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Review

Defence response of host plants for cyst nematode: A review on parasitism and defence

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ABSTRACT

The Cyst nematodes (CN), such as *Heterodera* spp. and *Globodera* spp. are key biotrophic pathogens inflicting high levels of damage to agricultural and horticultural crops. This review sheds light on the parasitism of the CN and molecular defence responses of infected plants. We highlight the role of effector proteins secreted from the oesophageal gland cells of the CN, hormone-signalling pathway, and miRNA regulation of gene expression that modulate the differentiation of the feeding site. In addition, we speak of the role of pattern-triggered immunity (PTI), effector-triggered immunity (ETI), resistance genes (R genes), and pathogenesis-related proteins in the immune defence responses of the CN. We conclude this review by discussing recent progress in genomic studies and molecular mechanisms involved in the recognition process of the infesting CN that provides scope for future investigations and the discovery of novel strategies to manage these biotrophic pathogens.

Contents

1. Introduction

Soil-borne pathogens are the important biotic constraints of agricultural and horticultural crops. Among biotic pathogens, plant-parasitic nematodes (PPN) cause significant damage to crop

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production worldwide. According to Nicol et al. (2011), the damage is estimated at more than US$80 billion annually. The Heteroderidae group of nematodes, known as cyst nematodes (CN), is an important pest of crops that leads to economic yield losses worldwide. The CN is the most complex group of sedentary endoparasitic nematodes because they spend most of their active lives within the roots of the host crops. The female CN is non-motile, globular (*Globodera* spp.) and lemon (*Heterodera* spp.) shaped, and it contains many embryonated eggs male is motile, which causes the stunting of the plants and leads to complete crop failure.

During infection, the CN first interacts with the roots as infective second-stage juveniles (J2). The J2 is motile that invades the root tips using stylet (Fig. 1). Cyst juveniles move intracellularly towards the vasculature. They then target a competent/spherical cell to initiate a feeding site to form a multinucleate syncytium (Moens et al., 2018). The syncytium is formed by fusing the neighbouring cells from an initial syncytial cell targeted by the CN after the invasion. It provides nutrients for developing CN (Sobczak and Golinowski, 2011). CN are biotrophic parasites because they feed on syncytia until complete reproduction. It can be controlled by cultural practice, crop rotation, sanitation, use of nematicides, and resistant cultivars. However, these management strategies are low output, expensive, and require a careful handling system. As a result, new techniques and resources to control CN are necessary that are non-toxic and suitable for the environment. Therefore, it is necessary to understand how plants interact with CN and how they respond against parasitism.

2. Role of effectors in host parasitism

The interactions between the host and pathogen are mediated by effectors, i.e., secreted proteins which play roles in parasitism. During the CN parasitism, these effectors initiate a signalling process that suppresses the host defence responses and facilitates infection. The increasing availability of genome sequences and genetic analyses has greatly encouraged scientists to understand plant-nematode interaction better. The effector proteins are CLC (cadiotrophin-lycytokine) signalling peptides, expressed in the oesophageal gland cell during infection in a plant with *H. glycines* encoded in the gene. A specific feature of these nematode CLEs is their processing from proteins containing single or multiple CLE motifs. CN acquires CLE peptides to change its host's behaviour, which favours syncytium formation (Wang et al., 2010).

Smant et al. (1998) identified β-1,4-Endoglucanases (cellulase) effector from the CN e.g., *Globodera rostochiensis* and *Heterodera glycines*. They found that effectors are involved in forming the feeding site, defence suppression signalling pathway, and alteration of phytohormones. Yang et al. (2019a and 2019b) identified the two effectors, Ha18764 and HaGland5, expressed in dorsal oesophageal

