



Revista Facultad Nacional de Agronomía
- Medellín

ISSN: 0304-2847

rfnagron_med@unal.edu.co

Universidad Nacional de Colombia
Colombia

Ávila Méndez, Kelly; Romero, Hernán Mauricio

Plant responses to pathogen attack: molecular basis of qualitative resistance

Revista Facultad Nacional de Agronomía - Medellín, vol. 70, núm. 2, 2017, pp. 8225-8235

Universidad Nacional de Colombia

Medellín, Colombia

Available in: <http://www.redalyc.org/articulo.oa?id=179951188011>

- How to cite
- Complete issue
- More information about this article
- Journal's homepage in redalyc.org

redalyc.org

Scientific Information System

Network of Scientific Journals from Latin America, the Caribbean, Spain and Portugal

Non-profit academic project, developed under the open access initiative

Plant responses to pathogen attack: molecular basis of qualitative resistance

Respuestas de las plantas al ataque de patógenos: bases moleculares de la resistencia cualitativa

doi: 10.15446/rfna.v70n2.64526

Kelly Ávila Méndez¹ and Hernán Mauricio Romero^{2*}

ABSTRACT

Keywords:

Host resistance
Non-host resistance
Zig-zag model
PTI
ETI
ETS

Pathogens attack plants to assimilate nutrients from them. All plant species have succeeded in overcoming pathogenic attack; therefore disease condition is not the rule but the exception. A co-evolutionary battle has equipped plants with sophisticated defense mechanisms and cognate pathogens with a corresponding arsenal of counter strategies to overcome them. Traditionally, plant-pathogen interaction has been associated with molecules involved in recognition processes giving rise to models such as the "zig-zag Model". However, this model is being re-evaluated because it is not consistent with the complexity of the interaction. Current models propose a holistic view of a process where the response is not always determined by the interaction of two molecules. This review discusses the main aspects related to qualitative responses in the plant-pathogen interaction and the new proposed models.

RESUMEN

Palabras claves:

Resistencia hospedero
Resistencia no
hospedero
Modelo zig-zag
PTI
ETI
ETS

Los patógenos atacan las plantas en un intento de asimilar los nutrientes de éstas. Todas las especies de plantas han tenido éxito para superar el ataque de patógenos, tanto que la condición de enfermedad no es la norma sino la excepción. Una batalla co-evolutiva ha dotado a las plantas con mecanismos de defensa sofisticados y a los patógenos afines con un arsenal correspondiente para superar dichas respuestas de defensa. Tradicionalmente, la interacción planta-patógeno se ha asociado a las moléculas que están involucradas en los procesos de reconocimiento, permitiendo el desarrollo de modelos que explican esta interacción, como el "Modelo zig-zag". Sin embargo, éste modelo está siendo revaluado debido a que no es consistente con la complejidad de la interacción. Los modelos actuales proponen una visión holística de un proceso en el que no siempre la respuesta va estar determinada por la interacción de dos moléculas. Esta revisión discute los principales aspectos relacionados con la respuesta cualitativa en la interacción planta-patógeno y los nuevos modelos biológicos propuestos.

¹ Corporación Centro de Investigaciones de Palma de Aceite, Cenipalma. AA 252171, Bogotá, Colombia.

² Facultad de Ciencias. Universidad Nacional de Colombia. AA 055051, Bogotá, Colombia

* Corresponding author <hmromeroa@unal.edu.co>

Plant diseases are a constant threat to agricultural production and thus to food security generating economic losses around the world. Pathogens that cause disease in plants include viruses, fungi, oomycetes, protozoa and nematodes (Pais *et al.*, 2013; Bigeard *et al.*, 2015). Traditionally the insects are excluded from this list; Agrios (2005), did not include them, but, actually the insects have been incorporated in the list of pathogens because there are evidences that the damage caused by insects could trigger a defense response similar to the one produced by common pathogens (Bever *et al.*, 2015; Conrath *et al.*, 2015; Stuart, 2015).

Global food security involves: food availability (production), access to food, and its utilization (for example nutritional aspects). At the same time, food security, presents a major imbalance in terms of growth and demand for food and world population. Thus, crop protection in terms of control of pests and diseases is a feasible strategy to reach the goals for food security (Savary *et al.*, 2012, Matthews *et al.*, 2013; Poppy *et al.*, 2014).

The traditional approach to control and respond to plant diseases has involved the use of pesticides, which, apart from the cost to the environment and human health, is not always able to reduce the incidence of the disease. Therefore, even with the application of pesticides, crop losses continue to occur, causing high production costs,

poor quality of products, and higher costs for the end consumer (Godfray *et al.*, 2010; Ronald, 2011; Fu and Dong, 2013; Lapin and Van den Ackerveken, 2013; Li *et al.*, 2013).

Due to the population growth estimated to reach 9 billion by 2050, the demand for food is high and so it is necessary to develop new varieties able to produce under limiting conditions such as high temperatures, water deficit, salinity and biotic stresses (Ronald, 2011; Mba *et al.*, 2012).

Climate change will have a direct impact on the incidence of pests and diseases of crops -affecting between 12% and 13% of crop yields. Bebbber and Gurr (2015), suggest that it is necessary to build a general framework for understanding the dynamics of plant communities at the large-scale, in order to generate predictions of change in plant communities over time. Such a framework would need to incorporate the environmental dependence of plant-pathogen interactions and plant-pathogen coevolution. These two features are particularly important in the face of climate change.

For example, in Colombia, in crops such as coffee, the increasing drought periods have been responsible for outbreaks in pests like the berry borer (Mba *et al.*, 2012). The following table shows some important diseases in different crops in Latin America to 2013.

Table 1. Principal diseases that affect important crops in Latin America.

Organisms	Scientific name/ Name of the disease	Affected crop
Fungus	<i>Hemileia vastatrix</i> /Coffee leaf rust	Coffee*
	<i>Phakopsora pachyrhizi</i> / Rust	Soybean
	<i>Mycosphaerella fijiensis</i> / Sigatoka negra	Banana*
	<i>Moniliophthora roreri</i> / Frosty pod rot	Cacao*
Oomycetes	<i>Phytophthora palmivora</i> /Bud rot	Oil Palm*
	<i>Phytophthora ramorum</i> / Sudden Oak death	Oak
Bacteria	<i>Burkholderia glumae</i> /Panicle blight	Rice*
	<i>Candidatus Liberibacter americanus</i> /Yellow Shoot or HLB	Citrics
Virus	Barley yellow dwarf luteoviruses (BYDV)	Wheat
	Banana bunchy top nanovirus (BBTV)	Banana
	Tomato yellow leaf curl begomovirus (TYLCV)	Tomato

*Diseases present in Colombia

Latin America is a highly diverse region in its ecosystems and the future of the biodiversity, and its associated ecological services depend on the ability to find a balance between conservation and development goals (Balvanera *et al.*, 2012; Mujica and Kroschel, 2013; Lee *et al.*, 2014; Bebbler and Gurr, 2015). In the case of Colombia, 37.3% of its area has an agricultural use, however, under a climate change scenario new diseases and pests would emerge and it is necessary to find alternative strategies for crop health management.

