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A Review on Molecular and Cellular Basis of Plant-Parasitic Root Knot Nematode-Host Interactions: Host Resistance

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Abstracts: **Root-knot nematodes (RKN), (*Meloidogyne* spp.) are obligate endoparasites of more than 3000 species of plants, which results in $70 billion worth of economic loss every year, worldwide. Controlling of obligated plant parasitic rootknot-nematode is generally difficult and also with the banning of many nematicides chemicals that control nematode, because of adverse environmental impacts, it is recommended to develop host resistance genes. Although, many R-gene confer resistance to RKN have been identified, the majority of these gene lose durability of resistance and affected by high temperature. As the results knowledge of molecular and cellular mechanism underlying host resistance condition is essential to develop durable resistance gene that provide stable resistance under different condition as well as provide resistance to many RKN species. Considering that, we have conducted extensive literature reviews on recently discovered diverse RKN resistance genes (structural and functional characterized) with their underlying mechanism of the resistance responses induced by different types of nematode resistance genes. In this review, several independent single dominant R genes confer resistance to RKN have been reported. These Resistance genes include: *Mi-gene, Ma-gene, PsoRPM2-gene, SacMi-gene and RMja genes* confer resistance to RKN in Tomato (*L. peruvianum*), *Prunus species* (*Myrobalan plum = Prunus cerasifera*), woody fruit tree (*Prunus sogdiana* and transgenic tobaccos) and Eggplants (*S. aculeatissimum) respectively. The structure, functions and mechanism of resistance mediated by these genes were summarized in this review.***

Keywords: **Meloidogyne spp, Rootknot nematodes, Resistance genes, Eggplants, Dominant R gene, Mi gene.**

1. INTRODUCTION

Root-knot nematodes (RKN), (*Meloidogyne spp*.) are obligate, sedentary endo-parasites of more than 3000 species of plants, that cause major crop losses on a worldwide scale which results in $70 billion worth of economic loss every year. The second stage juveniles (J2) hatch from the eggs in response to host-plant root exudates and invade the root just behind the apex, preferentially in the differentiation and elongation zone. Plant penetration is achieved by perforating cell walls with the combined effect of physical thrusting of the oral stylet and the enzymatic softening of the cell walls (Abad, *et al*., 2003). During parasitism, root knot-nematode secret parasitic protein called effectors that are produced by nematode amphids, hypodermis, and esophageal glands (dorsal and subventral) and involved in complicated nematode-plant molecular interactions such as invasion of roots, suppression of host immune defenses, and initiation and maintenance of permanent feeding structures (Barcala, *et al.,* 2010). As the results, root knot-nematodes are engaged in prolonged and intimate relationships with their host plants (up to six weeks) often involving complex morphological and physiological alterations of host cell into specialized cell called Giant cells. The Giants cells are essential for successful parasitism because this unique feeding structure provides nutrition to develop second juvenile larva (J2) in to adult. Root-knot nematodes are completely reliant on their giant cells as their sole source for food, and thus, the giant cells must be maintained throughout the nematode's life for its survival.

Plants are hosts for diverse microbes as well as for multicellular parasites like nematodes. In order to effectively protect themselves against the hazards of pathogens including nematodes, plants evolved various defense systems that range from physical barrier such as waxy cuticles and cell walls, to basal and inducible mechanisms in order to withstand the invasion by nematodes (Jones and Dangl, 2006). Basal defense responses – the first line of active defense – in plants are very often mediated via the detection of pathogen associated molecular patterns (PAMPs) nematode associated molecular pattern (NAMP) by membrane spanning proteins known as pattern-recognition receptors (PRRs). PAMPs include molecules that are associated with large classes of pathogens, such as lipopolysaccharide and chitin, the cell wall components of bacteria and fungi, as well as bacterial flagellin or virus-derived double-stranded RNA (Nurnberger, *et al.*, 2004). These PRRs induce PAMP triggered immunity (PTI) by triggering signaling cascades that initiate mitogen-activated protein kinase (MAPK) cascades, production of reactive oxygen species (ROS), production of antimicrobial compounds, altered ion fluxes, an increase in intracellular Ca2+ concentration, expression of pathogenesis related (defense) genes, changes in protein–protein interactions and localized callose deposition cell walls (Zipfel, 2009).

However, PAMP-triggered immunity (PTI) induces relatively low-intensity responses and provides less protection against the majority of pathogens (Chisholm, *et al.*, 2006). Besides, host-adapted pathogens nematodes can able to suppress PAMP-triggered immunity (PTI), often by delivering so-called effectors proteins into the host cytoplasm that interfere with intracellular signaling pathways induced by PTI mechanisms. In turn, plants have evolved mechanisms to recognize specific pathogen effector protein that suppress PTI, by the nucleotide-binding and leucine-rich repeat (NB-LRR) proteins encoded by disease resistance (R) genes and also induce effector-triggered immunity (ETI) (Van Ooijen, *et al*., 2007). NB-LRR proteins recognize effectors delivered to the host cytoplasm and induce a much stronger response than PTI, often associated with a type of cell death known as the hypersensitive response (HR). Some other plants have also evolved mechanism to recognize apoplastic effectors that by receptor-like proteins (RLPs) present in the plant plasma membrane and induce ETI. Although the components and recognition capacities of PTI receptors appear to be homogeneous in a given species, the recognition specificities of ETI are often highly variable both within and between populations of the same species.

In the evolutionary war between plant resistance and Root knot nematode virulence, resistance response may be considered a battle won by the plant. Plant host resistance to root knot-nematodes occur when plants, which have all of the components needed to be able to recognize effectors delivered into their cells and effectively respond to prevent the damaging manipulation of their resources by the intruder. The question "how product of plant resistance gene interact with root-knot nematodes' parasitic gene product" was described by two possible scenarios, in discussions about the molecular basis for this type of disease resistance in plants: (1) resistance that was determined by a host gene which encoded a polypeptide capable of interacting directly with a product from the pathogen (produced by a so-called avirulence gene) and somehow causing resistance in a single step, or (2) resistance that was conferred by a process of signal transduction in which the 'resistance' gene product serves as a pathogen perceptive molecule which in turn triggers a cascade of functionally conserved biochemical defence responses. Tales of the unexpected have also been revealed such as dual specificity of a resistance gene, the possibility that the resistance gene product may be located in the cytoplasm instead of being membrane bound, and that a so-called R-gene may not necessarily interact directly with an avirulence gene product of the pathogen. Recent advances in molecular genetics have lead to insights into the mechanisms by which plants either prevent pathogens from infecting them in the first place, or actively recognize and eliminate pathogens.

Controlling of obligated plant parasitic root-knot-nematode is generally difficult and also with the banning of many nematicides chemicals that control nematode, because of adverse environmental impacts, it is imperative that new safe disease control strategies for nematode management should be developed and implemented. Therefore, scientists are looking for alternative low-impact methods of nematode control, such as genetic and induced resistance, or the use of bio-control agents. In order to develop new and environmentally safe disease control strategies like resistance gene, it is essential to understand the molecular and cellular mechanisms of how RKN interact with host plants. In other words, it will be interesting to see how nematode effectors will be–directly or indirectly – recognized by the resistance genes product and how they interact as virulence factors with other plant components during the establishment of a parasitic relationship. The identification of nematode resistance genes as well as structural and functional characterization of these resistance genes is one step forward to understand these mechanisms. Therefore, the aims of this review was to survey comprehensively abundance literature on recently discovered diverse resistance genes to rootknot-nematode, structural and functional characterized Resistance genes as well as the mechanisms underlying the resistance responses induced by different types of nematode *resistance* genes.