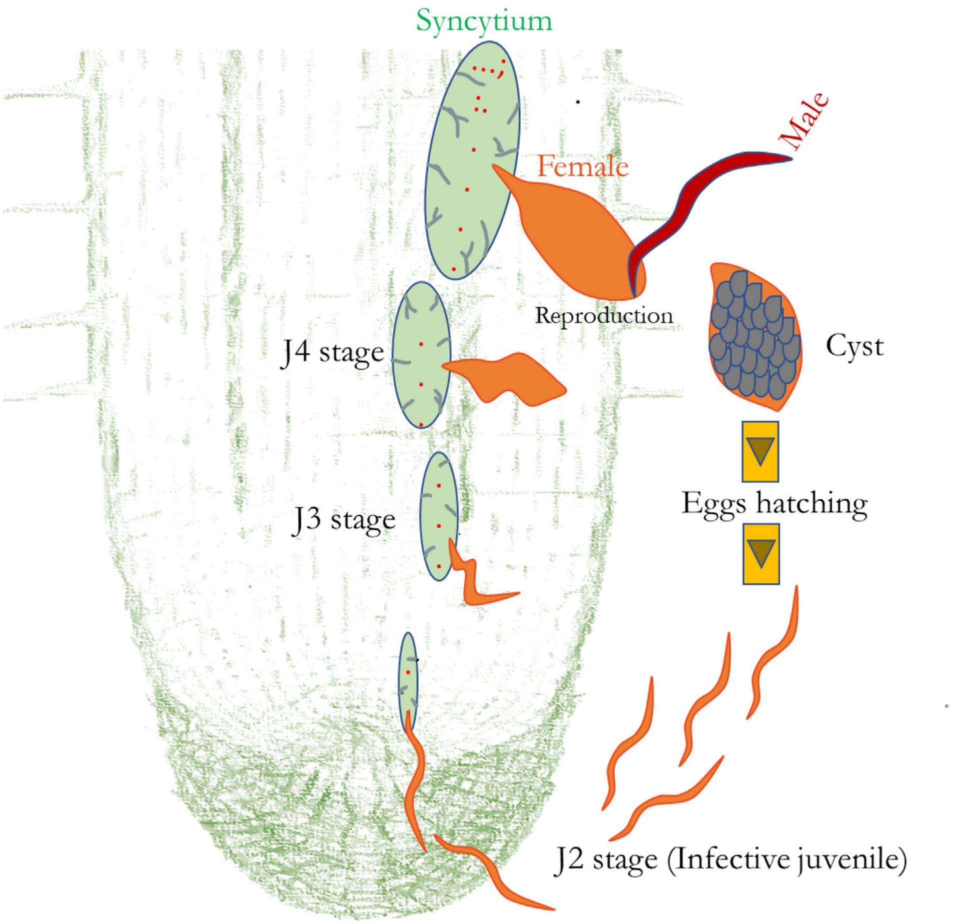

Fig. 1. An illustrated diagrammatic representation of infective juveniles (J2) of cyst nematode (CN) enters the root system, migrate through plant tissues, and develop a feeding site called syncytium. The juveniles (J2) become sedentary within the vascular tissues and CN, including *Heterodera* spp. and *Globodera* spp. acquire nutrients from the host-derived feeding sites, syncytia. Feeding sites lead to root swellings blocking water and nutrient supply within the plant body, thereby affecting the growth of the host plant. Adult CN females retain eggs inside the body, which form a cyst after death.

gland cells of *H. avenae*. The effector 'HaGland5′ promotes nematode parasitism and represses the defence-related genes; it reduces cell wall callose deposition and the burst of reactive oxygen species (ROS). On the other hand, the effector molecule 'Ha18764′ promotes parasitism by suppressing the plant pathogen-associated molecular pattern-triggered immunity (PTI) and effector-triggered immunity (ETI) during infection. The CN induces morphological and physiological changes within host plants through the secretion of an effector, which is involved in parasitism and promotes interaction with the host plant (Aharen et al., 2020). Hu et al. (2019) reported the effector 'Hg16B09′ expression in *H. glycines* using *in-situ* hybridization. They indicated that the upregulation of effector proteins in the parasitic stage juvenile establishes a metabolically hyperactive feeding site in the host plant by suppressing basal plant defences. Verma et al. (2022) investigated a cytoplasmic effector 'Hs2D01′ interaction with AtHAE, which is a leucine-rich repeat (LRR) receptor-like kinase found on the surface of cells that plays a crucial role in the parasitism by *H. schachtii*. They demonstrated that Hs2D01-AtHAE activates the cell wall enzymes that are essential for cell separation during abscission and lateral root emergence. Identifying the effector molecule is necessary to understand better the relationship between nematode effector and host cell protein. Verma et al. (2018) firstly reported one of the novel effectors, '30D08′ contributes to nematode parasitism by interacting with the nucleus and a host auxiliary spliceosomal protein (SMU2) to alter gene expression in feeding sites. Pogorelko et al. (2020) screened 51 effectors of the soybean cyst nematode (SCN) *Heterodera glycines*. They identified three effectors inhibiting effector-triggered immunity (ETI) and seven effectors as pattern-triggered immunity (PTI) suppressors. The effector proteins altered the host gene's expression and created specialized infection sites. In plants, autophagy is crucial for homeostasis, growth, senescence, and resistance to biotic and abiotic stressors. Autophagy aided in plant defences against bacterial, viral, and filamentous pathogens and emerged as a key target for microbial effectors. However, how plants engage in autophagy in nematode parasitism is mostly unknown. Recently, Chen et al. (2022) identified NMAS1 (Nematode Manipulator of Autophagy System 1), a novel and conserved effector from CN, using molecular and genetic analyses. They demonstrated that NMAS1, a virulence effector, can promote disease by targeting a crucial component of host autophagy and inhibiting PTI and defence-related cell death, which is mediated by membrane-associated and intracellular immune receptors. The CN effector that causes changes in the host is enlisted in Table 1.

