Chapter 6

A Molecular Vision of the Interaction of Tomato Plants and *Fusarium oxysporum* f. sp. *lycopersici*

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Abstract

Fusarium oxysporum causes vascular wilt disease in a broad range of crops, including tomato (*Solanum lycopersicum*). Tomato, a major and important vegetable crop, is susceptible to *F. oxysporum* f. sp. *lycopersici* (FOL), a biotrophic pathogen that is the causal agent of tomato wilt resulting in significant yield losses each year. Development of disease in susceptible tomato plants requires FOL to advance through a series of transitions, beginning with spore germination and culminating with establishment of a systemic infection. In addition, many host attributes, including the composition of root exudates, the structure of the root cortex, and the capacity to recognize and respond quickly to invasive growth of a pathogen, can impede the development of FOL. FOL divides into races on the basis of the ability of individual strains to overcome specific genes. This implies the presence of avirulence genes (Avr) in the fungus that is recognized by products of the corresponding genes. In tomato, resistance (R) genes against the wilt-inducing FOL are called immunity genes, and the interaction between these genes will determine the success of the infection.

Keywords: receptors, MAPK cascade, gene expression, effectors, pathogenicity

1. Introduction

Microorganisms have interacted with plants for millions of years. However, for these to be pathogenic, they must have virulence factors, secondary metabolites, and exoenzymes that allow them to access the interior of the plant through the leaves, root or wounds, or natural openings, to establish an interaction of compatibility with the host [1, 2]. One of the pathogens

that affect a considerable number of plant species is the fungus of the genus *Fusarium*, which causes the disease known as vascular wilt [3]. This genus is made up of a large set of species that possess many biological properties. In addition, it is characterized by the production of fusiform macroconidia that are widely distributed in soil and on organic substrates [4]. The species known as *Fusarium oxysporum* causes large losses to vegetable crops both in open field and in greenhouse production [5]. Special forms (f. sp.) have been assigned according to the specificity of the host, of which about 70 have been described f. sp. [6]. Among these special forms, *F. oxysporum* f. sp. *lycopersici* (FOL) affects the tomato crop (*Solanum lycopersicum*) and is one of the main limiting factors for its production. FOL is divided into physiological races based on its ability to infect specific cultivars [7]. Regardless of biological, chemical, or cultural measures, adequate management strategies to eliminate this pathogen are not currently available once the plants are infected and have *Fusarium* vascular wilt.

The disease development in susceptible tomato plants requires that FOL pass through a series of transitions, beginning with spore germination and culminating in the establishment of a systemic infection [8]. However, to reach this point, FOL requires avoiding the defense mechanisms that activate the plant-pathogen interaction [4]. The protection mechanism in tomato plants requires the perception of the pathogen through receptors of pathogen-associated molecular patterns (PAMPs) located in the plasma membrane, which triggers the basal defense system. This includes the influx of extracellular calcium (Ca) and mobilization of intracellular Ca to the cytosol, generation of reactive oxygen species (ROS), activation of mitogen-activated protein kinases (MAPKs) as well as calcium-dependent protein kinases (CDPKs) [9], and finally the induction of defense-related genes [10]. To avoid this defense system, FOL has the ability to secrete effectors such as the so-called proteins secreted in the xylem (SIX), which allows the infection to continue [11]. This implies the presence of avirulence (Avr) genes in the fungus, which is recognized by the products of the corresponding genes in the tomato, called R genes [12]. The interaction and compatibility of the Avr genes and R genes will result in the successful FOL infection or the survival of the tomato plant [13].

Despite the importance and necessity of controlling this disease, the molecular mechanisms of pathogenesis in tomato and the genetic basis for host specificity are still poorly understood.

This chapter presents the information necessary to obtain an understanding of fungal pathogenesis at the molecular level, allowing the characterization of actively expressed genes at different stages of plant infection or under various conditions.

2. *F. oxysporum* f. sp. *lycopersici* (FOL)

2.1. Host recognition by FOL

It is known that FOL can produce three types of asexual spores: (i) microconidia, (ii) macroconidia, and (iii) chlamydospores; while the sexual or teleomorphic phase is unknown. FOL can survive saprophytically in soil and organic waste in the absence of a host, either as mycelium or in all types of spores mentioned [14]. Chlamydospores are resistance structures capable of

remaining viable in the soil for several years according to environmental conditions, and this allows this pathogen to be dispersed rapidly with the movement of water, soil, or air [15, 16].

The presence of these reproductive structures of FOL in the development medium of tomato plant allows the plant-pathogen interaction to be initiated with a preinfection state, where the host recognition is carried out, and subsequently the germination of the spores, which will continue with the tissue infection [17].

In this stage, the identification of the host is vital for the initiation of the infection process, and this is done through the release of exudates from the host roots, as these compounds represent a carbon source for the fungus [18]. Its composition includes sugars, polysaccharides, amino acids, aliphatic, aromatic and fatty acids, sterols, phenolic compounds, enzymes, vitamins, plant growth regulators, and other secondary metabolites [19].

The specific compounds that FOL recognizes in its host have not been characterized. To initiate spore germination, it is known that exudates from the root of tomato plants stimulate the germination of FOL microconidia. In addition, a relationship was found between the stimulation of germination and the age of plants. The highest stimulation of germination was observed when the plants were 70 to 90 days old. Changes were also observed in root exudates such as the concentration of phenolic compounds and flavonoids or induced changes in the exudates by the degree of colonization of the arbuscular mycorrhizal fungus Glomus mosseae, modifying the spore germination and the degree of colonization [20, 21].

2.2. Signaling by MAPK

Mitogen-activated protein kinases (MAPKs) are proteins that have been evolutionarily conserved using cycles of phosphorylation and dephosphorylation for signal transduction. Activated MAPK kinase kinases (MAP3Ks) first phosphorylate two serine and/or threonine residues located within the activation loop of MAPK kinases (MAP2Ks). Activated MAP2Ks in turn trigger MAPK activation through dual phosphorylation of a highly conserved activation loop. Sequential activation of this pathway (MAP3Ks-MAP2Ks-MAPK) plays an essential role during the development of FOL. Activation of this signaling pathway will result in the expression of genes and transcripts necessary to regulate the infection process and the development of the disease, such as the expression of pathogenicity, infectious growth, or root attachment, once FOL identifies the host [22, 23].

Recent studies report that the physiological and developmental processes of FOL are regulated by three signaling pathways identified as *Fusarium oxysporum* MAP K (Fmk1), MAP kinase (Mpk1), and high-osmolarity glycerol response (Hog1) and are mediated by MAPKs. Each of these pathways has specific roles; in the case of Fmk1, it has functions related to virulence and fusion of hyphae. Mpk1 is related to characteristics of the cell wall as its integrity and remodeling, the growth and fusion of vegetative hyphae. Finally, Hog1 is linked to osmoregulation responses and stress responses. The three pathways are involved in the pathogenesis of FOL and in the development of the disease [24]. This was demonstrated by using RNA interference (RNAi) to silence these signaling pathways, which caused loss of surface hydrophobicity, reduction of invasion, hypovirulence, conidial size alteration, growth reduction, and a significant decrease in pathogenesis in tomato seedlings [25].

