Plant Physiology and Biochemistry 141 (2019) 332–342

Contents lists available at ScienceDirect

Plant Physiology and Biochemistry

journal homepage: www.elsevier.com/locate/plaphy

Review

Effective approaches to study the plant-root knot nematode interaction

Heba M.M. Ibrahim[a,*], Esraa M. Ahmad[a], Ainhoa Martínez-Medina[b], Mohammed A.M. Aly[a]

[a] Department of Genetics, Faculty of Agriculture, Cairo University, Giza, Egypt
[b] Molecular Interaction Ecology, German Centre for Integrative Biodiversity Research, Leipzig, Germany

ARTICLE INFO

Keywords:
Meloidogyne
Parasitism
Plant-nematode interaction
Root knot nematode
siRNA
Omics

ABSTRACT

Plant-parasitic nematodes cause major agricultural losses worldwide. Examining the molecular mechanisms underlying plant-nematode interactions and how plants respond to different invading pathogens is attracting major attention to reduce the expanding gap between agricultural production and the needs of the growing world population. This review summarizes the most recent developments in plant-nematode interactions and the diverse approaches used to improve plant resistance against root knot nematode (RKN). We will emphasize the recent rapid advances in genome sequencing technologies, small interfering RNA techniques (RNAi) and targeted genome editing which are contributing to the significant progress in understanding the plant-nematode interaction mechanisms. Also, molecular approaches to improve plant resistance against nematodes are considered.

1. Introduction

The world's rapid increase of the population growth rate in recent decades is one of the main challenges in terms of securing food supply. Plant-parasitic nematodes are considered among the most damaging plant pathogens worldwide (Trudgill and Blok, 2001). The damage by nematodes is estimated to cause a yearly loss of about 100 billion dollars in agricultural crops, despite all the currently used methods for nematode control (Coyne et al., 2018). In addition, the increase in global temperature due to climate changes is expected to affects nematode populations either by accelerating their life cycle as the soil temperature increases, or by changing host plant physiology which facilitates the infection process (Somasekhar and Prasad, 2012). For example, according to the NOAA global analysis for 2017, the 2017 average global temperature across land and ocean surface areas was 0.84 °C above the 20th century average of 13.9 °C (https://www.ncdc.noaa.gov/sotc/global/201713).

Nematodes are animals of the phylum Nematoda. They are multicellular organisms that have existed for about one billion years, and they are the second-most diverse animal lineage after insects. Some nematodes are free-living and others are animal or plant parasites.

Root-knot nematodes (RKNs; *Meloidogyne* spp.) cyst nematodes (*Heterodera* and *Globodera* spp.) and lesion nematodes (*Pratylenchus* spp.) are the three most important groups of nematodes, and can infect, feed on and reproduce on a vast range of plant species (Jones et al., 2013; Sikora et al., 2018).

Root knot nematodes (RKN), in particular *Meloidogyne* spp. and most prominently *M. incognita*, exhibit a broad host range and affect a multitude of wild plants and crops such as tomato, potato, and soybean (Abad and Williamson, 2010; Dutta et al., 2015; Jones et al., 2011). This polyphagous species has been even considered as one of the most damaging pathogens in the world (Trudgill and Blok, 2001). An online search provides an indication of the increasing interest worldwide in studying the relationship between RKN and their host plants (Cabrera et al., 2016). Therefore, in this review we first focus our discussion on the molecular aspects underlining the plant-RKN interaction. We further review current techniques used to study the molecular basis of the interaction such as high-throughput transcriptomics and genomics technologies and computational resources as well as gene cloning and silencing techniques. We finally summarize the several approaches to implement the knowledge about molecular mediators of the plant-RKN interaction together with genome engineering technologies towards reinforcing nematode resistance.

2. Biology of root knot nematodes (RKN)

2.1. RKN life cycle

Root knot nematodes (RKN; *Meloidogyne* spp.) are obligate sedentary endoparasites that require infecting a host plant to complete their life cycle (Singh and Phulera, 2015). The RKN life cycle can be summarized as illustrated in Fig. (1). It begins with the female laying eggs

* Corresponding author.
E-mail address: heba.ibrahim@staff.cu.edu.eg (H.M.M. Ibrahim).

https://doi.org/10.1016/j.plaphy.2019.06.009
Received 27 January 2019; Received in revised form 26 May 2019; Accepted 8 June 2019
Available online 09 June 2019
0981-9428/

Abbreviations

CRISPR/Cas9	Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR-Associated9
DAPG	2,4-Dacetylphloroglucinol
ES	Excretory/Secretory Proteins
ETI	Effector-Triggered Immunity
J2,3,4	Juvenile Stage 2, 3, 4
JA	Jasmonic Acid
NBS-LRR	Nucleotide-Binding Site Leucine-Rich Repeat
PAMP	Plant Pathogen-Associated Molecular Pattern
PLCP	Papain-Like Cysteine Proteases
PTI	PAMP-Triggered Immunity
QTL	Quantitative Trait Locus
RKN	Root Knot Nematode
RN	Reniform Nematode
RNAi	RNA Interference
SA	Salicylic Acid
SCL	SCARECROW-Like Transcription Factors
SNP	Single Nucleotide Polymorphism
TALEN	Transcription Activator-Like Effector Nuclease
TE	Transposable Elements

in the soil and/or in plant tissues. Infectious second-stage juveniles (J2) hatch from these eggs and enter roots of susceptible plants close to the root tips. The J2 root knot nematodes migrate intercellularly towards the vascular bundles where they initiate and establish their permanent feeding sites (J3 and J4). These feeding sites are made up of multiple multinucleate giant cells that can be easily recognized later as “knots” or “galls” on the roots where the nematodes feed and develop. The adult females then lay eggs, which give rise to new infectious juveniles.

When a RKN infests plant roots, it launches a sophisticated interactive relationship with the host cell. The nematode secretes effector proteins from the stylet to begin the parasitic process (Quentin et al., 2013). All biotrophic nematodes have an esophageal gland (which consists of one dorsal and two sub-ventral glands) where a number of effector proteins are secreted and then transferred to the host plant cells through the stylet. These effector proteins are required for establishing and maintaining the feeding site (Williamson and Hussey, 1996; Hussey, 1989). Some of these secreted proteins either modify the cell wall of the host plant and/or affect the progression of the host cell cycle, protein degradation, defense responses and transcriptional regulation (Akker and Birch, 2016; Davis et al., 2004).

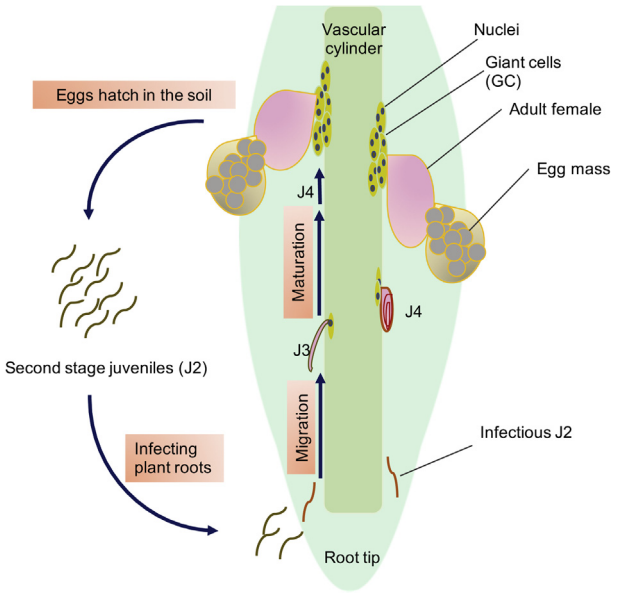

Fig. 1. Schematic model of the root knot nematode life cycle. The mature female releases eggs into the soil, where juvenile nematodes (J2) hatch. J2 juveniles may penetrate new susceptible plant roots and subsequently migrate intercellularly towards the vascular tissue. Then, the nematode induces formation of multinucleate giant cells to establish its feeding site (J3). Maturation of J3 continues to (J4), which in turn progress in maturation to adult females, or males under stressful condition. A female nematode will mature and form an egg sack to generate new nematode eggs.

2.2. The genomes of the RKN

The size of RKNs haploid genome was estimated to be around 86 Mb in size (Abad et al., 2008). However, genome sequencing of three RKN species was accomplished in 2017 using Illumina and 454 technologies and revealed an assembled sequence of 184, 236, and 258 Mb, for *M. incognita, M. javanica,* and *M. arenaria*, respectively (Blanc-Mathieu et al., 2017). By contrast, the genome assembly of facultative sexual nematode *M. hapla* was approximately 53 Mb (Blanc-Mathieu et al., 2017; Szitenberg et al., 2017). These results suggest polyploidy of the other three *Meloidogyne* species, since their genomes are 3–5 times bigger than the *M. hapla* genome (Blanc-Mathieu et al., 2017). Using more advanced computational analysis tools these analysis estimated the genomes of the above mentioned studied *Meloidogyne spp.* to harbor at least 43,718, 97,208, 103,001, and 14,700 protein coding genes for *M. incognita, M. javanica,* and *M. arenaria, and M. hapla,* respectively (Blanc-Mathieu et al., 2017; Szitenberg et al., 2017). Although both studies conducted analyses of these three *Meloidogyne* species (*M. incognita, M. javanica,* and *M. arenaria*), the results from Blanc-Mathieu et al. (2017) appeared to be more accurate since the N50 of the assembled genomes are much higher compared to the counterparts in the other study (Szitenberg et al., 2017). In addition, the assembled genomes sizes were confirmed with flow cytometry. The total size of the assembled genome of the model nematode *Caenorhabditis elegans* is comprised of 100 Mb (Hillier et al., 2005). By comparing the *M. incognita* genome architecture with related nematodes such as *C. elegans* and *Brugia malay* in previous studies, only one operon was found to be highly conserved among them (Abad et al., 2008). However, in a more recent discovery by Gahoi and Gautam (2017) 473 Excretory/Secretory (ES) proteins out of 1889 were predicted to have orthologues in *C. elegans* and only 561 protein appeared to be specific to *M. incognita*. Moreover, the study conducted in 2017 by Blanc-Mathieu et al. revealed significant differences in the genomic features of the sexual and asexual *Meloidogyne* species. The asexually reproducing species showed more duplicated regions as a result of being highly enriched with transposable elements (TE), which suggest genome plasticity and functional divergence of the duplicated regions (Blanc-Mathieu et al., 2017). Although the impact of that study was groundbreaking, generating contiguous assemblies of the asexual *Meloidogyne* genomes was still technically difficult using short read sequencing. The assemblies were more fragmented compared to *M. hapla* (N50 83,645), likely due to the genomic features of the asexual *Meloidogyne* spp., where TEs cover ca. 50% of the genomes (Blanc-Mathieu et al., 2017). In recent years however, using a high-quality long read genome sequencing method became available and affordable. For instance, a PacBio RSII long read-based assembly for the RKN *M. arenaria* was published that comprised 2224 contigs and that had a total assembly length of 284.05 Mb (Sato et al., 2018). The assembled genome had an N50 of 204,551 bp and was estimated to cover 94.8% of the coding region, while the previous genome assembly based on Illumina sequencing data showed an N50 contig length of 10,504 bp with a coverage of 91% of the coding region in (Szitenberg et al., 2017), and an N50 of 16,462 bp

with an assembly genome size of 258.07 Mb in Blanc-Matthieu et al. (2017). This highlights that emerging genome sequencing technologies have the power to produce high quality genomes of root knot nematodes and will enable comprehensive analysis of the evolution of RKN in the future.