3. Role of phytohormones and microRNA in nematode infestation

The involvement of phytohormones such as auxin, ethylene, salicylic acid, and jasmonic acid regulates the process in plants. These phytohormones also regulate the plant-nematode interaction, including controlling the plant defense system and developing nematode diseases. The phytohormones are key players in the formation of nematode-feeding sites. During the formation of feeding sites, nematodes interact with hormone homeostasis, giving complex results. Siddique et al. (2015) showed that the cytokinin hormone manipulates the host functions and establishes a long-term parasitic interaction by activating cytokinin signalling, cell cycle and progression. Cytokinin facilitates nematode development and infection during feeding site initiation and promotes syncytium expansion. Escudero Martinez et al. (2019) analyzed the effect of strigolactones (SLs), a novel class of phytohormones, during *H. schachtii* parasitism on *Arabidopsis*. They observed that SLs don't promote the hatching of CN but participate in host attraction and invasion. Dowd et al. (2017) have identified different expressions of cytokinin biosynthesis, catabolism, and signalling genes in response to infection developed by CN. They observed that CN manipulates the cytokinin signalling pathway and is responsible for cell cycle activation, which induces feeding site formation. Hu et al. (2017) demonstrated the ethylene signalling pathway's role in regulating root attractiveness in response to sugar beet cyst nematode. Ethylene and auxin are also involved in syncytia formation and control the nematode-induced regulatory networks in the host (Goverse and Bird, 2011).

Researchers have also studied the role of miRNA in plant nematode interaction. MicroRNAs (miRNAs) are non-coding RNAs that regulate the gene expression of the host plant and modulate the large-scale changes in the nematode feeding sites. Hewezi et al. (2016) reported the overexpression of 'miR827′ in the *Arabidopsis* to suppress the immune responses necessary to establish infection and cause disease (Table 2). The nematode-activated 'miR827′ targets the nitrogen limitation adaptation (NLA) gene, enhancing susceptibility to the CN. Piya et al. (2017) discovered that 'miR858′ contributes to transcriptome reprogramming during syncytia formation. The 'miR858′ regulates the target transcription factor MYB83, and constitutive overexpression reduces susceptibility to CN (Table 2). The miRNA targets the growth-regulating factor (GRF) genes for productive CN infections (Noon et al., 2019). Thus, the miRNA plays a diverse role in the biological process, especially in antagonistic responses against pests.

Table 1
List of CN effector genes for facilitating parasitism in plants.

Effector Gene	Nematode	Function	Reference
Ha18764	*Heterodera avenae*	Immune suppression by triggering PTI and ETI	Yang et al., 2019a
HaGland5	*H. avenae*	Repression of defence-related genes, the burst of ROS	Yang et al., 2019b
HsPGx	*H. schachtii*	Feeding site formation via parasitism protein	Aharen et al., 2020
Hg16B09	*H.glycines*	Suppression of plant innate immunity	Hu et al., (2019)
Hs30D08	*H. schachtii*	Feeding site formation via interaction with nucleus and host SMU2 protein	Verma et al., 2018
HsGLAND4	*H. schachtii*	Feeding site formation via interaction with the promoter of LTP genes	Barnes et al., 2018
HsPDI	*H. schachtii*	Syncytial feeding site formation *via* redox homeostasis	Habash et al., 2017
Hs32E03	*H. schachtii*	Alter the histone acetylation and depression of host rRNA genes.	Vijayapalani et al., 2018
GpIA7	*Globodera pallida*	Target the function of host EBP1 and hinder the plant cell cycle.	Coke et al., 2021
HaVAP1, HaVAP2	*H. avenae*	Knocking down and silencing both proteins hamper the parasitism.	Luo et al., 2019
GLAND5, GLAND6	*H. glycine*	Suppress the Pattern trigger immunity (PTI)	Pogorelko et al., 2020
RHA1B	*G. pallida*	Facilitates nematode parasitism by suppressing the ETI and hypersensitive response.	Kud et al., 2019
TUBG1, TUBG2	*H. schachtii*	Down-regulation of both genes is essential for successful parasitism and syncytium development	Różańska et al., 2018
NMAS1	*Globodera* spp.	Promoting disease by targeting a crucial component of host autophagy and inhibit PTI	Chen et al., 2022