2.3. Pathogenesis and virulence

The concepts of pathogenicity and virulence are often erroneously considered as synonyms. Its definition initially focused on the intrinsic properties of the pathogen. However, currently, the definition of these characteristics considers the contributions of the pathogen and the host in the development of the disease. Based on this, the concept of pathogenicity is described as the ability of a microorganism to cause damage in a host, while virulence is defined as the relative ability of a microorganism to cause damage in a host [26]. Following these definitions, we next describe the genes required for the development of the disease caused by FOL (**Figure 1**).

FOL infection process begins with the germination of spores on the host surface. It begins with the emergence of the germinal tube through the wall of the spore followed by the emergence of ramifications of this structure giving rise to fungal hyphae [27], which adhere to the root and continue with invasive growth and penetration of plant tissue. In this stage of penetration and colonization of the host, FOL requires expression of the Fmk1 gene. It is responsible for the coding of an MAPK, required for root adhesion and penetration, invasive

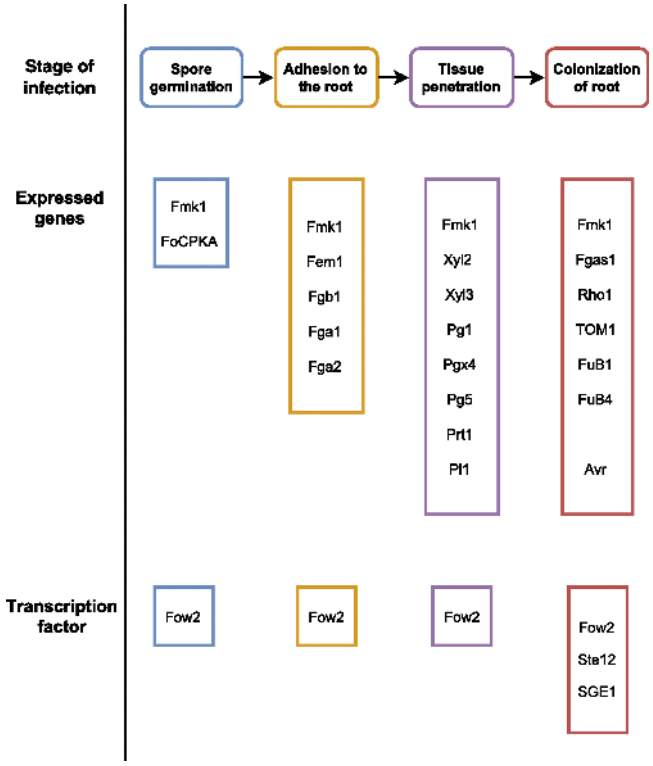

Figure 1. Relationship of genes and transcription factors activated during disease development of FOL.

pathogen growth, as well as secretion of pectinolytic enzymes and fusion of vegetative hyphae [28]. The Fmk1 MAPK cascade critically depends on the transcription factor Ste12, which controls the invasive growth and virulence downstream of the Fmk1 MAPK cascade. However, it is not linked to the regulation of root adhesion, suggesting that activation of Ste12 is independent of the MAPK pathway and that multiple pathways may converge on this transcription factor [29].

The participation of *Fusarium oxysporum* FOW2 gene, a type Zn(II) 2Cys6 transcription factor encoded by the gene designated by the same name, has also been indicated. It is highly conserved in the special forms of FOL, and its expression is essential for pathogenicity [30].

On the other hand, extracellular pH has been shown to act as a key signal for growth, differentiation, and virulence in pathogens [31]. Gene expression in fungi by environmental pH is regulated by a conserved signaling pathway, whose terminal component is the PacC/Rim1p zinc finger transcription factor. PacC is considered to act as a negative virulence regulator in FOL. Expression of this transcription factor is pH dependent, with high transcription levels under alkaline growth conditions and low transcription levels under acidic growth conditions. There was also a clear effect of pH and PacC on the expression of two genes that encode endopolygalacturonases [32].

The genes described related to the pathogenesis of FOL control various processes in the development of the pathogen. Such is the case of the cyclic AMP-dependent protein kinase A of *F. oxysporum* (FoCPKA) gene, which regulates multiple traits related to growth, microconidia formation, germ-tube shape, septation, and branching of hyphae by means of a cyclic adenosine monophosphate-dependent protein kinase A (cAMP) [33]. On the other hand, the Fgb1 gene encodes the β-subunit of the G protein that controls hyphae growth, development, and virulence through pathways dependent and independent of cAMP signals, while the α subunit is encoded by the Fga1 gene, whose silencing reduces the conidiation and pathogenicity of the fungus [34–36].

In a study on the cloning of the Fga2 gene, it was shown that the functions of the two Gα proteins overlap but are distinct. On the one hand, the Fga1 pathway regulates the growth and development of fungi, including morphogenesis and conidiation. In contrast, the Fga2 pathway plays a more crucial role in pathogenicity [37]. In addition, the loss of function of the Fgas1 gene, responsible for the expression of β-1,3-glucosyltransferases, dramatically affects the virulence of FOL, since it is linked to structural alterations of the cell wall [38].

Another gene related to the cell wall characteristics of FOL is Rho1, responsible for the coding of a putative Rho-type GTPase. It plays a crucial role in infection, avoiding recognition by the host defense system since its deletion in FOL leads to changes such as an increase in the amount of polymers in the cell wall, which serve as response activators in plants [39]. The Fow1 gene encodes a protein with high similarity to mitochondrial carrier proteins, which is specifically required for colonization in plant tissue since its absence generates a reduction in the virulence of FOL [40]. Likewise, the involvement of the Fpd1 gene has been described, which has as its possible function the coding for a transmembrane protein whose deficiency reduces the pathogenicity of FOL [41].

2.4. Lithic enzymes

The initiation of FOL infection requires degradation of the host cell wall through the action of a complex of enzymes with lytic activity such as xylanases, cellulases, pectinases, and polygalacturonases, which contribute to the penetration and colonization of the plant [42]. The genes xyl2 and xyl3 are responsible for the coding of xylanases, which degrade xylan. The xyl2 gene is expressed during the final stages of the disease, while xyl3 is present throughout the cycle [43]. The XlnR gene is known to be the main transcriptional activator of the xylanase genes. However, it was demonstrated that it is not determinant in the virulence of FOL, perhaps due to the presence of other xylanase genes whose expression is independent of this transcription factor [44].

The PG1 and PG5 genes are responsible for the expression of extracellular endopolygalacturonases, the latter expressed mostly during the early stages of infection [45, 46]. On the other hand, the characterization of several enzymes with lytic activity, such as PG1, exo-polygalacturonases (PG2 and PG3), an endoxylanase (XYL1), and an endopectate lyase (PL1), has been reported. Coded by genes pg1, pgx4, pg5, xyl2, xyl3, prt1, and pl1, these are expressed during different stages of interaction with the host plant indicating a possible role in the pathogenesis [47, 48]. While the absence of the Fpr1 protein (F-box protein, required for pathogenicity) results in the lack of expression of some enzymes involved in cell wall degradation, this is perceived as the inability of the pathogen to colonize the roots [49, 50].

3. Tomato plant

3.1. Pathogen recognition

Recognition of pathogen infection triggers an immunity system in the plant of two branches [13]. (i) In the first, common molecules are recognized in many classes of microorganisms, including those that are nonpathogenic and called immunity associated to pathogen-associated molecular patterns (PAMP)s or PAMP-triggered immunity (PTI). (ii) The second branch responds to factors of virulence and pathogenesis, so it is designated as effector-triggered immunity (ETI). Both mechanisms are described below (**Figure 2**).

