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RECOGNITION SYSTEM DURING HOST-PATHOGEN INTERACTION

Aparajita Dhar*, Pulak Bhaumik, M. Ranjana Devi

Department of Plant Pathology
Uttar Banga Krishi Viswavidyalaya, Pundibari, Cooch Behar
*Corrosponding Author: aparajitadhar94@gmail.com

Abstract

Depending upon the interaction between the host and pathogen during the process of pathogenesis mostly two types of resistance can be found viz., host resistance which are mostly governed by resistance genes and non-host resistance which are inducible and constitutive. Various signals are exchanged between the host and pathogen which leads to either virulence in pathogen or resistance in plants. Some of receptors such as PRRs in the host have the ability to recognize a wide range of microbial components, including fungal carbohydrates, bacterial proteins, and viral nucleic acids, apart from these other signalling compounds includes PAMPs and DAMPs. Different type of theories/hypothesis and models have been proposed in order to understand the signalling and recognition system during host pathogen interaction. However, there studies are limited to certain pathogen only, therefore more understanding and research is still needed in order to overcome the knowledge gap and for sustainable management of the pathogen.

Introduction

The potentiality to differentiate 'host' from 'non-host' plant is the most fundamental aspect of an immune system of plants. Basal resistance against several pathogens in plants is described by the term 'non-host resistance', is an evolutionarily ancient, multilayered resistance mechanism with inducible and constitutive components (Thordal-Christensen, 2003). Non-host resistance is active even in susceptible plants to restrict pathogen colonisation and is associated with the release of molecules like ligands or elicitors, which are derived from the pathogens and/or molecules such as oligogalacturonides and peptides, released by the host plant as endogenous elicitors, analogous to the 'danger signals' of the plant immune system (Matzinger, 2002). By contrast, host resistance referring to more recently evolved, acts within the species level and is controlled by polymorphic host genes, such as R (resistance) genes, the products of which interact, directly or indirectly, with secreted 'avirulence' proteins or effectors of the pathogen (Jones & Takemoto, 2004). The surface receptors detect both pathogen derived elicitors (pathogen-associated molecular patterns (PAMPs) if the molecule contains a conserved 'pattern') and avirulence effectors. They include receptor-like kinases (RLKs), receptor-like proteins (RLPs) and extracellular binding proteins that may form part of multicomponent recognition complexes. Intracellular receptors are the nucleotide-binding (NB), leucine-rich repeat (LRR) class of receptors for the detection of pathogen effectors (Altenbach & Robatzek, 2007; Tameling & Takken,). A signal transduction pathway for bacterial flagellin includes a LRR receptor kinase as well as a mitogen activated proteins (MAP) kinase cascade that activates defined transcription factors. (Rashid *et al.,* 2010).

Detection of pathogens

Investigation of the molecular basis of pathogen resistance shows a suite of cellular receptors that performs direct detection of pathogenic molecules. Pattern recognition receptors (PRRs) with in the cell membrane detect pathogen-associated molecular patterns (PAMPs) and wall-associated kinases (WAKs) detect damage-associated molecular patterns (DAMPs) that result from cellular damage during infection (Zipfel, 2014). Receptors with nucleotide-binding domains and leucine-rich

repeats (NLRs) are known to detect effectors that pathogens use to facilitate infection (Dangl *et al.,* 2013). PRRs, WAKs, and NLRs are responsible for initiation for one of many signalling cascades that have yet to be completely elucidated. Mitogen-activated protein kinases (MAPKs), G-proteins, calcium, ubiquitin, hormones, transcription factors (TFs), and epigenetic modifications operate the regulation of the expression of pathogenesis-related (PR) genes (Meng and Zhang, 2013). This leads to various responses preventing further infection by the pathogens: hypersensitive response (HR), Reactive Oxygen Species (ROS), cell wall modification, closure of stomata, or the production of various proteins and compounds that possess anti effect on pathogens (e.g., chitinases, protease inhibitors, defensins, and phytoalexins) (Juge,2006).

Detection of PAMPs and DAMPs by PRRs and WAKs

PRRs have the ability to recognize a wide range of microbial components, including fungal carbohydrates, bacterial proteins, and viral nucleic acids. These receptors often possess leucine-rich repeats (LRRs) which bind to extracellular ligands, transmembrane domains, necessary to localize in the plasma membrane, and cytoplasmic kinase domains for signal transduction through phosphorylation (Zipfel,2014). LRRs are highly divergent, associated with their ability to bind to different elicitors. Many PRRs depends on the regulatory protein brassinosteroid insensitive 1-associated receptor kinase 1 (BAK1) and other somatic embryogenesis receptor-like kinases (SERKs) (Monaghan and Zipfel, 2012). Extensive signalling is not always initiated, as some PRRs, upon activation, leads to the release of kinase domains that travel to the nucleus for triggering transcriptional reprogramming (Park and Ronald, 2012).