2.3. Resources for RKN research

Computational tools and publicly available databases facilitate better understanding of the different types of nematode parasitism and the genes and proteins involved in this process. For example, WormBase is an online database created by biologists and computer scientists to provide all the information concerning genomes and genes of currently 138 different nematode species. The *M. incognita* genome information, annotation, and gene prediction was incorporated in the WormBase database in 2014 (https://parasite.wormbase.org/Meloidogyne_incognita_prjea28837/Info/Index/). *Meloidogyne* genomic resource is an INRA-related database that specifically gives information about three of the root knot nematode species, *M. incognita, M. arenaria, and M. javanica* (https://meloidogyne.inra.fr). Another useful database for RKN is available at http://nematode.net/NN3_frontpage.cgi (Martin et al., 2015). This database gives information regarding functional genomics, transcriptomics, and proteomics of all parasitic roundworms. These online databases related to parasitic nematode genomes, transcriptomes, and proteomes provide valuable and useful information needed to speed up developing approaches to efficiently and sustainably control nematode infection and understanding the mechanism of the plant nematode interaction.

3. Molecular Plant-RKN interaction

3.1. Transcriptomics

Microarray and RNA deep sequencing provide novel and extensive insights into understanding the expression profiles of genes that participate in the parasitism process in both nematodes and their host plants. For instance, the microarray analysis that was performed by Ibrahim et al. (2011)a revealed differential expression of soybean genes in the galls formed on soybean roots (*Glycine max* L.) cultivar (cv.) William 82 during the compatible interaction with *M. incognita*. These changes include up- and down-regulation of genes related to cell wall remodeling and modification, mitosis and cell division, carbon and energy metabolism, and downregulation of genes involved in formation of defense-related compounds such as jasmonic acid (JA). Cabrera et al. (2014) analyzed the transcriptomic changes in *Arabidopsis thaliana* at early stages after infection with cyst nematodes and RKN and found that 1161 genes were up-regulated in giant cells, of which 529 genes were also induced in the syncytia, indicating that there is transcriptomic overlap induced by the two types of nematodes. All the genes dys-regulated in giant cell formation are affected by phytohormones, especially auxin and ethylene, such as the homeobox protein HAT1 and ethylene-responsive transcription factors like ESE3. Such studies emphasized the power of high throughput transcriptome sequencing (RNA-Seq) for RKN research.

3.2. RKN recruit plant hormone pathways

To establish their feeding sites, nematodes manipulate specific plant developmental pathways regulated by phytohormones. In addition, to colonize their host roots they regulate plant defenses by interacting with phytohormone-regulated defense pathways. This interface between development and defense results in complex patterns and renders it difficult to establish the specific role of different phytohormones in the RKN parasitism process (Gheysen and Mitchum, 2018). Moreover, the impact of phytohormones in plant-RKN interactions seems to be modulated by the host plant, the nematode species, and the infectious stage of the nematode. Here we highlight just some recent findings on the role of several hormonal-regulated pathways on RKN parasitism. For additional information in this topic readers are referred to the recent review by Gheysen and Mitchum (2018). Among plant hormones, auxins are key regulators of organogenesis, and thus it is not surprising that the establishment of RKN feeding sites is associated with local accumulation of auxins (Karczmarek et al., 2004). Accordingly, auxin mutants are less susceptible to RKN (Grunewald et al., 2009). Transcriptome analyses further show a complex temporal and spatial regulation pattern of auxin biosynthesis and signaling-related genes in RKN feeding sites (Cabrera et al., 2016, 2015). Although less studied, cytokinins are also proven to be involved in the RKN parasitism. This is not surprising due to their role in cell cycle control and nutrient mobilization. For instance, Arabidopsis plants with reduced cytokinin levels were found to be less susceptible to RKN (Lohar et al., 2004). Interestingly, De Meutter et al. (De Meutter et al., 2003) detected cytokinins in secretions from the RKN *M. incognita*, further indicating the importance of cytokinins on RKN parasitism. Regarding hormonal-regulated defensive pathways, several studies have shown the relevance of the salicylic acid (SA) and jasmonic acid (JA) pathways in the RKN-plant interaction. The SA pathway is generally involved in protection against biotrophic pathogens. According to the biotrophic nature of RKN, it is not surprising that the SA-pathway participates in the defense response mounted against RKN, although its role seems to be modulated by the parasitism stage (Martínez-Medina et al., 2017). Indeed, the elicitation of the SA pathway has been shown to reduce RNK infection (Molinari and Fanelli, 2013), although in some cases, this effect is not evident (Sanz-Alférez et al., 2008). Several studies have further suggested the ability of RKN to suppress the SA-related defenses in order to successfully colonize their host roots (Barcala et al., 2010; Martínez-Medina et al., 2017; Shukla et al., 2018). The JA-pathway is in general involved in plant defenses against necrotrophic pathogens and leaf chewing insects. Several studies have demonstrated that the elicitation of the JA-pathway enhances plant resistance to RKN (Cooper et al., 2005; Fujimoto et al., 2011; Nahar et al., 2011). However, analyses by using transgenic lines impaired in JA biosynthesis and signaling yield fragmented results. It seems that depending on the specific mutations of JA related genes, the plant can be susceptible to RKN (Bhattarai et al., 2008; Fan et al., 2015; Gleason et al., 2016; Kyndt et al., 2017; Sun et al., 2011). Besides the phyhormonal-pathways described above, other phyhormonal-pathways such as the ethylene-, abscisic acid- or the gibberellic acid-related pathways are also regulated during RKN parasitism, although they have been less extensively studied (Gheysen and Mitchum, 2018).

3.3. RKN effectors

Knowledge about RKN-secreted proteins and their interactions with the host cell during infection may provide a better understanding of the infection process. For instance, *in silico* analysis of the *Meloidogyne incognita* secretome and proteome resulted in the prediction of 1889 Excretory/Secretory (ES) proteins putatively secreted by the esophageal gland. Many of these proteins have orthologues in other living nematodes, while 561 (29.7%) of these proteins are specific to *M. incognita* (Gahoi and Gautam, 2017). ES proteins help in degrading the plant cell wall to facilitate nematode entrance, protecting nematodes from the plant defense responses and serve in establishing feeding sites.

Recently, scientists have identified several effectors secreted by RKN to facilitate parasitism by suppressing their hosts' immune response. The *Meloidogyne* effector protein MiMsp40 targets the plant pathogen-associated molecular pattern (PAMP)-triggered immunity (PTI). Overexpression of MiMsp40 in Arabidopsis plants resulted in strong infection and weak susceptible plants by suppressing PTI and/or ETI signals (effector-triggered immunity) and therefore increased plant susceptibility to nematodes as the number of galls and eggs significantly increased after 6 weeks of inoculation (Niu et al., 2016). Also, the effector

Mi8D05 was found to be actively expressed in *M. incognita* J2 when infecting plant roots. Silencing of this gene in the J2 resulted in a significant decrease in the infection rate (90%) in Arabidopsis plants (Xue et al., 2013). There are also effectors secreted by the RKN targeting plant transcription factors. The first such direct interaction was reported by Huang et al. (2006)a,b who found that the RKN signaling peptide 16D10 interacts directly with regulatory proteins in Arabidopsis, SCARECROW-like transcription factors (SCL), which altered the root growth patterns likely to favor nematode infection and accommodation. 16D10 functions as a regulator of two SCL transcription factors initiating SCL-mediated signal transduction cascades in infected cells to induce root cell proliferation and it also may be involved in feeding cell formation. Moreover, the *M. incognita* effector MiPFN3 supports feeding site formation by direct remodeling of the actin cytoskeleton of the plant cell resulting in giant cell formation (Leelarasamee et al., 2018). Another example is MiSGCR1, a small glycine- and cysteine-rich effector that was found to have a major role in successful infection by suppressing plant cell death due to hypersensitive response (Nguyen et al., 2018). Similar effects of suppressing the plant cell death were discovered with *M. enterolobii* and *M. graminicola* when silencing the nematode effectors MeTCT and MgGPP, respectively (Chen et al., 2017; Zhuo et al., 2017). Another protein, Mc1194, was revealed as an effector that facilitates the infection of *M. chitwoodi* by interacting with the protease and granulin domains of RD21A in Arabidopsis, which is a member of the papain-like cysteine proteases (PLCP) that are involved in programmed cell death (Davies et al., 2015). The cysteine proteinase RD21A was reported by Shindo et al. (2012) to play a role in the defense response against the necrotrophic fungal pathogen *Botrytis cinerea* in Arabidopsis. These examples illustrate that RKN employ a multitude of effectors to manipulate host plant roots. We suggest a schematic model (Fig. 2) to summarize this process. However, much is still unknown as most effectors remain uncharacterized to date.

4. Control strategies for plant parasitic nematodes

Several strategies are being used to control nematode infections in the field, which is very important for sustainable agriculture and food security. In the following we discuss the most recent conventional and non-conventional approaches to manage RKN infection of economically important plant species.

4.1. Traditional control strategies

Crop rotation (Chen and Tsay, 2006) and cover crops (Navarrete et al., 2016) are commonly applied to mitigate the damage of RKN. In addition, other techniques have been used and controlled nematode infection such as flooding and soil solarization (Ferris et al., 2012). However, these approaches are not completely successful because of the diverse RKN species and their broad host range. In addition, practices such as flooding are only successful in warm climates, require plenty of water and need flooding to be applied for a considerable amount of time, which may be harmful to the plant. Moreover, field solarization require stopping of cultivation for long periods. Thus, successful launch and continuation of agricultural practices to manage RKN infestation require serious and extensive planning and considerable investments. Beside flooding and solarization, soil fumigation has been used as another approach (Nelson et al., 2002). Crop yield can be dramatically affected by nematode infestation in nonfumigated soils. There are some fumigants that are currently being used in preplant treatments for management of RKN in vegetables, such as 1,3 D-metam sodium (Desaeger et al., 2017). Some of these fumigants are very effective against RKN, such as methyl bromide (Nelson et al., 2002). They are, however, greatly restricted in developed countries because of their dangerous implication on the environment and on human health (USDA ERS, 2000). On the other hand, studies have been conducted to utilize natural plant products and ammonia as fumigants against RKN populations to replace the highly toxic chemical fumigant compounds. For instance, the use of a mixture of lime and ammonium bicarbonate resulted in a release of an ammonia-releasing organic compound that had a nematocidal effect on plant-parasitic nematodes such as *Meloidogyne* and *Rotylenchulus* spp. (Oka and Pivonia, 2002; Su et al., 2015). In another study, an organic method included applying a mustard seed meal into the soil, such as yellow mustard alone or combined with another type such as Indian mustard as a fertilizer, where the mustard is a by-product of biodiesel fuel production from *Brassicaceae* plants (Meyer et al., 2015). However, most of the chemical fumigants exhibit a wide-spectrum and a stronger effect on RKN populations than their organic counterparts.