PAMPs are considered as conserved elements by different classes of microorganisms and are essential for survival and pathogenicity [51]. Among the molecules identified as PAMPs for FOL, some components of their cell walls such as chitin, glucan, and glycoproteins are considered in this group due to their interaction with the host [52, 53].

The synthesis of chitin is regulated by the chsV gene and its expression depends on the Fmk1-MAPK signaling pathway. This was demonstrated with mutants of this gene, as they were unable to infect and colonize tomato plants or to grow invasively in tomato fruit tissue. In addition to this, hypersensitivity to defense compounds produced by the host was observed [54, 55].

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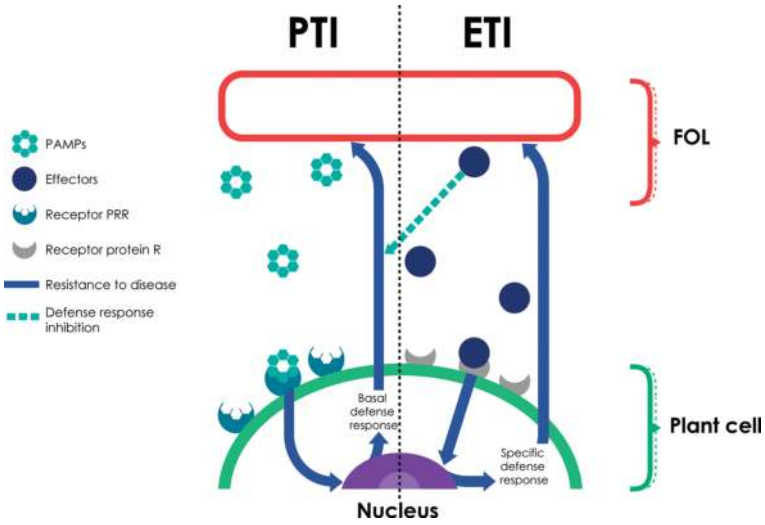

Figure 2. Scheme of activation of the defense system by PTI and ETI in tomato plant.

Glucans are also considered as elicitor molecules, although glucans may be present in the cell wall of both plants and fungi, β-1,6-glucan is specific to the cell wall of fungi, resulting in a potential PAMP [56]. Glycoproteins present in the cell wall of FOL, whose function is the adhesion of hyphae to plant tissue, are encoded by the Fem1 gene and are considered within this group [57]. Each of these elements can be recognized by the plant defense system since it has pattern recognition receptors (PRR) [58]. Plant PRRs are located on the surface of the plasma membrane and can be two types. The receptor-like kinases (RLK) contain a ligand-binding ectodomain, a single-pass transmembrane domain, and an intracellular kinase domain. Or they may be receptor-like proteins (RLPs) typically consisting of a repetitive domain rich in extracellular leucine, a transmembrane domain, and a short cytoplasmic tail [59–61].

To date, chitin has been the most extensively studied PAMPs; the presence of a receptor for chitin in rice cells has been detailed [62], while in *Arabidopsis thaliana*, an RLK-type lysin motif receptor-like protein (LysM RLK1) with an extracellular domain containing three predicted LysM motifs has been detailed. These studies have shown that the binding between the receptor and chitin is specific and direct. However, this interaction is not a simple ligand-binding reaction but could be accompanied by a conformational change of the receptor protein. This allows it to participate in signaling leading to gene induction and defense responses against pathogenic fungi [63, 64]. On the other hand, little is known about the mechanism of recognition of glucans as PAMPs in tomato plants. In soybeans, a glucan-elicitor–binding protein (GEBP) harbored a glucanase domain and a high-affinity glucan binding motif, which makes this protein a powerful tool to release and detect elicitor fragments of the pathogen [65].

3.2. Signaling and defense response

Recognition of pathogen elicitors that are released at the site of infection is rapidly followed by changes in ion flow and the production of reactive oxygen species. These events activate signaling cascades, which lead to the activation of the transcription factors involved in the activation of defense genes [66]. These responses are known to be regulated through complex signaling pathways involving various phytohormones. The FOL-activated signaling network integrates signals shared and mediated by synergistic or antagonistic interactions between salicylic acid (SA), jasmonic acid (JA), ethylene (ET), abscisic acid (ABA), and ROS [67, 68].

The SA plays an essential role in plant defense signaling since the recognition of FOL-derived components allows the accumulation of this phytohormone, with the subsequent establishment of local resistance in the infected region.

In the same way as the systemic resistance of the whole plant [69], the biosynthesis of SA is regulated by the Arabidopsis defense-related gene (SID2) [70]. This pathway requires the high-affinity protein SABP2, responsible for the conversion of methyl salicylic acid to SA [71], as well as the nonexpresser of pathogenesis-related (PR) genes positive regulator (NPR1) [72], which is regulated by the transcription factors of the TGA and WRKY family [73, 74]. On the other hand, the function of Ca as a second messenger has been characterized in numerous signaling pathways of plants, transporting a wide range of environmental and developmental stimuli to the physiological response [75]. An example is its participation in the regulation of SA levels through the interaction of a Ca/calmodulin with the transcription factor–enhanced disease susceptibility 1 (EDS1), through the activation of the Ca channels for the influx and subsequent mobilization of the intracellular Ca stores [76]. The increase of Ca in the cytoplasm is the first step in the signaling pathway of PAMP-triggered immunity (PTI). This elevation may occur in response to the perception of PAMPs, interactions of the R gene due to phosphorylation events, G protein signaling, and/or cyclic nucleotide increase [77].

The SA is crucial to induce the production of superoxide anion and hydrogen peroxide, by the activation of apoplastic peroxidase, and subsequently NADPH oxidase of the plasma membrane [78], which are connected to each other through the activation of Ca channels, as it has been pointed out that the increase of the cytoplasmic Ca coincides with the concomitant increase of ROS, or by the phosphorylation of proteins [79]. ROS are known for their direct antimicrobial role against pathogens as well as their relation to the activation of second messengers related to the expression of genes related to the production of response proteins [80], such as the peroxidases of class III, which are important due to their involvement in the reinforcement of the cell wall in the site of interaction with the pathogen, through catalysis of the reticulation of cell wall components including glycoproteins, lignin, and suberin [81]. Also, the oxidative burst is associated with the hypersensitivity response or programmed cell death, processes that inhibit the invasion of the pathogen through isolation [82].

Activation of MAPKs is critical in components of basal defense pathways as well as in more specific interactions involving R-gene–mediated resistance. The oxidative burst activates an MAPK cascade that induces the downstream defensive mechanisms regulated by SA, ET, JA,

and ABA. Responses may be ethylene synthesis, ROS production, pathogenesis-related (PR) protein expression, and cell death [83, 84].

On the other hand, jasmonates are involved in the reduction of FOL susceptibility in tomato plants, by increasing the activity of polyphenol oxidase [85]. Whereas in Arabidopsis plants, it has been observed that the response to *F. oxysporum* requires signaling pathways through ET, JA, SA, and the NPR1 gene, although it is independent of the function PAD4 and EDS1 [86]. The interactions between SA and JA signaling are complex, but research indicates an antagonistic relationship between them [87], while jasmonates and ET cooperate to synergistically induce defense genes such as PR1b, PR5, and PDF1.2 [88, 89]. Expression of the ERF1 gene responsive to ET and to JA is a common component in the pathways of both phytohormones [90]. It is suggested that ABA function affects disease resistance by suppressing basal and induced transcription of JA and ET response genes, which clarifies the antagonistic relationship between these hormones [91]. However, ABA has been reported to be involved in the production of callose for the early and efficient construction of papillae at sites of infection to counteract the pathogen [92]. On the other hand, signaling mediated by heterotrimer G proteins has been shown to suppress the induction of SA-, JA-, ET-, and ABA-dependent genes during the initial phase of infection with *F. oxysporum*, whereas at a later phase, it improves the JA-/ET-dependent genes like PDF1.2 and PR4 [93].

