato resistance protein | Jones et al., 2009; Sacco et al., 2009 |
| GpSPRY14.2 | SPRYSEC | Cytoplasm and nucleoplasm (TE) | Potato cytoplasmic linker protein (CLIP)-associated protein (SCLASP) | ✓ | | | At clasp1 KO susceptibility to Hs unchanged | Mei et al., 2018 |
| GrVAP1 | Venom allergen-like protein | nd | Tomato apoplastic papain-like cysteine protease (SIPOR3) | ✓ | | | roc3-3 SI mutant susceptibility to Gr unchanged; RCR2 necessary for Cl-2-mediated resistance | Lozano-Torres et al., 2012 |
| GrSPRYSEC-19 | SPRYSEC | nd | Tomato CC-NB-LRR resistance protein (SWF-6) | ✓ | | | Tomato resistance protein | Rehman et al., 2009; Postma et al., 2012 |
| GrCLE1 | CLE-like peptide | nd | Arabidopsis and potato CLAVATA2 (CLV2), Arabidopsis receptor-like kinase LRR-RLKs (EAM1 and EBM2) | | ✓ | | SCLU2 RNAi lines less susceptible to Gr | Lu et al., 2009; Guo et al., 2011; Chen et al., 2014 |

*(a) Effectors expressed in subventral glands (in blue), in dorsal glands (in green), and in hypodermis (in yellow); nd, not determined; IL, immunolocalisation; TE, transient expression in Nicotiana benthamiana leaves or Arabidopsis protoplasts. (b) DNA Binding effector. (c) Approaches used for target identification and validation (Y2H, yeast two hybrid; Co-IP, co-immunoprecipitation; pull-down or in vitro binding assay; BiFC, Bimolecular Fluorescence complementation or Luciferase Complementation). At, Arabidopsis thaliana; Pst, Pseudomonas subtilis DC3000; Mc, Meloidogyne chitwoodi; Sl, Solanum lycopersicum; OE lines, overexpressing lines; KO, T-DNA knockout line.*
CN G. rostochiensis GrVAP-1 and H. schachtii Hs4E02 (Lozano-Torres et al., 2012; Pogorelko et al., 2019) effectors in diverse host plants. Mc01194 and Hs4E02 target the same Arabidopsis PLCP, “Responsive to Dehydration 21A” (RD21A), to promote parasitism (Davies et al., 2015; Pogorelko et al., 2019). The expression of G. rostochiensis VAP1, which targets CRK3Pim in tomato, promotes susceptibility to G. rostochiensis and to the leaf mold Cladosporium fulvum (Lozano-Torres et al., 2012). It seems likely that other such molecular hubs are targeted by nematode effectors.

Other host functions targeted by RKN and CN effectors may be more related to the de novo nematode effectors. It seems likely that other such molecular hubs are targeted by Cladosporium fulvum tomato, promotes susceptibility to G. rostochiensis expression of G. rostochiensis parasitism (Davies et al., 2015; Pogorelko et al., 2019). The host plants. Mc01194 and Hs4E02 target the same Arabidopsis Torres et al., 2012; Pogorelko et al., 2019) effectors in diverse

EXPRESSION THROUGH THE MODULATION OF GENE EXPRESSION

The morphological, structural and metabolic changes associated with the ontogenesis of nematode feeding cells require the extensive reprogramming of plant gene expression (Szakasits et al., 2009; Favery et al., 2016). Gene expression is regulated principally in the nucleus, and several effectors are thought to target the nuclei of the cells destined to become feeding cells, as they have predicted plant-like nuclear or nucleolar localisation signals, and some have been detected in the nucleus following ectopic expression in Nicotiana benthamiana leaves. Nuclear translocation in host cells has been demonstrated by immunolocalisation for only three RKN effectors: the M. incognita MiEFF1 (Jouannet et al., 2012) and the M. javanica MnJULG1a (Lin et al., 2012) of unknown functions, and the M. graminicola MgGPP involved in plant defense suppression (Chen et al., 2017). All three were localized to giant cell nuclei. However, the targets of these effectors have yet to be characterized. Interestingly, some RKN and CN effectors have been shown to target key regulatory processes, including the epigenetic modification of histones, transcriptional regulation and mRNA splicing.

