The Review of Contemporary Scientific and Academic Studies
An International Multidisciplinary Online Journal
www.thercsas.com
ISSN: 2583-1380 Vol. 2 | Issue 10 | October 2022 Impact Factor: 4.736 (SJIF)

Plant Disease Resistance Mechanism: A Narrative Review

Md Estiarul Haque Pran (benzeneresearchcentre@gmail.com)
Research Scholar, Department of Biotechnology & Genetic Engineering,
Bangabandhu Sheikh Mujibur Rahman Science & Technology University Gopalganj, Bangladesh

 Crossref/DOI: https://doi.org/10.55454/rcsas.2.10.2022.006

Abstract: *Vertebrates have a highly adaptable immune system that depends on clonally generated antigen receptors by circulatory immune cells. These immune cells offer vertebrates antigen-specific immunity and reduce self-reactivity. Plants lack mobile immune cells. Every plant cell can mount an immunological response. Plants have a robust defense mechanism against pests and diseases. When pathogens escape mechanical barriers, plant receptors begin signaling pathways that drive gene expression. Genes and products make up a plant's immune system. Pathogens actively avoid and disrupt response pathways, favoring a decentralized immune system. Microorganisms may cause plant illness, growth, and reproduction. Plants' innate immune system has two branches. The first branch recognizes and responds to compounds present in nonpathogenic bacteria. The second replies to pathogen virulence factors through host targets. These plant defense chemicals give tremendous insights into molecular recognition, cell biology, and evolution across biological kingdoms. Recent study reveals plants have a complicated innate immune system that involves self-surveillance, systemic signaling, and chromosomal changes. Recent molecular advances have improved our knowledge of plant immunology for agricultural purposes. Understanding plant immunity will improve food, fiber, and biofuel crops. This study reviews plant immune system components, present knowledge, and future research goals in plant–pathogen interactions.*

Keywords: Defence Response, Disease Resistance, Leucine-Rich, Nucleotide-Binding, Plant Immunity

1. Introduction

The activation of signals in plant-pathogen interactions is a well-understood process that may lead to an immediate defensive response against a wide variety of plant infections. This defense mechanism aids the host plant in warding off more disease infection. The products of specialized host genes known as (resistance gene) R genes recognize particular pathogen effectors, triggering the plant's defensive signaling response. Harold Henry Flor's ground-breaking gene-for-gene model found a correlation between R genes and avirulence genes in the pathogen, which together produce an incompatible response (H. H. Flor, 1942). Recent molecular research considerably builds on the basic structure of H. H. Flor's gene-for-gene model, suggesting that plant resistance is governed by a complex regulatory mechanism. Components of the plant immune system contribute in pathogen detection, signal transduction, and defensive response. The zig-zag model describes how selective forces have led to the development of more complicated detection systems in plants and increasingly sophisticated escape mechanisms in diseases (J. D. G. Jones & Dangl, 2006).Scientists have discovered a large number of unique resistance (R) genes in plants, and they are using them in efforts to better our food supply. Instead of using harmful pesticides or other chemical methods to manage pests, plant resistance genes may be employed to create disease-resistant varieties. Using plant resistance genes in resistance breeding programs has several benefits, including the efficient decrease of pathogen development, minimum harm to the host plant, no pesticide input from farmers, and, most importantly, the environmentally benign nature of such crops.

However, traditional breeding for resistance is a time-consuming technique that often needs many hybrid generations to successfully introduce resistance genes from one species into the gene pool of another. Researchers believe their efforts will be aided by the complete functional investigations, cloning, characterization, and genetic transformation of plant resistance genes. Insects, nematodes, bacteria, fungi, viruses, and oomycetes are only some of the agricultural pests that need to be controlled efficiently and over the long term. Losses in worldwide productivity due to pathogens remain substantial despite the development of new resistant cultivars (Baker et al., 2010; Oerke & Dehne, 2004). How these factors influence immunity is the subject of this piece. Due to the specialized nature of most assessments, we won't be delving into every feature of every part. Instead, we want to provide an overarching theory of phytopathogen resistance supported by concrete evidence. Here, we'll discuss not just how infections have evolved to outsmart plants' defenses, but also which parts of the plant immune system are at play. This article also highlights several

The Review of Contemporary Scientific and Academic Studies
An International Multidisciplinary Online Journal
www.thercsas.com
ISSN: 2583-1380 Vol. 2 | Issue 10 | October 2022 Impact Factor: 4.736 (SJIF)

new findings in the realm of plant disease control systems, including plant resistance genes and their distribution.