Table 2
List of miRNA and their role in parasitism and defence.

miRNA for parasitism			
miRNA	CystNematode (CN)	Function	Reference
miR858	*Heterodera schachti*	Formation of syncytium by the regulating transcription factor, MYB83	Piya et al., 2017
miR827	*H. schachti*	Activation of nitrogen limitation adaptation gene enhances the CNs infection	Hewezi et al., 2016
miRNA396	*H. glycines*	Target the growth-regulating factor genes that are essential for CNs infection	Noon et al., 2019
miRNA for defence			
miR159-GmMYB33	*Heterodera glycines*	Modulate the GA-signalling and metabolism in the plant for defence	Lei et al., 2021
miR398	*Heterodera glycines*	Facilitate the plant resistance against CN	Tian et al., 2017
miR5032	*Heterodera glycines*	Overexpression of gene provide robust resistance against CN	Rambani et al., 2020

4. The host immune response against the CN infection

A successful pathogen can protect itself from plant-associated molecules that trigger defence signalling to avoid pathogen invasion. An elicitor is a diverse group of signal molecules recognized by the plant and induces defence against the pathogen. The immune response of plants can undergo two pathways to protect them from nematode invasion. First, the immune system is triggered by the pathogen-associated molecular patterns (PAMPs) to activate the PAMP-triggered immunity (PTI), and the second is the effector-triggered immunity (ETI) initiated by the effector protein produced by the nematode. Host plant cells have membrane-bound pattern recognition receptors (PRRs). It can recognize pathogen-associated molecules produced by a pathogen that activate the different types of immune responses. The first line of inducible defence, such as the burst of ROS triggers callose deposition. The first plant immune receptor, 'NILR1′ a leucine-rich repeat receptor-like kinase essential for the induction of basal immunity or PTI against the CN (Mendy et al., 2017). The role of mitogen-activated protein kinases (MAPKs) has been investigated as central components of cell signalling cascade against the *H. schachtii* parasitism in *Arabidopsis* spp. The MAPKs, such as MPK3 and MPK6 play a key role in the plant nematode interaction and activate the plant defence (Sidonskaya et al., 2016). McNeece et al. (2019) analyzed 32 MAPKs, of which nine have a defensive role and induced defence MAPK gene expression. The effector-triggered immunity is activated by R Proteins or resistance proteins present in the plant cell and recognizes the effectors of the pathogen and activate the hypersensitive response. In the case of CN, nematode-associated molecular patterns (NAMPs) play a wide role, initiating the defence signalling and modulating the plant immune responses. NAMPs role and its defence signalling initiation are represented in (Fig. 2). Manosalva et al. (2015) showed that nematode-conserved signalling molecules called ascarosides (ascr#18) acti-

