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Strategies of attack and defense in plant–oomycete interactions, accentuated for *Phytophthora parasitica* Dastur (syn. *P. Nicotianae* Breda de Haan)

Agnès Attard[1], Mathieu Gourgues[1], Eric Galiana, Franck Panabières, Michel Ponchet, Harald Keller*

Unité Mixte de Recherches, Interactions Plantes-Microorganismes et Santé Végétale, INRA1064-CNRS6192-UNSA, BP 167, 400 Route des Chappes, 06903 Sophia Antipolis, France

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Summary

Oomycetes from the genus *Phytophthora* are fungus-like plant pathogens that are devastating for agriculture and natural ecosystems. Due to their particular physiological characteristics, no efficient treatments against diseases caused by these microorganisms are presently available. To develop such treatments, it appears essential to dissect the molecular mechanisms that determine the interaction between *Phytophthora* species and host plants. Available data are scarce, and genomic approaches were mainly developed for the two species, *Phytophthora infestans* and *Phytophthora sojae*. However, these two species are exceptions from, rather than representative species for, the genus. *P. infestans* is a foliar pathogen, and *P. sojae* infects a narrow range of host plants, while the majority of *Phytophthora* species are quite unselective, root-infecting pathogens. To represent this majority, *Phytophthora parasitica* emerges as a model for the genus, and genomic resources for analyzing its interaction with plants are developing. The aim of this review is to assemble current knowledge on cytological and molecular processes that are underlying plant–pathogen interactions involving *Phytophthora*

Abbreviations: CBEL, cellulose-binding, elicitor and lectin activity; EST, expressed sequence tag; HR, hypersensitive response; NEP, necrosis and ethylene-inducing peptide; NLP, NEP-like protein; NPP1, necrosis-inducing *Phytophthora* protein 1; PAMP, pathogen-associated molecular pattern; PEP13, 13 amino acid minimal peptide within *Phytophthora* transglutaminase

*Corresponding author. Tel.: +33 492386594; fax: +33 492386587.
E-mail address: keller@sophia.inra.fr (H. Keller).

[1]These two authors contributed equally to this work.

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species and in particular *P. parasitica*, and to place them into the context of a hypothetical scheme of co-evolution between the pathogen and the host.
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Introduction

Plant pathogenic oomycetes have unique physiological characteristics and devastating effects on crops and natural ecosystems. By destroying the European potato monoculture, *Phytophthora infestans* conditioned the great famine that reduced the Irish population by 20% in 1845. This event is now considered as the origin of modern phytopathology (Scholthof, 2007). Since then, oomycete diseases have given rise to major changes in crop management and to the development of the first formulated fungicide (Bordeaux mixture) in the 1870s (Delmotte et al., 2006). Beyond these historical examples, oomycetes still have considerable economical and environmental impacts. *Phytophthora* and *Pythium* species are pathogenic for virtually all dicots, as well as for certain cereals (Erwin and Ribeiro, 1996), and they account for approximately $5 billion of damage worldwide (Stokstad, 2006).

Oomycetes were long considered as fungi, because they are heterotrophic, mycelium-forming

Table 1. Commonly used fungicide classes and their activity on oomycetes

Class	Fungicide (example)	Structure	Inhibitor of	Activity on oomycetes
Triazole	Flutriafol		Sterol synthesis; 14a-demethylase (CYP51)	Not active
Polyoxin	Polyoxorim (Polyoxin D)		Chitin synthesis; Chitin synthetase	Not active
Phenylamide	Metalaxyl		RNA polymerase-1	Active, but resistance evolves rapidly

organisms. Based on combinatorial analysis of molecular and morphological criteria (Barr, 1992; Baldauf et al., 2000), current taxonomy clusters oomycetes with photosynthetic organisms like brown algae or diatoms within the kingdom of stramenopiles. Mycelia from oomycetes are composed of non-partitioned hyphae that contain several diploid nuclei, thus contrasting to mycelia from filamentous fungi (Brasier and Sansome, 1975; Erwin and Ribeiro, 1996). Additionally, two major biochemical characteristics distinguish oomycetes from plant pathogenic fungi and directly influence field applications. Firstly, oomycete cell walls are primarily composed of β-1,3- and β-1,6 glucanes, and of cellulose (a β-1,4-glucane), whereas chitin, an essential component of fungal cell walls, is only marginally important (Bartinicki-Garcia and Wang, 1983). Secondly, oomycetes are unable to synthesize sterols, because they lack the squalene epoxydase and the 14α-demethylase enzymes required to convert sterol precursors (Wood and Gottlieb, 1978; Nes and Stafford, 1983; Tyler et al., 2006). As most of the traditionally used fungicides target chitin and sterol synthesis, they are inefficient against oomycetes (Table 1). Currently, pesticides used against oomycetes rely on the phenylamide metalaxyl, which specifically inhibits RNA polymerase-1 (Sukul and Spiteller, 2000). However, the first cases of metalaxyl resistance were reported less than 4 years after homologation of the compound in 1977 (Davidse et al., 1981), and resistance to metalaxyl is now a general characteristic of pathogenic *P. infestans* and *Phytophthora capsici* populations from potato and pepper, respectively (Lee et al., 1999; Parra and Ristaino, 2001). To date, pesticides that are adapted to prevent or cure oomycete diseases do not exist. In order to develop them, research has been focalized on understanding of the molecular mechanisms underlying oomycete pathogenicity and corresponding plant susceptibility or resistance responses.