4.2. Biological control strategies

Biopesticides can be defined as the pesticides made of living organisms or their products and they are used to defend plants against invading pathogens. The microorganisms used as biopesticides are ingested by the host organism (the plant pathogen) and can cause tissue

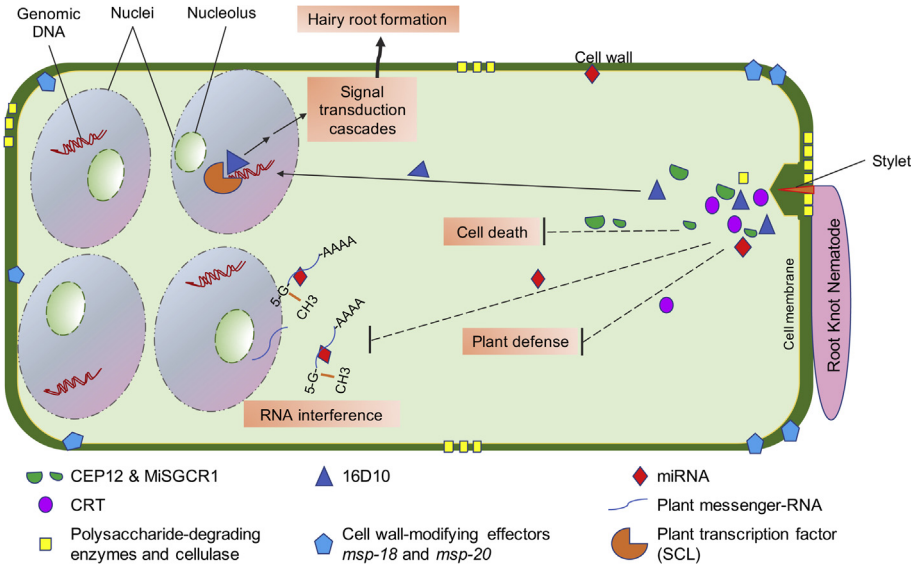

Fig. 2. Schematic model of the interaction of a sedentary parasitic nematode with its feeding cell. The RKN (purple) insert their stylet through the plant cell wall without penetrating the plasma membrane (invagination). Then, effectors are secreted from esophageal gland cells into the plant cell through the stylet, affecting cell processes on a large scale, including plant defense regulation, RNA interference, cell cycle, signal transduction, and tissue formation such as hairy root formation. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

destruction, and sometimes secrete toxic substances that affect the host organism (Tranier et al., 2014).

There are several nematode-antagonistic biocontrol agents that have different nematophagous properties and are classified into different categories accordingly. For instance, the two major groups are bacteria (Kiewnick and Sikora, 2006; Zeng et al., 2013) and fungi (Tranier et al., 2014). The mode of action of these biocontrol agents differ from each other and they could be specific to the nematode developmental stage. For instance, *Paecilomyces lilacinus* invades Meloidogyne spp. Eggs in tomato (Goswami et al., 2006). Another biocontrol agent studied to test its effect in the suppression of RKN infection consisted of two different strains of the fungus *Verticillium lecanii*. Soil inoculation with the two strains individually suppressed the RKN egg numbers. The two strains suppressed RKN even after being autoclaved, which indicated that the produced substance that inhibits nematodes is heat-stable (Meyer, 1998).

On the other hand, the saprophytic fungi *Arthrobotrys* spp., which are specifically RKN-antagonistic nematophous fungi. The mode of action of *Arthrobotrys* spp. fungi relies on capturing the nematodes by trapping them in three-dimensional hyphal network, followed by penetration of the nematode body and by secretion of extracellular enzymes that break down the nematode cuticle. These are called predatory fungi and they are specifically preying on nematodes (Huang et al., 2004).

There are several studies that have been conducted to identify biological control agents and their secreted substances that have nematode-antagonistic effects (Collange et al., 2011; Huang et al., 2004; Lamovšek et al., 2013; Tranier et al., 2014). One example of such substances produced by nematophagous fungi is the chymoelastase-like protease produced by *Verticillium chlamydosporium*, which has a nematocidal effect on *M. incognita* by hydrolyzing the outer egg shell (Segers et al., 1994). Moreover, The effect of the antiphytopathogenic 2,4-diacetylphloroglucinol (DAPG), produced by *Pseudomonas fluorescens*, was examined by Meyer et al. (2009) on two groups of nematodes. The first group was the plant-parasitic nematodes *Heterodera glycines, M. incognita, Pratylenchus scribneri* and X*iphinema americanum.* The second group consisted of the bacteria-feeding nematodes *C. elegans*, *Pristionchus pacificus*, and *Rhabditis rainai*. DAPG was toxic to *X. americanum* adults and reduced the hatching of *M. incognita* but stimulated the hatching of *C. elegans*. On the other hand, DAPG did not affect the viability of both after hatching. The effect of DAPG on RKN infecting watermelon was also studied by Meyer et al. (2016), where the number of RKN eggs was reduced by 28.9% in the cv. “Charleston Gray”, while it had no effect on cv. “Sugar Baby” infected by the same RKN, indicating that DAPG may have a plant genotype-dependent effect.

However, the use of biocontrol agents for defense against plant parasitic nematodes and pathogenic fungi is not fully commercialized because of biotic barriers such as the host range and susceptibility of different plants against those agents. Moreover, abiotic barriers such as

Box 1
The types of nematode target genes.

Parasitism-related genes (parasitomes).

A 21 bp siRNAs specifically targeting the gene FMRF amide-like peptide (flp) were sufficient to silence the gene in infectious stage juveniles (J2) of the potato cyst nematode *Globodera pallida* and the root knot nematode *M. incognita* (Dalzell et al., 2010). Moreover, suppression of two *M. incognita* genes, dual oxidase and a subunit of a signal peptidase required for processing of nematode secreted proteins, using RNAi resulted in reduction of the number of nematodes by 50% (Charlton et al., 2010). Moreover, two *FMRF amide-like peptide* genes (*flp-14* and *flp-18*) silenced *in vitro* and *in planta* in transformed tobacco lines affected the migration of *M. incognita* and their subsequent invasion of the root system. FLPs or neuropeptides are core components of all the biological processes of nematodes including feeding, locomotion parasitism and the sensory system, suggesting that neuropeptides would be promising targets in silencing studies to improve plant resistance against root knot nematodes (Papolu et al., 2013).

Further studies showed that Mi-CRT, a calreticulin (CRT) that is secreted by the nematode into the apoplastic space during infection, greatly affects plant defense. Knocking down *Mi-CRT* by RNAi reduced the ability of the nematode to infect nematode-susceptible *Arabidopsis thaliana* lines (Jaouannet et al., 2013). Shivakumara et al. (2017) reported that host-induced gene silencing of the *M. incognita* cell wall modifying enzyme effector genes *msp-18* and *msp-20* independently resulted in 43–70% and 42–67% reduction of *M. incognita* multiplication in eggplant, respectively.

There are at least 486 secreted proteins from *M. incognita* that are expressed during infection and are potentially involved in feeding site formation and host cell remodeling and reprograming to favor the nematode establishment. While these effector candidates have not been well studied so far, they may be promising targets for gene silencing to confer broad resistance against RKN to host plant (Bellafiore et al., 2008; Ali et al., 2017; Leelarasamee et al., 2018).

Development-related genes.

Silencing of specific nematode genes appears to have a profound effect on nematode development during infection, which may result in failure of the continuation of the infection. Urwin et al. (2002) found that silencing of genes encoding C-type cysteine proteinases inhibited the development of the nematode inside the roots and reduced the number of sperm cells formed by the mature male. Silencing this gene further resulted in a 60% reduction in the number of females that were able to reach the adult stage and produce eggs. This enzyme is synthesized in the intestine and is predicted to have a digestive function (Shingles et al., 2007). Furthermore, the *Mi-Rpn7* gene exhibited an influential role in *M. incognita* J2 motility and effectivity. When the J2 worms were subjected to uptake of a double stranded *Mi-Rpn7* RNA, the infection rate of the J2 was significantly reduced accompanied by interrupted locomotion, in addition to a 34% reduction of egg mass in transgenic composite soybean plants (Niu et al., 2012). *In planta* RNAi has been successfully used to silence four *M. incognita* developmental genes, namely L-lactate dehydrogenase, mitochondrial stress-70 protein precursor, ATP synthase beta-chain mitochondrial precursor, and tyrosine phosphatase, in an attempt to broaden resistance of soybean against the root-knot nematode, resulting in 94% reduction in gall formation on transformed soybean roots after challenge with RKN (Ibrahim et al., 2011a).

RNAi knockdown of heat-shock protein 90 (*hsp90*) and isocitrate lyase (*icl*) gene expression reduced root-knot nematode reproduction (Lourenço-Tessutti et al., 2015). These two genes are important in the nematode life cycle. Expression of RNAi constructs targeting *M. incognita hsp90* in *Nicotiana tabacum* plants resulted in a delay in the formation of galls and a reduction of the number of the newly formed eggs by 46%. However, silencing of *icl* did not affect the formation of nematode galls in the transformed plants, though it resulted in a 77% reduction in egg oviposition compared with the non-transformed plants.

Housekeeping genes.

Silencing housekeeping genes such as integrases, splicing factors, ribosomal protein 3a and 4, spliceosomal SR protein, coatomers, to name but a few, affected the reproductive fitness of the invading nematode and the success of the parasitism process (Klink et al., 2009; Yadav et al., 2006).

the physical and chemical nature of the rhizosphere may play a role. Since the effectiveness of these aforementioned traditional and biological control agents seems limited at best, there is a need to apply more suitable and targeted methods to control RKN infections. In the following, we discuss targeted molecular approaches that make use of RKN virulence genes for silencing as well as resources for plant resistance loci.

4.3. Molecular genetics strategies

The rapid progress in omics, biotechnology, and high-throughput next-generation sequencing methods have enriched our knowledge of the molecular aspects of the plant-nematode interactions and made it possible to incorporate and express endogenous and heterologous genes in plants to enhance plant resistance against nematodes. Genetic transformation strategies to achieve plant resistance against RKN include: a) transferring the resistance gene such as *Mi, Me,* and *Ma* from resistant plants to different plant species (Barbary et al., 2015; Claverie et al., 2011; Williamson et al., 1996), b) overexpression of different protease inhibitors (Lilley et al., 1999; Papolu et al., 2016; Tripathi et al., 2015) and c) gene silencing to target essential nematode genes that are required for successful establishment of nematode infection (Ibrahim et al., 2011b). Furthermore, it could be suggested to clone and overexpress the genes responsible for the biocontrol process from the corresponding agents such as *Paecilomyces javanicus* that may benefit plant protection efforts to activate and strengthen the plant immune response against infection with RKN.

Since RNAi technologies have been proven to be a potent strategy to control infection with multiple plant pathogens, we will focus on RNAi-based approaches. RNA interference (RNAi) is a natural defense mechanism that triggers degradation of mRNA to regulate gene expression at the post-transcriptional level and to degrade foreign RNA during virus infection in eukaryotes (Fire et al., 1998; Rosso et al., 2009; Sharp, 2001). The RNAi pathways in a model organism such as the free-living nematode *C. elegans* provided insights that helped develop new approaches to reach complete resistance against other nematodes such as RKN. RNAi has been used successfully in *C. elegans* to, for example, silence the *unc-22* gene, which is responsible for the non-essential myofilament protein in muscle cells (Fire et al., 1998). In addition, RNAi has been used in *C. elegans* to study the functions of 19,427 predicted *C. elegans* genes (Kamath et al., 2003).