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). EFR receptor (Ef-Tu receptor) recognizes the oligopeptide elf18. 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 induce ethylene synthesis, gene expression and PR (pathogen-related proteins), 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.*

Wall-associated kinases (WAKs) detect damage-associated molecular patterns (DAMPs)

Unlike the PRRs, other receptors interpret damage by recognizing cellular components, disrupted by pathogenic enzymes. WAKs consists of an N-terminal, extracellular galacturonan-binding domain which interacts with pectins in the cell wall, and cytoplasmic kinase domains, similar to the structure of PRRs. WAK1 and WAK2 perceive oligogalacturonic acid, resulting from plant cell wall pectin degradation by fungal enzymes (Brutus *et al.,* 2010).

Plant lectins are capable of recognizing carbohydrates that originate directly from pathogens or from damage incurred during infection. Many PAMPs and DAMPs consist of carbohydrates (i.e.,

lipopolysaccharides, oligogalacturonides, peptidoglycans, and cellulose) and are recognized by PRRs/WAKs with lectin domains, such as lectin receptor kinases (Lannoo and Van Damme 2014). Plants detect many extracellular molecules that possess an indication of pathogen infection (Gust *et al.,* 2017), like extracellular DNA, ATP, and NAD (P). Pathogens have undergone an evolution to interfere in the detection of PAMPs and reduce the efficacy of PTI. In order to recognitions of these infection-facilitating pathogen effectors, plants utilize more varied class of proteins (Andersen *et al.,* 2018).

NLRs Detect Pathogen Effectors

Effector molecules have ability to suppress basal defences and make the pathogen virulent. Plants have co-evolved with their pathogens, the R genes of plants are specific to these effector molecules, and they have co-evolved with effector molecules for recognizing them and to activate specific defence mechanism of plants. In nature every effector molecule (Avr1) has its correspondent resistance gene (R1), "gene for gene hypothesis". In absence of a specific R gene in plant Avr gene become effective in causing disease, but when it faces it's corresponding R gene it fails to produce any disease symptoms as R gene renders Avr gene paralysed. To evade this successful detection of pathogen by R genes of plants pathogen population continues to evolve, mutate and bring about changes in composition and structure of its effector molecules with the goal of that the newly synthesised effector molecules are no longer identified by the same R gene. These molecules are unstable and evolve very fast (Sarkar, 2015) NLRs, also known as R genes, are among the fastest evolving gene families. Their products, upon detection of pathogenic effectors, go through a conformational shift from a condensed, ADP-bound state to an open ATP-bound state with exposed N-terminal domains for the initiation of downstream signalling (Takken and Goverse, 2012). Most R proteins belong to a subgroup of a family of proteins which is called STAND (signal transduction ATPase with numerous domains). NBS-LRR (nucleotide-binding site; leucine rich repeats) proteins 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.,* 2014).

For signalling, the NBS-LRR-CC proteins generally require a GPI anchored protein named non-race specific disease resistance 1, while NBS-LRR-TIR proteins require an enhanced disease susceptibility 1 for signalling. Additionally, the NBS-LRR-CC proteins can be found in dicots and monocots whereas NBS-LRR-TIR are restricted only to dicots (Chiang and Coaker, 2015; Cui *et al.,* 2015). The mechanism that activates R proteins and the subsequent signalling 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). The recognition process could be modelled 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 is able to detect 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*, 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, cleave the RIN4, and this cleavage is detected by R proteins (Caplan *et al.,* 2008; Van der Hoorn and Kamoun, 2008).

Decoy hypothesis

The "decoy" protein possess a mimicry of 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 favours 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).

Zig-zag model

In the most basic interaction, the zig zag model reveals an interaction between the pathogen and the host. The interaction is 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 (Méndez and Romero, 2016).

This model is being re-evaluated, 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) and he 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. (Méndez and Romero, 2016).

Invasion model

This model was proposed by Cook *et al.* (2015), the authors took into consideration some limitations of the zig-zag model like 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, the only exception in the aspects related to the definition of the immunogenic molecules which 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 effective to an interaction model. In this sense, if a molecule has a role in a different process some evaluative forces can change them; producing changes in the interaction process or even in the fitness of the species (Méndez and Romero, 2016).

Multicomponent model

The model was proposed by Andolfo *et al.* (2016). According to him disadvantages of the zig-zag model is 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 Signalling (NTS) or PPRs Triggered Signalling (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) (Méndez and Romero, 2016).

Conclusions

Knowledge of plant–pathogen interactions will be undoubtedly continued to flourish in the 21st century, gone thorough by new molecular techniques and greater computational software. In addition to improving our knowledge of resistance, efforts will continue to alter crop genetics to develop better resistance. Continuing to alter the receptors necessary to initiate defence responses is likely the best route for development of resistance. NLRs may become a major tool of biotechnology, used to engineer resistance to any pathogen through the modified activity of the CRISPR/Cas9 system. 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. One recent approach utilizes the activation of Arabidopsis NLR RPS5 by *P. syringae* protease AvrPphB cleavage of PBS1 (Shao *et al.,* 2003). Understanding the pathogen recognitions, resistance and plant immunity will greatly benefit agricultural production by reducing crop loss, and contribute to our understanding of the molecular interactions and coevolution that underlies this crop field and numerous applications to other biological systems.