Genetic breeding is an old agricultural activity; humankind has domesticated plants and animals to increase yields and productivity. The main target for breeding has been the increase in production, and to achieve it, the effective control of pests and diseases is mandatory. Conventional breeding takes a long time to obtain an improved variety, however, techniques as induced mutagenesis or transgenesis have had a big impact on the production of crops, by speeding up the breeding process, and the production of new varieties through these non-conventional methods. Unfortunately, technical, economical and society problems are imposing new challenges for the use of these biotechnological tools for producing the new varieties.

Genome editing has emerged as a new tool of low cost, low environmental impact and high effectiveness to improve the quality of crop production. However, as in the traditional biotechnology (mutagenesis, transgenesis) one important requirement is the knowledge of the metabolic networks, and the identification of specific targets (genes) (Ma *et al.*, 2015; Quetier, 2016). There are numerous publications on genome editing (this review does not seek to cover them), but again, for the specific case of resistant to diseases, it is necessary to continue the efforts to understand the plant-pathogen relationships and to identify the key players (genes) on the pathogenicity (pathogen side) and resistance (plant side) (Beljah *et al.*, 2015).

This review will focus on the molecular response of plants to the presence of a pathogen, describing the molecular aspects of qualitative resistance. The models proposed to date are also discussed due to the high complexity of the biology of plant-pathogen interactions.

The plant immune system

Plant-pathogen interactions can be considered as a two-

way communication processes in which not only the plant is able to recognize a foreign organism and defend itself from it, but the pathogen must also be able to manipulate the biology of the plant to create an optimal environment for its own growth and development avoiding the plant response (Pritchard and Birch, 2011; Smale, 2012; Boyd *et al.*, 2013; Kushalappa *et al.*, 2016).

Plants, unlike animals, lack a defined immune system. They rely on the innate immunity of each cell and the systemic signals occurring at infection sites (Schulze-Lefert and Panstruga, 2011; Bonardi *et al.*, 2012; Lapin and Van den Ackerveken, 2013). However, with the particular characteristics of the plant defense system, the molecular mechanisms used by these organisms are similar to animals (Zipfel, 2014; Chiang and Coaker, 2015; Keller *et al.*, 2016).

Plant pathogens, in general, are divided into biotrophic and necrotrophic pathogens, although there is a third group, called hemibiotrophic (Spoel and Dong, 2012; Okmen and Doehlemann, 2014). The difference between these groups lies in their lifestyle. Biotrophic pathogens obtain their nutrients from living host tissue, while necrotrophic pathogens obtain their nutrients from dead host tissue, and for this reason the mechanisms used by each kind of pathogens to infect a plant is different (Koeck *et al.*, 2011; Lai and Mengiste, 2013).

Hemibiotrophic pathogens combine two strategies; they have an initial phase -biotrophic- in which the pathogen must evade the recognition from the host. This phase is followed by a necrotrophic stage in which toxins are secreted by the pathogen to induce host cell death; typically the visual symptoms start in this phase. Because of the presence of the asymptomatic biotrophic phase, the infection process with hemibiotrophic pathogens is difficult to understand and describe (Lee and Rose, 2010; Koeck *et al.*, 2011; Vleeshouwers and Oliver, 2014).

The genetic basis of plant resistance to pathogens is divided into qualitative resistance (monogenic resistance) and quantitative resistance (polygenic resistance) (Lopez, 2011). Qualitative resistance can be explained by the *gene-for-gene* model proposed in the fifties by Flor (1971), who determined the basis of inheritance of resistance to flax rust in flax cultivars. According to the type of interaction

with the pathogen, plant responses at the molecular level are divided into two types: i) non-host response and ii) host response. These two types of responses which differ mainly by the molecule type (both from the plant and the pathogen), involved in the process (Maekawa *et al.*, 2011; Schmidt and Panstruga, 2011; Li *et al.*, 2013) will be explained in the next two sections.

Non-host resistance

Non-host resistance, is defined as the event where a plant species in particular is resistant to different kind of pathogens (either bacteria, fungi, oomycetes, or viruses) but, these same pathogens can infect other plant species (Bent and Mackey, 2007; Fan and Doerner, 2012; Bellincampi *et al.*, 2014).

This response spectrum is caused by specific recognition processes between pathogen molecules called MAMPs (microbe-associated molecular patterns), which are recognized by PRR-type (pattern recognition receptors) membrane receptor proteins. PRR structures are types of receptor-like kinases (RLKs) that have functional modular domains (Beck *et al.*, 2012; Monaghan and Zipfel, 2012; Wu *et al.*, 2014a). However, MAMPs are molecules involved not only in the pathogenesis process; most of them, in fact, have been described as essential components of the cell, such as flg22. There are other types of MAMPs such as the HAMPs (herbivore-associated molecular patterns) and the DAMPs (damage-associated molecular patterns; originally called endogenous elicitors), but in general most literature talk about MAMPs to refer to this kind of molecules (Conrath *et al.*, 2015).

The molecular response triggered by the recognition of MAMPs is known as PTI (*PAMP-triggered immunity*) in which some molecular mechanisms associated with PTI include: production of ROS, Ca^{+2} cascades, and the activation of MAPK (*mitogen-activated protein kinases*) cascades, involving Ca^{+2} -dependent proteins that ultimately lead to transcriptional reprogramming (Bernoux *et al.*, 2011; Uma *et al.*, 2011; Yoshioka *et al.*, 2011; Bigeard *et al.*, 2015; Trapet *et al.*, 2015). Well-known case-studies include the following:

Bacterial PAMPs

- FLS2 receptor (receptor-like kinase flagellin sensing 2) of *Arabidopsis thaliana* that interacts specifically

with the oligopeptide flg22 of Gram-negative bacteria (Lu *et al.*, 2010; Albrecht *et al.*, 2012; Wang, 2012).

- EFR receptor (*Ef-Tu receptor*) recognizes the oligopeptide elf18. A particular characteristic that has been described only for plant species of the *Brassicaceae* family (Beck *et al.*, 2012; Wang, 2012).
- Receptor XA21: Identified in rice, associated with specific resistance to various bacterial strains of the *Xanthomonas oryzae* pv. *oryzae* species (Lee *et al.*, 2009).