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2. MOLECULAR GENETICS AND CELL BIOLOGY OF HOST RESISTANCE TO PLANT-PARASITIC ROOT-KNOT NEMATODES

Host resistance (R) gene to RKN is a gene which directly or in directly restrict the reproduction (eggs) and root galling of parasitic RKN. Host R genes encode intracellular immune receptors are called resistance (R) proteins. The majority of plant R genes are encode protein belongs to NB-LRR receptor family, which consist of a central nucleotide-binding (NB) domain and C-terminal Leucine-Rich Repeat (LRR) domain that structurally and functionally resemble mammalian nucleotide-oligomerization domain-like (NOD-like) receptors (Meyers, *et al*., 1999). Two types sub-class NBS-LRRs (NL) plant immune receptors: one encode an N-terminal domain with Toll/Interleukin-1 Receptor (TIR-NB-LRR, TNL), and the other one encode an N-terminal coiled-coil motif (CC-NB-LRR, CNL) (Dang, *et al.*, 2016). CNL and TNL genes act as receptors or co-receptors of pathogen-derived elicitors. Genome organization of many resistance genes encode both classes of NBS-LRR genes (TIR-type and CC-type/non-TIR) are commonly present in multigene clusters in plant genomes and can occur as true alleles across naturally variant genetic backgrounds. These R-proteins are generally constitutively expressed and act as modular and presumed to undergo intra- and inter-molecular reconfiguration upon effector recognition in order to activate plant immune defense (Dangl, *et al.,* 2013).

Molecular basis of resistance to parasitic is often determined by variation at single genetic loci encoding either factors mediating active recognition of, or susceptibility to the parasite. Recent advances in molecular genetics have lead to insights into the mechanisms by which plants either prevent pathogens from infecting them in the first place, or actively recognize and eliminate pathogens. Several independent single dominant R genes from different plants confer resistance for numerous species of root-knot nematode have been identified and mapped in different chromosomes. This review included the molecular and cellular basis of resistance mechanism mediated by R-genes includes, *Mi*, *Ma*, *Ma*, PsoRPM2, SacMi and *RMja* genes (Milligan, *et al*., 1998, Claverie, *et al*., 2011, Zhu, *et al*., 2017, Zhou, *et al*., 2018), confer resistance to RKN in Tomato (*L. peruvianum*), *Prunus* species (Myrobalan plum = *Prunus cerasifera*), woody fruit tree (*Prunus sogdiana* and transgenic tobaccos) and Eggplants (*S. aculeatissimum)* respectively.

Root-knot Nematode Host Mi-Resistance Genes Family

Gene confer resistance to root-knot nematode has been identified in numerous crop plants such as wild tomato, sweet potato and pepper (Milligan, *et al*., 1998, Chen, *et al*., 2007, Niu, 2007). The numerous tomato verities carries single dominant gene called Mi-1 that confers resistance to root-knot nematode species. In the early 1940, the Mi gene was first discovered in wild tomato (L. peruvianum) and then introduced into cultivated tomato (L. ycopersicon esculentumm) (Smith, 1944). The Mi-1 gene provides resistance to the three most damaging root-knot nematode species, *M. incognita*, *M. arenaria* and *M. javanica (*Milligan, *et al*., 1998, Williamson, 1998, Nombela, *et al*., 2003*).* Recently, numerous tomato cultivars have received Mi-R gene with help of *isozyme marker* and DNA linked marker *aps-1* and *Rex-1* respectively (Medina-Filho and Tanksley, 1983, Williamson, *et al*., 1994a). The Mi gene controls RKN at soil temperatures below 28°C and has commonly been used in tomato grown throughout the world.

However, the resistance conferred by the Mi gene has some critical limitations. Those are, Mi gene is not effective at soil temperatures above 28°C (Dropkin, 1969). Besides, repeating cultivation for long time and high numbers of pathogen inoculation produced some nematode population those have overcome the resistance conferred by Mi has also been reported. (Roberts, *et al*., 1990, Castagnone-Sereno, 1994, Kaloshian, *et al*., 1996). In addition, the presence of naturally occurring resistance-breaking populations such as *M. incognita*, *M. javanica* and *M. arenaria* has been reported (Maleita, *et al*., 2011). Another constraint of *Mi gene* is the susceptibility of Mi gene for some damaging RKN species, *M. hapla* or *M. enterolobi* (Williamson, 2006). The effect of resistance outcomes of Mi gene is also affected by gene dosage, depending on whether the resistant cultivars are heterozygous (Mimi) or homozygous (MiMi) as shown by (Tzortzakakis, *et al.,* 1998).

Structure and Functions Mi-Resistance Genes Family (Mi-1.1 and Mi-1.2)

Molecular studies of root-knot resistance gene, Mi-1 were carried out in the 1980's with the aims of both isolation of DNA markers for indirect selection for resistance and cloning the sequence. Although, efforts to localize the Mi gene have been hampered for many years because of the severe repression of recombination near this gene in *L. esculentum* lines carrying the introgressed *L. peruvianum* DNA (Messeguer, *et al*., 1991, Ho, *et al*., 1992, Liharska, *et al*., 1996). Recently, genetic mapping using molecular markers, and screening large populations of tomato for recombinants in

progeny from controlled genetic crosses of *L. peruvianum* plants with and without resistance (L. esculetum), resulted in localization of the gene to a small region of the genome of 65 kb short arm of chromosome 6 (Kaloshian, *et al*., 1998). Subsequently, DNA sequence analysis of this region (by sequencing 52 kb contiguous DNA) of the genome identified three closely related candidate genes: Mi-1.1, Mi-1.2 and Mi-1.3 (pseudo gene). Mi-1.3 is an apparent pseudogene because it lacks both the N- and C-terminal coding sequences and contains a deletion and several nonsense codons relative to *Mi-1.1* and *Mi-1.2*. The structures of Mi-1.1 and Mi-1.2 genes were studied through comparison of the cDNA and genomic sequences showed that each of Mi-1.1 and Mi-1.2 genes contains two introns at conserved positions near their 59 end. Intron one of Mi-1.1 and Mi-1.2 are 1306 and 556 bp respectively. Beside, intron one of both genes interrupts the untranslated region, whereas intron 2 interrupts the coding region. The position of the initiating ATG codon is conserved between the two genes and begins 42 bp 59 of intron 2. The 5-UTRs region of both genes were predicted 86 nucleotides. The lengths of the 3-UTR of *Mi-1.1* and *Mi-1.2* are 132 and 108 nucleotides, respectively. The two genes have an identical TATA box sequence (TATATTT) at 230 bp from the putative transcript start. In addition, *Mi-1.1* has a CAAT box sequence at 276 bp (Milligan, *et al*., 1998).

Functional analysis of Mi-1.2 gene using nematode-susceptible tomato line (Money maker) transformed with full construct of Mi-1.2 mediated by agrobacterium revealed that 14.7-kb DNA insert carrying *Mi-1.2* is sufficient to confer resistance to RKN species, M. Javanica and M. incognita that show similar of specificity of Mi resistance gene. Whereas similar experiment performed for Mi-1.2 failed to produce resistance phenotype of Mi-gene. All of the *Mi-1* family members in both susceptible and resistant tomato that appear to be intact genes are transcribed (Seah, *et al*., 2007). The predicted proteins encoded by Mi- 1.1 and Mi-1.2 were 1255 and 1255 amino acids respectively. The highest similarity of *Mi-1.2* to a gene whose product has known function is that to *Rpi-blb2* (82% identity), which is located on chromosome 6 in the corresponding genomic position to *Mi-1* in the wild potato *Solanum bulbocastanum* and confers broad resistance against the oomycete *Phytophthora infestans* (van der Vossen, *et al*., 2005). Mi-1.1 and Mi-1.2 each contain a predicted leucine zipper motif. A second region containing seven isoleucine/leucine heptad repeats not present in the other *R* genes spans residues 460 to 502 of Mi-1.2. These *heptad repeats* contain two proline residues, which would be predicted to cause a bend in the structure. The highest similarity among the leucine zipper–nucleotide binding–LRR proteins is in the 260–amino acid central conserved region suggestive of a conserved function for this part of the protein. This region contains two motifs, kinase-1a (P-loop) and kinase-2 consensus sequences that conform in sequence and spacing to those found in known ATP and GTP binding proteins (Traut, 1994).