There are several strategies to use RNAi to produce plants with modified defense responses against different pathogens at the transcriptional and post-transcriptional levels, such as virus-induced gene silencing (VIGS) and microRNA (miRNA)-mediated gene silencing (Mmeka et al., 2014). Navarro et al. (2006) first reported the involvement of miR393 as an antibacterial miRNA in the plant defense machinery to limit the growth of *Pseudomonas syringae* in Arabidopsis plants. miR393 represses auxin signaling and negatively regulates the mRNAs of transport inhibitor response 1, auxin signaling F-box proteins 2 and 3 (TIR1, AFB2, and AFB3). miR393 was also found to be upregulated upon infection. Another group of 60 miRNAs from 25 miRNA families were identified in soybean cultivars after infection by SCN that putatively target genes with functions such as oxidative activity, ion and nucleic acid binding (Tian et al., 2017). In *M. incognita,* the expression of several miRNA genes was up-regulated during infection and, in turn, affected the expression of their target genes in cotton (*Gossypium hirsutum*) (Pan et al., 2018) and tomato (*Solanum lycopersicum*) (Kaur et al., 2017). Co-down-regulation of six genes was achieved where infection was reduced to about 44% by silencing the genes *drh-3*, *tsn-1*, *rrf-1*, *xrn-2*, *mut-2* and *alg-1* individually, which are components of the RNA interference pathway of *M. incognita.* In addition, knocking down the genes *drh-3* and *mut-2* disturbed nematode development (Iqbal et al., 2016).

Dutta et al. (2015) suggested an integrative approach that uses multiple RNAi constructs targeting several nematode processes as well as tissue-specific plant promoters, which are wound-inducible or plant parasitic nematode-inducible, to control expression of these RNAi constructs. Although RNA silencing occurs in a highly sequence-specific manner, off-target silencing of endogenous plant genes or genes from non-pathogenic microbes can be a problem. Off-target gene silencing can be minimized by (1) thorough bioinformatics analysis to minimize the risk of silencing non-targeted genes with RNAi constructs, (2) targeting the 3′ and 5’ untranslated regions (UTRs) as these are highly variable between kingdoms, (3) targeting species-specific genes; these genes can be detected using comparative nematode genomics. This thorough analysis will also result in avoiding the use of gene families with high degree of sequence similarity between the plant and animal kingdoms. These can be considered as biosafety requirements.

In general, three types of nematode-specific genes are being used as targets for RNAi approaches, i.e. genes facilitating nematode parasitism, nematode developmental genes, and housekeeping genes (Box 1). Studies targeting genes involved in nematode parasitism included the *M. incognita* calreticulin Mi-CRT (Jaouannet et al., 2013) and the cell wall-modifying enzymes *msp-18* and *msp-20* (Shivakumara et al., 2017). RNAi fragments have been successfully used to target *Meloidogyne* parasitism genes expressed in the sub-ventral or dorsal glands of different plant parasitic nematode species. As a result, the parasitism process was remarkably affected and notable interference detected using ELISA (enzyme-linked immunosorbent assay) and quantitative real-time PCR (Dinh et al., 2015; Guozhong G. Huang et al., 2006; Jaouannet et al., 2013; Kapur-Ghai et al., 2014; Papolu et al., 2016; Sindhu et al., 2009; Xue et al., 2013).

Development-related genes from the RKN *M. incognita* include *Mi-Rpn7*, whose downregulation interfered with locomotion in J2 juveniles (Niu et al., 2012), L-lactate dehydrogenase, mitochondrial stress-70 protein precursor, ATP synthase beta-chain mitochondrial precursor, and tyrosine phosphatase (Ibrahim et al., 2011a) as well as heat-shock protein 90 (*hsp90*) and isocitrate lyase (*icl*) (Lourenço-Tessutti et al., 2015). RNAi targeting these genes severely affected RKN infection rates. Finally, RNAi of nematode housekeeping genes such as ribosomal and spliceosomal proteins disturbs the reproductive and parasitic success (Klink et al., 2009; Yadav et al., 2006). While targeting these types of genes indeed has a profound effect on the nematodes by greatly reducing the infection success, developmental genes and housekeeping genes may not be suitable for plant protection approaches, since these are often highly conserved genes among animals and even across phyla. However, RNAi against parasitism genes can be a powerful and highly specific method to protect plants while avoiding off-target effects, since these often include species-specific proteins such as effectors.

4.3.1. Exploiting plant resistance mechanisms

Plants exhibit two layers of induced resistance against microbial and animal pathogens, referred to as pathogen-associated molecular patterns (PAMP)-triggered immunity (PTI) and effector-triggered immunity (ETI). The first barrier of the host plant defense, however, is the epidermal cell wall, which consists of about 40% cellulose, hemicelluloses, xyloglucan, pectin, and various proteoglycans (Ausubel, 2005; Boller and Felix, 2009). For example, some proteins naturally released in the exudates of soybean seeds were found to have nematocidal properties against *M. incognita*. Proteomic approaches and *in vitro* activity assays indicated the existence of 63 exuded proteins, including a β-1,3-glucanase, a chitinase, a lectin, a trypsin inhibitor, and a lipoxygenase, all of which are related to plant defense. The soybean exudates were able to reduce the hatching of nematode eggs and to cause 100% mortality of second-stage juveniles (J2). The pretreatment of *M. incognita* J2 juveniles with these exudates resulted in a 90% reduction of the gall number in tobacco plants. These findings suggested that exuded proteins are directly involved in plant defense against soil pathogens including nematodes during seed germination (Rocha et al., 2015). However, in a recent study Tsai et al. (2019) discovered a *de novo* chemoattractant that is synthesized on Arabidopsis seeds and that

has a positive effect on different RKN species by attracting RKN J2 to invade the newly emerged seedling roots.

Phytohormones play roles in plant-nematode interactions as well. Cytokinin signaling after infection of plants with *H. schachtii* participates in reprogramming of gene expression in infected roots to initiate the syncytium. Cytokinin-insensitive plants are more susceptible to nematodes, which highlights the importance of cytokinin for nematode development. However, elevated cytokinin signaling due to overexpression of *MYB108* and *MYB30* in Arabidopsis results in activation of the plant immune response against the pathogen, suggesting that temporal and spatial fine-tuning of cytokinin signaling by the nematode is required for the infection program (Shanks et al., 2016).

There are other resistance genes studied in plants to develop resistant cultivars. In tomato, the *Mi* gene stimulates necrosis at *M. incognita* feeding sites at early points of infection (Bartlem et al., 1998). In potato, the *H1* gene causes hypersensitivity and necrosis in the syncytium-surrounding cells during syncytium initiation by *G. rostochiensis* (Bartlem et al., 1998).

Using the sequence motifs of resistance genes isolated from tobacco and Arabidopsis, Leister et al. (1996) were able to isolate potato resistance genes against nematode infection. One of these genes was linked to the nematode resistance loci *Gro1* and *R7* responsible for resistance against *Phytophthora infestans*. In wheat, the *Heterodera avenae* resistance gene *Cre3* that belongs to the nucleotide binding site-leucine rich repeat (NBS-LRR) class of plant resistance genes was isolated and mapped to the wheat chromosome 2D (Lagudah et al., 1997). In the soybean cultivars Peking and PI88788, six QTLs including *Rhg1* and *Rhg4* were previously mapped using bi-parental mapping techniques and were confirmed to be related to resistance.

The first genetic mapping for RKN resistance quantitative trait loci (QTLs) was reported by (Tamulonis et al., 1997). They identified two QTLs on chromosome 10 using RFLP markers, i.e. Linkage Group (LG)-O and LG-G. The resistance alleles were found to be originally derived from the ancestral soybean cultivar Palmetto (PI 96354). Li et al. (2001) flanked the QTL region on chromosome 10 using SSR markers, recognizing two SNP markers within the region in PI 437654 resistance to reniform nematode (RN) (Ha et al., 2007). Another RKN resistance QTL was found in 27 soybean cultivars on chromosome 10 (Ha et al., 2004), which was derived from PI 567516C. More recently, other studies identified the QTL, SNP markers and candidate genes responsible for soybean PI 567516C resistance against southern RKN and RN. A genetic linkage map was constructed using 238 SSR and 687 SNPs. This map revealed three QTLs located on chromosomes 10, 13 and 17 responsible for soybean resistance against RKN and two QTLs located on chromosomes 11 and 18 against RN (Jiao et al., 2015). Several SNP markers and candidate genes showing resistance to RKN were identified in different soybean plants (Pham et al., 2013; Xu et al., 2013) and in other RKN resistant plants such as cotton, cowpea, and grapevine (Barbary et al., 2015; Kumar et al., 2016; Santos et al., 2018; Smith et al., 2018; Warmerdam et al., 2018). Bi-parental mapping populations is a technique used to detect and identify the QTLs in populations produced from bi-parental crosses controlling resistance against soybean cyst nematode SCN. However, this method identified only limited allelic diversity related to resistance mechanisms, and its genomic resolution is limited because of the recombination percentage due to the formation of the recombinant inbred line (RIL) populations (Vuong et al., 2015). Taken together, combining new (GWAS) and established (QTL mapping) techniques to identify resistance loci in cultivated and natural soybean lines proves to be a powerful resource for breeding of RKN resistance in soybean. Introgression of resistance genes can not only be highly effective to protect crops from RKN, but such lines are not considered as genetically modified crops, so that they can be broadly applied in agricultural settings.

4.4. Genome engineering approaches

The rapid advances in gene editing technologies are now enabling rapid targeted gene knock-out in plant genomes. There are four main approaches of genome editing techniques, namely homologous recombination-dependent gene targeting, recombinase-mediated site-specific gene integration, oligonucleotide-directed mutagenesis and nuclease-mediated site-specific genome modifications (Cardi and Neal Stewart, 2016). These approaches have the potential to empower breeding of broadly nematode-resistant cultivars in a wide range of crops and herbs, including soybean, tomato and potato. The successful utilization of CRISPR/Cas9-directed genome editing in plant species has been reported in chickpea, the legume models *G. max*, and *M. truncatula* (Li et al., 2015; Meng et al., 2017). The CRISPR/Cas9 technology allows high-throughput gene editing at the genomic scale (Yang et al., 2017). Genome editing may help improving specific characteristics of plants with a limited genetic pool and lack of resistance sources. An emblematic case would be the modification of functional SNPs in the *SHMT* gene (Serine Hydroxymethyltransferase) in order to confer resistance to nematodes or to modify miRNA target sites in *NBS-LRR* genes (nucleotide-binding site leucine-rich repeat) ensuring the up-regulation of certain functional *R*-genes (Leonetti et al., 2018). Further, CRISPR/Cas9 genome editing protocols have been established in *C. elegans* (Friedland et al., 2013; Zamanian and Andersen, 2016), highlighting potential applications of the technology for studying RKNs more effectively in the future. While plants subjected to CRISPR/Cas9 gene editing are considered genetically modified and are thus subject to severe regulations especially in Europe, the technology is a powerful tool for the research of RKN and plant protection.