Fungal and oomycetes PAMPs

- CeBIP and CERK1 receptor: LysM domains were initially identified as carbohydrate-binding domains in bacteria (Monaghan and Zipfel, 2012). Evidence that these domains (LysM- RLKs) are involved in PTI activity come from their identification in rice (CeBIP) and in *Arabidopsis* (CERK1) (Miya *et al.*, 2007; Macho and Zipfel, 2014), where these domains bind together and specifically recognize chitin fragments.
- EiX1 and EiX2 receptors: EIX (*ethylene-inducing xylanase*) proteins which induce ethylene synthesis and PR (*pathogen-related proteins*) gene expression, are plant elicitors identified in tobacco and tomatoes. Their action is associated with a HR response (Ron and Avni, 2004).
- Cf-9: identified in tomato was the first protein LRR-RLP and confers resistance to the fungus *Cladosporium fulvum*.

In the case of oomycetes, the PAMPs and the PRR have not been described yet. There are reports with some approximations like the soluble beta- glucan-binding protein (GBP) from soybean (*Glycine max*) that recognizes heptaglucosides from the oomycete *Phytophthora sojae*. Additionally, other PAMPs have been identified that can trigger immune signaling in fungi or oomycetes. For example, plants can recognize fungal ergosterol and other oomycete PAMPs including arachidonic acid, elicitors, the transglutaminase-derived immunogenic epitope Pep13. However, in all of these cases, the PRR proteins have not been identified so far (Zipfel, 2014).

This first line of defense response is usually effective against some pathogens, however, the pathogen has adapted its molecular infection mechanisms to evade or suppress the PTI, secreting proteins (called effectors), that

trigger what is known as a host resistance mechanism (Monaghan and Zipfel, 2012; Couto and Zipfel, 2016). This plant-pathogen interaction has been explained by the zig-zag Model proposed by Jones and Dangl (2006) which suggests a co-evolutionary response process involving two plant immunity branches (PTI and ETI) and a transition phase (ETS). The details about this model will be described in the final section.

In addition to the mechanisms of PTI previously described, new evidence suggests that plants also use RNA silencing mechanisms as a defense mechanism. In this case, the plant has specific miRNA sequences that regulate gene expression and defend cells against invasive “nucleic acids”, whether they are transposons, transgenes or viruses (Zvereva and Pooggin, 2012).

The first miRNA identified to be involved in PTI was miR393 in *Arabidopsis thaliana* in response to *Pseudomonas syringae*. miR393 is induced by flg22 and then suppresses auxin signaling by negatively regulating mRNAs of auxin receptors, transport inhibitor response 1 (TIR1), AFB2 and AFB3, which allow plants to prioritize defense signaling over plant growth, and trigger a series of defense responses. The role of miRNAs in PTI has also been demonstrated in fungal and oomycete infection, for example, osa-miR7695 was found to accumulate in rice treated with blast fungal mycelia (Fei *et al.*, 2016; Huang, 2016).

Host resistance

Molecular events during ETI (effector-triggered immunity) processes overlap with PTI. This branch of plant immunity occurs within the cell and originates once the host recognizes the effectors secreted by the pathogen, in which plant resistance (R) proteins can perceive these effectors initiating a defense response, including oxidative burst, accumulation of hormones such as salicylic acid (SA) and NOI (nitrogen oxide), MAPK cascades, changes in calcium levels, transcriptional reprogramming and synthesis of antimicrobial compounds, expression of *pathogenesis related* (PR) genes (Hein *et al.*, 2009; Coll *et al.*, 2011; De Bruyne *et al.*, 2014; Stael *et al.*, 2015).

Depending on the type of pathogen, the plant can induce programmed cell death (PCD) processes, also termed hypersensitive response (HR). These processes seek to block the advance of biotrophic pathogens to avoid

an infection in different host tissues. In this process, chloroplasts play a key role in the production of ROS-type molecules and NOI (Robert-Seilantantz *et al.*, 2007; Lopez, 2011; Presti *et al.*, 2015). For necrotrophic pathogens, the plant cell wall is the first line of defense providing a dynamic interface for interaction with necrotrophic pathogens. The interaction includes serving as a rich source of carbohydrates for the growth of pathogens; acting as a physical barrier to restrict the progression of the pathogens, and playing a role as an integrity sensory system that can activate intracellular signaling cascades in which plant hormones like jasmonic acid (JA) and ethylene (ET) play a major role in the defense response against these pathogens (Vleesschauwer *et al.*, 2014).

R proteins and activation

R proteins recognize effectors and activate the defense-signaling network (Hogenhout *et al.*, 2009; Song *et al.*, 2009; Gururani *et al.*, 2012). Generally, this type of resistance confers complete and specific resistance; that is why it is also called race-specific resistance (de Jonge *et al.*, 2011; Saintenac *et al.*, 2013). The R proteins are codified by NB-LRR genes, one of the largest and most variable gene families found in plants (Collier and Moffett, 2009).

Most R proteins belong to a subgroup of a family of proteins called STAND (*signal transduction ATPase with numerous domains*). NBS-LRR (*nucleotide-binding site; leucine rich repeats*) proteins that are subdivided into two subclasses depending on their N-terminal domain, -TIR- (*Toll/Interleukin-1 receptors*) domain or -CC- (*coiled coil*) domain, and are known as NBS-LRR-TIR and NBS-LRR-CC, respectively (Marone *et al.*, 2013; Wu *et al.*, 2014a).

For signaling, the NBS-LRR-CC proteins generally required a GPI anchored protein named non-race specific disease resistance 1, while NBS-LRR-TIR proteins require an enhanced disease susceptibility 1 for signaling. Additionally, the NBS-LRR-CC proteins are found in dicots and monocots whereas NBS-LRR-TIR are restricted to dicots (Chiang and Coaker, 2015; Cui *et al.*, 2015). The mechanism that activates R proteins and the subsequent signaling cascade in ETI is still being debated. Related to recognition, the simplest model is the direct interaction model in which there is a physical interaction between the pathogen effector and the R protein. An example of this mode of interaction

occurs between the pita CC-NB-LRR immune receptor in rice and the AvrPita effector of the fungus *Magnaporthe grisea* (Liu *et al.*, 2011).

There are no particular characteristics that distinguish the way in which these proteins can sense different classes of pathogens (Collier and Moffett, 2009). However, the recognition process could be modeled in a more complex way through an indirect recognition. This form of recognition has led to the development of alternative recognition models:

Guard hypothesis. The guard hypothesis suggests that R proteins can detect changes or alterations caused by the effector to the host “guard” protein. One of the cases reported for this model corresponds to the RIN4 (*RPM1 interacting protein 4*) protein of *A. thaliana*, which is associated with two CC-NB-LRR-RMP1 and RPS2-type proteins. RIN4 is the target protein for AvrRpm1 and Avrpt2 effectors which, because of their protease activity, induce cleavage of RIN4, and this cleavage is detected by R proteins (Caplan *et al.*, 2008; Van der Hoorn and Kamoun, 2008).