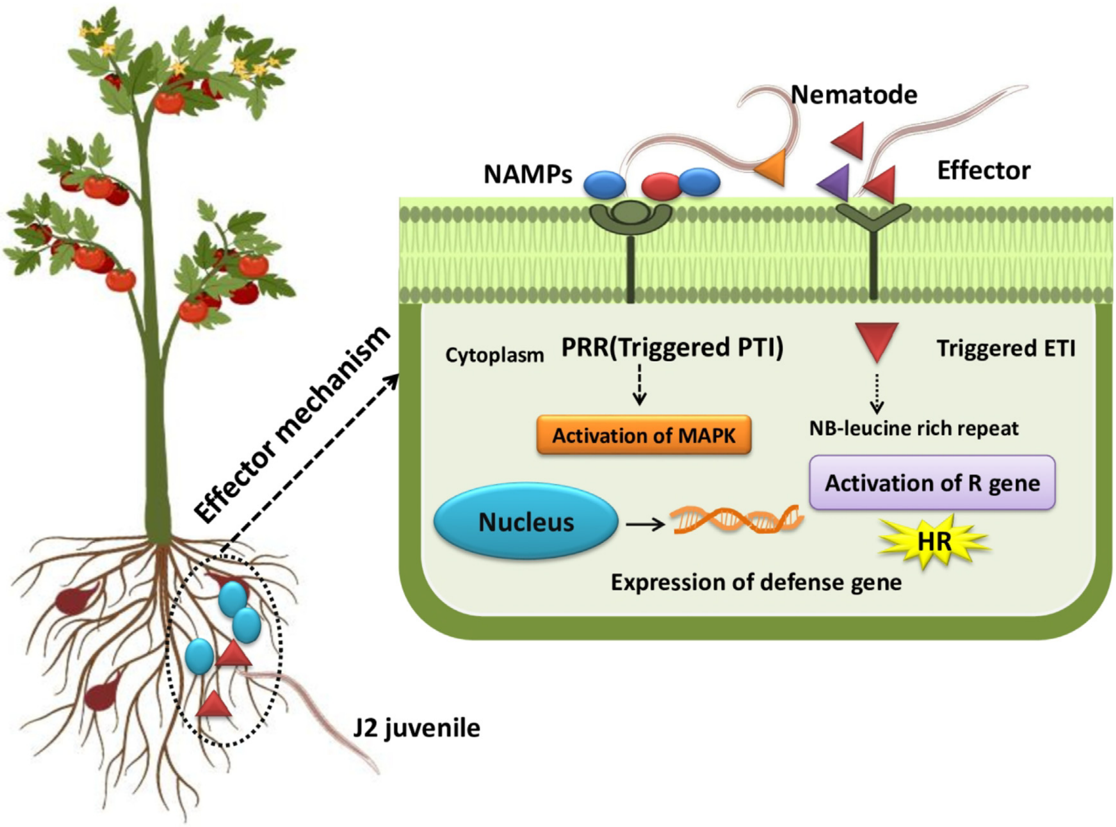

Fig. 2. Interaction between plant immune receptor and defence signalling components. Nematode associated molecular patterns (NAMPs) recognized by the plant membrane PRR (Pattern-Recognition Receptors) that triggers PTI (Pathogen Triggered Immunity), and activate the production of effector protein triggers the ETI (Effector-Triggered Immunity) that started the hypersensitive (HR) against the nematode.