5. Conclusions

Nematode infections are widely spread worldwide causing devastating crop losses and traditional control methods are not sufficient in countering the threat. Thus, understanding the molecular basis of plant-nematode interactions and identifying key genes and proteins involved in the infection process and the plant resistance response will help in developing new techniques to produce plant lines more resistant to nematode infection. In this review we explored the different methods and techniques used to understand the molecular basis of the interaction between the plant and RKN, such as computational resources and next generation sequencing of genomes and transcriptomes, in addition to the advances in using gene cloning and silencing techniques (RNAi) to control the nematode infection. For instance, omics technologies offer a powerful toolset for effective targeted approaches that could be used to help understanding the interaction between plant and RKN. With the advances of bioinformatics and computational biology, analyzing the omics large-scale data now provides a strong support for identification of interacting biological components and pathways involved in parasitism and plant response. These approaches find RKN effectors to be potential targets for gene silencing or knock-out by their expression profiles. Also, it could be suggested to utilize genes from biocontrol agents such as *Paecilomyces javanicus* to activate and strengthen the plant immune response against infection with RKN. In addition, identifying and characterizing QTLs and actual candidate defense genes against RKN in resistant plants will enhance our understanding of RKN mediated resistance. It will also provide a valuable tool for breeding programs by efficiently incorporating RKN resistance into improved cultivars. However, these approaches must be cautiously applied to avoid emergence of new hyper-virulent RKN populations and pleiotropic effects on plant growth and fruit quality that could reduce crop yields. In conclusion, in this review we pointed out the important roles of genome engineering technologies to study the basis of RKN resistance and to understand the molecular aspects behind the interaction with their host plant towards plant protection against nematode resistance. Moreover, we suggest a high-quality sequencing and

assembly by combining long-read sequencing that covers highly repetitive sequences of RKN in addition to using high-density genetic mapping for RKN to reinforce detection and identification of virulence genes and hence improve our understanding of the plant pathogen interaction.

Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Funding resources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

H. M. M. Ibrahim, wrote the manuscript, collected the literature, designed the article, drew the figures of this manuscript, and revised the manuscript. E. M. Ahmad, participated in collecting the literature, writing, and revising the manuscript. A. Martínez-Medina, added references and participated in writing and revising the manuscript. M. A. M. Aly, contributed to the writing of the manuscript, suggested and added references, critically revised the manuscript and approved it for publication. All authors have read and approved the manuscript.

Acknowledgements

We are grateful to Stefan Kusch (RWTH Aachen University, Germany) for critical revision and proofreading of the manuscript. Esraa M. Ahmad was supported by the Faculty of Agriculture (Cairo University, Egypt).

References

Abad, P., Gouzy, J., Aury, J.-M., Castagnone-Sereno, P., Danchin, E.G.J., Deleury, E., Perfus-Barbeoch, L., Anthouard, V., Artiguenave, F., Blok, V.C., Caillaud, M.-C., Coutinho, P.M., Dasilva, C., De Luca, F., Deau, F., Esquibet, M., Flutre, T., Goldstone, J.V., Hamamouch, N., Hewezi, T., Jaillon, O., Jubin, C., Leonetti, P., Magliano, M., Maier, T.R., Markov, G.V., McVeigh, P., Pesole, G., Poulain, J., Robinson-Rechavi, M., Sallet, E., Ségurens, B., Steinbach, D., Tytgat, T., Ugarte, E., van Ghelder, C., Veronico, P., Baum, T.J., Blaxter, M., Bleve-Zacheo, T., Davis, E.L., Ewbank, J.J., Favery, B., Grenier, E., Henrissat, B., Jones, J.T., Laudet, V., Maule, A.G., Quesneville, H., Rosso, M.-N., Schiex, T., Smant, G., Weissenbach, J., Wincker, P., 2008. Genome sequence of the metazoan plant-parasitic nematode Meloidogyne incognita. Nat. Biotechnol. 26, 909–915. https://doi.org/10.1038/nbt.1482.

Abad, P., Williamson, V.M., 2010. Plant nematode interaction: a sophisticated dialogue. Adv. Bot. Res. 53, 147–192. https://doi.org/10.1016/S0065-2296(10)53005-2.

Akker, S.E. Den, Birch, P.R.J., 2016. Opening the effector protein toolbox for plant – parasitic cyst nematode interactions. Mol. Plant 9, 1451–1453. https://doi.org/10.1016/j.molp.2016.09.008.

Ali, M.A., Azeem, F., Abbas, A., Joyia, F.A., Li, H., Dababat, A.A., 2017. Transgenic strategies for enhancement of nematode resistance in plants. Front. Plant Sci. 8, 750. https://doi.org/10.3389/fpls.2017.00750.

Ausubel, F.M., 2005. Are innate immune signaling pathways in plants and animals conserved? Nat. Immunol. 6, 973–979. https://doi.org/10.1038/ni1253.

Barbary, A., Djian-Caporalino, C., Palloix, A., Castagnone-Sereno, P., 2015. Host genetic resistance to root-knot nematodes, Meloidogyne spp. In: Solanaceae: from Genes to the Field. Pest Manag. Sci, . https://doi.org/10.1002/ps.4091.

Barcala, M., García, A., Cabrera, J., Casson, S., Lindsey, K., Favery, B., García-Casado, G., Solano, R., Fenoll, C., Escobar, C., 2010. Early transcriptomic events in microdissected Arabidopsis nematode-induced giant cells. Plant J. https://doi.org/10.1111/j.1365-313X.2009.04098.x.

Bartlem, D., Jones, M.G.K., Heinrich, T., 1998. Molecular aspects of plant-nematode interactions and their exploitation for resistance strategies. Australas. Plant Pathol. 27, 59. https://doi.org/10.1071/AP98007.

Bellafiore, S., Shen, Z., Rosso, M.-N., Abad, P., Shih, P., Briggs, S.P., 2008. Direct identification of the Meloidogyne incognita secretome reveals proteins with host cell reprogramming potential. PLoS Pathog. 4, e1000192. https://doi.org/10.1371/journal.ppat.1000192.

Bhattarai, K.K., Xie, Q.-G., Mantelin, S., Bishnoi, U., Girke, T., Navarre, D.A., Kaloshian, I., 2008. Tomato susceptibility to root-knot nematodes requires an intact jasmonic acid signaling pathway. Mol. Plant Microbe Interact. 21, 1205–1214. https://doi.org/10.1094/mpmi-21-9-1205.

Blanc-Mathieu, R., Perfus-Barbeoch, L., Aury, J.M., Da Rocha, M., Gouzy, J., Sallet, E., Martin-Jimenez, C., Bailly-Bechet, M., Castagnone-Sereno, P., Flot, J.F., Kozlowski, D.K., Cazareth, J., Couloux, A., Da Silva, C., Guy, J., Kim-Jo, Y.J., Rancurel, C., Schiex, T., Abad, P., Wincker, P., Danchin, E.G.J., 2017. Hybridization and polyploidy enable genomic plasticity without sex in the most devastating plant-parasitic nematodes. PLoS Genet. 13, e1006777. https://doi.org/10.1371/journal.pgen.1006777.

Boller, T., Felix, G., 2009. A renaissance of elicitors: perception of microbe-associated molecular patterns and danger signals by pattern-recognition receptors. Annu. Rev. Plant Biol. 60, 379–406. https://doi.org/10.1146/annurev.arplant.57.032905.105346.

Cabrera, J., Barcala, M., Fenoll, C., Escobar, C., 2016. The power of omics to identify plant susceptibility factors and to study resistance to root-knot nematodes. Curr. Issues Mol. Biol. 19, 53–72.

Cabrera, J., Bustos, R., Favery, B., Fenoll, C., Escobar, C., 2014. NEMATIC: a simple and versatile tool for the in silico analysis of plant-nematode interactions. Mol. Plant Pathol. 15, 627–636. https://doi.org/10.1111/mpp.12114.

Cabrera, J., Díaz-Manzano, F.E., Fenoll, C., Escobar, C., 2015. Developmental pathways mediated by hormones in nematode feeding sites. Adv. Bot. Res. 73, 167–188. https://doi.org/10.1016/bs.abr.2014.12.005.

Cardi, T., Neal Stewart, C., 2016. Progress of targeted genome modification approaches in higher plants. Plant Cell Rep. https://doi.org/10.1007/s00299-016-1975-1.

Charlton, W.L., Harel, H.Y.M., Bakhetia, M., Hibbard, J.K., Atkinson, H.J., McPherson, M.J., 2010. Additive effects of plant expressed double-stranded RNAs on root-knot nematode development. Int. J. Parasitol. 40, 855–864. https://doi.org/10.1016/j.ijpara.2010.01.003.

Chen, J., Lin, B., Huang, Q., Hu, L., Zhuo, K., Liao, J., 2017. A novel Meloidogyne graminicola effector, MgGPP, is secreted into host cells and undergoes glycosylation in concert with proteolysis to suppress plant defenses and promote parasitism. PLoS Pathog. 13, e1006301. https://doi.org/10.1371/journal.ppat.1006301.

Chen, P., Tsay, T.T., 2006. Effect of crop rotation on *Meloidogyne* spp. and *Pratylenchus* spp. populations in strawberry fields in Taiwan. J. Nematol. 38, 339–344.

Claverie, M., Dirlewanger, E., Bosselut, N., Van Ghelder, C., Voisin, R., Kleinhentz, M., Lafargue, B., Abad, P., Rosso, M.-N., Chalhoub, B., Esmenjaud, D., 2011. 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. 156, 779–792. https://doi.org/10.1104/pp.111.176230.

Collange, B., Navarrete, M., Peyre, G., Mateille, T., Tchamitchian, M., 2011. Root-knot nematode (Meloidogyne) management in vegetable crop production: the challenge of an agronomic system analysis. Crop Protect. 30, 1251–1262. https://doi.org/10.1016/j.cropro.2011.04.016.

Cooper, W.R., Jia, L., Goggin, L., 2005. Effects of jasmonate-induced defenses on root-knot nematode infection of resistant and susceptible tomato cultivars. J. Chem. Ecol. 31, 1953–1967. https://doi.org/10.1007/s10886-005-6070-y.

Coyne, D.L., Cortada, L., Dalzell, J.J., Claudius-Cole, A.O., Haukeland, S., Luambano, N., Talwana, H., 2018. Plant-parasitic nematodes and food security in sub-Saharan Africa. Annu. Rev. Phytopathol. 56, 381–403. https://doi.org/10.1146/annurev-phyto-080417-045833.

Dalzell, j. j, McMaster, S., Fleming, C.C., Maule, A.G., 2010. Short interfering RNA-mediated gene silencing in Globodera pallida and Meloidogyne incognita infective stage juveniles. Int. J. Parasitol 40 (1), 91–100. https://doi.org/10.1016/j.ijpara.2009.07.003.

Davies, L.J., Zhang, L., Elling, A.A., 2015. The Arabidopsis thaliana papain-like cysteine protease RD21 interacts with a root-knot nematode effector protein. Nematology 17, 655–666. https://doi.org/10.1163/15685411-00002897.

Davis, E.L., Hussey, R.S., Baum, T.J., 2004. Getting to the roots of parasitism by nematodes. Trends Parasitol. 20, 134–141. https://doi.org/10.1016/J.PT.2004.01.005.