Genomic tools for analyzing the interaction between *Phytophthora parasitica* and plants

Most of the current knowledge on the molecular interactions between *Phytophthora* and plants arose from research involving two species, *Phytophthora sojae* and *P. infestans*. Draft genome sequences from both species (as well as from *Phytophthora ramorum*) are now available (Nusbaum et al., 2006; Tyler et al., 2006), and will help to accelerate the identification of genes that determine the molecular dialogue between these species and plants. However, *P. infestans* is a foliar pathogen, while most other species are soilborne, root-infecting pathogens. Furthermore, *P. infestans* and *P. sojae* have narrow host ranges, whereas most *Phytophthora* species attack a broad spectrum of plants. In addition, *P. infestans* and *P. ramorum* are poorly amenable to large-scale analyses of expressed, compatibility-related genes, due to the low pathogen biomass within infected tissues, and due to the woody nature of the infected tissue, respectively.

As a consequence, several laboratories have focused on the more representative species, *P. parasitica* Dastur (syn. *P. nicotianae* Breda de Haan). *P. parasitica* is a soilborne pathogen infecting both herbaceous and woody hosts in a range of about 60 different plant families, including the Solanaceae (Figure 1) and other cultivated crops of worldwide importance (Erwin and Ribeiro, 1996). Technical procedures for this species, like *in vitro* inoculation and transformation protocols, are now available (Colas et al., 1998; Bottin et al., 1999; Gaulin et al., 2002; Le Berre et al., 2007). Genomic resources are evolving, and a bacterial artificial chromosome library allowed to confirm the size of the *P. parasitica* genome (Shan and Hardham, 2004). At 95.5 Mb, the *P. parasitica* genome is similar to *P. sojae*, which has been estimated at 90–95 Mb (Mao and Tyler, 1991; Voglmayer and Greilhuber, 1998). However, it

Figure 1. Symptoms of stem rot disease on a tomato (cv. Saint Pierre) plant, and details of progressive rotting (inset). The photograph was taken 6 days after inoculation with zoospore suspensions of a Spanish *Phytophthora parasitica* isolate from the Sophia Antipolis *Phytophthora* collection.

distinguishes *P. parasitica* from *P. ramorum* and *P. infestans*, which have significantly different genomes sizing 65 and 240 Mb, respectively (Tyler et al., 2005; Tooley and Therrien, 1987). To profile *P. parasitica* gene expression during different phases of the life cycle, expressed sequence tag (EST) libraries were created. They represent 3405 unique *P. parasitica* genes that are expressed by *in vitro* growing mycelium (Panabieres et al., 2005), and during the late stages of the compatible interaction with tomato (Le Berre et al., 2007). Smaller EST collections were generated from zoospores and germinated cysts of *P. parasitica* (Skalamera et al., 2004; Shan et al., 2004a). About 80% of the obtained sequences were also found within the *P. ramorum*, *P. sojae* or *P. infestans* genomes. However, 10–15% of the ESTs did not match any available sequence data for *Phytophthora* species (Le Berre et al., 2007). The corresponding sequences are supposed to reflect