2. Biotrophic and Necrotrophic Plant Pathogens

Pathogens infect plants for a variety of reasons, including their lifestyle preferences. Pathogens that are adapted to feed on live plant tissue are called biotrophic. Some of these infections have coevolved in close proximity to their host plant, becoming obligate biotrophs that need natural substrates for growth in the laboratory. On artificial medium, non-obligatory biotrophs may thrive, but neither obligate nor non-obligate biotrophs can thrive as saprophytes. Biota can only feed on certain organisms. Biotrophs are mostly found in the leaf and the intercellular spaces between mesophyll cells (Voegele et al., 2003). Some organisms generate feeding structures called haustoria, which invaginate the plasma membrane of host cells to provide an optimal milieu for food retrieval. In contrast to obligate parasites, necrophilic pathogens have a more distant and casual interaction with their host. They may colonize damaged plant tissues and often create poisons that harm the host tissue before they can fully establish themselves. Outside of a host, necrotrophs may develop into saprophytes. It grows well in laboratory conditions using artificial medium (De Wit, 2007).

3. Basis of Plant Defense

Plant infections not only lower harvest rates, but also lower quality produce compounds that are bad for people. The resistance of pathogens to modern pesticides and antimicrobials is also on the rise. Therefore, other methods of disease control are needed. Plant disease resistance genes are the basis of many crop improvement programs, and molecular marker methods and biotechnology are being utilized to enhance these programs. The present pest and disease concerns, as well as abiotic difficulties, need extensive research into plant resistance genes (Chisholm et al., 2006). Pathogen selection pressure has resulted in the evolution of plant post-invasion resistance systems. Dominant resistance genes are responsible for controlling these defensive systems, and their products may either directly or indirectly detect certain pathogen effectors, setting off effective defense responses. In most cases, R-protein-activated resistance is restricted to strains of a certain pathogen that also produce the corresponding effector protein (Avr protein). Hypersensitive response (HR) is often associated with this resistance and results in the rapid death of the invading cell and, in some cases, a few neighboring cells. In order to properly combine numerous resistance sources and create novel disease resistance approaches in agriculture, structural and functional analyses of plant resistance genes and R-gene loci are required. Furthermore, it is crucial to understand the plant pathogen interaction in order to achieve the aforementioned goals (Halterman et al., 2003).

Plants in the wild are always at risk of contracting diseases brought on by pathogenic microorganisms and pests. To survive and fight off these dangers, plants have developed a highly developed immune system. Upon detecting a pathogen-derived signature, hundreds of immune receptors may activate one of two defensive mechanisms in plants (pathogen-associated molecular patterns-triggered immunity [PTI] or effector-triggered immunity [ETI]). When resistance (R) proteins are activated, ETI is triggered, and infected cells die. There are several R proteins, which belong to the NBS-LRR/NLR (nucleotide-binding domain and leucine-rich repeats) family of intracellular receptors. More than 300 functional R genes have been found since 1992, demonstrating the rapid expansion of research into and identification of these genes in light of their critical role in crop protection during the last 30 years. The "arms race" between R genes and pathogens is dynamic and may be expensive for the plant. Since R proteins may initiate apoptosis, their expression is tightly regulated in the genome via mechanisms including as methylation and micro RNAs. While much has been accomplished, many problems remain, such as those concerning the evolution and regulation of R genes, the method of action of R genes, and the initiation of downstream immunological signaling by R genes and their associated proteins (Xue et al., 2020).