The defense responses that are activated by these pathways in tomato plants involve the increase of defense enzymes such as phenylalanine ammonium lyase and peroxidase [94], as well as the synthesis and accumulation of proteins related to pathogenesis, such as chitinases and b 1–3 glucanases. These proteins act synergistically to inhibit the growth of the fungus [95]. Programmed cell death can be induced by α-tomatine, which has a fungicidal action, in addition to its potential role as an activator of tyrosine kinase signaling pathways and the monomeric GTP-binding protein (G protein) that leads to Ca elevation and the ROS burst in FOL cells [96]. The regulation of plant immune responses is mediated by transcription factors of the WRKY family, which are functionally connected by forming a transcriptional network composed of positive and negative feedback loops within a network of partially redundant elements, some of which hold central positions that allow the activation of fast and efficient defense programs [97].

3.3. Effector protein recognition

Once the first line of defense is activated through recognition of PAMPs, FOL employs mechanisms that allow it to suppress such activated responses. During the infection process, it secretes small proteins rich in cysteine (effector or virulence proteins). The function of these proteins is to promote infection and colonization in the host plant, by disrupting various cellular processes such as signal transduction or modifying the proteins in the host plant [98].

The set of these effectors determines the specificity of the host, as well as the ability of the pathogen to manipulate the host immunity [99, 100]. In FOL, these effectors are designated as proteins secreted in the xylem (SIX) and six genes have been reported to encode them [101].

These genes related to pathogenicity are located on a small chromosome within the FOL genome [102].

Recognition of effectors occurs through receptors known as R proteins, which contain at the amino terminus a predicted conserved central domain that functions as a nucleotide-binding site (NBS) and a variable number of leucine-rich repeats (LRR) in the extreme C-terminal [103]. It is considered that this LRR domain of proteins could contribute to the recognition of various ligands derived from pathogens, while the amino-terminal domain determines the specificity of signaling. These receptors are also referred to as NBS-LRR [104–106]. The way in which R proteins activate the signal transduction pathway leading to plant defense is not yet fully understood, but recognition of pathogens is thought to trigger nucleotide-dependent conformational changes that may induce oligomerization, thus providing a scaffold for the activation of downstream signaling components [107].

The perception of the effectors triggers the second branch of the plant defense system or ETI. This is based on the gene-for-gene hypothesis, where resistance to disease is thought to be conferred by R genes, or immunity (I) genes in tomato, but requires the coincidence of avirulence genes (Avr) from FOL [12]. This is why FOL is divided into physiological races based on the ability of the individual strains to overcome the tomato-specific immunity genes (**Figure 3**). Therefore, compatible or incompatible interactions are controlled by three avirulence genes (Avr 1–3) in FOL and the corresponding resistance genes (I-I3) in tomato [108].

The SIX4 protein has been identified as a virulence effector designated as Avr1 gene, and the mature protein is made up of 184 amino acids and contains 6 cysteines in its structure. Its expression was initially reported for race FOL 1 and is required to activate resistance mediated by gene I and I-1. In addition, it is related to the suppression of disease resistance linked to the I-2 gene and the I-3 gene for tomato [109]. The SIX3 protein corresponds to the Avr2 gene, which is made up of 144 amino acids and contains 2 repeated cysteines. It is required for the development of disease symptoms, as demonstrated by its deletion, resulting in a reduction in virulence. This protein can be recognized by the I-2 resistance gene [11].

Expression of the Avr3 gene encoding the SIX1 protein is essential for virulence in tomato. Its structure consists of 189 amino acids and contains 8 repeated cysteines. Its recognition is necessary to activate the resistance through the I-3 gene. A relation between the expression of this gene and Avr1, for the evasion of resistance activated by I-3, has been suggested. The Avr3 gene requires the presence of live plant cells, and its secretion is performed immediately after the penetration of the root cortex [110–112]. Another important effector protein in the pathogenicity of FOL is SIX6. It is made up of 199 amino acids and contains 7 cysteines. It is expressed in early and late stages of infection and its expression suppresses the cellular death triggered by the I-2 protein and requires the presence of live host cells [113]. Close homologs have been found in other special forms for the SIX6 and SIX7 effectors, suggesting that these genes may have a more general role in pathogenicity [114].

The expression of Avr genes in FOL is regulated by the transcription factor SIX Gene Expression 1 (SGE1). Although its expression is not required for the vegetative growth of the fungus, it is essential for the pathogenicity of FOL, by playing an important role during

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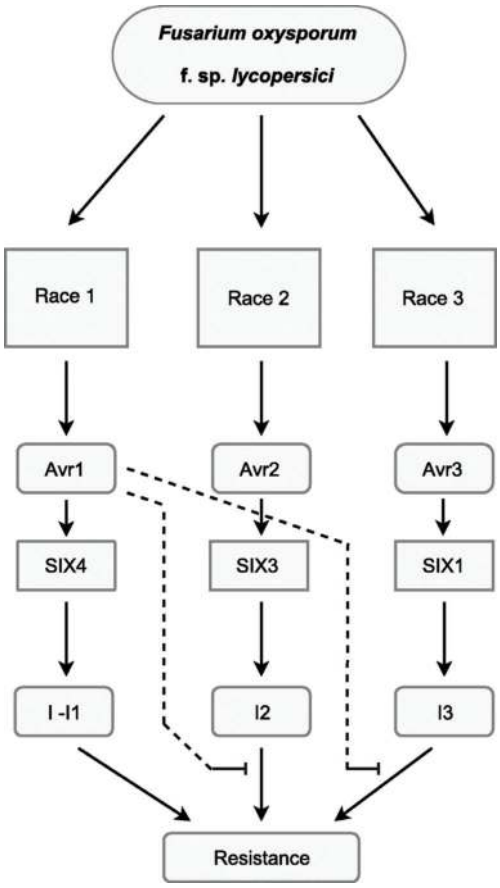

Figure 3. Classification of the physiological races of FOL according to the interaction of Avr genes of FOL and immunity genes in tomato.

parasitic growth, which produces an extensive growth in the plant and leads to the symptoms of the disease [115].

3.4. Overcoming defense response

One of the strategies of FOL to overcome the tomato defense response is the participation of chitinases, through the synergistic action of two proteases that are required for the complete separation of the binding domain of class I and class IV chitinase of tomato, allowing full virulence of FOL [116].

Detoxification of α-tomatine by the action of the enzyme tomatinase in FOL has also been identified. It is encoded by the TOM1 gene, which plays an essential role for the successful infection of the fungus [117]. The role of fusaric acid, which plays an important role in fungal pathogenicity,

has also been described by decreasing the cell viability of the plant. It is directly related to programmed cell death through damage to photosynthetic machinery, increase in protease activity, ROS production, low regulation of antioxidant enzyme activities, and positive regulation in lipid peroxidation, as well as the disorder of the nitrogen metabolism resulting in the collapse of the cell [118–120]. Its biosynthesis requires expression of the FUB1 and FUB4 genes [121], and L-aspartate is suggested as the precursor amino acid in the biosynthetic pathway [122].