A potential kinase-3a motif that differs somewhat from the published consensus (Traut, 1994) but is highly conserved among nucleotide binding–LRR genes. Additional conserved regions include a hydrophobic domain containing the sequence GLPL, which is almost invariant among nucleotide binding– LRR genes described to date (Hammond-Kosackand Jones, 1997). The C-terminal region of Mi-1.1 and Mi-1.2 can be arranged into z14 LRRs of z24 amino acids. This framework is most similar to that of Prf. The consensus sequence of the LRR of Mi-1.2 is aXXLXXLXXLXa (X) 12 (where a indicates an aliphatic amino acid residue and X indicates any amino acid; a consensus is assigned if the amino acid is present in 50% of the residues at a particular position in the repeat. This consensus most strongly resembles that for the cytoplasmic class of nucleotide binding–LRR proteins (Jones and Jones, 1996).

Mi-9 gene confer resistance to the same spectrum of RkN species (M. javanica, M. arenaria and M. incognita) as Mi-1, but which provide stable resistance in higher temperature, has been mapped on short arm of chromosomes 6 as Mi-1 in *S. arcanum* (Ammiraju, *et al*., 2003). Molecular studies using RNA interference (RNAi) to silence genes in the *Mi-1* family indicate that *Mi-9* is a homologue of *Mi-1* (Jablonska, *et al*., 2007).

Molecular and Cellular Mechanism of Resistance Mediated by Mi-Genes

In tomato, the R *gene* locus *Mi-1* contains two genes that encode two proteins, Mi-1.1 and Mi-1.2, which have high sequence similarity and contain NBS-LRR motifs (Milligan, *et al*., 1998). Mi-1.1 does not function in pest resistance; *Mi-1.2* confers race-specific resistance against RKNs, potato aphids (*Macrosiphum euphorbiae*), and whiteflies (*Bemisia tabaci*) (Milligan, *et al*., 1998, Nombela, *et al*., 2003). Mechanism of resistance mediated by Mi-1 genes has been proposed to be involved in specific recognition of pathogen products, effectors. Based on the absence of a signal peptide, it is proposed that Mi-1.2 is probably localized in cytoplasm. The Mi-1.2 gene resistance response to RKN infection, cellular *hypersensitive response* (HR) occurs near the anterior end of the nematode at 12 hours after inoculation. This corresponds roughly to the time when the nematode would be expected to inject effectors initiate giant cell. This

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coinciding of time of effectors injection and HR is consistent with the hypothesis that Mi-1.2 resistance mediated through gene-to-gene model. In other word, Mi-recognizes something (effectors) that the nematode injects into the plant cell that triggered resistance response, localized hypersensitive response (HR) at and surrounding areas of giant cell initiation (Ho, *et al*., 1992, Milligan, *et al*., 1998, Dangl and Jones, 2001). Despite extensive efforts during the past two decades, molecular mechanisms connecting Mi-1.2 R-mediated effector recognition with regulatory processes involved in basal defense and PTI are largely elusive.

However, the molecular, histological and histo-chemical studies of mechanism of Mi-1.2 resistance response have reported that NBS domain of the Mi-1.2 R protein can be autoactivated to trigger defense signaling in tomato (Tameling, *et al*., 2002, Lukasik-Shreepaathy, *et al*., 2012). The LRR domain of the Mi-1.2 protein has many roles in the regulation of RKN recognition and HR signaling (Hwang and Williamson, 2003). Resistance to *Meloidogyne* is speculated to be regulated by a protein kinase acting either early in *Mi-1.2* signal transduction or upstream of Mi-1.2 and is required for *Mi-1.2*-mediated RKN resistance (de Ilarduya, *et al*., 2001, Martinez de Ilarduya, *et al*., 2004). Notably, the chaperones Hsp90-1 and Sgt1 are involved in the formation of the Mi-1.2 signaling complex (Bhattarai, *et al*., 2007) (**Figure 1**). Virus inducing gene silencing, the plant receptor-like kinase somatic embryogenesis receptor kinase 3 (SERK3)/brassinosteroid insensitive 1-associated kinase 1 (BAK1), (SlSERK1) revealed a role for SlSERK1 in Mi-1-mediated resistance to potato aphids, but not to RKNs (Peng, *et al*., 2011).

Transcript analysis has revealed that several genes encoding heat shock transcription factors (Hsfs) and heat shock proteins (Hsps) (Hsp90) are essential for *Mi-1.2*-mediated resistance to RKNs by functioning as a chaperone of the R protein signaling complex during pathogen attack (Bhattarai, *et al*., 2007). Using, virus-induced gene silencing (VIGS) in tomato, the heat shock protein HSP90-1 and the co-chaperone SGT1 were shown to be required for resistance mediated by the R gene Mi-1 (Meloidogyne spp.) and potato aphids (Macrosiphumeuphorbiae). In addition, VIGS also identified the involvement of a mitogen-activated protein kinase (MAPK) cascade including the MAPK kinase (MAPKK) LeMKK2 and the MAPKs LeMAPK1, LeMAPK2 and LeMAPK3 in Mi-1 resistance against potato aphids (Li, *et al*., 2006b). Furthermore, recent studies have reported that Mi.1.2 R-proteins directly interfere with transcriptional regulators (SlWRKY72a and SlWRKY72b) to activate the transcriptional network controlling *Mi-1.2*-triggered ETI immunity (Bhattarai, *et al*., 2010).

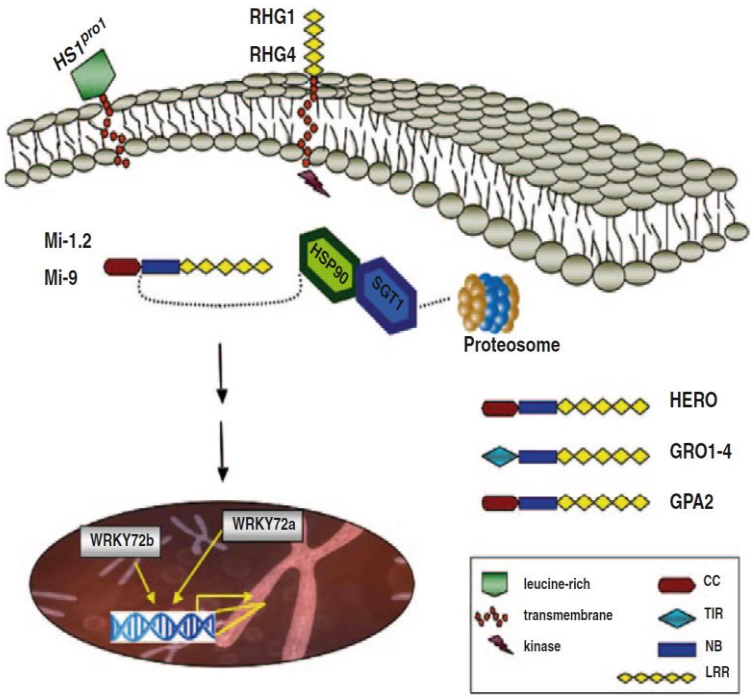

Figure: 1 Structures and localization of nematode resistance proteins and components of the Mi-1.2 signaling pathway. *Abbreviations*: CC, coiled-coil; TIR, toll-interleukin receptor-like; NB, nucleotide-binding; LRR, leucine-rich repeat (Adapted from Abed, *et al*., 2011)

The functional link between Mi-1 and WRKY72-like TFs appears a step of direct defense activation. Mechanism of Mi-1-triggered ETI may require transcriptional up-regulation of SlWRKY72a and SlWRKY72b, which in turn boosts basal defense responses controlled by these TFs. A role of WRKY72-type TFs in Mi-1-mediated resistance is consistent with the fact that both Mi-1 and AtWRKY72 appear to utilize SA-independent defense mechanisms (Bhattarai, *et al*., 2008). To sum up, the mechanisms mediated by Mi-1.2 resistance response to RKN infection are characterized by early hypersensitive response (HR), a highly strong and effective defense reaction in tomato (Solanumlycopersicum) and similar to the Me3 R gene in pepper (Capsicum annuum), in contrast to late necrosis of imperfect giant cells, as for the Me1 R gene of pepper and the Rk R gene of cowpea (Williamson, 1998, Pegard, *et al*., 2005, Das, *et al*., 2008). The Mi-1.2 NBS domain of the Mi-1.2 R protein can be autoactivated to trigger defense signaling in tomato (Tameling, *et al*., 2002, Lukasik-Shreepaathy, *et al*., 2012). The LRR domain of the Mi-1.2 protein has many roles in the regulation of RKN recognition and HR signaling (Hwang and Williamson, 2003). The chaperones Hsp90-1 and Sgt1 are involved in the formation of the Mi-1.2 signaling complex (Bhattarai, *et al*., 2007). The involvement of a mitogen-activated protein kinase (MAPK) cascade including LeMAPK1, LeMAPK2 and LeMAPK3 in Mi-1 resistance against potato aphids (Li, *et al*., 2006b). The Mi.1.2 R-proteins directly interfere with transcriptional regulators (SlWRKY72a and SlWRKY72b) to activate the transcriptional network controlling *Mi-1.2*-triggered ETI immunity.