Decoy hypothesis. The “decoy” protein mimics the pathogen effector target, so the decoy functions mainly to restrict the pathogen but is not involved in the immune response (van der Hoorn and Kamoun, 2008). This model has been discussed mainly from the evolutionary point of view, it is expected that in the presence of the *R gene*, natural selection favors the decoy protein, but in the absence of the *R gene*, natural selection will cause the protein to decrease its affinity for the effector (Saintenac *et al.*, 2013; Wu *et al.*, 2015). Van der Hoorn and Kamoun (2008), explain the new model and offer four study cases to explain the model as follows:

Plant-pathogen interaction models

As we previously explained, each immunity branch has specific molecules, but, knowing the molecules and the process that produce them is not the only information that we need to understand the plant immunity. The next section provides information about the zig-zag model that until today is still the most accepted model. However, there are updated or new versions of the model.

Zig-zag model. In the most basic interaction, the zig zag model involves an interaction between the pathogen and

the host. The interaction can be divided in four phases:

- Phase 1: plants detect MAMPs via PRRs to trigger PAMP-triggered immunity (PTI).
- Phase 2: successful pathogens deliver effectors that interfere with PTI, resulting in effector-triggered susceptibility (ETS).
- Phase 3: an effector can be recognized by an NB-LRR protein, activating effector-triggered immunity (ETI), which after surpassing a defined threshold induces hypersensitive cell death (HR).
- Phase 4, pathogen strains that have lost certain effector are selected. They might have also gained a new set of effectors to respond to the plant defense.

This model is being reevaluated, as some authors argue that describing a pathosystem as a model of interaction between molecules is a reductionist view of a process that is clearly highly complex. Other authors express concerns regarding the confusion that could arise from the terms of avirulence genes, virulence genes and effectors (Cook *et al.*, 2014; Pritchard and Birch, 2014). The intent of this debate is not to invalidate any model, but to draw attention to certain issues discussed in the opinion article by Pritchard and Birch (2014), who describe six limitations of the zig-zag Model:

1. Molecular approach: It does not include DAMP. Therefore, it is suggested that the model is restricted to interactions with biotrophic pathogens.
2. Environmental context: By excluding the environmental factor it eliminates the effects of the interaction of the environment with the species that could affect the activation or suppression of molecular processes.
3. Organization of interaction events: The authors suggest that interaction events do not occur in organized phases, but, on the contrary, they can be stochastic processes.
4. Timescale: A model without a timescale does not allow for an adequate explanation of Phase 4 of the model (Phase 4: Gain / loss of effectors).
5. Physical scale: As in point 4 above, there is no population context to which it must be subjected for the gain or loss of effectors.
6. Qualitative model

Authors like Fei and collaborators (2016) have completed the 4 phases of the model introducing the effect that miRNAs have on the response of ITP and TSI. For example, miR393, which targets genes that are involved

in auxin signaling (TIR1, AFB2, and AFB3) is induced upon treatment with flg22. The repression of auxin signaling during infection enhances host PTI by hormone crosstalk. Effectors from pathogens can suppress the levels of plant miRNAs, such as miR393, to enhance susceptibility. However, the miR482 family, a negative regulator of plant Resistance (R) genes, can also be repressed upon detection of effectors to enhance effector-triggered immunity (ETI). Thus, although the zig-zag model is still maintained in its most basic sense as far as lines of defense are concerned, nevertheless, it is accepted that depending on the pathosystem, the model could have more components and could be updated if necessary.

Invasion model. This model was proposed by Cook *et al.* (2015), the authors took into consideration some limitations of the zig zag model such as: the model is restricted in terms of what microbe-associated molecule patterns (MAMPs) the plants can perceive through pattern recognition receptors (PRRs).

The invasion model has been explained in a similar way than the the zig-zag model, except in the aspects related to the definition of the immunogenic molecules. The authors suggest that these molecules must be represented as a continuum, and they argue that these molecules play other roles beyond the pathogenicity. Thus, the evolution can affect these molecules and have effects in an interaction model. In this sense, if a molecule has a role in a different process some evolutive forces can alter them, producing changes in the interaction process or even in the fitness of the species.

Multicomponent model. The model was proposed by Andolfo *et al.* (2016). Like in the previous model, the authors start showing the disadvantages of the zig-zag model such as the fact that the model only describes two perception layers (PTI and ETI).

The multicomponent model has two components: activation and modulation, and it is divided in three phases as follows:

- 1) Interaction: two principal effects are detected: i) modifications of virulence factor targets and ii) specific alterations of primary plant metabolism.
- 2) Activation: modifications of virulence factor targets

induce the Nibblers Triggered Signaling (NTS) or PPRs Triggered Signaling (PTS), mediated by R-genes activation. Metabolic alterations induce a feedback regulation of primary metabolic pathways resulting in a Hormone Tempered Resistance (HTR).

- 3) Modulation or effective resistance stage, the NTS/PTS, and the HTR converge to confer a resistance specific to the lifestyle of pathogen (Pathogen lifestyle-Specific Resistance, PSR).

In this case, the authors try to emphasize that the model will be determined specifically by the pathogen's life cycle. On the other hand, this model is in certain way connected with a new approach in which R genes and effectors are described like independent molecules, in a way that better articulate all the plant-pathogen related information for using molecular techniques to open a new era in crop breeding.

The two last models do not pretend to invalidate the original zig-zag model; the idea with these new perspectives is to bring a new concept in plant immunity with a holistic vision of a process that is not only related to a molecular interaction. Also, the model try to take into account other aspects that can affect the fitness of the pathogen and the host.

Final considerations

The advent of omics technologies has introduced a new and wide range of identification tools not only for one gene but also for areas of the genome that are associated with the pathogen response and the pathogen's effectors (Brauer *et al.*, 2014; Vayssier-Taussat *et al.*, 2014; Thynne *et al.*, 2015). Genomic studies should focus on identifying these areas of the genome, as they allow for visualizing the plant's response mechanisms and even making predictions about the evolution of these areas.

In silico approaches allow generating different views, not only at the species level but also at the population level, to describe, based on genome information, the evolution of plants to achieve durable resistance to diseases (Burdon and Thrall, 2014; Karasov *et al.*, 2014; Knief, 2014; Brown, 2015).

As mentioned at the beginning of this review, the growing demand for food production is generating new challenges

to maintain crop production rates. Different authors suggest that genome editing technologies will allow to introduce or modify characteristics of interest that ensure high quality productions and quantity of different crops (Andolfo *et al.*, 2016; Baltes and Voytas, 2015; Hendel *et al.*, 2015; Kole *et al.*, 2015).

Three mechanisms for genome editing are recognized: ZFN (Zinc Finger Nucleases), TALEN (TAL effector nucleases) and CRISPR/Cas9. These technologies seek to modify the genome introducing DBS (double strand breaks), under the control of specific nucleases, such action may cause deletions, insertions or modifications in the genome that can result from the DNA repair mechanisms NHEJ (Non-homologous end joining) and HR (Homologous recombination) (Huang *et al.*, 2016; Mahesh, 2016; Nagamangala *et al.*, 2015; Weeks *et al.*, 2016).