A suite of cellular sensors capable of direct detection of harmful chemicals is shown by the molecular foundation of pathogen resistance. Pathogen-associated molecular patterns (PAMPs) are recognized by pattern recognition receptors (PRRs) in the cell membrane, while damage-associated molecular patterns (DAMPs) are recognized by wall-associated kinases (WAKs) as a consequence of cellular damage during infection (Zipfel, 2014).

Receptors with nucleotide-binding domains and leucine-rich repeats may identify effector chemicals utilized by pathogens to enhance infection (NLRs). To yet, the precise signaling pathways initiated by PRRs, WAKs,

and NLRs remain unclear (Dangl, 2013). Pathogenesis-related (PR) gene expression may be regulated by a wide variety of stimuli, including mitogen-activated protein kinases (MAPKs), G-proteins, ubiquitin, calcium, hormones, and transcription factors (TFs). So many reactions are available to stop the spread of illness in this manner. Some of them include the release of reactive oxygen species (ROS), the hypersensitive response (HR), the closing of stomata, changes to the cell wall, and the creation of a wide range of anti-pest proteins and chemicals (such as chitinases, defensins, phytoalexins, and protease inhibitors) (Loon et al., 2006). Molecular approaches have shed light on the complex network of organelles and protein and non-protein molecules that plants use to ward off pathogens and control their defensive responses. Those variables may modify the responses of other signaling systems, including the growth and abiotic stress response pathways. For a full understanding of plant-pathogen interactions, we need to describe in detail the molecular interactions that take place when a compatible pathogen interacts with plant tissue.

4. Virulence of Pathogen Is Dependent on Attack and Evasion

When exposed to a wide range of pathogen species and subspecies, plant populations develop a similarly diverse repertoire of immune receptors and defense strategies. For their part, plant pathogens have evolved defensive mechanisms to circumvent or prevent detection by their hosts. Pathogens were able to overcome PAMP-triggered immunity (PTI) via the secretion of effectors (Loon et al., 2006). To deliver its effectors into the cytoplasm of wheat, the bacteria Xanthomonastranslucens use a type III secretion system that looks like a tube (Boch&Bonas, 2010). Other Xanthomonas species use a type VI secretion system to transport effectors extracellularly (Gardiner et al., 2014). Horizontal gene transfer is another way that pathogens might acquire new, dangerous traits. the movement of genes that have an influence on another species from one species to another. For instance, tan spot disease in wheat may be caused by the transfer of the necrosis-inducing Tox A gene from Parastagonospora nodorum to Pyrenophoratriticirepentis (Friesen et al., 2006). At this time, plants have a defensive mechanism called effector-triggered immunity (ETI) that can identify and respond to such effectors. The fact that certain diseases feed on live tissue while others feed off of dead tissue necessitates a range of remedies. Unfortunately, the hypersensitive reaction (HR) that is supposed to prevent biotroph infection rather promotes necrotroph infection (Glazebrook, 2005). By rapidly switching between biotrophy and necrotrophy and secreting effectors in waves that vary with tissue and infection stage, hemi-biotrophs are able to deceive the plant (Toru & Stergiopoulos, 2016).

5. Evolution of Plant Immune System: Primary & Secondary

Plants' evolution has been influenced in part by their interactions with microbes since 480 million years ago. Plants perceive biotic interactions and trigger a defensive or a favorable response to fight infections and insects and to enable contact with beneficial organisms. Plants can detect PAMPs and effectors to combat pathogens (J. D. G. Jones & Dangl, 2006). PAMPs are microbially conserved compounds that activate PAMP-triggered immunity (PTI), a plant's earliest active response to microbiological sensing. PTI generates reactive oxygen species, deposits callose at infection sites, and activates pathogen-responsive genes, inhibiting microbial development. Plant infections produce effector molecules (virulence factors) to improve their fitness on plant hosts. Effectors may function in the cell or extracellular matrix. Effectors decrease PTI and are identified as avirulent (Avr) factors by R-proteins extracellularly or intracellularly, triggering effector-triggered immunity (ETI). New effectors may inhibit ETI, causing effector-triggered susceptibility (ETS). A hypersensitive response (HR) is a sort of localized programmed cell death that prevents pathogen or insect proliferation. Jones and Dangl (2006) describe PTI and ETI as zigzag stepwise evolution. PAMPs, Avr factors, PRRs, and R-proteins have a foggy border; hence PTI and ETI should be seen as a continuum. Spoel and Dong (2012) said plant defense is a complex innate immune system that involves self-surveillance, systemic signaling, and chromosomal changes (Zicola, 2016).