Root-knot Nematodes Host Ma-Resistance Genes

The Ma resistance gene has been identified in *Prunus* species, Myrobalan plum (*Prunus cerasifera*), a near-wild allogamous species found in temperate and Mediterranean climates (Eremin, 1978). In those species, Ma gene confer high degree of dominant resistance to more than 30 root-knot nematode including, *M. arenaria*, *M. incognita*, *M. javanica*, *M. hispanica* and *M. hapla*. (Esmenjaud, *et al*., 1997). Resistance conferred by Ma gene is very unique in its being stable, broad and even provide control to RKN like *M. floridensis* for which no natural host resistance gene has not yet discovered (Esmenjaud, *et al*., 1997) as well as provide resistance for highly invasive root-knot nematode species, *Meloidogyne mayaguensis* which overcomes the most common resistance genes such as Mi-1 gene in tomato, Me gene in papper and Rk gene in cowpea. (Williamson, 1998, Rubio-Cabetas, *et al*., 1999, Brito, *et al*., 2007, Kiewnick, *et al*., 2009, Castagnone-Sereno, 2012). Besides, Ma R-gene provide stable resistance under high temperature (Esmenjaud, *et al*., 1996a) under which the first identified and cloned resistance gene (Mi-gene) was the lost the ability to provide stable resistance to RKN in tomato and aphid (Dropkin, 1969). The *Ma* gene, from *P. cerasifera*, was the first TNL gene, conferring resistance to RKNs, cloned in a woody perennial plant. Conversely to the *Mi-1* tomato CNL R gene (Milligan, *et al*., 1998), the *Ma* gene confers a heat-stable and complete-spectrum resistance to RKNs (Claverie, *et al*., 2011), and no natural or selected virulent isolates have been detected yet (Khallouk, *et al*., 2013). Besides these attractive biological properties, this gene displays a unique C-terminal structure, which is only found in the *Prunus* and *Malus* genera, made of five PL domains completing the TIR-NBS-LRR canonical part (Van Ghelder and Esmenjaud, 2016).

The two key features of resistance are its spectrum (horizontal component) and strength (vertical component). In other word, durable resistance is a resistance that remains effective for long period of extensive use in agriculture in conductive environment for the disease (Johnson, 1981). The resistance conferred by the *Ma* gene is both full spectrum and strong. This key feature has been demonstrated in genetic studies based on an evaluation procedure involving the application of high and continuous inoculum pressure. In inter-specific Prunus hybrids, the resistance conferred by Ma alone or by a combination of Ma and RMia has not been overcome when challenged, under glasshouse conditions, for 2–4 years of exposure to continuous *M. incognita* inoculum pressure (Khallouk, *et al*., 2013).

Structure and Functions Ma-Resistance Gene

Resistance to M. *arenaria* in Myrobalan plum (*Prunus species*) is controlled by the Ma major resistance genes that are completely dominant and confer a non-host behavior that totally prevents the multiplication of the nematode. The Ma genes have been identified in highly heterologous and self incompatible near-wild cultivars (Eremin, 1978). After the *Mi-1* gene from tomato (Milligan, *et al*., 1998), the *Ma* gene is the second cloned gene confer resistance to RKN and located on chromosome 7 of Prunus species *(Prunus cerasifera)*. The *Ma* gene belongs to the TNL family of the NBS-LRR class of genes instead of the CNL family of *Mi-1* (Milligan, *et al*., 1998). Further recombinant analysis and BAC sequencing identified a cluster of three TIR-NBS-LRR (TNL) genes, one of which is probably the *Ma* gene (Esmenjaud, 2009). The *Ma* gene has the longest full-length cDNA size (2,048 deduced amino acids) of all TNL genes cloned to date. Ma gene TNL structure is completed by a huge post-LRR (PL) sequence (1,088 amino acids) comprising five repeated

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carboxyl-terminal PL exons with two conserved motifs. The amino-terminal region (213 amino acids) of the LRR exon is conserved between alleles and contrasts with the high inter-allelic polymorphisms of its distal region (111 amino acids) and of PL domains. The *Ma* gene highlights the importance of these uncharacterized PL domains, which may be involved in pathogen recognition through the decoy hypothesis or in nuclear signaling (Claverie, *et al*., 2011).

Molecular and Cellular Mechanism Mediated Ma-Resistance Genes

The recently cloned Ma confers a complete-spectrum resistance to RKN (*M. incognita*, *M. arenaria* and *M. javanica*). This R-gene (Ma) triggers a hypersensitive-like reaction characterized by the complete absence of galls. This gene has the peculiarity to have been identified in a highly heterozygous and self-incompatible material from, moreover, a near-wild (unfixed) origin (Eremin, 1978). The positional cloning strategy for *Ma* has shown that the Ma gene belongs to the TNL family of the NBS-LRR class of genes instead of the CNL family of Mi-1 (Milligan, *et al*., 1998). It belongs to the Toll interleukin-1 receptor nucleotide-binding site leucine-rich repeat class of resistance genes (NB-LRR-TNL). The major structural difference between TNL1 and other known TNLs resided in the presence of five PL exons at C-terminal region. The deduced amino-acid sequence of this PL region of the corresponding protein, the function of which is completely unknown, is longer than the rest of the gene (i.e. TIR, NB, NLL and LRR domains) (Meyers, *et al*., 2003).

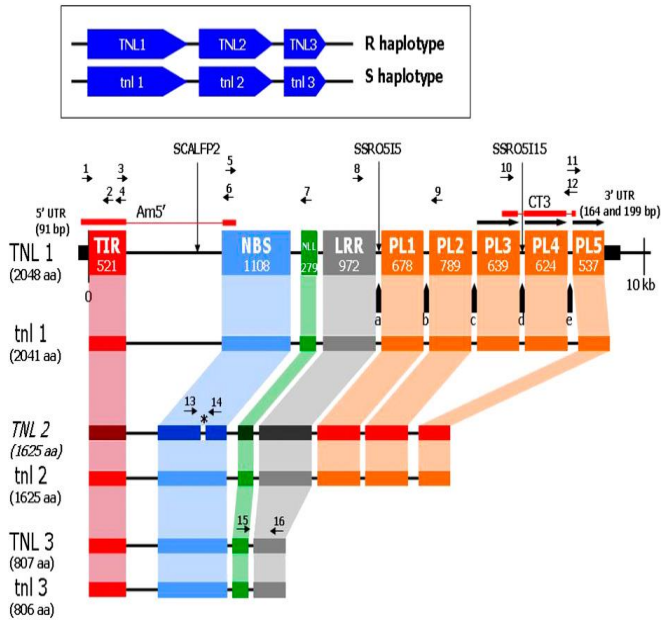

Figure 2: Exon and intron structure and size (in bp) of the TNL cluster from the R and S haplotypes. PL1 to PL5 are the C-terminal post-LRR exons. Vertical arrows indicate polymorphic markers; a to e = SSR sequences as follows: a = (TC) 33, b = (TC)18, c = (TC)21, d = (TC)21(TA)10, and e = (CT)27 (CAGA) (CA)6. Direct repeats of sequences in PL3 to PL5 are indicated by horizontal arrows above the DNA sequence. Thick black lines at each end of TNL1 are the 5# UTR (79 bp) and 3# UTR (two transcript variants of 164 and 199 bp), respectively. Red bars above TNL1 are the TNL1-specific cDNA fragments Am5# and CT3. Values at the left end of each gene are the total amino acids (aa) deduced from the sequenced full-length cDNA sequence or from the predicted cDNA (other genes). The TNL2 pseudogene (in italics), after correction of the single-base frameshift mutation in the NBS (indicated by the star), is shown in darker colors. Primers used for the full-length cDNA sequence and sequence verifications are shown by arrows with numbers and correspond, from 5# to 3#, respectively, to Am5#-2F (1), TIRGC1-R1 (2), TIRNBSGC1-F (3), TIRGC1-R2 (4), NBSGC1-F (5), TIRNBSGC1-R (6), NBSNLLGC1-R (7), EpisLRR-F1 (8), EpisLRR-R1 (9), CT3-Fo (10), Ic-CT3- Ba (11), CT3-Ba (12), NBSGC2-F (13), NBSGC2-R (14), NLR-F2 (15), and NLR-R (16)