CRISPR/Cas9 is currently proposed as a simple and useful alternative for genome editing, since it allows the modification of multiple sites along the genome. Several case studies have been reported in plants using this technology (Fauser *et al.*, 2014; Jia and Nian, 2014; Lowder *et al.*, 2015; Shan *et al.*, 2014). Weeks and collaborators (2014) present a complete review of the different case studies that have been developed in species such as *Arabidopsis thaliana*, wheat and rice using CRISPR-Cas9 technology, and it is expected that soon more and more advances in the breeding for disease resistance will come from the use of this technology.

The information available on plant-pathogen interactions has raised many questions. Certain questions are focused on the “simplicity” with which these very diverse mechanisms have been described, as we can see in the new models mentioned. The dynamic and comprehensive approach is what is now referred to as biological dynamic networks, where different aspects of the model, even evolutionary aspects, must be taken account (Pritchard and Birch, 2011; Niks *et al.*, 2015).

According to Vleesschauwer *et al.* (2014), studies in rice are providing new insights, often revealing unique complexities, for this reason the description of a biological process is not only related to the molecules per se, it is necessary to analyze the organism to describe how these plant-pathogen

relationships can modulate the interaction in a niche and in a population.

REFERENCES

- Albrecht C, Boutrot F, Segonzac C, Schwessinger B, Gimenez-Ibanez S, Chinchilla D, Rathjen JP, de Vries SC and Zipfel C. 2012. Brassinosteroids inhibit pathogen-associated molecular pattern-triggered immune signaling independent of the receptor kinase BAK1. *Proceedings of the National Academy of Sciences* 109(1): 303–308. doi: 10.1073/pnas.1109921108.
- Andolfo G, Iovieno, P, Frusciante L and Ercolano M. 2016. Genome-Editing Technologies for Enhancing Plant Disease Resistance. *Frontiers in Plant Science* (December): 1813. doi: org:10.3389/fpls.2016.01813
- Baltes N and Voytas D. 2015. Enabling plant synthetic biology through genome engineering. *Trends in Biotechnology* 33(2): 120–131. doi: 10.1016/j.tibtech.2014.11.008
- Balvanera P, Uriarte M, Leñero L, Altesor A, DeClerck G, Hall J, Lara A, Lateral P, et al. 2012. Ecosystem services research in Latin America: The state of the art. *Ecosystem Services* 2:56-70. doi: 10.1016/j.ecoser.2012.09.006
- Bebber D and Gurr S. 2015. Crop-destroying fungal and oomycete pathogens challenge food security. *Fungal Genetics and Biology* 74:62-64. doi: 10.1016/j.fgb.2014.10.012
- Beck M, Heard W, Mbengue M and Robatzek S. 2012. The INs and OUTs of pattern recognition receptors at the cell surface. *Current Opinion in Plant Biology* 15(4): 367–374. doi: 10.1016/j.copbi.2012.05.004.
- Beljah K, Chaparro A, Kamoun S, Patron N, and Nekrasov V. 2015. Editing plant genomes with CRISPR/Cas9. *Current Opinion in Biotechnology* 32:76-84. doi: 10.1016/j.copbi.2014.11.007
- Bellincampi D, Cervone F and Lionetti V. 2014. Plant cell wall dynamics and wall-related susceptibility in plant-pathogen interactions. *Frontiers in Plant Science* 5: 228. doi: 10.3389/fpls.2014.00228.
- Bent AF and Mackey D. 2007. Elicitors, effectors, and R genes: the new paradigm and a lifetime supply of questions. *Annual Review of Phytopathology* 45: 399–436. doi: 10.1146/annurev.phyto.45.062806.094427.
- Bernoux M, Ellis JG and Dodds PN. 2011. New insights in plant immunity signaling activation. *Current Opinion in Plant Biology* 14(5): 512–518. doi: 10.1016/j.copbi.2011.05.005.
- Bever JD, Mangan SA and Alexander HM. 2015. Maintenance of Plant Species Diversity by Pathogens. *Annual Review of Ecology, Evolution, and Systematics*, 46(1): 305–325. doi: 10.1146/annurev-ecolsys-112414-054306
- Bigeard J, Colcombet J and Hirt H. 2015. Signaling mechanisms in pattern-triggered immunity (PTI). *Molecular Plant* 8(4): 521–539. doi: 10.1016/j.molp.2014.12.022.
- Bonardi V, Cherkis K, Nishimura MT and Dangl JL. 2012. A new eye on NLR proteins: focused on clarity or diffused by complexity. *Current Opinion in Immunology* 24(1): 41–50. doi: 10.1016/j.coi.2011.12.006.
- Boyd LA, Ridout C, O'Sullivan DM, Leach JE and Leung H. 2013. Plant-pathogen interactions: disease resistance in modern agriculture. *Trends in Genetics* 29(4): 233–240. doi: 10.1016/j.tig.2012.10.011.