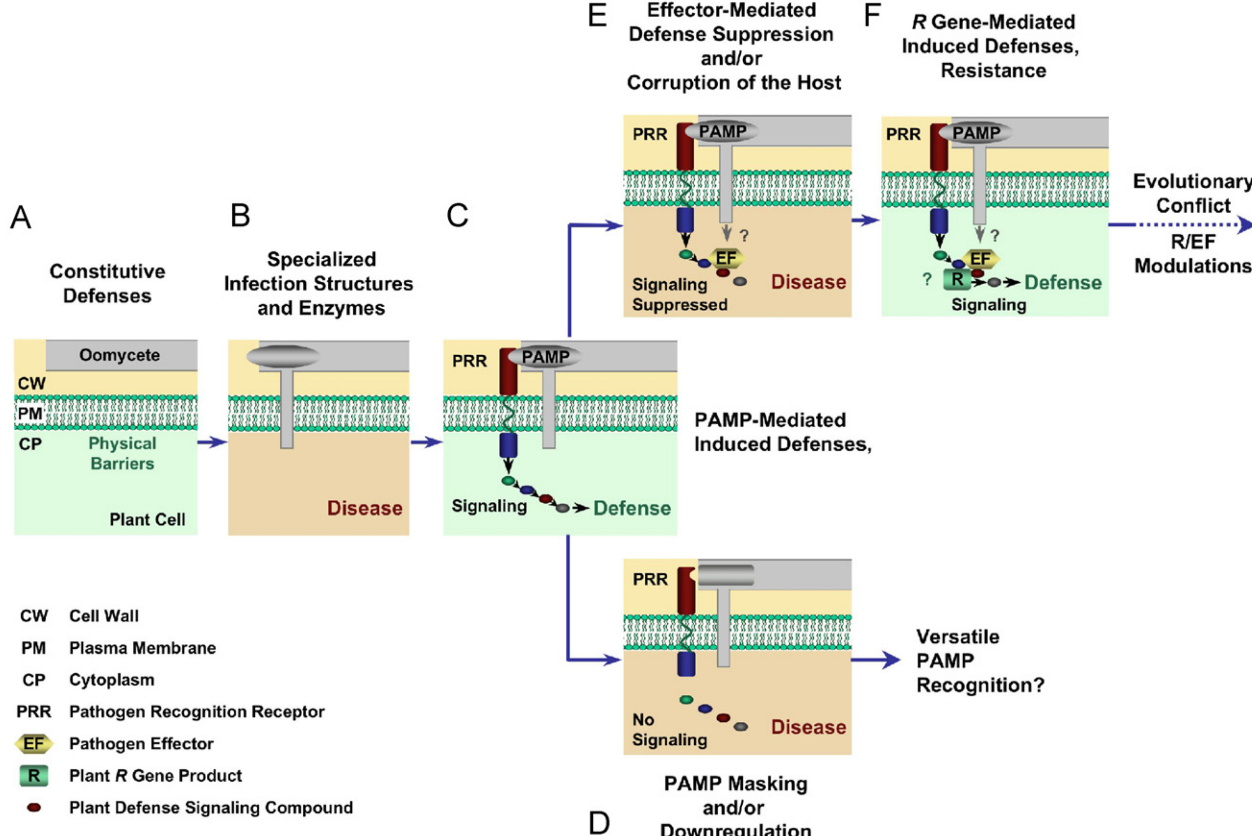

Figure 2. Hypothetical evolutionary scheme for the interaction between plants and oomycetes. The scheme has been adapted from the generally approved model for plant–bacteria interactions (Chisholm et al., 2006; Ingle et al., 2006; Jones and Dangl, 2006). The text describes characteristics that have been confirmed for plant–oomycete interactions, and it highlights gaps in our knowledge. (A) In plants, epicuticular waxes, the cuticle, and the cell walls form physical barriers that generally hinder infection by non-pathogenic (e.g. saprophytic) oomycetes. (B) Plant pathogens developed infection structures (e.g. appressoria) and functions (e.g. lytic enzymes) to penetrate the host and to become infectious. (C) As a consequence, specific receptor-mediated recognition mechanisms emerged, which allow plant species to perceive conserved motifs within essential structural or functional macromolecules (PAMPs) from the pathogen. The perception of PAMPs triggers signaling cascades that induce defense machanisms. (D) In order to avoid the triggered defenses, oomycetes are supposed to either mask PAMPs, or to downregulate their production during the critical phases of infection. (E) Alternatively, specific virulence functions (effectors) are supposed to interfere with the host cell metabolism, or to suppress defense signaling. (F) Recognition of these virulence functions, or their activity, by specific *R* gene products is then presumed to initiate an additional layer of defense signaling, which triggers the so-called "genetic", or "gene for gene-mediated", resistance. Presently, the oomycete–plant interplay is supposed to be stacked in an evolutionary conflict, where pathogens aim at diversifying the recognized virulence functions, and where plant varieties aim at holding them up by the development of novel recognition specificities. The intracellular interference of oomycete effectors with defense signaling (shown in E), as well as the intracellular recognition of these effectors, or their activities, by *R* gene products (F), still requires demonstration for plant–oomycete interactions.

species-specific genes, which probably account for the capacity of *P. parasitica* to infect a wide host range.