References

Altenbach D, Robatzek S. 2007. Pattern recognition receptors: from the cell surface to intracellular dynamics. Molecular Plant–Microbe Interactions. 20: 1031–1039.

Andersen , E J., Ali , S., Byamukama , E., Yen, Y., and Nepal, M P. ,2018. Disease Resistance Mechanisms in Plants. *Genes* , 339; doi:10.3390

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

Brutus, A., Sicilia, F., Macone, A., Cervone, F., De Lorenzo, G. A. 2010. Domain swap approach reveals a role of the plant wall-associated kinase 1 (WAK1) as a receptor of oligogalacturonides. Proc. Natl. Acad. Sci. USA, 107, 9452–9457

Caplan JL, Mamillapalli P, Burch-Smith TM, Czymmek K and Dinesh-Kumar SP. 2008. Chloroplastic protein NRIP1 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

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/annurevphyto-080614-120114.

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

Dangl,J.L.,Horvath,D.M.,Staskawicz, B.J. 2013. Pivoting the plant immune system from dissection to deployment. Science, 341, 746–751

Gust, A.A.; Pruitt, R.; Nürnberger, T. 2017. Sensing danger: Key to activating plant immunity. Trends Plant Sci. 22, 779–791

Jones DA, Takemoto D. 2004. Plant innate immunity – direct and indirect recognition of general and specific pathogen-associated molecules. Current Opinion in Immunology 16: 48–62.

Juge, N.2006. Plant protein inhibitors of cell wall degrading enzymes. Trends Plant Sci. 11, 359–367.

Lannoo, N.; Van Damme, E.J.2014. Lectin domains at the frontiers of plant defense. Front. Plant Sci., 5, 397

Lee SW, Han SW, Sririyanum M, Park CJ, Seo YS and Ronald PC. 2009. A type I-secreted, sulfated peptide triggers XA21mediated innate immunity. Science 326(5954): 850–853. doi: 10.1126/science.1173438.

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.

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.

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

Marone D, Russo MA, Laidò G, De Leonardis AM and Mastrangelo AM. 2013. Plant nucleotide binding site-leucinerich repeat (NBS-LRR) genes: active guardians in host defense responses. International Journal of Molecular Science 14(4): 7302– 7326. doi: 10.3390/ijms14047302.

Matzinger P. 2002. The danger model: a renewed sense of self. Science 296: 301–305.

Méndez K. A and Romero H. M. 2017. Plant responses to pathogen attack: molecular basis of qualitative resistance .Agron. 70(2): 8225-8235

Meng, X.; Zhang, S. 2013. MAPK cascades in plant disease resistance signaling. Ann. Rev. Phytopathol, 51, 245–266

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.; Zipfel, C. Plant pattern recognition receptor complexes at the plasma membrane. 2012. Curr. Opin. Plant Biol. 15, 349–357

Park, C.-J.; Ronald, P.C. Cleavage and nuclear localization of the rice xa21 immune receptor. 2012. Nat. Commun., 3, 920.

Pritchard L and Birch PR. 2014. The zigzag model of plantmicrobe interactions: is it time to move on. Molecular Plant Pathology 15(9): 865–870. doi: 10.1111/mpp.12210.

Rashid R., Bhat, J. A., Malik, A., Bhat, Z. A., Dar, W. A., Untoo, S. A., and Ganaie, M Y. 2010. Molecular Basis of Host Pathogen Interaction. *International Journal of Applied Agricultural Research.* ISSN 0973-2683 5(1):35–45

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.

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

Sarkar, A., Sinha, A., Sarma, B. K. and Singh, H.B. 2015. Plant pathogen interaction and host defense responses . *Improved Production Technologies in Vegetable Crops.* 246.

Shao, F.; Golstein, C.; Ade, J.; Stoutemyer, M.; Dixon, J.E.; Innes, R.W. 2003 Cleavage of Arabidopsis PBS1 by a bacterial type III effector. Science, 301, 1230–1233.

Takken,F.L and Goverse,A. 2012. How to build a pathogen detector: Structural basis of NB-LRR function. Curr. Opin. Plant Biol., 15, 375–384.

Tameling WIL, Takken FLW. (in press). Resistance proteins: scouts of the plant innate immune system. European Journal of Plant Pathology (published online: 27 September 2007).

Thordal-Christensen H. 2003. Fresh insights into processes of nonhost resistance. Current Opinions in Plant Biology 6: 351–357.

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.

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 S, Shan L and He P. 2014. Microbial signature-triggered plant defense responses and early signaling mechanisms. Plant Science 228: 118–126. doi: 10.1016/j.plantsci.2014.03.001.

Zipfel, C. Plant pattern-recognition receptors. Trends Immunol. 2014, 35, 345–351.