- Brauer EK, Singh DK and Popescu SC. 2014. Next-generation plant science: putting big data to work. *Genome Biology* 15(1): 301. doi: 10.1186/gb4149.
- Brown JK. 2015. Durable resistance of crops to disease: a Darwinian perspective. *Annual Review of Phytopathology* 53: 513–539. doi: 10.1146/annurev-phyto-102313-045914.
- Burdon JJ and Thrall PH. 2014. What have we learned from studies of wild plant-pathogen associations?—the dynamic interplay of time, space and life-history. *European Journal of Plant Pathology* 138(3): 417–429. doi: 10.1007/s10658-013-0265-9.
- Caplan JL, Mamillapalli P, Burch-Smith TM, Czymbek K and Dinesh-Kumar SP. 2008. Chloroplastic protein NR1P1 mediates innate immune receptor recognition of a viral effector. *Cell* 132(3): 449–462. doi: 10.1016/j.cell.2007.12.031.
- Chiang, Y.-H., & Coaker, G. (2015). Effector triggered immunity: NLR immune perception and downstream defense responses. *The Arabidopsis Book*, 13, e0183. doi: 10.1199/tab.0183
- Coll NS, Epple P and Dangl JL. 2011. Programmed cell death in the plant immune system. *Cell Death and Differentiation* 18(8): 1247–1256. doi: 10.1038/cdd.2011.37.
- Collier SM and Moffett P. 2009. NB-LRRs work a “bait and switch” on pathogens. *Trends in Plant Science* 14(10): 521–529. doi: 10.1016/j.tplants.2009.08.001
- Cook DE, Mesarich CH and Thomma BP. 2015. Understanding plant immunity as a surveillance system to detect invasion. *Annual Review of Phytopathology* 53: 541–563. doi: 10.1146/annurev-phyto-080614-120114.
- Conrath U, Beckers GJM, Langenbach CJG and Jaskiewicz MR. 2015. Priming for enhanced defense. *Annual Review of Phytopathology*, 53(JUNE): 97–119. doi: 10.1146/annurev-phyto-080614-120132
- Couto D and Zipfel C. 2016. Regulation of pattern recognition receptor signalling in plants. *Nature Reviews Immunology* 16: 537–552. doi: 10.1038/nri.2016.77
- Cui H, Tsuda K and Parke, JE. 2015. Effector-Triggered Immunity: from pathogen perception to robust defense. *Annual Review of Plant Biology* 66: 487–511. doi: 10.1146/annurev-arplant-050213-040012
- De Bruyne L, Höfte M and De Vleeschauwer D. 2014. Connecting growth and defense: the emerging roles of brassinosteroids and gibberellins in plant innate immunity. *Molecular Plant* 7(6): 943–959. doi: 10.1093/mp/ssu050.
- De Jonge R, Bolton MD and Thomma BPHJ. 2011. How filamentous pathogens co-opt plants: the ins and outs of fungal effectors. *Current Opinion in Plant Biology* 14(4): 400–406. doi: 10.1016/j.pbi.2011.03.005.
- Fan J and Doerner P. 2012. Genetic and molecular basis of nonhost disease resistance: complex, yes; silver bullet, no. *Current Opinion in Plant Biology* 15(4): 400–406. doi: 10.1016/j.pbi.2012.03.001.
- Fausser F, Schimi S and Puchta H. 2014. Both CRISPR/Cas-based nucleases and nickases can be used efficiently for genome engineering in *Arabidopsis thaliana*. *Plant Journal* 79(2): 348–359. doi: 10.1111/tpj.12554
- Fei Q, Zhang Y, Xia, R and Meyers B. 2016. Small RNAs add zing to the zig-zag model of plant defenses. *MPMI*. 29(3):165-169. doi:10.1094/MPMI-09-15-0212-FI
- Flor HH. 1971. Current status of the gene-for-gene concept. *Annual Review of Phytopathology* 9(1): 275–296. doi: 10.1146/annurev.py.09.090171.001423.
- Fu ZQ and Dong X. 2013. Systemic acquired resistance: turning local infection into global defense. *Annual Review of Plant Biology* 64: 839–863. doi: 10.1146/annurev-arplant-042811-105606.
- Godfray HC, Beddington JR, Crute IR, Haddad L, Lawrence D, Muir JF, Pretty J, Robinson S, Thomas SM and Toulmin C. 2010. Food security: the challenge of feeding 9 billion people. *Science* 327(5967): 812–818. doi: 10.1126/science.1185383.
- Gururani MA, Venkatesh J, Upadhyaya CP, Nookaraju A, Pandey SK and Park SW. 2012. Plant disease resistance genes: current status and future directions. *Physiological and Molecular Plant Pathology* 78: 51–65. doi: 10.1016/j.pmp.2012.01.002.
- Hein I, Gilroy EM, Armstrong MR and Birch PR. 2009. The zig-zag-zig in oomycete-plant interactions. *Mol Plant Pathology* 10(4): 547–562. doi: 10.1111/j.1364-3703.2009.00547.x.
- Hendel A, Fine EJ, Bao G and Porteus MH. 2015. Quantifying on- and off-target genome editing. *Trends in Biotechnology* 33(2): 132–140. doi: 10.1016/j.tibtech.2014.12.001
- Hogenhout SA, Van der Hoorn RAL, Terauchi R and Kamoun S. 2009. Emerging concepts in effector biology of plant-associated organisms. *Molecular Plant-Microbe Interactions* 22(2): 115–122. doi: 10.1094/MPMI-22-2-0115.
- Huang S, Weigel D, Beachy RN and Li J. 2016. A proposed regulatory framework for genome-edited crops. *Nature Genetics*, 48(2): 109–111. doi: 10.1038/ng.3484
- Huang J, Yang M and Zhang X. 2016. The function of small RNA in plant biotic stress response. *Journal Of Integrative Plant Biology* 58(4): 312-327. doi: 10.1111/jipb.12463
- Jia H and Nian W. 2014. Targeted genome editing of sweet orange using Cas9/sgRNA. *PLoS ONE* 9(4). doi: 10.1371/journal.pone.0093806
- Jones JDG and Dangl JL. 2006. The plant immune system. *Nature* 444(7117): 323–329. doi: 10.1038/nature05286.
- Karasov TL, Horton MW and Bergelson J. 2014. Genomic variability as a driver of plant-pathogen coevolution. *Current Opinion in Plant Biology* 18: 24–30. doi: 10.1016/j.pbi.2013.12.003.
- Keller H, Boyer L and Abad P. 2016. Disease susceptibility in the zig-zag model of host microbe interactions: only a consequence of immune suppression?. *Molecular Plant Pathology*. 17(4):475-479. doi: 10.1111/mpp.12371
- Knief C. 2014. Analysis of plant microbe interactions in the era of next generation sequencing technologies. *Frontiers in Plant Science* 5: 216. doi: 10.3389/fpls.2014.00216.
- Koeck M, Hardham AR and Dodds PN. 2011. The role of effectors of biotrophic and hemibiotrophic fungi in infection. *Cell Microbiology* 13(12): 1849–1857. doi: 10.1111/j.1462-5822.2011.01665.x.
- Kole C, Muthamilarasan M, Henry R, Edwards D, Sharma R, Abberton M, ... Prasad M. 2015. Application of genomics-assisted breeding for generation of climate resilient crops: progress and prospects. *Front Plant Sci*, 6(August): 563. doi: 10.3389/fpls.2015.00563
- Kushalappa AC, Yogendra KN and Karre S. 2016. Plant Innate Immune Response: Qualitative and Quantitative Resistance. *Critical Reviews in Plant Sciences* 35(1): 38–55. doi: 10.1080/07352689.2016.1148980