Molecular and Cellular Mechanism Mediated Ma-Resistance Genes

The recent histological study clearly showed that resistance mediated by the *Ma* gene is associated with cell necroses (arresting the nematode development) and the corresponding HLR phenotypes occurring in either the vascular cylinder, the meristematic apical or bud regions, or the cortex. Differential staining with toluidine blue revealed dark-blue and blue-green coloration of HLR cell compounds and suggested accumulation of phenolics. Under UV light, some compounds

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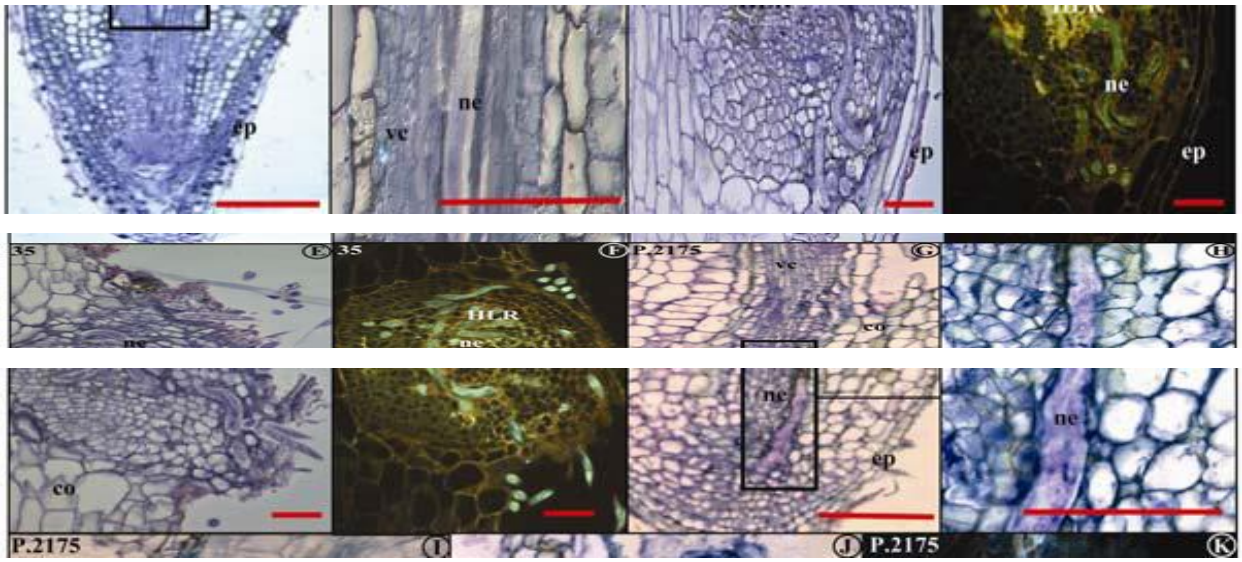
emitted yellow-orange fluorescence with a lower intensity than in resistant pepper CM334 (Pegard, *et al*., 2005), in which a high content of phenolics such as chlorogenic acid has been detected. In resistant accessions (P.2175 and 35) the first signs of cellular necrosis were localized in the vascular cylinder at 3 dpi (Khallouk, *et al*., 2011). The *Ma* gene does not induce an early resistance phenomenon due to a physical or chemical barrier to penetration. This situation is contrary to CM334 pepper (carrying the *Me7* gene), in which J2s are preferably blocked in the epidermal layer of cells (Pegard, *et al*., 2005) and might trigger an active early post-penetration biochemical defense mechanism. All the tested RKN species whether mitotic or meiotic (*M. floridensis*), whereas Mi-1 confers a more restricted spectrum of resistance. This suggests that the Ma-R protein recognizes nematode signals or effectors common to a wide range of *Meloidogyne species*. It is highly probable that this gene recognizes a crucial effector or guards a virulence/effector target that RKN species have in common. In other words, the absence of coevolution, the wide-spectrum and high-level resistance conferred by the *Ma* gene may be best explained by an indirect interaction, guard hypothesis (Van der Biezen and Jones, 1998, Dangl and Jones, 2001) between the resistance gene product and the nematode Avr factors. Alternatively, in the context of the decoy hypothesis proposed by Van der Hoorn and Kamoun (2008), at least one of the PL exons might mimic a conserved host target (as hypothesized for the WRKY domain of SLH1 by Noutoshi, *et al.*, 2005) common to *Meloidogyne species* and unrelated plant pathogens and lead to a direct interaction. In the TNL1/*Ma* gene, not only the PL domains but also the end of the LRR domain and the gene regulatory region show extensive polymorphism. In this case, we may suppose that the "guarded" host product or the host decoy is targeted by independent Avr products from one or more pathogens species that are not apomictic RKN (Khallouk, *et al*., 2011).

Recent, histochemical study of resistance mechanism mediated by of Ma-R gene showed that motile J2s neither swelled nor developed into J3s, and initiation of feeding sites was never observed. This complete absence of gall symptoms is associated with cell necroses and corresponding hypersensitive-like reaction (HLR) phenotypes occurring either in the stele or in the meristematic apical region or in the cortex. Nematode attacks often disorganized the meristematic apical tissues, which induced the development of subterminal lateral roots replacing primary terminal apices and, thus, provided an active resistance reaction to HLR damage. Microscopic observations of stained resistance root sections revealed dark blue color characteristic of an HLR around the nematode at different dates. The earliest HLR was characterized at 3 dpi in our study (Fig. 3A and B). Such reactions occurred in either the vascular cylinder (Fig. 3A and G), the meristematic or bud regions (Fig. 3C and E), or the cortex (Fig. 3I). The intensity of staining seemed to be higher at later dates (40 dpi) (Fig. 3I and J). When root sections were examined under UV light, the yellow or orange autofluorescence (Fig. 3D, F, and K), exhibiting the presence of aromatic compounds, was seen within the cells and in cell walls. In our figures, we could observe clear signs of nematode death at 23 dpi (Fig. 3G and H). In *Ma*-resistant accessions, observations of development of roots in apical regions consecutive to nematode attacks showed the emergence of newly formed lateral roots from buds formed just upward of the apices (Fig. 3L to P). These sub-terminal lateral roots emerged from the stele as a consequence of disorganization of tissues observed in the meristematic terminal regions (Fig. 3Q to S).