PRRs identify several microbial components. PRRs identify fungi, bacteria, and viruses (Niehl et al., 2016). These receptors feature extracellular ligand-binding leucine-rich repeats, transmembrane domains, and cytoplasmic kinase domains. LRRs are diverse due to their capacity to bind to different elicitors. BAK1 and SERKs are involved in several PRRs (Prince et al., 2014). Signaling isn't usually extensive. When activated, certain PRRs release kinase domains that go to the nucleus (Park & Ronald, 2012). PRRs detect numerous molecules (Prince et al., 2014). That's bacterial flagellin, EF-Tu, and peptidoglycan, fungal chitin, xylanase, oomyceteelicitins, viral double-stranded RNA, and insect aphid-derived elicitors. Wheat PRRs TaLRK10,

The Review of Contemporary Scientific and Academic Studies
An International Multidisciplinary Online Journal
www.thercsas.com
ISSN: 2583-1380 Vol. 2 | Issue 10 | October 2022 Impact Factor: 4.736 (SJIF)

TaRLP1.1, and TaRLK-R1-3 have been connected with rust resistance (Puccinia fungus) by detection of fungal PAMPs (Feuillet & Schachermayr, 1997).

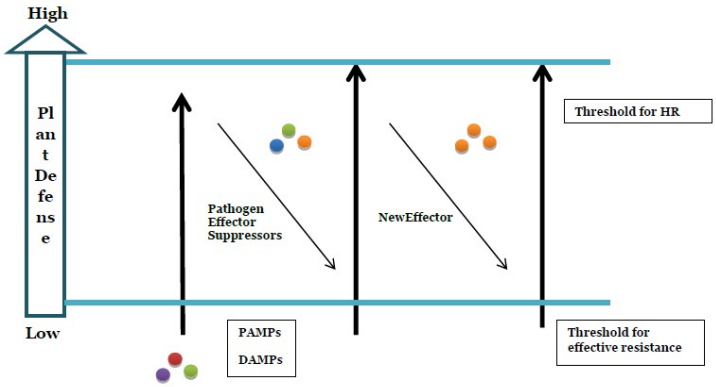

Figure 1: Zigzag model as described by Jones and Dangl (J. D. G. Jones &Dangl, 2006)

Other sensors detect harm by identifying cellular components damaged by pathogen enzymes. Arabidopsis WAK1 perceives oligogalacturonides. WAKs have an N-terminal galacturonan-binding domain that interacts with cell wall pectins and cytoplasmic kinase domains, like PRRs (Hefetz et al., 2014). WAK1 and WAK2 detect oligogalacturonic acid from fungal pectin breakdown. Plant lectins identify pathogen- or infection-caused carbohydrates. PAMPs and DAMPs include carbs (i.e. cellulose, peptidoglycans, oligogalacturonides, and lipopolysaccharides). PRRs/WAKs with lectin domains recognize these. Plants can detect infection-causing extracellular substances, Extracellular DNA, ATP and NADP. Pathogens have developed to hide PAMPs, reducing PTI's efficacy. Cladosporiumfulvum and Magnaportheoryzae generate chitin-binding proteins (Avr4 and Slp1) (Presti et al., 2015). Pathogens emit effectors that impede plant defense; plants have evolved to resist utilizing the zig-zag paradigm. Plants identify infection-facilitating pathogen effectors through a separate class of proteins.