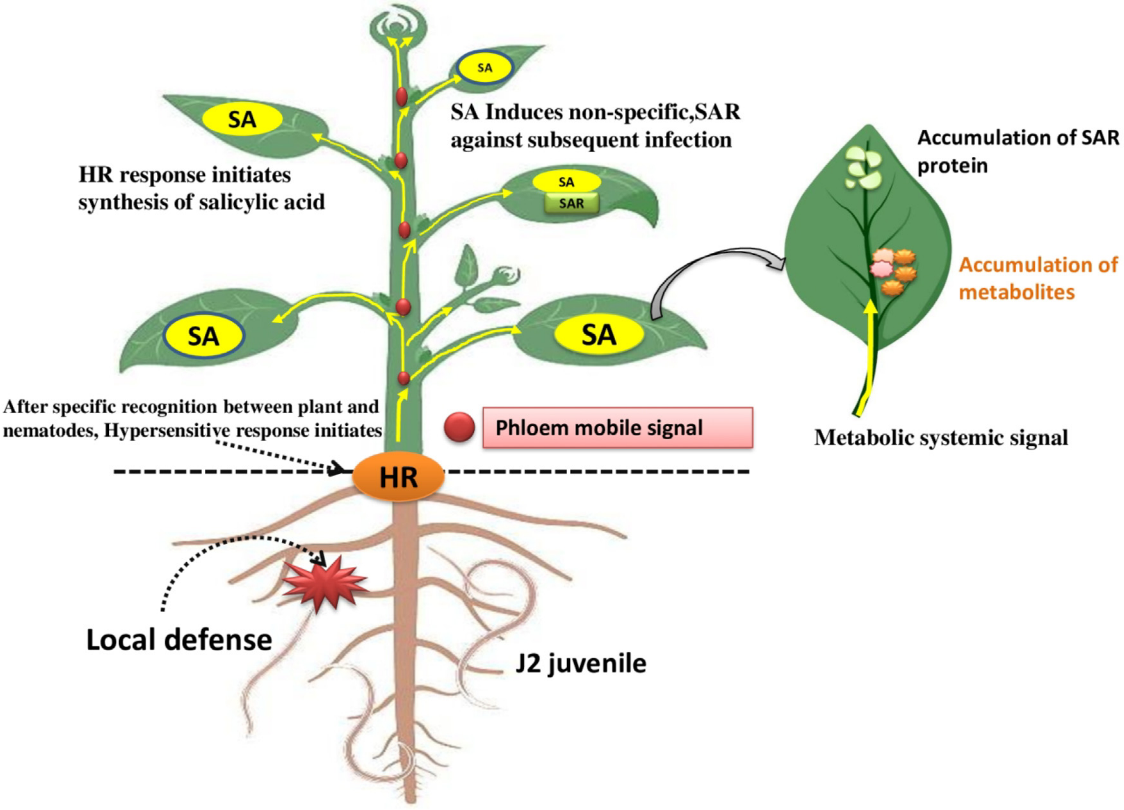

Fig. 3. The role of SA against the nematode infection through inducing SAR (Systematic Acquired Resistance) activates the pathogenesis-related proteins in the distant tissue of the host plant.

vate plant immune response. Ascarosides are NAMPs specific to nematodes and perceived by plants, activating conserved immune reactions. The plant cells have some receptor proteins, such as polygalacturonase-inhibiting proteins (PGIPs), which regulate camalexin and indole-glucosinolate biosynthetic pathways during the nematode parasitism (Shah et al., 2017).

5. Systemic acquired resistance and defence marker genes

The local host responses are activated at the local infestation site, causing the hypersensitive response that prevents subsequent infection. Host plants develop resistance against various pathogens through the hormone-mediated signals known as systemic acquired resistance (SAR). SAR enhances the defence potential of host plants and activates the pathogenesis-related genes in other host tissues, which are not exposed to infection and provide protection against future attacks. Several signalling molecules are involved in SAR. In the case of a necrotrophic pathogen, jasmonic acid (JA)-mediated signalling pathways play a significant role in plant resistance against the pathogen. Salicylate (SA) also plays an important regulatory role in biotrophic pathogens like cyst nematodes (Fig. 3). SA signalling synthesis specific function in defence response against the CN is not well known. Matthews et al. (2014) investigated thirty-one *Arabidopsis* genes involved in the SA and JA synthesis and signalling against the cyst nematodes CN. They found that some *Arabidopsis* genes, such as *AtNPR1*, *AtTGA2*, and *AtPR-5,* primarily associated with SA regulation, signalling, and synthesis enhanced resistance towards the CN. Several changes in gene expression, including the activation of pathogenesis-related proteins, occur in potato leaves after root infection with a cyst nematode. Molecular methods are used to extract plant genes and express their up-regulated genes upon nematode infection. In Egypt, Elkobrosy et al. (2021) first reported the characterization of *Globodera rostochiensis* at the molecular level. In particular, they demonstrated how this nematode affected the responses of the defence genes in the infected potato. The functional transcriptome of infected and non-infected potato plants was examined, and approximately 57 up-regulated and 22 down-regulated genes were identified. These reported genes provided broad-spectrum data about the plant nematode interaction. Contradictory information exists regarding the function of PR proteins in interactions with parasitic organisms. Some studies suggest that PR proteins are activated and involved in plant defence. Temperature variation causes changes in plant transcriptome activity (activation of resistance genes H1 and Gro1-4, as well as genes PR1, PR2, PR3, and PR6, responsible for the establishment of a defensive response to infection)(Lavrova et al., 2017). Their finding reveals the expression of the genes involved in the immune reaction in potato roots to the *Globodera rostochiensis*. Guo et al. (2019) reported that the R*hg*1 gene encodes the resistance against SCN responsible for developing resistance in soybean. They suggested that overexpression of Rhg1-GmAAT activated the jasmonic acid (JA) pathway causing resistance toward the SCN. Singh et al. (2020) highlighted the role of the ascorbate oxidase (AO) enzyme in their study. AO works as an effective systemic defence compound that protects plants against the *H. schachtii*. CN defence-related gene ‘GmSAMT1′ called Salicylic acid methyltransferase is involved in salicylic acid biosynthesis and signal transduction pathway and plays a defensive role against *H.glycines* (Lin et al., 2013). The defence related genes are enlisted in Table 3.