The Hs32E03 effector of H. schachtii alters the acetylation of histones by interacting with the Arabidopsis histone deacetylase (HDAC) HDT1 and FK506 binding protein, FKBP53 (Vijayapalani et al., 2018) in the nucleus. HDT1 and FKBP53 repress the transcription of rRNA genes, with HDT1 deacetylating histone H3 at Lys-9. Hs32E03 has been shown to inhibit HDAC, and an assessment of histone modifications in Hs32E03-expressing Arabidopsis lines based on chromatin immunoprecipitation revealed that these lines had abnormally high levels of acetylation in rDNA regions. As expected, rRNA levels were high in the line showing a low expression of Hs32E03 and displaying higher levels of CN infection. Interestingly, lower levels of rRNA were detected in the line highly expressing Hs32E03, due to the hypermethylation of rDNA promoters, resulting in an inhibition of nematode development. These findings highlight the importance of rRNA levels for syncytium formation, as protein overproduction is required, which in turn necessitates the synthesis of additional ribosomes. Hs32E03 is the first nematode effector for which a role has been reported in the epigenetic regulation of plant gene expression to promote parasitism.

Several other nuclear effectors have been shown to target transcription factors directly. The M. incognita Mi16D10 effector, which has a C-terminal CLE-like domain, interacts with SCARECROW-like transcription factors from both tomato and Arabidopsis (Huang et al., 2006). SCARECROW transcription factors are involved in root radial patterning, particularly in endoderm differentiation, and they act in concert with a short root transcription (SHR) factor (Hirsch and Oldroyd, 2009). Plants overexpressing Mi16D10 have larger root systems, implicating this effector in the modulation of root development. Another example is provided by the H. schachtii effector Hs10A07, which is secreted into the cytoplasm and then phosphorylated by an Arabidopsis kinase. This phosphorylation leads to its translocation into the nucleus, where it interacts with a second protein, IAA16, an Aux/IAA transcription factor, to modulate ARF expression (Hewezi et al., 2015).

Other effectors may modulate gene transcription directly by binding to DNA. Examples include H. glycines HgGLAND4 (Barnes et al., 2018) and the M. incognita 7H08 effector (Zhang et al., 2015). HgGLAND4 has been shown to bind specifically to the promoters of LTP genes implicated in plant defense, suppressing their expression (Barnes et al., 2018). Mi7H08
has been shown to be imported into the nucleus, and to activate the transcription of a reporter gene in planta, but the host genes regulated by this effector have yet to be identified (Zhang et al., 2015).

Finally, a H. schachtii effector, Hs30D08, has been shown to interfere with mRNA splicing, thereby altering gene expression in feeding sites (Verma et al., 2018). RNA splicing is required to remove introns from pre-mRNA and to join the protein-coding sequences (exons) together during the translation of mRNA into protein. Alternative splicing (AS) may occur, and this represents another way of regulating gene expression and increasing protein diversity. In Arabidopsis, 70% of genes may be alternatively spliced, and AS has been shown to play a significant role in plant development, and in responses to abiotic and biotic stresses (Reddy et al., 2013; Yang et al., 2014). Hs30D08 has been shown to interact with an actor of the spliceosome machinery, the auxiliary spliceosomal protein SMU2, in Arabidopsis (Verma et al., 2018). Transcriptomic analyses of Arabidopsis lines expressing the Hs30D08 confirmed its function in modulating AS and gene expression. Future investigations will shed light on the role of splicing and AS in feeding cell formation and plant responses to CN and RKN.

CONCLUSION AND PERSPECTIVES

The repertoire of putative RKN and CN effectors is extremely large, and proteinaceous effectors have been shown to target diverse compartments, manipulating many host plant functions to orchestrate the suppression of plant defenses, the formation of feeding sites and the promotion of nematode survival and reproduction. Moreover, the arsenal of plant pathogens is not restricted to proteinaceous effectors. They also secrete other molecules, such as secondary metabolites, glycolipids, hormones analogs, or small RNAs, to alter plant functions (Weiberg et al., 2013; Manosalva et al., 2015; Collemare et al., 2019). However, few data are available concerning the functions of effectors and the plant processes they target. The elucidation of effector function and the identification of host targets during parasitism thus remain major challenges. The large-scale identification of effector targets, particularly in crops, would be an important breakthrough potentially leading to the discovery of new processes involved in plant-nematode dialog. Comparison of RKN- and CN-targets will shed light on processes involved in their specific parasitic strategies and host ranges.

Functional analyses of effector targets may lead to the identification of susceptibility genes with potential for use in resistance breeding (De Almeida Engler et al., 2005; van Schie and Takken, 2014). In addition, “hubs,” susceptibility factors frequently targeted by different pathogens, may constitute ideal candidates for the design of broad-host range resistance in plants. However, these susceptibility genes are often crucial for plant physiology and development. Interfering with host protein recognition by pathogen effectors may be an interesting way of preserving important plant functions whilst breaking the susceptibility of the plant to pathogens. The breeding of new crops harboring point mutations that are less susceptible to diseases may be achieved with new technologies, such as the TILLING and CRISPR/Cas9 technologies, which are increasingly widely used (Engelhardt et al., 2018; Zaiedi et al., 2018). Improvements in our understanding of effector/target functions are required if we are to block plant-microbe compatible interactions and engineer durable disease resistance.

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