6. Effectors of Plant Pathogens Suppress Primary Innate Immune Responses

The real pathogens of plants and animals may circumvent or inhibit the fundamental innate immune system's basal defenses. Many viruses, bacteria, fungi, and oomycetes that infect animals have learned to evade or inhibit MAMP detection and the accompanying triggering of primary defensive responses (Martinon, 2005). Plant and animal pathogenic bacteria have four secretory systems, with the type III secretion system (TTSS) proving to be the most important for virulence. In order to inject several effectors into the host plant and cause disease, plant-pathogenic bacteria rely on the TTSS. Numerous plant pathogenic bacterial effectors have been demonstrated to inhibit initial defensive responses in plants after being injected with TTSS (Fig. 4b), with as many as 30–40 effectors described for certain bacteria (Defense et al., 2004). Suppression mechanisms have been identified for a subset of effectors; for example, the P. syringae effectors AvrPto, AvrRpt2, and AvrRpm1 all attenuate responses elicited by MAMPs. Disease is encouraged by AvrPtoB because it inhibits the plant's hypersensitive response (HR) and activates the abscisic acid (ABA) pathway. Many plant-harming bacteria generate coronatine, a jasmonic acid (JA) analogue that inhibits salicylic acid (SA)-induced defenses (Hauck et al., 2003).

Mechanisms and roles of effector delivery in fungi and oomycetes are less well known. Tomatoes infected with the fungus Cladosporiumfulvum have ten effectors secreted into the intercellular space by the fungus. When the Avr2 effector attaches to the plant cysteine protease Rcr3, it limits its activity, whereas the Avr4 effector shields the fungus from the destructive effects of plant chitinases. As shown by the effectors of the rice blast fungus Magnaporthegrisea and the potato late blight oomycete pathogen, among others, other fungal and oomycete effectors function within host cells. However, oomycete effectors often encode an RXLR motif, which has been hypothesized to enhance effector absorption into the plant cell, suggesting that the method by which fungal effectors are carried into plant cells is still poorly understood. The malaria parasite Plasmodium falciparum has been shown to rely on this motif to invade mammalian host cells (Bhattacharjee et al., 2006).

https://doi.org/10.55454/rcsas.2.10.2022.006

The Review of Contemporary Scientific and Academic Studies
An International Multidisciplinary Online Journal
www.thercsas.com
ISSN: 2583-1380 Vol. 2 | Issue 10 | October 2022 Impact Factor: 4.736 (SJIF)

Figure 2: Pattern-Triggered Immunity (PTI) in plants.

7. Effector-Triggered Secondary Immune Responses

When pathogens of animals breach physical barriers like the epithelium of the skin or gut, TLRs on phagocytes detect them and signal for the phagocyte to engulf and destroy the invader. Phagocytes also serve as a bridge between the innate and adaptive immune systems by stimulating B and T cells to produce cell-mediated and humoral immune responses in response to antigens presented to their receptors. Because of their limited immunological capabilities, plants are unable to eliminate pathogens from their intercellular spaces and vascular systems. In order to avoid being stopped by the body's first line of defense, true pathogens generate effectors that dampen or otherwise compromise this line of protection. An effector or effector-mediated disruption of host targets initiates a secondary defensive response in plants that protects them against real infections (Chisholm et al., 2006).

Resistance proteins (RPs) keep tabs on these effectors or their alterations and set off RP-mediated secondary defensive responses that often result in an HR (a localized programmed cell death response) and other locally induced defense responses that halt the pathogen's growth (Fig. 4c). Thus, RPs detect disrupted host targets specifically, but the induced HR is broad-spectrum in its efficacy against plant pathogens. Depending on the plant pathogen, effectors may target many domains within the same host component, each of which is monitored by a separate RP. An example of a host target is the A. thaliana RIN4 protein, which is guarded by two RPs (RPM1 and RPS2) and targeted by three TTSS-dependent bacterial effectors (AvrRpm1, AvrB, and AvrRpt2). The guard model elaborates on how the host's secondary defenses might detect effector-induced perturbations of the target without directly detecting the effectors themselves. More often than not, RPs learn about effectors via oblique means. Several bacterial pathogens, including Ralstoniasolanacearum, have been shown to contain effectors that are directly identified by RPs (Deslandes et al., 2003).