If FOL manages to evade the defenses of tomato plants, infection and the development of symptoms of vascular wilting will occur. Effects include leaf detachment and leaf epinasty, followed by slower leaf growth, progressive wilt, defoliation, and inevitably death [123].

4. Conclusion

In this way, it is clear that both FOL and the tomato plant are in a long competition of defensive mechanisms to ensure their survival when the plant-pathogen interaction occurs.

FOL genomic analyzes have revealed the evolutionary characteristics of genes associated with FOL adaptation to their hosts, getting to understand the specificity for these. Molecular biology studies have evidenced the genes that are expressed in FOL interactions with their hosts at different stages of infection. However, a greater level of understanding with regard to the interaction mechanisms is needed. Future efforts will be needed to investigate the role of effector proteins in FOL-host interactions.

A study of elicitor molecules of natural or synthetic origin that are recognized as PAMPs and can trigger a nonspecific defense response is necessary. The obtained knowledge will further improve tolerance to vascular wilt of tomato plants by FOL infection.

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References

[1] Chisholm ST, Coaker G, Day B, Staskawicz BJ. Host-microbe interactions: Shaping the evolution of the plant immune response. Cell. 2006;**124**(4):803-814

[2] Schulz B, Boyle C. The endophytic continuum. Mycological Research. 2005;**109**(6):661-686

[3] de Sain M, Rep M. The role of pathogen-secreted proteins in fungal vascular wilt diseases. International Journal of Molecular Sciences. 2015;**16**(10):23970-23993

[4] Di Pietro A, Madrid MP, Caracuel Z, Delgado-Jarana J, Roncero MIG. *Fusarium oxysporum*: Exploring the molecular arsenal of a vascular wilt fungus. Molecular Plant Pathology. 2003;**4**(5):315-325

[5] McGovern RJ. Management of tomato diseases caused by *Fusarium oxysporum*. Crop Protection. 2015;**73**:78-92

[6] Lievens B, Rep M, Thomma BP. Recent developments in the molecular discrimination of formae speciales of *Fusarium oxysporum*. Pest Management Science. 2008;**64**(8):781-788

[7] Armstrong GM, Armstrong JK. Formae Speciales and races of *Fusarium oxysporum* causing wilts of the Cucurbitaceae. Phytopathology. 1978;**68**:19-28

[8] Gordon TR. *Fusarium oxysporum* and the *Fusarium* wilt syndrome. Annual Review of Phytopathology. 2017;**55**(1):23-39

[9] Zipfel C. Pattern-recognition receptors in plant innate immunity. Current Opinion in Immunology. 2008;**20**(1):10-16

[10] Ramamoorthy V, Raguchander T, Samiyappan R. Induction of defense-related proteins in tomato roots treated with *Pseudomonas fluorescens* Pf1 and *Fusarium oxysporum* f. sp. *lycopersici*. Plant and Soil. 2002;**239**(1):55-68

[11] Houterman PM, Ma L, van Ooijen G, de Vroomen MJ, Cornelissen BJC, Takken FLW, et al. The effector protein Avr2 of the xylem-colonizing fungus *Fusarium oxysporum* activates the tomato resistance protein I-2 intracellularly. The Plant Journal. 2009;**58**(6):970-978

[12] Flor HH. Current status of the gene-for-gene concept. Annual Review of Phytopathology. 1971;**9**(1):275-296

[13] Jones JDG, Dangl JL. The plant immune system. Nature. 2006;**444**(16):323-329

[14] Akhter A, Hage-Ahmed K, Soja G, Steinkellner S. Potential of *Fusarium* wilt-inducing chlamydospores, *in vitro* behaviour in root exudates and physiology of tomato in biochar and compost amended soil. Plant and Soil. 2016;**406**(1-2):425-440

[15] Park D. Some aspects of the biology of *Fusarium oxysporum* Schl. in soil. Annals of Botany. 1959;**23**(1):35-49

[16] McKeen CD, Wensley RN. Longevity of *Fusarium oxysporum* in soil tube culture. Science. 1961;**134**(3489):1528-1529

[17] Recorbet G, Steinberg C, Olivain C, Edel V, Trouvelot S, Dumas-Gaudot E, et al. Wanted: Pathogenesis-related marker molecules for *Fusarium oxysporum*. The New Phytologist. 2003;**159**(1):73-92

[18] Jones DL, Hodge A, Kuzyakov Y. Plant and mycorrhizal regulation of rhizodeposition. The New Phytologist. 2004;**163**(3):459-480

[19] Bertin C, Yang X, Weston LA. The role of root exudates and allelochemicals in the rhizosphere. Plant and Soil. 2003;**256**(1):67-83

[20] Steinkellner S, Mammerler R, Vierheilig H. Microconidia germination of the tomato pathogen *Fusarium oxysporum* in the presence of root exudates. Journal of Plant Interactions. 2005;**1**(1):23-30

[21] Scheffknecht S, Mammerler R, Steinkellner S, Vierheilig H. Root exudates of mycorrhizal tomato plants exhibit a different effect on microconidia germination of *Fusarium oxysporum* f. sp. *lycopersici* than root exudates from non-mycorrhizal tomato plants. Mycorrhiza. 2006;**16**(5):365-370

[22] Hamel L-P, Nicole M-C, Duplessis S, Ellis BE. Mitogen-activated protein kinase signaling in plant-interacting fungi: Distinct messages from conserved messengers. Plant Cell Online. 2012;**24**(4):1327-1351

[23] Zhao X, Mehrabi R, Xu J-R. Mitogen-activated protein kinase pathways and fungal pathogenesis. Eukaryotic Cell. 2007;**6**(10):1701-1714

[24] Segorbe D, Di Pietro A, Pérez-Nadales E, Turrà D. Three *Fusarium oxysporum* mitogen-activated protein kinases (MAPKs) have distinct and complementary roles in stress adaptation and cross-kingdom pathogenicity. Molecular Plant Pathology. 2017;**18**(7):912-924

[25] Pareek M, Rajam MV. RNAi-mediated silencing of MAP kinase signalling genes (Fmk1, Hog1, and Pbs2) in *Fusarium oxysporum* reduces pathogenesis on tomato plants. Fungal Biology. 2017;**121**(9):775-784

[26] Casadevall A, Pirofski LA. Host-pathogen interactions: Redefining the basic concepts of virulence and pathogenicity. Infection and Immunity. 1999;**67**(8):3703-3713

[27] Kang Z, Buchenauer H. Cytology and ultrastructure of the infection of wheat spikes by *Fusarium culmorum*. Mycological Research. 2000;**104**(9):1083-1093

[28] Di Pietro A, Garcõ FI, Roncero MIG. A MAP kinase of the vascular wilt fungus *Fusarium oxysporum* is essential for root penetration and pathogenesis. Molecular Microbiology. 2001;**39**(5):1140-1152

[29] Rispail N, Di Pietro A. *Fusarium oxysporum* Ste12 controls invasive growth and virulence downstream of the Fmk1 MAPK Cascade. Molecular Plant-Microbe Interactions. 2009;**22**(7):830-839