- Lai Z and Mengiste T. 2013. Genetic and cellular mechanisms regulating plant responses to necrotrophic pathogens. *Current Opinion in Plant Biology* 16(4): 505–512. doi: 10.1016/j.pbi.2013.06.014.
- Lapin D and Van den Ackerveken G. 2013. Susceptibility to plant disease: more than a failure of host immunity. *Trends in Plant Science* 18(10): 546–554. doi: 10.1016/j.tplants.2013.05.005.
- Lee S-J and Rose JKC. 2010. Mediation of the transition from biotrophy to necrotrophy in hemibiotrophic plant pathogens by secreted effector proteins. *Plant Signaling & Behavior* 5(6): 769–772. doi: 10.4161/psb.5.6.11778.
- Lee SW, Han SW, Sriyanum M, Park CJ, Seo YS and Ronald PC. 2009. A type I-secreted, sulfated peptide triggers XA21-mediated innate immunity. *Science* 326(5954): 850–853. doi: 10.1126/science.1173438.
- Lee D, Edmeades S, Nys E, McDonald A and Janssen Y. 2014. Developing local adaptation strategies for climate change in agriculture: A priority-setting approach with application to Latin America. *Global Environmental Change* 29: 78–91. doi: 10.1016/j.gloenvcha.2014.08.002
- Li Y, Huang F, Lu Y, Shi Y, Zhang M, Fan J and Wang W. 2013. Mechanism of plant-microbe interaction and its utilization in disease-resistance breeding for modern agriculture. *Physiological and Molecular Plant Pathology* 83: 51–58. doi: 10.1016/j.pmp.2013.05.001.
- Liu J, Elmore JM, Lin Z-JD and Coaker G. 2011. A receptor-like cytoplasmic kinase phosphorylates the host target RIN4, leading to the activation of a plant innate immune receptor. *Cell Host & Microbe* 9(2): 137–146. doi: 10.1016/j.chom.2011.01.010.
- Lopez C. 2011. Descifrando las bases moleculares de la resistencia cuantitativa. *Acta Biologica Colombiana* 16(2): 3.
- Lowder LG, Zhang D, Baltes NJ, Paul JW, Tang X, Zheng X, ... et al. 2015. A CRISPR/Cas9 Toolbox for Multiplexed Plant Genome Editing and Transcriptional Regulation. *Plant Physiology* 169(2): 971–85. doi: 10.1104/pp.15.00636
- Lu D, Wu S, Gao X, Zhang Y, Shan L and He P. 2010. A receptor-like cytoplasmic kinase, BIK1, associates with a flagellin receptor complex to initiate plant innate immunity. *Proceedings of the National Academy of Sciences* 107(1): 496–501. doi: 10.1073/pnas.0909705107.
- Ma X, Zhang Q, Zhu Q, Liu W, Chen Y, Qiu R, Wang B et al. 2015. A Robust CRISPR/Cas9 System for Convenient, High-Efficiency Multiplex Genome Editing in Monocot and Dicot Plants. *Molecular Plant* 8(8): 1274–1284. doi: 10.1016/j.molp.2015.04.007
- Mahesh S. 2016. The State of Art of New Transgenic Techniques in Plant Breeding: A Review. *Journal of Advances in Biology & Biotechnology* 9(4): 1–11. doi: 10.9734/JABB/2016/27846
- Macho AP and Zipfel C. 2014. Plant PRRs and the activation of innate immune signaling. *Molecular Cell* 54(2): 263–272. doi: 10.1016/j.molcel.2014.03.028.
- Maekawa T, Kufer TA and Schulze-Lefert P. 2011. NLR functions in plant and animal immune systems: so far and yet so close. *Nature Immunology* 12(9): 817–826. doi: 10.1038/ni.2083.
- Marone D, Russo MA, Laidò G, De Leonardis AM and Mastrangelo AM. 2013. Plant nucleotide binding site-leucine-rich repeat (NBS-LRR) genes: active guardians in host defense responses. *International Journal of Molecular Science* 14(4): 7302–7326. doi: 10.3390/ijms14047302.
- Mba C, Guimaraes E and Ghosh K. 2012. Re-orienting crop improvement for the changing climatic conditions of the 21st century. *Agriculture & Food Security*. 1:7. doi: 10.1186/2048-7010-1-7
- Mattews, R., Rivington, M., Muhammed, S., Newton, A., Hallet, P., 2013. Adapting crops and cropping systems to future climates to ensure food security: The role of crop modelling. *Global Food Security*. 2(1): 24–28. doi: 10.1016/j.gfs.2012.11.009
- Miya A, Albert P, Shinya T, Desaki Y, Ichimura K, Shirasu K, Narusaka Y, Kawakami N, Kaku H and Shibuya N. 2007. CERK1, a LysM receptor kinase, is essential for chitin elicitor signaling in Arabidopsis. *Proceedings of the National Academy of Sciences* 104(49): 19613–19618. doi: 10.1073/pnas.0705147104.
- Monaghan J and Zipfel C. 2012. Plant pattern recognition receptor complexes at the plasma membrane. *Current Opinion in Plant Biology* 15(4): 349–357. doi: 10.1016/j.pbi.2012.05.006.
- Mujica N and Kroschel J. 2013. Pest intensity-crop loss relationships for the leafminer fly *Liriomyza huidobrensis* (Blanchard) in different potato (*Solanum tuberosum* L.) varieties. *Crop Protection* 6–16. doi: 10.1016/j.cropro.2012.12.019
- Nagamangala Kanchiswamy C, Sargent DJ, Velasco R, Maffei ME and Malnoy M. 2015. Looking forward to genetically edited fruit crops. *Trends in Biotechnology* 33(2): 62–64. doi: 10.1016/j.tibtech.2014.07.003
- Niks RE, Qi X and Marcel TC. 2015. Quantitative resistance to biotrophic filamentous plant pathogens: concepts, misconceptions, and mechanisms. *Annual Review of Phytopathology* 53: 445–470. doi: 10.1146/annurev-phyto-080614-115928.
- Okmen B and Doehlemann G. 2014. Inside plant: biotrophic strategies to modulate host immunity and metabolism. *Current Opinion in Plant Biology* 20: 19–25. doi: 10.1016/j.pbi.2014.03.011.
- Pais M, Win J, Yoshida K, Etherington GJ, Cano LM, Raffaele S, Banfield MJ, Jones A, Kamoun S and Saunders DG. 2013. From pathogen genomes to host plant processes: the power of plant parasitic oomycetes. *Genome Biology* 14(6): 211. doi: 10.1186/gb-2013-14-6-211.
- Poppy G, Jepson P, Pickett A and Birkett A. 2014. Achieving food and environmental security: new approaches to close the gap. *Philosophical Transactions of the Royal Society B* 369: 1–6. doi: 10.1098/rstb.2012.0272
- Presti L, Lanver D, Schweizer G, Tanaka S, Liang L, Tollot M, Zuccaro A, Reissmann S and Kahmann R. 2015. Fungal effectors and plant susceptibility. *Annual Review of Plant Biology* 66: 513–545. doi: 10.1146/annurev-arplant-043014-114623.
- Pritchard L and Birch P. 2011. A systems biology perspective on plant-microbe interactions: biochemical and structural targets of pathogen effectors. *Plant Science* 180(4): 584–603. doi: 10.1016/j.plantsci.2010.12.008.
- Pritchard L and Birch PR. 2014. The zigzag model of plant-microbe interactions: is it time to move on. *Molecular Plant Pathology* 15(9): 865–870. doi: 10.1111/mpp.12210.
- Quetier, F. 2016. The CRISPR-Cas9 technology: Closer to the ultimate toolkit for targeted genome editing. *Plant Science*. 242:65–76. doi: 10.1016/j.plantsci.2015.09.003
- Robert-Seilaniantz A, Navarro L, Bari R and Jones J. 2007. Pathological hormone imbalances. *Current Opinion in Plant Biology* 10(4): 372 – 379. doi: 10.1016/j.pbi.2007.06.003.