8. Interaction of R Gene with Effector

8.1 Gene Model

The hypothesis that through time, a host and its parasite develop genetic systems that are complimentary to one another, so that for every gene in the host that confers resistance, there is a gene in the parasite that confers susceptibility. Corresponding genes are those from both species that interact with one another; for example, if a gene in the host conditions resistance, then a gene in the parasite must also condition avirulence. Either directly or indirectly (via the evolution of an avirulence gene), the protein encoded by the resistance gene serves as a receptor for a ligand secreted by the parasite. Receptor–ligand interactions serve as the recognition event that initiates the resistant phenotype's defensive responses via cellular signal transduction (Flor, 1971). Pathogenicity and resistance to Melampsoralini linseed rust were shown to be inherited in a manner that is now known as the gene-for-gene theory, first shown by Flor (1946, 47). Host and parasite evolved complimentary genic systems, as shown by the observation that "for each gene regulating rust response in the host, there is a particular gene conditioning pathogenicity in the parasite." Proof of concept varies from case to case, however it has been applied to different host pathogen combinations such viruses, bacteria, fungus, nematodes, insects, and a flowering plant.

8.2 Guard model

The R gene detects effectors in this way, although it is indirect. R gene products interact with their pathogen counterparts only under very specific conditions (effector). This theory proposes that the R proteins protect another protein, which they interact with. When the R protein detects interference with the guardee protein, resistance is activated. Here, the virulence factor seems to bind to a guardee protein that is either the virulence factor's intended target or a structural imitation of the virulence factor's target. That way, plant defenses may focus on combating a particular pathogenesis technique rather than trying to keep up with constantly shifting pathogen forms. The guardee protein is changed after a pathogen interaction, making it detectable by the R gene products in plants (Van Der Hoorn &Kamoun, 2008).

The Review of Contemporary Scientific and Academic Studies
An International Multidisciplinary Online Journal
www.thercsas.com
ISSN: 2583-1380 Vol. 2 | Issue 10 | October 2022 Impact Factor: 4.736 (SJIF)

8.3 Decoy Model

In plant populations with polymorphic R genes, the guarded effector target is susceptible to two conflicting natural selection processes. R gene polymorphism refers to the presence/absence of functional R genes in plant populations. In the absence of a functioning R gene, natural selection may reduce the guardee's binding affinity with the effector, enabling it to avoid detection and modification. In the presence of a functioning R gene, natural selection may prefer guardees with better effector interaction to increase pathogen detection (Van Der Hoorn &Kamoun, 2008).

These two conflicting selection pressures on the guardee's effector interaction create an evolutionarily unstable scenario that might be eased by a host protein called "decoy." It specializes in R protein effector perception but doesn't affect illness or resistance. Decoys resemble effector targets to capture pathogens in recognition events. Decoys may arise from effector targets via gene duplication and evolution or by emulating them (target mimicry). The Decoy Model suggests that the R protein is a decoy that monitors the effector target and mimics the operational effector target, but only acts in perception of pathogen effectors without adding pathogen fitness without its corresponding R protein. This Decoy Model varies from the traditional and refined Guard Models, which suggest that effector modification of the guarded effector target enhances pathogen fitness (Van Der Hoorn &Kamoun, 2008).

9. Induced Systemic Resistance in Plants

Systemic acquired resistance (SAR) protects plants against pathogens by developing outside of main and secondary immune responses. Infecting leaves or stems causes systemic resistance and local primary and secondary immune responses (Grant & Lamb, 2006). SAR is effective against a broad variety of pathogens and depends on plant hormones such as salicylic acid, jasmonic acid, ethylene, and abscisic acid. Hormone-dependent defense mechanisms fight microbes and insects. The kind of plant pathogen influences local and systemic resistance and hormone dependency. Biotrophic and necrotrophic pathogens, controlled by various hormones, elicit different forms of induced resistance (Qiu et al., 2008).