[30] Imazaki I, Kurahashi M, Iida Y, Tsuge T. Fow2, a Zn(II)2Cys6-type transcription regulator, controls plant infection of the vascular wilt fungus *Fusarium oxysporum*. Molecular Microbiology. 2007;**63**(3):737-753

[31] Eshel D, Miyara I, Ailing T, Dinoor A, Prusky D. pH regulates endoglucanase expression and virulence of *Alternaria alternata* in persimmon fruit. Molecular Plant-Microbe Interactions. 2002;**15**(8):774-779

[32] Caracuel Z, Roncero MIG, Espeso EA, González-Verdejo CI, García-Maceira FI, Di Pietro A. The pH signalling transcription factor PacC controls virulence in the plant pathogen *Fusarium oxysporum*. Molecular Microbiology. 2003;**48**(3):765-779

[33] Kim HS, Park SY, Lee S, Adams EL, Czymmek K, Kang S. Loss of cAMP-dependent protein kinase a affects multiple traits important for root pathogenesis by *Fusarium oxysporum*. Molecular Plant-Microbe Interactions. 2011;**24**(6):719-732

[34] Jain S, Akiyama K, Mae K, Ohguchi T, Takata R. Targeted disruption of a G protein α subunit gene results in reduced pathogenicity in *Fusarium oxysporum*. Current Genetics. 2002;**41**(6):407-413

[35] Jain S, Akiyama K, Kan T, Ohguchi T, Takata R. The G protein β subunit FGB1 regulates development and pathogenicity in *Fusarium oxysporum*. Current Genetics. 2003; **43**(2):79-86

[36] Delgado-Jarana J, Martínez- Rocha A, Roldán-Rodríguez R, Groncero M, Di Pietro A. G-protein β subunit Fgb1 regulates hyphal growth, development, and virulence through multiple signalling pathways. Fungal Genetics and Biology. 2005;**42**(1):61-72

[37] Jain S, Akiyama K, Takata R, Ohguchi T. Signaling via the G protein α subunit FGA2 is necessary for pathogenesis in *Fusarium oxysporum*. FEMS Microbiology Letters. 2005;**243**(1):165-172

[38] Caracuel Z, Martínez-Rocha AL, Di Pietro A, Madrid MP, Roncero MIG. *Fusarium oxysporum* gas1 encodes a putative β-1, 3-glucanosyltransferase required for virulence on tomato plants. Molecular Plant-Microbe Interactions. 2005;**18**(11):1140-1147

[39] Martínez-Rocha AL, Roncero MIG, López-Ramirez A, Mariné M, Guarro J, Martínez-Cadena G, et al. Rho1 has distinct functions in morphogenesis, cell wall biosynthesis and virulence of *Fusarium oxysporum*. Cellular Microbiology. 2008;**10**(6):1339-1351

[40] Inoue I, Namiki F, Tsuge T. Plant colonization by the vascular wilt fungus *Fusarium oxysporum* requires FOW1, a gene encoding a mitochondrial protein. Plant Cell Online. 2002;**14**(8):1869-1883

[41] Kawabe M, Mizutani K, Yoshida T, Teraoka T, Yoneyama K, Yamaguchi I, et al. Cloning of the pathogenicity-related gene FPD1 in *Fusarium oxysporum* f. Sp. *lycopersici*. Journal of General Plant Pathology. 2004;**70**(1):16-20

[42] Roncero M, Hera C, Ruiz-Rubio M, Garcia-Maceira FI, Madrid MP, Caracuel Z, et al. *Fusarium* as a model for studying virulence in soilborne plant pathogens. Physiological and Molecular Plant Pathology. 2003;**62**(2):87-98

[43] Ruiz-Roldán MC, Di PA, Huertas-González MD, Roncero MIG. Two xylanase genes of the vascular wilt pathogen *Fusarium oxysporum* are differentially expressed during infection of tomato plants. Molecular and General Genetics MGG. 1999;**261**(3):530-536

[44] Calero-Nieto F, Di Pietro A, Roncero MIG, Hera C. Role of the transcriptional activator XlnR of *Fusarium oxysporum* in regulation of xylanase genes and virulence. Molecular Plant-Microbe Interactions. 2007;**20**(8):977-985

[45] Di Pietro A, Roncero MIG. Cloning, expression, and role in pathogenicity of pg1 encoding the major extracellular endopolygalacturonase of the vascular wilt pathogen *Fusarium oxysporum*. Molecular Plant-Microbe Interactions. 1998;**11**(2):91-98

[46] García-Maceira FI, Di Pietro A, Huertas-González MD, Ruiz-Roldán MC, Roncero MI. Molecular characterization of an endopolygalacturonase from *Fusarium oxysporum* expressed during early stages of infection. Applied and Environmental Microbiology. 2001;**67**(5):2191-2196

[47] Huertas-González MD, García Maceira FI, Roncero MIG, Ruiz-Roldán MC, Di Pietro A. Cloning and characterization of pl1 encoding an in planta-secreted pectate lyase of *Fusarium oxysporum*. Current Genetics. 1999;**35**(1):36-40

[48] Roncero MI, Di Pietro A, Ruiz-Roldán MC, Huertas-González MD, Garcia-Maceira FI, Méglecz E, et al. Role of cell wall-degrading enzymes in pathogenicity of *Fusarium oxysporum*. Revista Iberoamericana de Micología. 2000;**17**(1):S47-S53

[49] Duyvesteijn RGE, Van Wijk R, Boer Y, Rep M, Cornelissen BJC, Haring MA. Frp1 is a *Fusarium oxysporum* F-box protein required for pathogenicity on tomato. Molecular Microbiology. 2005;**57**(4):1051-1063

[50] Jonkers W, Rodrigues CDA, Rep M. Impaired colonization and infection of tomato roots by the Δ frp1 mutant of *Fusarium oxysporum* correlates with reduced CWDE gene expression. Molecular Plant-Microbe Interactions. 2009;**22**(5):507-518

[51] Thomma B, Nürnberger T. Of PAMPs and effectors: The blurred PTI-ETI dichotomy. The Plant Cell. 2011;**23**(1):4-15

[52] Schoffelmeer EAM, Klis FM, Sietsma JH, Cornelissen BJC. The cell wall of *Fusarium oxysporum*. Fungal Genetics and Biology. 1999;**27**(2-3):275-282

[53] Felix G, Regenass M, Boller T. Specific perception of subnanomolar concentrations of chitin fragments by tomato cells: Induction of extracellular alkalinization, changes in protein phosphorylation, and establishment of a refractory state. The Plant Journal. 1993;**4**(2):307-316

[54] Madrid MP, Di Pietro A, Roncero MIG. Class V chitin synthase determines pathogenesis in the vascular wilt fungus *Fusarium oxysporum* and mediates resistance to plant defence compounds. Molecular Microbiology. 2002;**47**(1):257-266

[55] Martín-Urdíroz M, Roncero MIG, González-Reyes JA, Ruiz-Roldán C. ChsVb, a class VII chitin synthase involved in septation, is critical for pathogenicity in *Fusarium oxysporum*. Eukaryotic Cell. 2008;**7**(1):112-121

[56] Fesel PH, Zuccaro A. β-glucan: Crucial component of the fungal cell wall and elusive MAMP in plants. Fungal Genetics and Biology. 2016;**90**:53-60

