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Plant responses to pathogen attack: molecular basis of qualitative resistance

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

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ABSTRACT

Keywords:
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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 clave:
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.

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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, Mattews *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. Bebber 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	*Hemileia vastatrix /Coffee leaf rust*	Coffee*
	Phakopsora pachyrhizi / Rust	Soybean
	Mycosphaerella fijiensis / Sigatoka negra	Banana*
	Moniliophthora roreri/ Frosty pod rot	Cacao*
Oomycetes	*Phytophthora palmivora*/Bud rot	Oil Palm*
	Phytophthora ramorum/ Sudden Oak death	Oak
Bacteria	*Burkholderia glumae/Panicle blight*	Rice*
	Candidatus Liberibacter americanus /Yellow Shoot or HLB	Citrics
Virus	Barley yellow dwarf luteoviruses (BYDV)	Wheat
	Banana bunchy topo 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; Bebber 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 its 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 reprograming (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 fulvus).*

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, elicitins, 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 *pathogeneses 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-Seilaniantz *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.

Multicompent 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 it 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.

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