De Meutter, J., Tytgat, T., Witters, E., Gheysen, Greetje, Van Onckelen, H., Gheysen, Godelieve, 2003. Identification of cytokinins produced by the plant parasitic nematodes Heterodera schachtii and Meloidogyne incognita. Mol. Plant Pathol. 4, 271–277. https://doi.org/10.1046/j.1364-3703.2003.00176.x.

Desaeger, J., Dickson, W., Locascio, S.J., 2017. Methyl bromide alternatives for control of root-knot nematode (Meloidogyne spp.) in tomato production in Florida. J. Nematol. 49, 140–149. https://doi.org/10.21307/jofnem-2017-058.

Dinh, P.T.Y., Zhang, L., Mojtahedi, H., Brown, C.R., Elling, A.A., 2015. Broad Meloidogyne resistance in potato based on RNA interference of effector gene 16D10. J. Nematol. 47, 71–78.

Dutta, T.K., Banakar, P., Rao, U., Moffett, P., Day, B., 2015. MINI REVIEW ARTICLE the status of RNAi-based transgenic research in plant nematology. https://doi.org/10.3389/fmicb.2014.00760.

Fan, J.W., Hu, C.L., Zhang, L.N., Li, Z.L., Zhao, F.K., Wang, S.H., 2015. Jasmonic acid mediates tomato's response to root knot nematodes. J. Plant Growth Regul. 34, 196–205. https://doi.org/10.1007/s00344-014-9457-6.

Ferris, H., Griffiths, B.S., Porazinska, D.L., Powers, T.O., Wang, K.-H., Tenuta, M., 2012. Reflections on plant and soil nematode ecology: past, present and future. J. Nematol. 44, 115–126.

Fire, A., Xu, S., Montgomery, M.K., Kostas, S.A., Driver, S.E., Mello, C.C., 1998. Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. Nature 391, 806–811. https://doi.org/10.1038/35888.

Friedland, A.E., Tzur, Y.B., Esvelt, K.M., Colaiacovo, M.P., Church, G.M., Calarco, J.A., 2013. Heritable genome editing in C. elegans via a CRISPR-Cas9 system. Nat Methods 10, 741–743. https://doi.org/10.1038/nmeth.2532.

Fujimoto, T., Tomitaka, Y., Abe, H., Tsuda, S., Futai, K., Mizukubo, T., 2011. Expression profile of jasmonic acid-induced genes and the induced resistance against the root-

knot nematode (Meloidogyne incognita) in tomato plants (Solanum lycopersicum) after foliar treatment with methyl jasmonate. J. Plant Physiol. 168, 1084–1097. https://doi.org/10.1016/j.jplph.2010.12.002.
Gahoi, S., Gautam, B., 2017. Genome-wide analysis of Excretory/Secretory proteins in root-knot nematode, Meloidogyne incognita provides potential targets for parasite control. Comput. Biol. Chem. 67, 225–233. https://doi.org/10.1016/j.compbiolchem.2017.01.014.
Gheysen, G., Mitchum, M.G., 2018. Phytoparasitic nematode control of plant hormone pathways. Plant Physiol. 179, 1212–1226. https://doi.org/10.1104/pp.18.01067.
Gleason, C., Leelarasamee, N., Meldau, D., Feussner, I., 2016. OPDA has key role in regulating plant susceptibility to the root-knot nematode Meloidogyne hapla in Arabidopsis. Front. Plant Sci. 7, 1–11. https://doi.org/10.3389/fpls.2016.01565.
Goswami, B.K., Pandey, R.K., Rathour, K.S., Bhattacharya, C., Singh, L., 2006. Integrated application of some compatible biocontrol agents along with mustard oil seed cake and furadan on Meloidogyne incognita infecting tomato plants. J. Zhejiang Univ. - Sci. B 7, 873–875. https://doi.org/10.1631/jzus.2006.b0873.
Grunewald, W., Cannoot, B., Friml, J., Gheysen, G., 2009. Parasitic nematodes modulate PIN-mediated auxin transport to facilitate infection. PLoS Pathog. 5, 3–9. https://doi.org/10.1371/journal.ppat.1000266.
Ha, B.-K., Robbins, R.T., Han, F., Hussey, R.S., Soper, J.F., Boerma, H.R., 2007. SSR mapping and confirmation of soybean QTL from PI 437654 conditioning resistance to reniform nematode. Crop Sci. 47, 1336. https://doi.org/10.2135/cropsci2006.10.0645.
Ha, B.K., Bennett, J.B., Hussey, R.S., Finnerty, S.L., Boerma, H.R., 2004. Pedigree analysis of a major QTL conditioning soybean resistance to southern root-knot nematode. Crop Sci. 44, 758–763. https://doi.org/10.2135/cropsci2004.0758.
Hillier, L.W., Coulson, A., Murray, J.I., Bao, Z., Sulston, J.E., Waterston, R.H., 2005. Genomics in C. elegans: so many genes, such a little worm. Genome Res. 15, 1651–1660. https://doi.org/10.1101/gr.3729105.
Huang, G., Allen, R., Davis, E.L., Baum, T.J., Hussey, R.S., 2006. Engineering broad root-knot resistance in transgenic plants by RNAi silencing of a conserved and essential root-knot nematode parasitism gene. Proc. Natl. Acad. Sci. Unit. States Am. 103, 14302–14306. https://doi.org/10.1073/pnas.0604698103.
Huang, Guozhong, Dong, R., Allen, R., Davis, E.L., Baum, T.J., Hussey, R.S., 2006. A root-knot nematode secretory peptide functions as a ligand for a plant transcription factor. Mol. Plant Microbe Interact. 19, 463–470. https://doi.org/10.1094/MPMI-19-0463.
Huang, X., Zhao, N., Zhang, K., 2004. Extracellular enzymes serving as virulence factors in nematophagous fungi involved in infection of the host. Res. Microbiol. 155, 811–816. https://doi.org/10.1016/j.resmic.2004.07.003.
Hussey, R.S., 1989. Disease-inducing secretions of plant-parasitic nematodes. Annu. Rev. Phytopathol. 27, 123–141. https://doi.org/10.1146/annurev.py.27.090189.001011.
Ibrahim, H.M.M., Alkharouf, N.W., Meyer, S.L.F., Aly, M.A.M., Gamal El-Din, A.E.K.Y., Hussein, E.H.A., Matthews, B.F., 2011a. Post-transcriptional gene silencing of root-knot nematode in transformed soybean roots. Exp. Parasitol. 127, 90–99. https://doi.org/10.1016/j.exppara.2010.06.037.
Ibrahim, H.M.M., Hosseini, P., Alkharouf, N.W., Hussein, E.H.A., Gamal El-Din, A.E.K.Y., Aly, M.A.M., Matthews, B.F., 2011b. Analysis of Gene expression in soybean (Glycine max) roots in response to the root knot nematode Meloidogyne incognita using microarrays and KEGG pathways. BMC Genomics. https://doi.org/10.1186/1471-2164-12-220.
Iqbal, S., Fosu-Nyarko, J., Jones, M.G.K., 2016. Genomes of parasitic nematodes (Meloidogyne hapla, Meloidogyne incognita, Ascaris suum and Brugia malayi) have a reduced complement of small RNA interference pathway genes: knockdown can reduce host infectivity of M. incognita. Funct. Integr. Genom. 16, 441–457. https://doi.org/10.1007/s10142-016-0495-y.
Jaouannet, M., Magliano, M., Arguel, M.J., Gourgues, M., Evangelisti, E., Abad, P., Rosso, M.N., 2013. The root-knot nematode calreticulin mi-CRT is a key effector in plant defense suppression. Mol. Plant Microbe Interact. 26, 97–105. https://doi.org/10.1094/MPMI-05-12-0130-R.
Jiao, Y., Vuong, T.D., Liu, Y., Li, Z., Noe, J., Robbins, R.T., Joshi, T., Xu, D., Shannon, J.G., Nguyen, H.T., 2015. Identification of quantitative trait loci underlying resistance to southern root-knot and reniform nematodes in soybean accession PI 567516C. Mol. Breed. 35, 131. https://doi.org/10.1007/s11032-015-0330-5.
Jones, J., Gheysen, G., Fenoll, C., Carmen, 2011. Genomics and Molecular Genetics of Plant-Nematode Interactions. Springer. https://doi.org/10.1007/978-94-007-0434-3.
Jones, J.T., Haegeman, A., Danchin, E.G.J., Gaur, H.S., Helder, J., Jones, M.G.K., Kikuchi, T., Manzanilla-López, R., Palomares-Rius, J.E., Wesemael, W.M.L., Perry, R.N., 2013. Top 10 plant-parasitic nematodes in molecular plant pathology. Mol. Plant Pathol. 14, 946–961. https://doi.org/10.1111/mpp.12057.
Kamath, R.S., Fraser, A.G., Dong, Y., Poulin, G., Durbin, R., Gotta, M., Kanapin, A., Le Bot, N., Moreno, S., Sohrmann, M., Welchman, D.P., Zipperlen, P., Ahringer, J., 2003. Systematic functional analysis of the Caenorhabditis elegans genome using RNAi. Nature 421, 231–237. https://doi.org/10.1038/nature01278.