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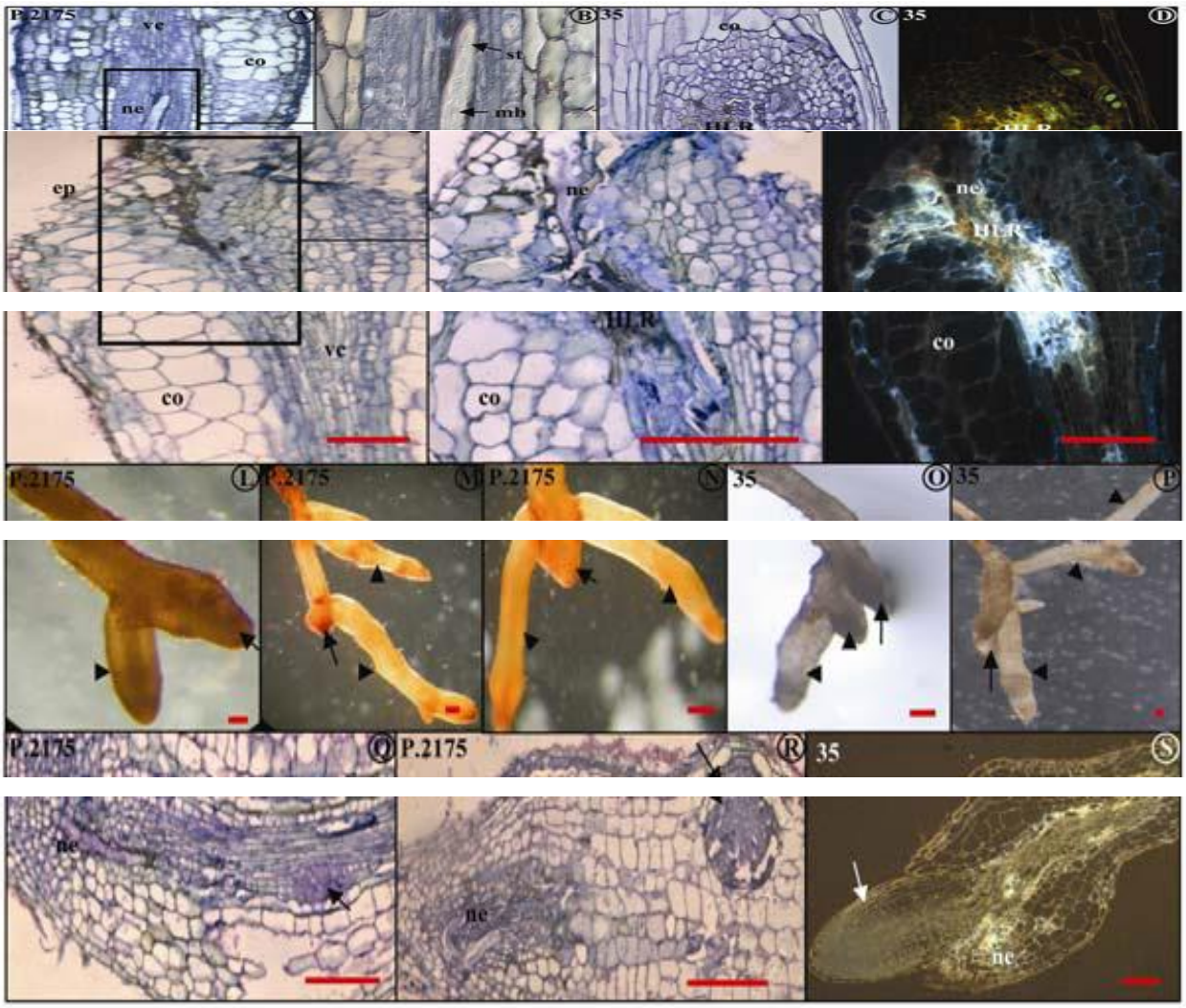

Figures: 3 Incompatible interaction in resistant accessions (P.2175 and 35). **A, C, E, G, and I,** Sections stained with toluidine blue showing hypersensitive-like reactions (HLRs) associated with second-stage juveniles (J2s). **B, H, and J,** Magnification of A, G, and I, respectively. **D, F, and K,** Unstained sections observed under UV showing yellow and orange fluorescence illustrating HLR around J2s. **L to P,** Lateral roots neoformed (arrowheads) near damaged apices (arrows). **Q,R, and S,** Sections showing damaged meristematic apical tissues (arrow) and correlative emergence of lateral roots (section S is unstained and observed under UV); ep = epidermis, co = cortex, vc = vascular cylinder, ne = nematode, mb = median bulb, st = stylet. Bars = 100 µm (except L to P, where bars = 500 µm). Adapted from Khallouk, *et al*., 2013).

Further investigations are required in order to understand more accurately the underlying mechanisms involved in the HLR mediated by the *Ma* gene in *Prunus spp*., at both cellular and molecular levels.

Root-knot Nematodes Host PsoRPM2 Resistance Genes

The PsoRPM2 (*Prunus sogdiana* RESIST PATHOGEN *M. incognita*) gene can rapidly and significantly increase its expression in response to M. incognita invasion and thus enhance the RKN resistance of transgenic tobacco lines, suggesting that it is likely involved in disease resistance, which is similar to previous studies on the GHNTR1 gene (Zhang, *et al*., 2015).

Structure and Functions of PsRPM2 Resistance Genes

Homologous cloning shows that the CDS of PsoRPM2 had a length of 3297 bp and was flanked by a 92-bp 30-UTR and a 225-bp 50-UTR. Genomic DNA sequencing revealed no introns within PsoRPM2, and PsoRPM2 was found to contain a TIR domain (139 aa), a NB-ARC domain (267 aa), and LRR domain (300 aa). The TIR domain contained three conserved

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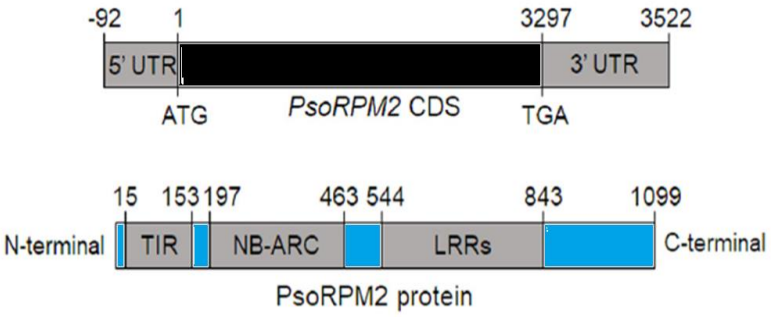
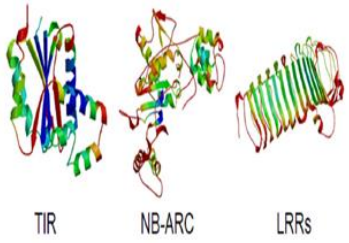
motifs, the NBS-ARC domain contained a P-loop and kinases 1, 2, and 3 motifs, and the LRR domain contained 13 leucine-rich repeats. The CDS regions of PsoRPM2 genes in resistance and susceptible P. *sogdiana* plants were identical. Phylogenetic analysis suggests that PsoRPM2 was closely related to homologous proteins of Prunus mume, Prunus *persica*, and Malus *domestica* (**Figure: 4**) (Zhu, *et al*., 2017).



A



B

Figure: 4 PsoRPM2 cloning and protein analysis. The mRNA clone of PsoRPM2 generated by 30-RACE (lane 1), 50-RACE (lane 2), and full-length amplification (lane 3). M: DNA marker. (**A**) Schematic representations of PsoRPM2. (**B**) The predicted 3-dimensional structures of the TIR, NB-ARC, and LRR domains within PsoRPM2.

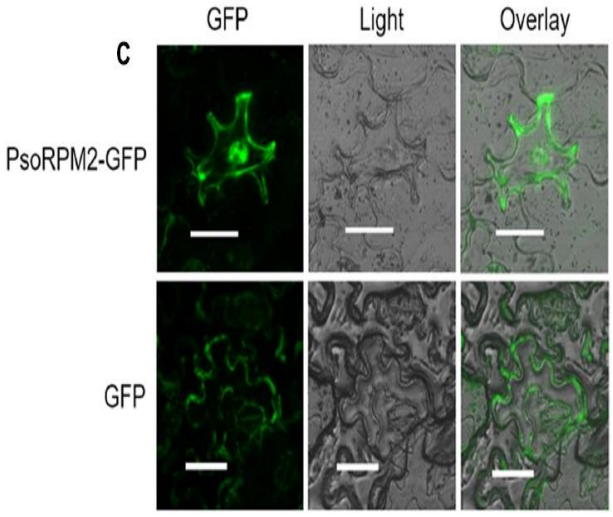


Figure: 5 PsoRPM2 expression profile and subcellular localization of PsoRPM2 protein. (A) PsoRPM2 expression in various tissues of resistant (upper two panels) and susceptible (under two panels) P. sogdiana plants. RPII was used as a reference gene. (B) PsoRPM2 expression in root tips following M. incognita infection measured using qRT-PCR. The

results show the means _ SD based on three biologic repetitions, each with three technical repetitions. Different letters denote a significant difference at $p < 0.05$ (Tukey's test). (C) Protein localization analysis showing PsoRPM2-GFP in the cytoplasm and nucleus of N. benthamiana epidermal cells. Bar = 40 mm.