6. Molecular and genomics strategies for the CN

Molecular and genomic approaches improved the understanding regarding the plant nematode interaction and provided an opportunity to develop effective strategies against nematode infec-

Table 3
List of defence genes for the resistance against the CN infection in plants.

Defence Gene	Cyst Nematode (CN)	Host Plant	Function	Reference
AtMYB59	*Heterodera schachtii*	*Arabidopsis thaliana*	Reduce the susceptibility of the host	Wiśniewska et al., 2021
WI12Rhg1	*Heterodera glycines*	*Soybean*	Interact with DELLAs proteins that contribute to hormone signalling pathways.	Dong and Hudson, 2022
AtHRS1	*H. schachtii*	*A. thaliana*	Interfere with the development of cyst-induced syncytia and reduce the number of females.	Wiśniewska et al., 2022
At3g59930	*H. schachtii*	*A. thaliana*	Overexpression of the gene enhances the resistance to CN	Hawamda et al., 2022
Hg-rps23, Hg-snb1, and Hg-cpn1	*H. glycines*	*Soybean*	Enhance the broad-spectrum resistance via host-induced silencing.	Zhang et al., 2022a, 2022b
Glyma.06g036700	*H. glycines*	*Soybean*	Expression of the cupredoxin family proteins enhances the CNs resistance.	Zhang et al., 2022a, 2022b

tion. Novel genomic technologies enhanced crop sustainability by overexpressing 'R' genes, quantitative trait loci (QTL), and RNA interference. In the last decade, QTL played a key role in controlling CN. Jiao et al. (2015) identified the quantitative trait loci contributing to underlying resistance to CN. Swaminathan et al. (2018) detected the QTL mapping to CN resistance with the help of SNP (single nucleotide polymorphisms) markers. SNP tools provide data to study yield and disease resistance. Significant progress in RNAi-based plant protection strategies has been applied against nematode diseases.

RNAi is a powerful tool that regulates silencing gene expression, such as post-transcriptional gene silencing (PTGS), and inhibits translation and transcriptional gene silencing. Tian et al. (2019) reported that RNAi gene silencing reduces the populations of SCN and enhances host resistance. RNA interference decreases the pathogenicity of the CN. The genetic basis of broad-based resistance to SCN has also been reported, and the impact of 'rhg1′ and 'Rhg4′ genes for interaction with nematodes is highlighted by research (Patil et al., 2019). Marker-assisted selection (MAS) has also been developed. The three functional competitive allele-specific PCR (KASP) marker assays were sufficient for high-throughput marker-assisted selection for SCN resistance (Shi et al., 2015). There is no doubt that genetic tools have facilitated the identification of resistance genes and promoted the development of resistant varieties by improving desirable traits. Identifying the 'Rhg1′ and 'Rhg4′ genes improved the cyst nematode susceptible lines through the gene-editing (Liu et al., 2017; Bayless et al., 2018). Therefore, genome editing tools can modify specific targeted sequences and can be used to develop resistant varieties. The RNA-seq-based identification of resistance genes against the CN revealed that breeding nematode-resistant varieties is the safest and most effective method to manage plant diseases (Jiang et al., 2021).

7. Conclusion and future perspectives

CN are regarded as the biggest hazard to crop productivity worldwide due to their extensive host range. In recent years, it has become clear that nematode secretory effector proteins play a key role in the formation of feeding sites and the control of host cell machinery. Infection sites are established using a variety of procedures. There is no question that the host cell is regulated by phytohormone signalling and a variety of transcription factors, which also play a vital role in the immune response and emergence of symptoms in host plants. Additionally, we talked about how gene expression controls the nematode pest and initiates defensive reactions. The current understanding of molecular mechanisms supports the latest discoveries of novel genes and proteins implicated in the host-specific defence against CN. The development of RNAi (RNA interference) technology has emerged as a powerful technique for controlling the nematode population through gene silencing in light of genomic studies. So, with the aid of current developments in genetic, genomic, and molecular research, researchers were inspired to develop new tools for nematode resistance and strategies to better understand plant nematode interactions.

Author contributions

All authors contributed equally to this manuscript. Authors have read, critiqued and approved it for publication.

Disclosure statement

No potential conflict of interest was reported by the author (s).

Declaration of Competing Interest

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

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