Kapur-Ghai, J., Kaur, M., Goel, P., 2014. Development of enzyme linked immunosorbent assay (ELISA) for the detection of root-knot nematode Meloidogyne incognita. J. Parasit. Dis. 38, 302–306. https://doi.org/10.1007/s12639-013-0246-0.
Karczmarek, A., Overmars, H., Helder, J., Goverse, A., 2004. Feeding cell development by cyst and root-knot nematodes involves a similar early, local and transient activation of a specific auxin-inducible promoter element. Mol. Plant Pathol. 5, 343–346. https://doi.org/10.1111/j.1364-3703.2004.00230.x.
Kaur, P., Shukla, N., Joshi, G., VijayaKumar, C., Jagannath, A., Agarwal, M., Goel, S., Kumar, A., 2017. Genome-wide identification and characterization of miRNAome from tomato (Solanum lycopersicum) roots and root-knot nematode (Meloidogyne incognita) during susceptible interaction. PLoS One 12, e0175178. https://doi.org/10.1371/journal.pone.0175178.
Kiewnick, S., Sikora, R.A., 2006. Biological control of the root-knot nematode Meloidogyne incognita by Paecilomyces lilacinus strain 251. Biol. Control 38, 179–187. https://doi.org/10.1016/j.biocontrol.2005.12.006.
Klink, V.P., Kim, K.H., Martins, V., MacDonald, M.H., Beard, H.S., Alkharouf, N.W., Lee, S.K., Park, S.C., Matthews, B.F., 2009. A correlation between host-mediated expression of parasite genes as tandem inverted repeats and abrogation of development of female Heterodera glycines cyst formation during infection of Glycine max. Planta 230, 53–71. https://doi.org/10.1007/s00425-009-0926-2.
Kumar, P., He, Y., Singh, R., Davis, R.F., Guo, H., Paterson, A.H., Peterson, D.G., Shen, X., Nichols, R.L., Chee, P.W., 2016. Fine mapping and identification of candidate genes for a QTL affecting Meloidogyne incognita reproduction in Upland cotton. BMC Genomics 17. https://doi.org/10.1186/S12864-016-2954-1.
Kyndt, T., Nahar, K., Haeck, A., Verbeek, R., Demeestere, K., Gheysen, G., 2017. Interplay between carotenoids, abscisic acid and jasmonate guides the compatible rice-Meloidogyne graminicola interaction. Front. Plant Sci. 8, 951. https://doi.org/10.3389/fpls.2017.00951.
Lagudah, E.S., Moullet, O., Appels, R., 1997. Map-based cloning of a gene sequence encoding a nucleotide-binding domain and a leucine-rich region at the Cre3 nematode resistance locus of wheat. Genome. https://doi.org/10.1139/g97-087.
Lamovšek, J., Urek, G., Trdan, S., 2013. Biological control of root-knot nematodes (Meloidogyne spp.): microbes against the pests. Acta Agric. Slov. 101, 263–275. https://doi.org/10.2478/acas-2013-0022.
Leelarasamee, N., Zhang, L., Gleason, C., 2018. The root-knot nematode effector MiPFN3 disrupts plant actin filaments and promotes parasitism. PLoS Pathog. 14, e1006947. https://doi.org/10.1371/journal.ppat.1006947.
Leister, D., Ballvora, A., Salamini, F., Gebhardt, C., 1996. A PCR-based approach for isolating pathogen resistance genes from potato with potential for wide application in plants. Nat. Genet. 14, 421–429. https://doi.org/10.1038/ng1296-421.
Leonetti, P., Accotto, G.P., Hanafy, M.S., Pantaleo, V., 2018. Viruses and phytoparasitic nematodes of cicer arietinum L.: biotechnological approaches in interaction studies and for sustainable control. Front. Plant Sci. 9, 319. https://doi.org/10.3389/fpls.2018.00319.
Li, Z., Jakkula, L., Hussey, R.S., Tamulonis, J.P., Boerma, H.R., 2001. SSR mapping and confirmation of the QTL from PI96354 conditioning soybean resistance to southern root-knot nematode. Theor. Appl. Genet. 103, 1167–1173. https://doi.org/10.1007/s001220100672.
Li, Z., Liu, Z.B., Xing, A., Moon, B.P., Koellhoffer, J.P., Huang, L., et al., 2015. Cas9-guide RNA directed genome editing in soybean. Plant Physiol 169, 960–970. https://doi.org/10.1104/pp.15.00783.
Lilley, C., Devlin, P., Urwin, P., Atkinson, H., 1999. Parasitic nematodes, proteinases and transgenic plants. Parasitol. Today 15, 414–417. https://doi.org/10.1016/S0169-4758(99)01513-6.
Lohar, D.P., Schaff, J.E., Laskey, J.G., Kieber, J.J., Bilyeu, K.D., Bird, D.M.K., 2004. Cytokinins play opposite roles in lateral root formation, and nematode and Rhizobial symbioses. Plant J. https://doi.org/10.1111/j.1365-313X.2004.02038.x.
Lourenço-Tessutti, I.T., Souza Junior, J.D.A., Martins-de-Sa, D., Viana, A.A.B., Carneiro, R.M.D.G., Togawa, R.C., de Almeida-Engler, J., Batista, J.A.N., Silva, M.C.M., Fragoso, R.R., Grossi-de-Sa, M.F., 2015. Knock-down of heat-shock protein 90 and isocitrate lyase gene expression reduced root-knot nematode reproduction. Phytopathology 105, 628–637. https://doi.org/10.1094/PHYTO-09-14-0237-R.
Martin, J., Rosa, B.A., Ozersky, P., Hallsworth-Pepin, K., Zhang, X., Bhonagiri-Palsikar, V., Tyagi, R., Wang, Q., Choi, Y.J., Gao, X., McNulty, S.N., Brindley, P.J., Mitreva, M., 2015. Helminth.net: expansions to Nematode.net and an introduction to Trematode.net. Nucleic Acids Res. 43, D698–D706. https://doi.org/10.1093/nar/gku1128.
Martínez-Medina, A., Appels, F.V.W., van Wees, S.C.M., 2017. Impact of salicylic acid- and jasmonic acid-regulated defences on root colonization by Trichoderma harzianum T-78. Plant Signal. Behav. 12. https://doi.org/10.1080/15592324.2017.1345404.
Meng, Y., Hou, Y., Wang, H., Ji, R., Liu, B., Wen, J., et al., 2017. Targeted mutagenesis by CRISPR/Cas9 system in the model legume Medicago truncatula. Plant Cell Rep 36, 371–374. https://doi.org/10.1007/s00299-016-2069-9.
Meyer, S.L.F., 1998. HortTechnology., HortTechnology. American Society for Horticultural Science.
Meyer, S.L.F., Everts, K.L., Gardener, B.M., Masler, E.P., Abdelnabby, H.M.E., Skantar, A.M., 2016. Assessment of DAPG-producing Pseudomonas fluorescens for management of Meloidogyne incognita and Fusarium oxysporum on watermelon. J. Nematol. 48, 43–53.
Meyer, S.L.F., Rice, C.P., Zasada, I.A., 2009. DIBOA: fate in soil and effects on root-knot nematode egg numbers. Soil Biol. Biochem. 41, 1555–1560. https://doi.org/10.1016/j.soilbio.2009.04.016.
Meyer, S.L.F., Zasada, I.A., Rupprecht, S.M., Vangessel, M.J., Hooks, C.R.R., Morra, M.J., Everts, K.L., 2015. Mustard seed meal for management of root-knot nematode and weeds in tomato production. HortTechnology 25, 192–202.
Mmeka, E.C., Adesoye, A., Ubaoji, K.I., Nwokoye, A.B., 2014. Gene silencing technologies in creating resistance to plant diseases. Int. J. Plant Breed. Genet. 8, 100–120. https://doi.org/10.3923/ijpbg.2014.100.120.
Molinari, S., Fanelli, E., 2013. Expression of Tomato Salicylic Acid (SA) - Responsive Pathogenesis - Related Genes in 15.
Nahar, K., Kyndt, T., De Vleesschauwer, D., Höfte, M., Gheysen, G., 2011. The jasmonate pathway is a key player in systemically induced defense against root knot nematodes in rice. Plant Physiol. 157, 305–316. https://doi.org/10.1104/pp.111.177576.
Navarrete, M., Djian-Caporalino, C., Mateille, T., Palloix, A., Sage-Palloix, A.M., Lefèvre, A., Fazari, A., Marteu, N., Tavoillot, J., Dufils, A., Furnion, C., Pares, L., Forest, I., 2016. A resistant pepper used as a trap cover crop in vegetable production strongly decreases root-knot nematode infestation in soil. Agron. Sustain. Dev. 36. https://