- Ron M and Avni A. 2004. The receptor for the fungal elicitor ethylene-inducing xylanase is a member of a resistance-like gene family in tomato. *Plant Cell* 16(6): 1604–1615. doi: 10.1105/tpc.022475.
- Ronald P. 2011. Plant genetics, sustainable agriculture and global food security. *Genetics* 188(1): 11–20. doi: 10.1534/genetics.111.128553.
- Saintenac C, Zhang W, Salcedo A, Rouse MN, Trick HN, Akhunov E and Dubcovsky J. 2013. Identification of wheat gene Sr35 that confers resistance to Ug99 stem rust race group. *Science* 341(6147): 783–786. doi: 10.1126/science.1239022.
- Savary A, Ficke A and Aubertot J. 2012. Crop losses due to diseases and their implications for global food production losses and food security. *Food Security*. doi: 10.1007/s12571-012-0200-5
- Schmidt SM and Panstruga R. 2011. Pathogenomics of fungal plant parasites: what have we learnt about pathogenesis. *Current Opinion in Plant Biology* 14(4): 392–399. doi: 10.1016/j.pbi.2011.03.006.
- Schulze-Lefert P and Panstruga R. 2011. A molecular evolutionary concept connecting nonhost resistance, pathogen host range, and pathogen speciation. *Trends in Plant Science* 16(3): 117–125. doi: 10.1016/j.tplants.2011.01.001.
- Shan Q, Wang Y, Li J and Gao C. 2014. Genome editing in rice and wheat using the CRISPR/Cas system. *Nature Protocols* 9(10): 2395–410. doi: 10.1038/nprot.2014.157
- Smale ST. 2012. Transcriptional regulation in the innate immune system. *Current Opinion in Immunology* 24(1): 51–57. doi: 10.1016/j.coi.2011.12.008.
- Song J, Win J, Tian M, Schormack S, Kaschani F, Ilyas M, van der Hoorn RAL and Kamoun S. 2009. Apoplastic effectors secreted by two unrelated eukaryotic plant pathogens target the tomato defense protease Rcr3. *Proceedings of the National Academy of Sciences* 106(5): 1654–1659. doi: 10.1073/pnas.0809201106.
- Spoel SH and Dong X. 2012. How do plants achieve immunity? Defence without specialized immune cells. *Nature Reviews Immunology* 12(2): 89–100. doi: 10.1038/nri3141.
- Stael S, Kmiecik P, Willems P, Van Der Kelen K, Coll NS, Teige M and Van Breusegem F. 2015. Plant innate immunity--sunny side up. *Trends in Plant Science* 20(1): 3–11. doi: 10.1016/j.tplants.2014.10.002.
- Stuart, 2015. Insect effectors and gene-for-gene interactions with host plants. *Current Opinion in Insect Science*. Vol 9: 56-61. doi: org/10.1016/j.cois.2015.02.010
- Thynne E, McDonald MC and Solomon PS. 2015. Phytopathogen emergence in the genomics era. *Trends in Plant Science* 20(4): 246–255. doi: 10.1016/j.tplants.2015.01.009.
- Trapet P, Kulik A, Lamotte O, Jeandroz S, Bourque S, Nicolas-Francès V, Rosnoblet C, Besson-Bard A and Wendehenne D. 2015. No signaling in plant immunity: a tale of messengers. *Phytochemistry* 112: 72–79. doi: 10.1016/j.phytochem.2014.03.015.
- Uma B, Rani TS and Podile AR. 2011. Warriors at the gate that never sleep: non-host resistance in plants. *Journal of Plant Physiology* 168(18): 2141–2152. doi: 10.1016/j.jplph.2011.09.005.
- Van der Hoorn RAL and Kamoun S. 2008. From guard to decoy: a new model for perception of plant pathogen effectors. *The Plant Cell* 20(8): 2009–2017. doi: 10.1105/tpc.108.060194.
- Vayssier-Taussat M, Albina E, Citti C, Cosson JF, Jacques MA, Lebrun MH, Le Loir Y, Ogliastro M, Petit MA, Roumagnac P and Candresse T. 2014. Shifting the paradigm from pathogens to pathobiome: new concepts in the light of meta-omics. *Frontiers in Cellular and Infection Microbiology* 4: 29. doi: 10.3389/fcimb.2014.00029.
- Vleeshouwers VG and Oliver RP. 2014. Effectors as tools in disease resistance breeding against biotrophic, hemibiotrophic, and necrotrophic plant pathogens. *Molecular Plant and Microbe Interactions* 27(3): 196–206. doi: 10.1094/MPMI-10-13-0313-IA.
- Vleeshouwers VG, Xu J., and Hofte. 2014. Making sense of hormone-mediated defense networking: from rice to Arabidopsis. *Frontiers in Plant Science*. Vol 5. Article 611. doi: 10.3389/fpls.2014.00611.
- Wang ZY. 2012. Brassinosteroids modulate plant immunity at multiple levels. *Proceedings of the National Academy of Sciences* 109(1): 7–8. doi: 10.1073/pnas.1118600109.
- Weeks DP, Spalding MH and Yang B. 2016. Use of designer nucleases for targeted gene and genome editing in plants. *Plant Biotechnology Journal* 14(2): 483–495. doi: 10.1111/pbi.12448
- Wu CH, Krasileva KV, Banfield MJ, Terauchi R and Kamoun S. 2015. The “sensor domains” of plant NLR proteins: more than decoys. *Frontiers in Plant Science* 6: 134. doi: 10.3389/fpls.2015.00134.
- Wu S, Shan L and He P. 2014a. Microbial signature-triggered plant defense responses and early signaling mechanisms. *Plant Science* 228: 118–126. doi: 10.1016/j.plantsci.2014.03.001.
- Wu L, Chen H, Curtis C and Fu, Z. Q. 2014b. Go in for the kill. *Virulence* 5(7): 710–21. doi: 10.4161/viru.29755
- Yoshioka H, Mase K, Yoshioka M, Kobayashi M and Asai S. 2011. Regulatory mechanisms of nitric oxide and reactive oxygen species generation and their role in plant immunity. *Nitric Oxide* 25(2): 216–221. doi: 10.1016/j.niox.2010.12.008.
- Zipfel C. 2014. Plant pattern-recognition receptors. *Trends in Immunology* 35(7). doi: 10.1016/j.it.2014.05.004
- Zvereva A and Poggin M. 2012. Silencing and Innate Immunity in Plant defense against viral and non-viral pathogens. *Viruses*. 4: 2578-2597. doi: 10.3390/v4112578