Initiation of infection

The lifestyle of *P. parasitica* and its molecular interaction with plants might be characterized by an evolutionary scheme (Figure 2). The species is able to grow and reproduce in the absence of live plant material *in vitro*, on organic debris and in humus soil (Tsao, 1969). It is thus supposed to originate from saprophytic oomycetes. *Phytophthora* species form diploid oospores, which are able to survive in the soil or in decomposing plants for several years and thus constitute highly persistent conservation structures (Weste, 1983; Drenth et al., 1995). However, the main mean for oomycete propagation is a consequence of asexual reproduction. Typically, mycelium differentiates sporangia that either detach and germinate directly or liberate biflagellated, highly motile zoospores without a cell wall. Zoospores propagate in soil water and are attracted to the elongation and differentiation zones of plant roots (Figure 3A). *P. parasitica* spores apparently do not have plant species-specific root preferences, thus contrasting to *P. sojae* zoospores, which are attracted specifically to roots exuding the isoflavones daidzein and genistein (Morris and Ward, 1992; Morris et al., 1998). *P. parasitica* zoospores can also be transported passively by splash water to leaf surfaces, where they are attracted to wound sites (Figure 3B) before encystment and germination (Galiana et al., 2005). Spores of the oomycete have been shown to secrete PcVsv1, a protein containing multiple thrombospondin type 1 repeats otherwise found in adhesins of animals and malarial parasites, but not in plants, green algae or true fungi (Robold and Hardham, 2005). This protein, as well as mucin-like glycoproteins and other surface-binding proteins that have been identified in pre-infection stages of *P. infestans* and *P. parasitica*, are presumed to assure host adhesion of the zoospores (Gornhardt et al., 2000; Panabieres et al., 2005). Encysted spores on both roots and leaves then attract further zoospores to form clumps of cysts (Figure 3A, B). This phenomenon of self-attraction appears to be a strategy to increase the likelihood of infection (Tyler, 2002). It is known as the "homing response"

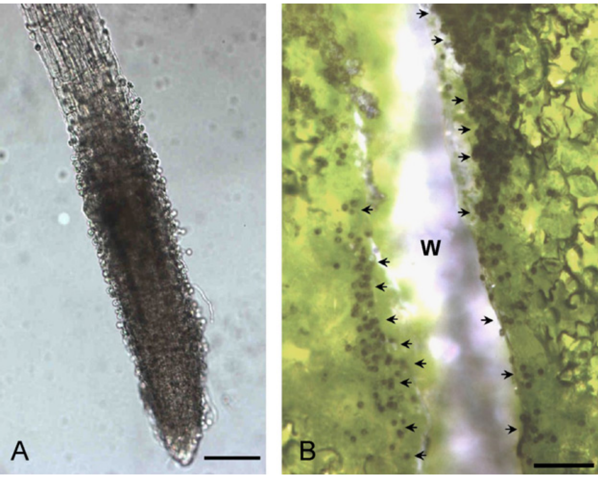

Figure 3. Clumps of encysted *P. parasitica* zoospores on plant surfaces. (A) At the elongation and differentiation zones of root tips from *Arabidopsis thaliana*, and (B) around wound openings (W) in the leaf epidermis from *Nicotiana tabacum* (arrows). The bar represents 100 μm.