10. Adaptation of Pathogens to Secondary Innate Immune Responses

The arms race between plants and their pathogens has led to a variety of adaptations to primary, secondary, and perhaps systemic generated defensive responses. Novel effectors have evolved as a result of co-evolution between plants and pathogens; these effectors no longer interact directly with RPs or perturb host targets in ways that are detectable by RPs. Changes in effector gene mutations are determined by the effector's importance to the pathogen's virulence and/or competitive abilities outside the host when facing antagonistic microorganisms or other hostile conditions (Stergiopoulos et al., 2007). Some effector genes can be mutated to produce effectors with subtle amino acid changes that reduce or avoid RP recognition while maintaining virulence functions, while others can be deleted entirely from the pathogen genome, preventing RP recognition. This indirect interaction between RP and effector-modified host target is strongly correlated with effector loss, lending credence to the guard hypothesis. Consequently, it is speculated that the pathogen's pathogenicity is unaffected by the loss of the effector, as the role it played is likely supplied by functionally related effectors. It is especially rapid in resistant plants that carry the matching RP for some harmful bacteria for the effector gene to be lost due to genome rearrangements, including excision of the effector gene. It is also taken into account that the modes of adaptive evolution depend not only on the virulence function of an effector but also on the lifestyle of the pathogen that carries that effector (biotrophic or necrotrophic) (D. A. Jones &Takemoto, 2004).

11. Structure, Localization and Activation of RPs

Pathogens use effectors to influence host plant cells both externally and inside. Therefore, RPs within plant cells or outside (with a transmembrane anchor) identify perturbations of host targets inside or outside the host cells. All RPs have an LRR, and intracellular RPs feature a nucleotide binding (NB) domain preceded by a transient receptor potential (TIR) or leucine zipper (LZ) domain (Chisholm et al., 2006). The mechanism of effector-mediated RP-mediated activation of secondary defensive responses has been partly unraveled in a select few circumstances. AvrRpm1, AvrB, and AvrRpt2 are three bacterial effectors that interact with the plant protein RIN4.

https://doi.org/10.55454/rcsas.2.10.2022.006

The Review of Contemporary Scientific and Academic Studies
An International Multidisciplinary Online Journal
www.thercsas.com
ISSN: 2583-1380 Vol. 2 | Issue 10 | October 2022 Impact Factor: 4.736 (SJIF)

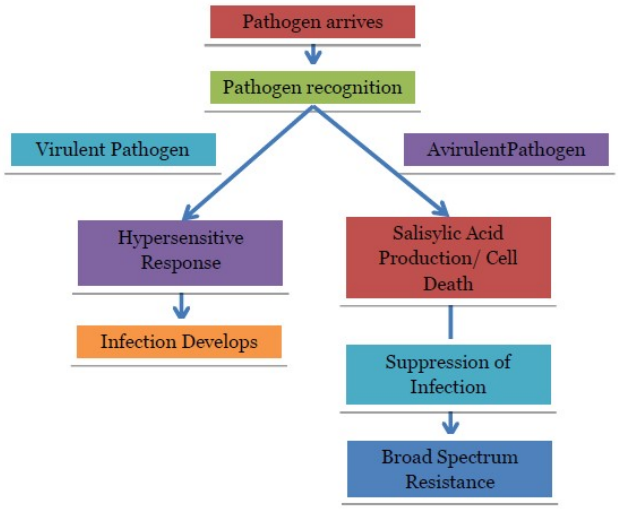

Figure 3: Plant pathogen interaction and development of disease resistance.

Phosphorylation of RIN4 by AvrRpm1 and AvrB. (Rooney et al., 2005). What is expected to trigger the NB-LRR cytoplasmic protein RPM1. In contrast, AvrRpt2 is a cysteine protease that is activated inside the host cell and cleaves the RIN4 protein, activating the cytoplasmic NB-LRR protein RPS2, and therefore mediating the secondary defensive response. The extracellular effector Avr2 of the fungal tomato pathogen C. fulvum interacts with and inhibits the extracellular cysteine protease Rcr3, which is necessary for activation of the extracellular RLP Cf-2 to induce secondary defensive responses. The exact molecular basis for Rcr3's activation of Cf-2 remains elusive. Cytoplasmic NB-LRR proteins need both intramolecular and intermolecular alterations to become active. When a nucleotide diphosphate is exchanged for a nucleotide triphosphate, an activation domain called the NB domain is triggered. The LRR domain is hypothesized to be involved in effector-perturbed host targets or direct recognition of effectors. By phosphorylating transcription factors like TGAs and WRKYs, MAMP- and effector-induced PRR- and RP-mediated defense signaling activates genes encoding antimicrobial proteins or proteins that catalyze the generation of antimicrobial chemicals like phytoalexins or reactive oxygen species. Most pathogen effectors inhibit PRR-mediated primary defenses, but some can also inhibit RP-mediated secondary defenses (Abramovitch et al., 2006).