The *PsoRPM2* protein belongs to the TIR-NB-ARC-LRR subfamily, which is similar to Ma (Claverie, *et al*., 2011), but different from the Mi-1 and the GHNTR1 proteins belong to the CC-NB-ARCLRR subfamily (Milligan, *et al*., 1998, Zhang, *et al*., 2015). The difference between CC and TIR domains may affect the R gene function during plant immunity (Shirasu, 2009). The NB-ARC domain in the middle of R proteins has been suggested to act as an elicitor, which may maintain an intramolecular interaction with the LRR domain during the inactive protein state (Tameling, *et al*., 2002, Steinbrenner, *et al*., 2015). The NB-ARC domain structure of the *PsoRPM2* protein was most similar to the ced-4 protein (Yan, *et al*., 2004). The ced-4 protein mediated apoptosis (Yan, *et al*., 2004), indicating that the NB-ARC domain may achieve the nematode resistance signal of PsoRPM2. This indicated that the NB-ARC domain of PsoRPM2 may induce RKN resistant signaling. The number of repeats of the LRR domain differs between different nematode proteins and its 3D structure was predicted to have a horseshoe structure (Takken and Goverse, 2012). This domain of PsoRPM2 may be associated with pathogen recognition and promotion of disease resistance as previously reported (Krasileva, *et al*., 2010). In our PsoRPM2 transgenic tobacco lines, L1–4 were associated with a remarkable reduction of M. *incognita* susceptibility. However, the level of RKN resistance varied between the four *PsoRPM2*-expressing transgenic lines. L1 displayed almost no nematode infection symptoms and has the highest expression of the four transgenic lines. In combination with the expression of the PsoRPM2 gene in resistance *P. sogdiana* and the resistance to RKN of transgenic tobaccos revealed that higher expression level of the PsoRPM2 gene usually induced stronger RKN resistance, which is consistent with a previously reported observation for Mi-1.2 transgenic tomatoes (Milligan, *et al*., 1998). In addition, PsoRPM2-expressing transgenic tobacco lines all exhibited early flowering, which implies that PsoRPM2 is also involved in plant reproductive development. Furthermore, the PsoRPM2 gene enhanced the plant RKN-resistance and interacted with its chaperone protein complex (Zhu, *et al*., 2017). PsoRPM2-HSP90-1-SGT1-RAR1 may also possibly have formed a complex in *P. sogdiana*, and the resistant mechanism of the PsoRPM2 gene may be similar to other R genes that require assistance from the co-chaperone protein complex (Kadota, *et al*., 2010).

Root-knot Nematodes Host Rmja-Resistance Genes

The *Ma* gene, from *P. cerasifera*, was the first TNL gene, conferring resistance to RKNs, cloned in a woody perennial plant (Claverie, *et al*., 2011). Several other RKNs *R* genes with more restricted resistance spectra have been identified (Saucet, *et al*., 2016). These are the *RMia* gene from peach, which is most probably a TNL located in a 92-kb interval on the chromosome 2 (Duval, *et al*., 2014) and the *RMja* gene from almond which confers a resistance to *M. javanica* but not to *M. incognita*. A low-resolution mapping strategy carried out on few progenies localized the *RMja* gene on the chromosome 7 (linkage group 7) (Van Ghelder, *et al*., 2010). We localized the *RMja* gene between two SSR markers that cover a window of 0.14 cM. This region corresponds to a physical interval of 99 kb in the peach genome v2.0.a1. The high-resolution mapping strategy conducted on 1448 total F2 almond seedlings revealed a single recombination event for each of the flanking markers, LRR25 and KIN35. Internal primers named LRR5 and EndKin designed within this final interval, amplified fragments that eliminated any recombination events allowing us to refine the *RMja* gene localization.

Root-knot Nematodes Host (Sac Mi)-Resistance Genes

Root-knot nematodes, *Meloidogyne* spp., cause considerable damage in eggplant production. RKN R-genes SacMi transferred to *S. aculeatissimum* through successful inter-specific hybridization between *S. aculeatissimum* and cultivated eggplant. Partial SacMi-R gene was obtained from cDNA obtained from transcriptome sequencing of *S. aculeatissimum* (Zhou, *et al*., 2016). Subsequently, full-length cDNA of the *SacMi* gene was obtained using the technique of rapid-amplification of cDNA ends (RACE). The open reading frame of the *SacMi* gene was 4014 bp and encoded a protein of 1338 amino acids. Sequence analysis indicated that *SacMi* belong to the non- Toll/Interleukin-1 receptor (TIR)-NBS-LRR type disease-resistance genes (Zhou, *et al*., 2018). The deduced protein sequence of *SacMi* ORF contained typical NBS domains including P-loop, RNBS-A-nonTIR, Kinase-2, RNBS-B, RNBS-C, GLPL, RNBS-D-nonTIR. The conserved NBS region resembles an ATPase domain present in proteins regulating programmed cell death. The C-terminus LRR domain is considered to be an effector-binding domain, and has been hypothesized to participate in specific recognition of pathogen effector molecules.

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The expression patterns of *SacMi* were investigated to gain insight into its involvement in *M. incognita* resistance. The quantitative RT-PCR showed that *SacMi* is expressed at low levels in uninfected roots, but was up-regulated by infection with *M. incognita*. Silencing of *SacMi* enhanced susceptibility of *S. aculeatissimum* plants to *M. incognita*, suggesting the possible involvement of *SacMi* in resistance against *M. incognita* infection (Zhou, *et al*., 2018). The *SacMi* is expressed at low levels in uninfected roots of *S. aculeatissimum*, but infection with *M. incognita* significantly enhanced the expression level of *SacMi*, indicating that *SacMi* might be associated with the *M. incognita* resistance in *S. aculeatissimum*. Phytohormones such as salicylic acid (SA), jasmonate (JA), and abscisic acid (ABA) are important regulators in the complex signaling cascades and are involved in the defense responses. SA and JA signaling pathways have been demonstrated to be mutually antagonistic and the ABA has mostly been considered to act as a negative regulator of disease resistance. SA was reported to be an important component of the signaling that leads to *Mi-1*-mediated defense response to root-knot nematode in tomato, while JA-dependent signaling does not play a role in *Mi-1*-mediated defense, but an intact JA signaling pathway is required for tomato susceptibility to RKNs. In *Arabidopsis*, SA treatment increased the expression of *SSI4*, which encoded a putative protein belonging to the TIR-NBS-LRR class of R proteins. However, there are also some opposite cases, like $Hs1^{pro-1}$, a nematode resistance gene in sugar beet, was not induced by external stimuli including SA, JA, ABA and gibberellic acid (GA). In this study, *SacMi* was activated not only by SA but also by Me JA and ABA, suggesting *SacMi* may play a potential role in mediating cross-talk between defense-signaling pathways. The exact role of these hormones and the cross-talk between them during the defense response to RKNs still remains to be discovered (Zhou, *et al*., 2018).