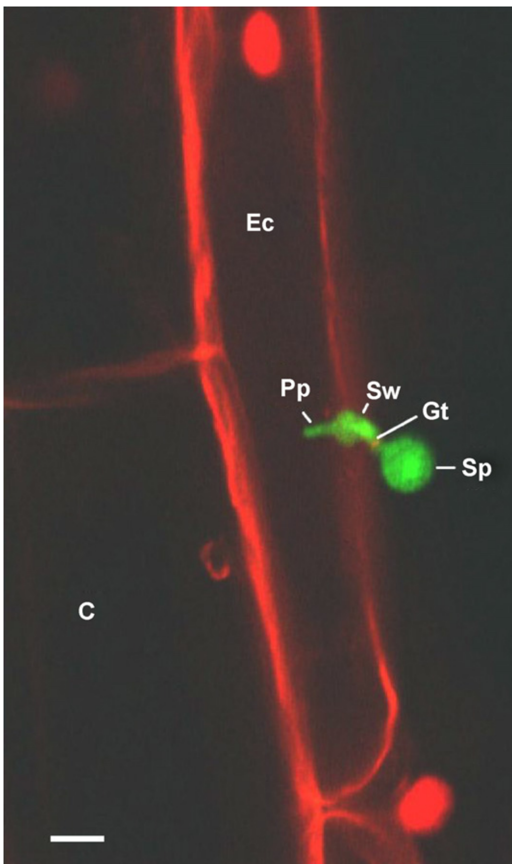

Figure 4. Penetration of *P. parasitica* into tomato roots. Zoospores from a strain expressing GFP under the control of the *P. parasitica* translation initiation factor 1 gene promoter (Le Berre et al., 2007) were applied to tomato roots *in vitro*. Spores (Sp) germinate, and the germination tube (Gt) forms an appressorium-like swelling (Sw) to push aside joined epidermal cells (Ec), and to enter a penetration peg (Pp) in between them. The absence of cytoplasmic propidium iodine stain (red fluorescence) indicates that plant cells are alive. The confocal laser scanning micrograph was taken 3 h post-inoculation. The bar represents 10 μm.

(Deacon and Donaldson, 1993) and is probably due to chemical signaling involving calcium (Reid et al., 1995).

Once encysted on plant surfaces, Ca^{2+}-dependent signaling triggers germination of *P. parasitica* spores to initiate infection (Warburton and Deacon, 1998). Germ tubes then enter directly into the intercellular spaces through wound openings on leaves, or form swellings that allow penetration between epidermal cells on root surfaces (Figure 4). In true fungi, polyols and trehalose mediate the osmoregulation of spores and the generation of turgor pressure in appressoria (Thines et al., 2000; Foster et al., 2003). *Phytophthora* species are considered as being unable to accumulate these compounds (Kim and Judelson, 2003), and only one report describes the accumulation of low arabitol concentrations in *P. infestans* spores (Tereshina et al., 2000). It has been suggested that *P. parasitica* rather regulates turgor pressure through the accumulation of proline (Ambikapathy et al., 2002), and that the amino acid is also involved in the formation of appressorium-like structures. However, it remains to be demonstrated whether *P. parasitica* germ tube swellings on plant roots are infection structures that are homologous to fungal appressoria.

When entering the host, germlings from *P. parasitica* have to adapt nutrient uptake to the apoplastic environment. Penetrating hyphae probably use plasma membrane H^+-ATPases to generate an electrochemical gradient, thus favoring fluxes of compounds from the plant to the oomycete cytoplasm (Shan et al., 2006). This hypothesis is supported by the finding that the gene coding for the *P. parasitica* H^+-ATPase, PMA1, shows strongest expression in germinating cysts. Plasma membrane H^+-ATPases are highly conserved across kingdoms, and expression of the corresponding genes has also been observed in germinating spores from fungi (Struck et al., 1996, 1998). However, the *P. parasitica* PMA1 H^+-ATPase is supposed to have a specialized role in the oomycete's life cycle, because an additional 155 amino acid cytoplasmic loop between transmembrane domains 8 and 9 is not found in similar proteins from other organisms (Shan et al., 2006).

Recognition by the host cells

To get into contact with the host cell plasma membrane for establishing the initial phase of interaction, *P. parasitica* has to overcome the plant cell wall. A large array of genes expressed by the oomycete encode proteins with similarities to hydrolytic enzymes probably involved in cell wall degradation (Panabieres et al., 2005; Le Berre et al., 2007). *P. parasitica* and several other *Phytophthora* species harbor a cell wall-associated glycoprotein that has no homology with published sequences, but that possesses a domain similar to the cellulose-binding domain of fungal glycanases. CBEL (cellulose-binding, elicitor, and lectin activity) binds to cellulosic substrates and is supposed to be involved in cell wall apposition in *P. parasitica*, and in the attachment of oomycete hyphae to host cell walls (Gaulin et al., 2002). However, plants have evolved mechanisms to recognize invading pathogens through the perception of conserved motifs in pathogen-derived molecules that are not subject to evolutionary diversification (Figure 2C). Receptor-mediated recognition of such pathogen-associated molecular patterns (PAMPs) triggers signaling cascades involving Ca^{2+}-fluxes and MAP kinase-mediated protein phosphorylations, which eventually activate an array of plant defense responses. The induced resistance mechanisms include the synthesis of lytic enzymes, the production of toxic compounds and reactive oxygen species, the reinforcement of the cell wall and, in some cases, cellular suicide. The pathogen-induced events that lead to programmed cell death are called the hypersensitive response (HR) (Nimchuk et al., 2003). Cells from *Nicotiana tabacum* and from *Arabidopsis thaliana* recognize the cellulose-binding domain from *P. parasitica* CBEL as a PAMP, and subsequently trigger the HR (Gaulin et al., 2006).