[57] Schoffelmeer EAM, Vossen JH, van Doorn AA, Cornelissen BJC, Haring MA. FEM1, a *Fusarium oxysporum* glycoprotein that is covalently linked to the cell wall matrix and is conserved in filamentous fungi. Molecular Genetics and Genomics 2001;**265**(1):143-152

[58] Boller T, He SY. Innate immunity in plants: An arms race between pattern recognition receptors in plants and effectors in microbial pathogens. Science. 2009;**324**(5928):742-744

[59] Monaghan J, Zipfel C. Plant pattern recognition receptor complexes at the plasma membrane. Current Opinion in Plant Biology. 2012;**15**(4):349-357

[60] Zipfel C. Plant pattern-recognition receptors. Trends in Immunology. 2014;**35**(7):345-351

[61] Wang G, Ellendorff U, Kemp B, Mansfield JW, Forsyth A, Mitchell K, et al. A genome-wide functional investigation into the roles of receptor-like proteins in *Arabidopsis*. Plant Physiology. 2008;**147**(2):503-517

[62] Kaku H, Nishizawa Y, Ishii-Minami N, Akimoto-Tomiyama C, Dohmae N, Takio K, et al. Plant cells recognize chitin fragments for defense signaling through a plasma membrane receptor. Proceedings of the National Academy of Sciences of the United States of America. 2006;**103**(29):11086-11091

[63] Wan J, Zhang X-C, Neece D, Ramonell KM, Clough S, Kim S, et al. A LysM receptor-like kinase plays a critical role in chitin signaling and fungal resistance in *Arabidopsis*. Plant Cell Online. 2008;**20**(2):471-481

[64] Iizasa E, Mitsutomi M, Nagano Y. Direct binding of a plant LysM receptor-like kinase, LysM RLK1/CERK1, to chitin *in vitro*. The Journal of Biological Chemistry. 2010;**285**(5): 2996-3004

[65] Umemoto N, Kakitani M, Iwamatsu A, Yoshikawa M, Yamaoka N, Ishida I. The structure and function of a soybean b-glucan-elicitor-binding protein. Proceedings of the National Academy of Sciences. 1997;**94**(3):1029-1034

[66] Métraux JP. Recent breakthroughs in the study of salicylic acid biosynthesis. Trends in Plant Science. 2002;**7**(8):332-334

[67] Glazebrook J. Contrasting mechanisms of defense against biotrophic and necrotrophic pathogens. Annual Review of Phytopathology. 2005;**43**(1):205-227

[68] Loake G, Grant M. Salicylic acid in plant defence—The players and protagonists. Current Opinion in Plant Biology. 2007;**10**(5):466-472

[69] Tsuda K, Sato M, Glazebrook J, Cohen JD, Katagiri F. Interplay between MAMP-triggered and SA-mediated defense responses. The Plant Journal. 2008;**53**(5):763-775

[70] Wildermuth MC, Dewdney J, Wu G, Ausubel FM. Isochorismate synthase is required to synthesize salicylic acid for plant defence. Nature. 2001;**414**(6863):562-565

[71] Tripathi D, Jiang Y-L, Kumar D. SABP2, a methyl salicylate esterase is required for the systemic acquired resistance induced by acibenzolar- S -methyl in plants. FEBS Letters. 2010;**584**(15):3458-3463

[72] ZQ F, Yan S, Saleh A, Wang W, Ruble J, Oka N, et al. NPR3 and NPR4 are receptors for the immune signal salicylic acid in plants. Nature. 2012;**486**(7402):228-232

[73] Zhang Y, Tessaro MJ, Lassner M, Li X. Knockout analysis of *Arabidopsis* transcription factors TGA2, TGA5, and TGA6 reveals their redundant and essential roles in systemic acquired resistance. Plant Cell Online. 2003;**15**(11):2647-2653

[74] Li J, Brader G, Palva ET. The WRKY70 transcription factor: A node of convergence for jasmonate-mediated and salicylate-mediated signals in plant defense. Plant Cell Online. 2004;**16**(2):319-331

[75] Lecourieux D, Ranjeva R, Pugin A. Calcium in plant defence-signalling pathways. The New Phytologist. 2006;**171**(2):249-269

[76] Du L, Ali GS, Simons KA, Hou J, Yang T, Reddy ASN, et al. Ca^{2+}/calmodulin regulates salicylic-acid-mediated plant immunity. Nature. 2009;**457**(7233):1154-1158

[77] Ma W, Berkowitz GA. The grateful dead: Calcium and cell death in plant innate immunity. Cellular Microbiology. 2007;**9**(11):2571-2585

[78] Kimura M, Kawano T. Salicylic acid-induced superoxide generation catalyzed by plant peroxidase in hydrogen peroxide-independent manner. Plant Signaling & Behavior. 2015;**10**(11):e1000145

[79] Kurusu T, Yagala T, Miyao A, Hirochika H, Kuchitsu K. Identification of a putative voltage-gated Ca^{2+} channel as a key regulator of elicitor-induced hypersensitive cell death and mitogen-activated protein kinase activation in rice. The Plant Journal. 2005;**42**(6):798-809

[80] Mandal S, Mitra A, Mallick N. Biochemical characterization of oxidative burst during interaction between *Solanum lycopersicum* and *Fusarium oxysporum* f. sp. *lycopersici*. Physiological and Molecular Plant Pathology. 2008;**72**(1-3):56-61

[81] Almagro L, Gó Mez Ros LV, Belchi-Navarro S, Bru R, Barceló AR, Pedreñ OMA. Class III peroxidases in plant defence reactions. Journal of Experimental Botany. 2009;**60**(2):377-390

[82] Bae H, Kim MS, Sicher RC, Bae H-J, Bailey BA. Necrosis- and ethylene-inducing peptide from *Fusarium oxysporum* induces a complex cascade of transcripts associated with signal transduction and cell death in *Arabidopsis*. Plant Physiology. 2006;**141**(3):1056-1067

[83] Pedley KF, Martin GB. Role of mitogen-activated protein kinases in plant immunity. Current Opinion in Plant Biology. 2005;**8**(5):541-547

[84] Berrocal-Lobo M, Molina A. *Arabidopsis* defense response against *Fusarium oxysporum*. Trends in Plant Science. 2008;**13**(3):145-150

[85] Thaler JS, Owen B, Higgins VJ. The role of the jasmonate response in plant susceptibility to diverse pathogens with a range of lifestyles. Plant Physiology. 2004;**135**(1): 530-538

[86] Berrocal-Lobo M, Molina A. Ethylene response factor 1 mediates *Arabidopsis* resistance to the soilborne fungus *Fusarium oxysporum*. Molecular Plant-Microbe Interactions. 2004;**17**(7):763-770

[87] Kunkel BN, Brooks DM. Cross talk between signaling pathways in pathogen defense. Current Opinion in Plant Biology. 2002;**5**(4):325-331

[88] Xu Y, Chang P, Liu D, Narasimhan M. Plant defense genes are synergistically induced by ethylene and methyl jasmonate. The Plant. 1994;**6**(8):1077-1085

[89] Manners J, Penninckx I, Vermaere K. The promoter of the plant defensin gene PDF1.2 from *Arabidopsis* is systemically activated by fungal pathogens and responds to methyl jasmonate but not to salicylic. Plant Mol. 1998;**38**(6):1071-1080

[90] Lorenzo O, Piqueras R, Sánchez-Serrano JJ, Solano R. Ethylene response factor1 integrates signals from ethylene and jasmonate pathways in plant Defense. Plant Cell Online. 2003;**15**(1):165-178