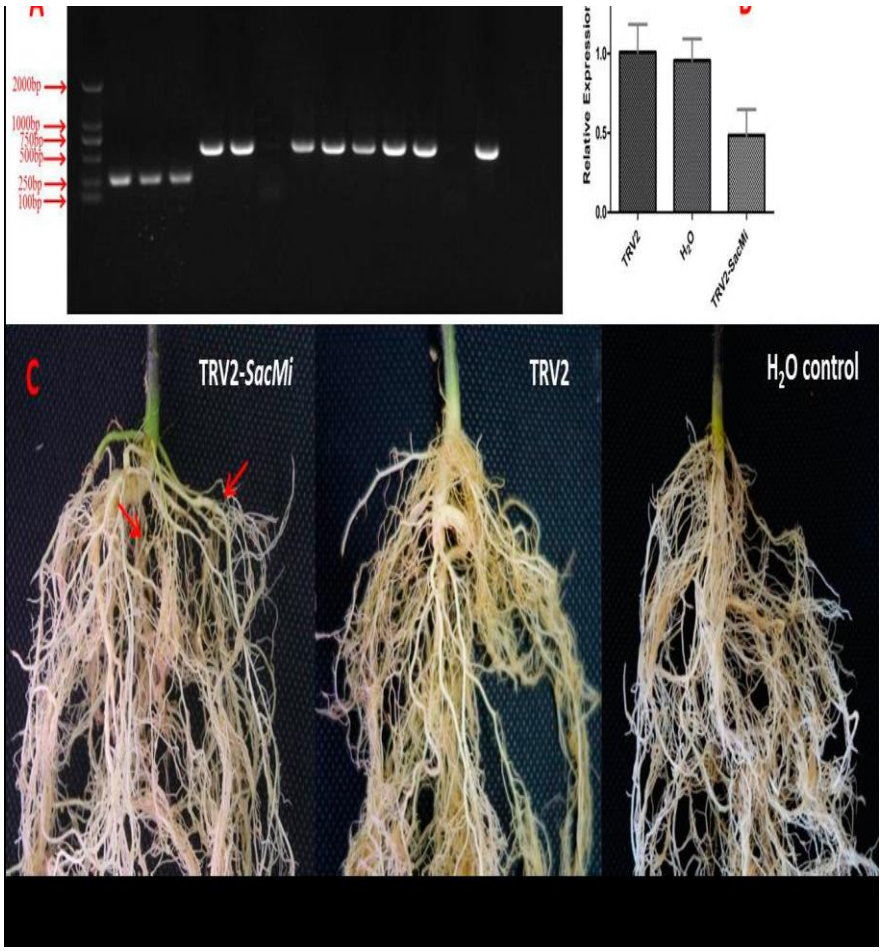

Figure 6: VIGS of *SacMi* increases the sensitivity to *M. incognita* in *S. aculeatissimum*. (**A**) PCR detection of TRV2-*SacMi* and TRV transcripts in vivo. M: Marker, 1–3: plants inoculated with TRV2; 4–13: plants inoculated with TRV2-*SacMi*; 14–15: H2O control; (**B**) qRT-PCR analysis of *SacMi* mRNA transcript levels in *SacMi*-silenced plants, empty TRV2 vector control plants and H2O control plants; (**C**) Symptoms of TRV2-*SacMi* or TRV2 silenced or H2O control *S. aculeatissimum* plants infected by *M. incigna*.

3. THEORETICAL MODEL FOR MOLECULAR AND CELLULAR BASIS OF RKN-HOST INTERACTION IN RESISTANCE CONDITION

Gene-to-gene model is a sophisticated mechanisms by which plant perceive pathogen attack and trigger an effective innate immune response. A well-characterized perception mechanism is based on resistance (*R*) genes in plants whose products confer recognition of cognate avirulence (Avr) proteins in the pathogen. This gene-for-gene hypothesis was introduced by Flor in the 1940s, and dozens of R-Avr *gene* combinations have since been characterized (Dangl and Jones, 2001). The products of *R* genes (Resistance protien) act as receptors (receptor-like proteins carrying Leu-rich repeats (LRRs)) that directly interact with the products of Avr genes (Effectors) ligand-receptor model (Keen, 1990). Indeed, direct binding of a few R-Avr combinations was found, consistent with a receptor-ligand mode of action (Jia, *et al*., 2000, Deslandes, *et al*., 2003, Dodds, *et al*., 2006, Ueda, *et al*., 2006). Gourd model explain the mechanism of host-pathogen interaction in that R proteins act by monitoring (guarding) the effector target and that modification of this target by the effector results in the activation of the R protein, which triggers disease resistance in the host (Van der Biezen and Jones, 1998, Dangl and Jones, 2001). Meanwhile, it has become evident that many Avr proteins contribute to pathogen virulence on plants lacking the cognate *R* gene. Avr proteins are now considered to be part of a larger repertoire of pathogen-secreted proteins that are called effectors to stress their presumed intrinsic virulence function. Avr recognition by plants has been coined effector-triggered immunity to contrast it with pathogen-associated molecular pattern (PAMP)–triggered immunity (Chisholm, *et al*., 2006, Jones and Dangl, 2006). Decoy Model implies that the effector target monitored by the R protein is a decoy that mimics the operative effector target but only functions in perception of pathogen effectors without contributing pathogen fitness in the absence of its cognate R protein. This Decoy Model is distinct from the classical and refined Guard Models that imply that the manipulation of the guarded effector target by the effector benefits pathogen fitness in the absence of the R protein.

In host resistant condition, the feeding cell initiation and development are arrested, resulting in the death of RKN. Plant R-gene grouped in two subclass TIR-NBS-LRR (TNL) and non-TIR NBS-LRR. Given their modular organization and distinctive domain functions, TNLs act as a multi-function tool for plant immunity. Indeed, the leucine-rich repeat (LRR) domain is polymorphic and often described by its ability to detect pathogens through direct or indirect effector recognition (Jones and Dangl, 2006). However, identification of the avirulence gene (effectors) which is able to induce a resistance response in a gene-for-gene specific manner in the presence of the corresponding *R* gene still challenging. It has been proposed that plant R-gene likely the encoding resistance protein which directly or indirectly–recognized avirulence product which mediated the activation of host defense response either ETI or PTI pathways that triggered defense response such hypersensitive response. The molecular and cellular mechanisms of resistance mediated by host R-genes confer resistance to RKN are still limited.

4. SUMMARY AND CONCLUSIONS

Root-knot nematodes (RKN), (*Meloidogyne* spp.) are obligate, sedentary endo-parasites of more than 5500 species of plants, that cause major crop losses on a worldwide scale which results in $70 billion worth of economic loss every year (Blok, *et al*., 2008). Recently, several genes confer resistance to RKN, have been identified and transferred from wild to relative cultivar. These are Mi-gene, Ma-gene, *PsoRPM2*-gene, *SacMi*-gene, RMja-gene, *SacMi*-gene and *PsoRPM2*-gene confer resistance to various number of RKN species, in Tomato (L. peruvianum), *Prunus* species (*Prunus cerasifera*), woody fruit tree (*Prunus sogdiana* and transgenic tobaccos) and Eggplants (*S. aculeatissimum)* respectively. These single dominant genes share several structural motifs (NBS-LRR) and grouped in to two NBS-LRR gene families: TIR-NBS-LRR (TNL) and non-TIR-NBS-LRR. The majority of RKN host resistance genes, Ma-gene, SacMi-gene, RMja-gene are belongs to interleukin-1 receptor (TIR)-NBS-LRR type disease-resistance genes. In contrast, the *Mi-1* tomato R-geneis belongs to CNL R gene. Mechanism of resistance mediated by the well known, Mi-1 R-gene, conferring resistance to RKN species, *M. incognita*, *M. arenaria* and *M. javanica*, are characterized by early hypersensitive response (HR), a highly strong and effective defense reaction in tomato. Molecular mechanism of host Mi-1 gene resistance response is supported by the chaperones Hsp90-1 and Sgt1 that participate in the formation of the Mi-1.2 signaling complex. In addition, the mitogen-activated protein kinase (MAPK) cascade including LeMAPK1, LeMAPK2 and LeMAPK3 are involved in Mi-1 resistance against potato aphids (Li, *et al*., 2006b). Furthermore, the Mi.1.2 R-proteins directly interfere with transcriptional regulators (SlWRKY72a and SlWRKY72b) to activate the transcriptional network controlling *Mi-1.2*-triggered ETI immunity. The Ma-R gene, conferring resistance to all tested RKN species in woody perennial plant,

associated with cell necroses (arresting the nematode development) and the corresponding HLR phenotypes occurring in either the vascular cylinder, the meristematic apical or bud regions, or the cortex with accumulation of phenolics. In conclusion, the mechanism mediated by host resistance gene to RKN, are varied in timing, location, and nature of the resistant reaction depending on the plant genotype, the particular resistance gene, and the *Meloidogyne* species.

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Conflict of Interest:

The authors declare there is no potential conflict of interest.

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