Several *P. parasitica* PAMPs of different molecular structures were characterized, which are highly conserved within this and other *Phytophthora* species. All known PAMPs are either cell wall compounds of the oomycete or motifs of secreted proteins, thus being accessible to specific plant cell surface receptors. Cell wall preparations from *P. parasitica* have been reported to trigger defense responses in tobacco (Bottin et al., 1994). The active compounds are probably glucans with a minimal branched (1,3–1,6) hepta-β-glucoside motif similar to that found in *P. sojae*, and for which a plasma membrane receptor was identified in soybean cells (Umemoto et al., 1997; Fliegmann et al., 2004). This hypothesis is supported by the finding that heterologous expression of the soybean glucan receptor cDNA in tobacco results in resistance to *P. parasitica* (Kakitani et al., 2001). Another *P. parasitica* cell wall-localized PAMP, which is present in at least 10 different *Phytophthora* species, is a 13 amino acid stretch within a transglutaminase. This enzyme is supposed to ensure the polymerization of cell wall proteins and

to organize the oomycete cellular architecture (Brunner et al., 2002). The 13 amino acid stretch (PEP13) within the enzyme is necessary for transglutaminase activity (Brunner et al., 2002), sufficient for receptor binding on parsley cells (Nürnberger et al., 1994), and able to induce intracellular defense signaling cascades (Kroj et al., 2003). Among the secreted *P. parasitica* proteins harboring a PAMP, the 24 kDa necrosis-inducing *Phytophthora* protein 1 (NPP1) is able to trigger a light-dependent HR in tobacco and other dicots, but not in monocots (Fellbrich et al., 2002; Qutob et al., 2006). NPP1 and other necrosis and ethylene-inducing peptide-like proteins (NLPs) found in diverse microorganisms are believed to exert a toxic function on lipid bilayers and are, therefore, considered as pathogenicity factors (Qutob et al., 2006). Interestingly, the *P. sojae* protein is expressed when the interaction with soybean switches from biotrophy to necrotrophy (Qutob et al., 2002).

All *Phytophthora* species abundantly secrete 10 kDa proteins, which form a superfamily called elicitins. On tobacco and some *Brassica* species, elicitins induce the defense mechanisms that lead to the HR (Ricci et al., 1989; Bonnet et al., 1996). Moreover, an application of elicitins to tobacco conditions the plants to resist to subsequent infections by pathogenic strains of *P. parasitica* and other pathogens. The resistance induced by elicitins is systemic and durable, and shows the characteristics of "systemic acquired resistance", a widespread defense mechanism in plants (Keller et al., 1996). The biological function of elicitins is related to their ability to bind sterols as well as various fatty acids (Mikes et al., 1998; Osman et al., 2001) and to transport them between membranes (Vauthrin et al., 1999). Mutant elicitins, which are not able to bind sterols, are also unable to bind to the specific tobacco plasma membrane receptors, and cannot induce plant defense (Osman et al., 2001). Because *Phytophthora* species do not synthesize sterols, elicitins are supposed to transport these essential compounds from the host cell plasma membrane to the pathogen (Ponchet et al., 1999). No minimal PAMP motif can be assigned for elicitins, because their three-dimensional structure, resulting from three disulfide bridges, is required for sterol loading and receptor binding. The entire protein has thus to be considered as a PAMP. The EST sequencing project for *P. parasitica* led to the identification of 10 different elicitin classes (Panabieres et al., 2005; Le Berre et al., 2007). Most abundantly expressed are the class 1 proteins of parasiticein, which are encoded by at least 4 genes (*ParA1*.1–*ParA1*.4), varying only by mutations in the 3′ untranslated regions (Panabieres et al., 2005). Proteins encoded by genes from the parasiticein classes 5 and 6 (PAR5 and PAR6) have N-terminal sequence similarities with a phospholipase from *P. capsici*, thus suggesting an involvement of PAR5 and PAR6 in membrane remodeling (Nespoulous et al., 1999).