[91] Anderson JP, Badruzsaufari E, Schenk PM, Manners JM, Desmond OJ, Ehlert C, et al. Antagonistic interaction between abscisic acid and jasmonate-ethylene signaling pathways modulates defense gene expression and disease resistance in *Arabidopsis*. Plant Cell Online. 2004;**16**(12):3460-3479

[92] Flors V, Ton J, Jakab G. Abscisic acid and callose: Team players in defence against pathogens? Journal of Phytopathology. 2005;**153**(7-8):377-383

[93] Trusov Y, Sewelam N, Rookes J, Kunkel M. Heterotrimeric G proteins-mediated resistance to necrotrophic pathogens includes mechanisms independent of salicylic acid-, jasmonic acid/ethylene- and abscisic acid-mediated defense signaling. The Plant. 2009; **58**(1):69-81

[94] Mandal S, Mallick N, Mitra A. Salicylic acid-induced resistance to *Fusarium oxysporum* f. sp. *lycopersici* in tomato. Plant Physiology and Biochemistry. 2009;**47**(7):642-649

[95] Sinha M, Singh R, Kushwaha G, Iqbal N. Current overview of allergens of plant pathogenesis related protein families. The Scientific World Journal. 2014;**2014**:543195

[96] Ito S, Ihara T, Tamura H, Tanaka S, Ikeda T. α-Tomatine, the major saponin in tomato, induces programmed cell death mediated by reactive oxygen species in the fungal pathogen *Fusarium oxysporum*. FEBS Letters. 2007;**581**(17):3217-3222

[97] Eulgem T, Somssich I. Networks of WRKY transcription factors in defense signaling. Current Opinion in Plant Biology. 2007;**10**(4):366-371

[98] He P, Shan L, Sheen J. Elicitation and suppression of microbe-associated molecular pattern-triggered immunity in plant–microbe interactions. Cellular Microbiology. 2007; **9**(6):1385-1396

[99] Ma L, Houterman P, Gawehns F, Cao L. The AVR2–SIX5 gene pair is required to activate I-2-mediated immunity in tomato. The New Phytologist. 2015;**208**(2):507-518

[100] Oliveira-Garcia E, Valent B. How eukaryotic filamentous pathogens evade plant recognition. Current Opinion in Microbiology. 2015;**26**:92-101

[101] Houterman P, Speijer D, Dekker H. The mixed xylem sap proteome of *Fusarium oxysporum*-infected tomato plants. Molecular Plant. 2007;**8**(2):215-221

[102] Kashiwa T, Kozaki T, Ishii K, Turgeon B. Sequencing of individual chromosomes of plant pathogenic *Fusarium oxysporum*. Fungal Genetics and Biology. 2017;**98**(1):46-51

[103] McHale L, Tan X, Koehl P, Michelmore RW. Plant NBS-LRR proteins: Adaptable guards. Genome Biology. 2006;**7**(4):212

[104] Caplan J, Padmanabhan M, Dinesh-Kumar S. Plant NB-LRR immune receptors: From recognition to transcriptional reprogramming. Cell Host & Microbe. 2008;**3**(3):126-135

[105] Eitas T, Dangl J. NB-LRR proteins: Pairs, pieces, perception, partners, and pathways. Current Opinion in Plant Biology. 2010;**13**(4):472-477

[106] Elmore J, Lin Z, Coaker G. Plant NB-LRR signaling: Upstreams and downstreams. Current Opinion in Plant Biology. 2011;**14**(4):365-371

[107] Takken F, Albrecht M, Tameling W. Resistance proteins: Molecular switches of plant defence. Current Opinion in Plant Biology. 2006;**9**(4):383-390

[108] Inami K, Yoshioka-Akiyama C, Morita Y, Yamasaki M. A genetic mechanism for emergence of races in *Fusarium oxysporum* f. Sp. *lycopersici:* Inactivation of avirulence gene AVR1 by transposon insertion. PLoS One. 2012;**7**(8):e44101

[109] Houterman P, Cornelissen B, Rep M. Suppression of plant resistance gene-based immunity by a fungal effector. PLoS Pathogens. 2008;**4**(5):e1000061

[110] van der Does H, Duyvesteijn R. Expression of effector gene SIX1 of *Fusarium oxysporum* requires living plant cells. Fungal Genetics and Biology. 2008;**45**(9):1257-1264

[111] Rep M, Van Der DH, Meijer M. A small, cysteine-rich protein secreted by *Fusarium oxysporum* during colonization of xylem vessels is required for I-3-mediated resistance in tomato. Molecular Microbiology. 2004;**53**(5):1373-1383

[112] Rep M, Meijer M, Houterman P. *Fusarium oxysporum* evades I-3-mediated resistance without altering the matching avirulence gene. Molecular Plant: Microbe Interactions. 2005;**18**(1):15-23

[113] Gawehns F, Houterman P, Ichou F. The *Fusarium oxysporum* effector Six6 contributes to virulence and suppresses I-2-mediated cell death. Molecular Plant: Microbe Interactions. 2014;**27**(4):336-348

[114] Lievens B, Houterman P, Rep M. Effector gene screening allows unambiguous identification of *Fusarium oxysporum* f. sp. *lycopersici* races and discrimination from other formae speciales. FEMS Microbiology Letters. 2009;**300**(2):201-215

[115] Michielse C, van WR, Reijnen L. The nuclear protein Sge1 of *Fusarium oxysporum* is required for parasitic growth. PLoS Pathogens. 2009;**5**(10):e1000637

[116] Jashni M, Dols I, Iida Y, Boeren S. Synergistic action of a metalloprotease and a serine protease from *Fusarium oxysporum* f. Sp. *lycopersici* cleaves chitin-binding tomato chitinases, reduces their. Molecular Plant: Microbe Interactions. 2015;**28**(9):996-1008

[117] Pareja-Jaime Y, Roncero M. Tomatinase from *Fusarium oxysporum* f. sp. *lycopersici* is required for full virulence on tomato plants. Molecular Plant: Microbe Interactions. 2008;**21**(6):728-736

[118] Singh V, Upadhyay R. Fusaric acid induced cell death and changes in oxidative metabolism of *Solanum lycopersicum* L. Botanical Studies. 2014;**55**(1):66-77

[119] Wu H, Yin X, Zhu Y, Guo S, Wu C, Lu Y. Nitrogen metabolism disorder in watermelon leaf caused by fusaric acid. Physiological and Molecular Plant Pathology. 2007; **71**(1-3):69-77

[120] Singh V, Singh H, Upadhyay R. Role of fusaric acid in the development of "*Fusarium* wilt"symptoms in tomato: Physiological, biochemical and proteomic perspectives. Plant Physiology and Biochemistry. 2017;**118**:320-332

[121] Niehaus E, Bargen K von, Espino J. Characterization of the fusaric acid gene cluster in *Fusarium fujikuroi*. Applied Microbiology 2014;**98**(4):1749-1762

[122] Studt L, Janevska S, Niehaus E. Two separate key enzymes and two pathway-specific transcription factors are involved in fusaric acid biosynthesis in *Fusarium fujikuroi*. Environmental Microbiology. 2016;**18**(3):936-956

[123] Michielse C, Rep M. Pathogen profile update: *Fusarium oxysporum*. Molecular Plant Pathology. 2009;**10**(3):311-324