doi.org/10.1007/s13593-016-0401-y.
Navarro, L., Dunoyer, P., Jay, F., Arnold, B., Dharmasiri, N., Estelle, M., Voinnet, O., Jones, J.D.G., 2006. A plant miRNA contributes to antibacterial resistance by repressing auxin signaling. Science 312, 436–439. https://doi.org/10.1126/science.1126088.
Nelson, S.D., Locascio, S.J., Allen, L.H., Dickson, D.W., Mitchell, D.J., 2002. Soil flooding and fumigant alternatives to methyl bromide in tomato and eggplant production. Hortscience 37, 1057–1060.
Nguyen, C.-N., Perfus-Barbeoch, L., Quentin, M., Zhao, J., Magliano, M., Marteu, N., Da Rocha, M., Nottet, N., Abad, P., Favery, B., 2018. A root-knot nematode small glycine and cysteine-rich secreted effector, MiSGCR1, is involved in plant parasitism. New Phytol. 217, 687–699. https://doi.org/10.1111/nph.14837.
Niu, J., Jian, H., Xu, J., Chen, C., Guo, Q., Liu, Q., Guo, Y., 2012. RNAi silencing of the Meloidogyne incognita Rpn7 gene reduces nematode parasitic success. Eur. J. Plant Pathol. 134, 131–144. https://doi.org/10.1007/s10658-012-9971-y.
Niu, J., Liu, P., Liu, Q., Chen, C., Guo, Q., Yin, J., Yang, G., Jian, H., 2016. Msp40 effector of root-knot nematode manipulates plant immunity to facilitate parasitism. Sci. Rep. 6, 19443. https://doi.org/10.1038/srep19443.
Oka, Y., Pivonia, S., 2002. Use of ammonia-releasing compounds for control of the root-knot nematode Meloidogyne javanica. Nematology 4, 65–71. https://doi.org/10.1163/156854102760082212.
Pan, X., Nichols, R.L., Li, C., Zhang, B., 2018. MicroRNA-target gene responses to root knot nematode (Meloidogyne incognita) infection in cotton (Gossypium hirsutum L.). Genomics. https://doi.org/10.1016/J.YGENO.2018.02.013.
Papolu, P.K., Dutta, T.K., Tyagi, N., Urwin, P.E., Lilley, C.J., Rao, U., 2016. Expression of a cystatin transgene in eggplant provides resistance to root-knot nematode, Meloidogyne incognita. Front. Plant Sci. 7, 1122. https://doi.org/10.3389/fpls.2016.01122.
Papolu, P.K., Gantasala, N.P., Kamaraju, D., Banakar, P., Sreevathsa, R., Rao, U., 2013. Utility of host delivered RNAi of two FMRF amide like peptides, flp-14 and flp-18, for the management of root knot nematode, Meloidogyne incognita. PLoS One 8, e80603. https://doi.org/10.1371/journal.pone.0080603.
Pham, A.-T., McNally, K., Abdel-Haleem, H., Roger Boerma, H., Li, Z., 2013. Fine mapping and identification of candidate genes controlling the resistance to southern root-knot nematode in PI 96354. Theor. Appl. Genet. 126, 1825–1838. https://doi.org/10.1007/s00122-013-2095-8.
Quentin, M., Abad, P., Favery, B., Rivas, S., Reymond, P., 2013. Plant Parasitic Nematode Effectors Target Host Defense and Nuclear Functions to Establish Feeding Cells, vol. 312 57–1. https://doi.org/10.3389/fpls.2013.00053.
Rocha, R.O., Morais, J.K.S., Oliveira, J.T.A., Oliveira, H.D., Sousa, D.O.B., Souza, C.E.A., Moreno, F.B., Monteiro-Moreira, A.C.O., Antonino De Souza, J.D., Grossi De Sá, M.F., Vasconcelos, I.M., 2015. Proteome of soybean seed exudates contains plant defense-related proteins active against the root-knot nematode Meloidogyne incognita. J. Agric. Food Chem. 63, 5335–5343. https://doi.org/10.1021/acs.jafc.5b01109.
Rosso, M.N., Jones, J.T., Abad, P., 2009. RNAi and functional genomics in plant parasitic nematodes. Annu. Rev. Phytopathol. 47, 207–232. https://doi.org/10.1146/annurev.phyto.112408.132605.
Santos, J.R.P., Ndeve, A.D., Huynh, B.-L., Matthews, W.C., Roberts, P.A., 2018. QTL mapping and transcriptome analysis of cowpea reveals candidate genes for root-knot nematode resistance. PLoS One 13, e0189185. https://doi.org/10.1371/journal.pone.0189185.
Sanz-Alférez, S., Mateos, B., Alvarado, R., Sánchez, M., 2008. SAR induction in tomato plants is not effective against root-knot nematode infection. Eur. J. Plant Pathol. 120, 417–425. https://doi.org/10.1007/s10658-007-9225-6.
Sato, K., Kadota, Y., Gan, P., Bino, T., Uehara, T., Yamaguchi, K., Ichihashi, Y., Maki, N., Iwahori, H., Suzuki, T., Shigenobu, S., Shirasu, K., 2018. High-quality genome sequence of the root-knot nematode Meloidogyne arenaria genotype A2-O. Genome Announc. 6 e00519-18. https://doi.org/10.1128/genomeA.00519-18.
Segers, R., Butt, T.M., Kerry, B.R., Peberdy, J.F., 1994. The nematophagous fungus Verticillium chlamydosporium produces a chymoelastase-like protease which hydrolyses host nematode proteins in situ. Microbiology 140, 2715–2723. https://doi.org/10.1099/00221287-140-10-2715.
Shanks, C.M., Rice, J.H., Zubo, Y., Schaller, G.E., Hewezi, T., Kieber, J.J., 2016. The role of cytokinin during infection of Arabidopsis thaliana by the cyst nematode Heterodera schachtii. Mol. Plant Microbe Interact. 29, 57–68. https://doi.org/10.1094/MPMI-07-15-0156-R.
Sharp, P.A., 2001. RNA interference–2001. Genes Dev. 15, 485–490. https://doi.org/10.1101/gad.880001.
Shindo, T., Misas-Villamil, J.C., Hörger, A.C., Song, J., van der Hoorn, R.A.L., 2012. A role in immunity for Arabidopsis cysteine protease RD21, the ortholog of the tomato immune protease C14. PLoS One 7, e29317. https://doi.org/10.1371/journal.pone.0029317.
Shingles, J., Lilley, C.J., Atkinson, H.J., Urwin, P.E., 2007. Meloidogyne incognita: molecular and biochemical characterisation of a cathepsin L cysteine proteinase and the effect on parasitism following RNAi. Exp. Parasitol. 115, 114–120. https://doi.org/10.1016/j.exppara.2006.07.008.
Shivakumara, T.N., Chaudhary, S., Kamaraju, D., Dutta, T.K., Papolu, P.K., Banakar, P., Sreevathsa, R., Singh, B., Manjaiah, K.M., Rao, U., 2017. Host-Induced Silencing of Two Pharyngeal Gland Genes Conferred Transcriptional Alteration of Cell Wall-Modifying Enzymes of Meloidogyne incognita vis-à-vis Perturbed Nematode Infectivity in Eggplant. Front. Plant Sci. 8, 473. https://doi.org/10.3389/fpls.2017.00473.
Shukla, N., Yadav, R., Kaur, P., Rasmussen, S., Goel, S., Agarwal, M., Jagannath, A., Gupta, R., Kumar, A., 2018. Transcriptome analysis of root-knot nematode (*Meloidogyne incognita*)-infected tomato (*Solanum lycopersicum*) roots reveals complex gene expression profiles and metabolic networks of both host and nematode during susceptible and resistance responses. Mol. Plant Pathol. 19, 615–633. https://doi.org/10.1111/mpp.12547.
Sikora, R.A., Coyne, D., Hallmann, J., Timper, P., 2018. Plant_Parasitic_Nematodes_in_Subtropical.
Sindhu, A.S., Maier, T.R., Mitchum, M.G., Hussey, R.S., Davis, E.L., Baum, T.J., 2009. Effective and specific in planta RNAi in cyst nematodes: expression interference of four parasitism genes reduces parasitic success. J. Exp. Bot. 60, 315–324. https://doi.org/10.1093/jxb/ern289.
Singh, R., Phulera, S., n.d. Plant Parasitic Nematodes: the Hidden Enemies of Farmers.
Smith, H.M., Smith, B.P., Morales, N.B., Moskwa, S., Clingeleffer, P.R., Thomas, M.R., 2018. SNP markers tightly linked to root knot nematode resistance in grapevine (Vitis cinerea) identified by a genotyping-by-sequencing approach followed by Sequenom MassARRAY validation. PLoS One 13, e0193121. https://doi.org/10.1371/journal.pone.0193121.
Somasekhar, N., Prasad, J.S., 2012. Plant – nematode interactions: consequences of climate change. In: Crop Stress and its Management: Perspectives and Strategies. Springer Netherlands, Dordrecht, pp. 547–564. https://doi.org/10.1007/978-94-007-2220-0_17.
Su, L., Ruan, Y., Yang, X., Wang, K., Li, R., Shen, Q., 2015. Suppression on plant-parasitic nematodes using a soil fumigation strategy based on ammonium bicarbonate and its effects on the nematode community. Sci. Rep. 5, 17597. https://doi.org/10.1038/srep17597.
Sun, Y., Yin, J., Cao, H., Li, C., Kang, L., Ge, F., 2011. Elevated CO2 influences nematode-induced defense responses of tomato genotypes differing in the JA pathway. PLoS One 6. https://doi.org/10.1371/journal.pone.0019751.
Szitenberg, A., Salazar-Jaramillo, L., Blok, V.C., Laetsch, D.R., Joseph, S., Williamson, V.M., Blaxter, M.L., Lunt, D.H., 2017. Comparative genomics of apomictic root-knot nematodes: hybridization, ploidy, and dynamic genome change. Genome Biol. Evol. 9, 2844–2861. https://doi.org/10.1093/gbe/evx201.
Tamulonis, J.P., Luzzi, B.M., Hussey, R.S., Parrott, W.A., Boerma, H.R., 1997. RFLP mapping of resistance to southern root-knot nematode in soybean. Crop Sci. 37, 1903. https://doi.org/10.2135/cropsci1997.0011183X003700060039x.
Tian, B., Wang, S., Todd, T.C., Johnson, C.D., Tang, G., Trick, H.N., 2017. Genome-wide identification of soybean microRNA responsive to soybean cyst nematodes infection by deep sequencing. BMC Genomics 18, 572. https://doi.org/10.1186/s12864-017-3963-4.
Tranier, M.-S., Pognant-Gros, J., Quiroz, R.D. la C., González, C.N.A., Mateille, T., Roussos, S., 2014. Commercial biological control agents targeted against plant-parasitic root-knot nematodes. Braz. Arch. Biol. Technol. 57, 831–841. https://doi.org/10.1590/S1516-8913201402540.
Tripathi, L., Babirye, A., Roderick, H., Tripathi, J.N., Changa, C., Urwin, P.E., Tushemereirwe, W.K., Coyne, D., Atkinson, H.J., 2015. Field resistance of transgenic plantain to nematodes has potential for future African food security. Sci. Rep. 5, 8127. https://doi.org/10.1038/srep08127.
Trudgill, D.L., Blok, V.C., 2001. A < scp > POMICTIC < /scp > , P < scp > OLYPHAGOUS < /scp > R < scp > OOT < /scp > -K < scp > NOT < /scp > N < scp > EMATODES < /scp > : exceptionally Successful and Damaging Biotrophic Root Pathogens. Annu. Rev. Phytopathol. 39, 53–77. https://doi.org/10.1146/annurev.phyto.39.1.53.
Tsai, A.Y.L., Higaki, T., Nguyen, C.N., Perfus-Barbeoch, L., Favery, B., Sawa, S., 2019. Regulation of root-knot nematode behavior by seed-coat mucilage-derived attractants. Mol. Plant. https://doi.org/10.1016/j.molp.2018.11.008.
Urwin, P.E., Lilley, C.J., Atkinson, H.J., 2002. Ingestion of double-stranded RNA by preparasitic juvenile cyst nematodes leads to RNA interference. Mol. Plant Microbe Interact. 15, 747–752. https://doi.org/10.1094/MPMI.2002.15.8.747.
USDA ERS, U.S.D. of A.E.R.S, 2000. Economic Implications of the Methyl Bromide Phaseout 1–12.
Vuong, T.D., Sonah, H., Meinhardt, C.G., Deshmukh, R., Kadam, S., Nelson, R.L., Shannon, J.G., Nguyen, H.T., 2015. Genetic architecture of cyst nematode resistance revealed by genome-wide association study in soybean. BMC Genomics 16. https://doi.org/10.1186/s12864-015-1811-y.
Warmerdam, S., Sterken, M.G., van Schaik, C., Oortwijn, M.E.P., Sukarta, O.C.A., Lozano-Torres, J.L., Dicke, M., Helder, J., Kammenga, J.E., Goverse, A., Bakker, J., Smant, G., 2018. Genome-wide association mapping of the architecture of susceptibility to the root-knot nematode *Meloidogyne incognita* in *Arabidopsis thaliana*. New Phytol. 218, 724–737. https://doi.org/10.1111/nph.15034.
Williamson, V.M., Hussey, R.S., 1996. Nematode pathogenesis and resistance in plants. Plant Cell 8, 1735–1745. https://doi.org/10.1105/tpc.8.10.1735.
Williamson, V.M., Hussey, R.S., Szabò, V., Frost, L.N., Schmidt, R., Biezen, E.A. Van der, Moores, T., Dean, C., Daniels, M.J., Jones, J.D.G., 1996. Nematode pathogenesis and resistance in plants. Plant Cell 8, 1735–1745. https://doi.org/10.1105/tpc.8.10.1735.
Xu, X., Zeng, L., Tao, Y., Vuong, T., Wan, J., Boerma, R., Noe, J., Li, Z., Finnerty, S., Pathan, S.M., Shannon, J.G., Nguyen, H.T., 2013. Pinpointing genes underlying the quantitative trait loci for root-knot nematode resistance in palaeopolyploid soybean by whole genome resequencing. Proc. Natl. Acad. Sci. U.S.A. 110, 13469–13474. https://doi.org/10.1073/pnas.1222368110.
Xue, B., Hamamouch, N., Li, C., Huang, G., Hussey, R.S., Baum, T.J., Davis, E.L., 2013. The 8D05 parasitism gene of Meloidogyne incognita is required for successful infection of host roots. Phytopathology 103, 175–181. https://doi.org/10.1094/PHYTO-07-12-0173-R.
Yadav, B.C., Veluthambi, K., Subramaniam, K., 2006. Host-generated double stranded RNA induces RNAi in plant-parasitic nematodes and protects the host from infection. Mol. Biochem. Parasitol. 148, 219–222. https://doi.org/10.1016/j.molbiopara.2006.03.013.
Yang, N., Wang, R., Zhao, Y., 2017. Revolutionize genetic studies and crop improvement

with high-throughput and genome-scale CRISPR/Cas9 gene editing technology. Mol. Plant 10, 1141–1143. https://doi.org/10.1016/j.molp.2017.08.001.

Zamanian, M., Andersen, E.C., 2016. Prospects and challenges of CRISPR/Cas genome editing for the study and control of neglected vector-borne nematode diseases. FEBS J 283, 3204–3221. https://doi.org/10.1111/febs.13781.

Zeng, Q., Huang, H., Zhu, J., Fang, Z., Sun, Q., Bao, S., 2013. A new nematicidal compound produced by Streptomyces albogriseolus HA10002. Antonie van Leeuwenhoek. Int. J. Gen. Mol. Microbiol. 103, 1107–1111. https://doi.org/10.1007/s10482-013-9890-8.

Zhuo, K., Chen, J., Lin, B., Wang, J., Sun, F., Hu, L., Liao, J., 2017. A novel *Meloidogyne enterolobii* effector MeTCTP promotes parasitism by suppressing programmed cell death in host plants. Mol. Plant Pathol. 18, 45–54. https://doi.org/10.1111/mpp.12374.