Avoidance of recognition and host manipulation

PEP13, NLPs, and elicitins are perceived by independent plant cell surface receptors, triggering diverging (for PEP13 and NLP) or converging (for NLP and elicitins) defense signaling cascades that lead (NLP and elicitins) or not (PEP13) to the HR (Fellbrich et al., 2002; Kanneganti et al., 2006). In order to overcome the first layer of resistance, the pathogen had to develop specific mechanisms that make it possible to avoid recognition (Figure 2D) and/or to repress defense (Figure 2E). Avoidance of recognition through gene repression has been described for the *ParA1* genes. Although *ParA1* is constitutively expressed during vegetative growth, parasiticein production is downregulated during compatible *P. parasitica* interactions with tomato and tobacco (Colas et al., 2001). Similar results were found for the analog of the *ParA1* gene in *P. infestans*, *Inf1*, which is downregulated during potato infection (Kamoun et al., 1997). However, to date it has not been clarified how *P. parasitica* avoids the onset of innate immunity, which is triggered by the recognition of the other PAMPs described above.

EST sequencing led to the identification of expressed genes that may be involved in counteracting PAMP-mediated defense responses (Panabieres et al., 2005; Le Berre et al., 2007). Among them is an analog of GIP, which is a *P. sojae* member of a family encoding glucanase inhibitors that interact with soybean endo-β-1,3-glucanases during infection (Rose et al., 2002). Two families of Kazal-like protease inhibitors, EPI1 and EPI10, were identified from *P. infestans*, and are supposed to interact with extracellular defense proteases from tomato (Tian et al., 2004, 2005). Extracellular protease inhibition might be part of a common infection strategy for *Phytophthora* species, because *P. parasitica* expresses a gene similar to *epi1* (Panabieres et al., 2005). The secretion of proteins inhibiting the hydrolytic activity of plant defense enzymes is considered as the *Phytophthora* "counter defense" to infect the host (Kamoun, 2006).

Other oomycete proteins are probably addressed to the host cell cytoplasm, where they might interact with plant proteins to corrupt the host metabolism (Figure 2E). Such a function for disease development would be similar to bacterial systems, where virulence effectors are directly injected into the plant cell cytoplasm (Grant et al., 2006). In the absence of an injection system similar to the bacterial type III secretion system, it remains nevertheless enigmatic how a putative oomycete effector would transit to the interior of a host cell (Ellis et al., 2006). At present, only 2 proteins were identified as putative *Phytophthora* effectors, AVR3A from *P. infestans* and AVR1B from *P. sojae* (Shan et al., 2004b; Armstrong et al., 2005). The intrinsic function of these proteins is unknown, but transient expression experiments indicate that at least AVR3A is able to repress the host resistance response triggered by the elicitin INF1 (Bos et al., 2006). A characteristic of the proteins is the presence of a peptide signal and a preserved motif (RxLR), which is supposed to be involved in the translocation of these proteins into the host cell cytoplasm by a mechanism similar to the one employed by the malaria parasite, *Plasmodium falciparum* (Hiller et al., 2004; Kamoun, 2006). During the biotrophic phase of interaction with host cells, *Phytophthora* species are supposed to form intracellular feeding structures that are functional analogs of haustoria. Fungal haustoria are enriched with putative effector molecules (Catanzariti et al., 2006), and it seems likely that *Phytophthora* species use similar specialized structures to deliver effectors into the host cell cytoplasm during the biotrophic phase of the compatible interaction. Genome sequences from *P. infestans*, *P. ramorum*, and *P. sojae* allow the prediction of at least 100 genes in each genome coding for proteins harboring the RxLR motif (Kamoun, 2006). However, the expressed sequence collection from *P. parasitica*, which was obtained from preinfection stages, and from late time points during the interaction with tomato, allowed the identification of only 3 genes encoding putative RxLR proteins (J.Y Le Berre and F. Panabières, unpublished). Because the EST collection does not contain expressed sequences from the early biotrophic interaction, this under-representation probably confirms the hypothesis that genes coding for cytoplasmic effectors are predominantly expressed during the haustorial stage. However, it has to be reminded that to date no clear-cut experimental proof for a protein translocation between the oomycete and the host cell cytoplasma has been reported.

Resistance genes and resistance breeding

The emergence of microbial effectors counteracting PAMP-triggered defenses led to the evolution of plant proteins able to specifically identify these proteins. This evolution resulted in genetic resistance following the "gene-for-gene" model (Flor, 1956, 1971). It has been shown that single dominant plant resistance (*R*) genes encode proteins that interact directly or indirectly with microbial effectors (Figure 2F; Jones and Dangl, 2006). Dominant genes from the pathogen encoding the recognized effectors are subsequently considered as avirulence (*Avr*) genes. Matching R/Avr combinations allow the plants to activate defense mechanisms and the HR through signaling cascades that crosstalk with PAMP-triggered immunity (Wiermer et al., 2005). In the absence of a functional R protein, or in the presence of a modified AVR effector, pathogens avoid recognition and trigger disease. Therefore, *Avr* genes are under constant diversifying selection, leading to an evolutionary conflict with plants harboring corresponding *R* genes (Allen et al., 2004).

Only two matching *R* and *Avr* genes have been cloned and characterized that confer resistance to *Phytophthora* species. RPS1b from soybean and R3a from potato recognize the Avr proteins Avr1b from *P. sojae* and Avr3a from *P. infestans*, respectively (Ballvora et al., 2002; Gao et al., 2005; Huang et al., 2005). R/Avr recognition probably occurs in the plant cell cytoplasm, because the cytoplasmic transient coexpression of *Avr* and *R* genes leads to HR induction, thus supporting the hypothesis that Avr proteins are effectors, which are translocated from the oomycete to the interior of host cells (Armstrong et al., 2005). Single dominant *R* genes conferring resistance to *P. parasitica* have been described in tomato (Rattan and Saini, 1979) and tobacco (Van Jaarsveld et al., 2002), but none have yet been cloned and characterized.

Introgression of dominant resistance genes into susceptible cultivars has frequently been used to manage *Phytophthora* resistance. Eleven *R* genes from the wild potato species, *Solanum demissum*, have been introduced into modern potato cultivars (Van der Lee et al., 2001). However, *P. infestans* races quickly evaded the new single gene-mediated resistance properties of the cultivars (Goodwin, 1999; Garelik, 2002). *R* gene introgression thus has shown its limits for increasing *Phytophthora* resistance, and alternative breeding programs have to be developed to render oomycete resistance durable. Genetic engineering approaches, which were based on the pathogen-inducible expression of

transgenes encoding properly targeted PAMPs, have shown to account for the creation of *P. parasitica* resistance in tobacco (Keller et al., 1999; Belbahri et al., 2001). Recently it has been shown that the transgenic, pathogen-inducible expression of a constitutively active form of MAPK kinase, which is a signaling compound in PAMP-triggered immunity, leads to resistance of potato to *P. infestans* (Yamamizo et al., 2006). To manage durable oomycete resistance, similar biotechnological approaches might be combined with classical monogenic resistance breeding strategies.

Conclusions and perspectives

During the last decade, our understanding of the molecular bases underlying incompatible plant–oomycete interactions advanced considerably through the availability of genomic tools for the model plant, *Arabidopsis thaliana*. Recently, the research efforts on *A. thaliana* were extended to understand the molecular mechanisms involved in compatibility. The identification of plant genes, which are required for successful infection by pathogens, revealed that host plants contribute substantially to the creation of an environment that favors colonization (O'Connell and Panstruga, 2006).

Research efforts on the dissection of the molecular dialog between plants and oomycetes were mainly focalized on *Hyaloperonospora parasitica*, *P. sojae*, and *P. infestans*. However, the majority of agronomically important oomycetes are soil-borne pathogens with a broad-spectrum host range. To represent such oomycetes, *P. parasitica* is emerging, and genomic tools for this species are now becoming available. Data from EST collections suggest that pathogenesis of *P. parasitica* involves the standard repertoire of factors needed to colonize plants, such as cell wall-degrading enzymes, plus a set of novel proteins that probably manipulate plant physiology. The challenge for future research would be to understand (I) what is the action of these proteins, (II) where is their activity localized, (III) when is it expressed, and (IV) what is the plant's role in the outcome of the interaction. A genomic sequencing program for *P. parasitica* would allow comparative analyses with the available *Phytophthora* genomes, and probably lead to conclusions on common mechanisms for all species, and on specific functions that are required for the invasion of a large host range.

To analyze plant targets for *P. parasitica* proteins, genomic tools need to be developed for corresponding host plants. Tobacco, the historical host for *P. parasitica*, is now entering the genomics era. Fifty-six thousand ESTs, collected from tobacco plants exposed to various environmental conditions, have been sequenced. These sequences will be used to create a tobacco-specific microarray of expressed genes (http://www.estobacco.info) that will allow plant gene expression profiling during the interaction with *P. parasitica*. Transient and stable gene overexpression and knock-down experiments became routine for this plant, thus allowing functional genomics. Furthermore, tobacco is an excellent model plant for proteomics and metabolomics, and it accounts for the majority of data that fills the corresponding databases. Nevertheless, research on the compatible interaction between *P. parasitica* and host plants would certainly accelerate through the availability of an established pathosystem for *A. thaliana*.

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