12. Major Class of R Protein

Plant resistance genes may be categorized by their amino acid motif organization and membrane spanning domains. LRRs (Leucine rich repeats) are recognition specificity components present in most R proteins (J. D. G. Jones, 2001). First-class R-gens encode cytoplasmic proteins with a nucleotide-binding site (NBS), a C-terminal leucine rich repeat (LRR), and a putative coiled coil domain (CC). Arabidopsis RPS2 and RPM1 resist P. syringae, while tomato I2 resists Fusariumoxysporum. Second-class resistance genes are cytoplasmic proteins containing LRR and NBS motifs and a TIR-like N-terminal domain. The tobacco N, flax L6, and RPP5 genes belong to this class (Lawrence et al., 1995). Extracytoplasmicleucine rich repeats (eLRR) are the third major family of NBS-less resistance genes (TrD). eLRRs are not directly involved in pathogen identification and defense gene activation, but they are necessary for specific defense proteins like PGIPs (Centre et al., 1997). C. fulvum resistance genes (Cf-9, Cf-4, and Cf-2) contain an extracellular LRR, a membrane-spanning domain, and a short cytoplasmic C terminus (J. D. G. Jones, 2001). The rice Xa21 Xanthomonas resistance gene includes extracellular LRR, transmembrane, and serine-threonine kinase domains. Fifth-class resistance genes include putative extracellular LRRs, a PEST (Pro-Glu-Ser-Thr) protein degradation domain (only in Ve2), and short protein motifs (ECS) that may target the protein for receptor-mediated endocytosis (e.g. tomato Ve1 and Ve2 genes) Ve1 and Ve2 are PAMP receptors. Arabidopsis RPW8 comprises a membrane protein domain (TrD) linked to a putative coiled coil domain (CC). Arabidopsis RRS1-R, a novel member of the TIReNBSeLRR R protein family, offers resistance to the bacterial phytopathogenRalstoniasolanacearum. RRS1-R features a WRKY domain and C-terminal nuclear localization signal (NLS). The WRKY domain is a 60-amino-acid region with a zinc-finger-like motif at its Nterminus. Enzymatic R-genes do not include LRR or NBS groups. The maize Hm1 gene protects against

https://doi.org/10.55454/rcsas.2.10.2022.006

The Review of Contemporary Scientific and Academic Studies
An International Multidisciplinary Online Journal
www.thercsas.com
ISSN: 2583-1380 Vol. 2 | Issue 10 | October 2022 Impact Factor: 4.736 (SJIF)

southern corn leaf blight-causing Cochlioboluscarbonum (Johal& Briggs, 1992). Cereal resistance genes like Hm1 encode proteins with unique roles. The Pto protein in P. syringae has a Ser-Thr kinase domain but no LRRs, whereas the Rpg1 gene in barley provides stem rust resistance by encoding a receptor kinase-like protein with two tandem protein kinase domains but no known receptor sequences. Recessive resistance is frequent in viral systems, despite most resistance genes being dominant. Barley mlo, Arabidopsis RRS1-R, rice xa13, and xa5 are recessive resistance genes. Functional genomics methods and whole genome sequencing of various agricultural plants have made identifying and using R-genes simpler (Brueggeman et al., 2002).

13. Engineering Plant Resistance to Pathogens

The discovery of R genes has led to disease-resistant crops. Using insertional mutagenesis or map-based cloning, resistant plants may be made. By inserting DNA into a gene's coding or regulatory region, insertional mutagenesis disrupts gene expression. Then, plasmid rescue is utilized to clone plant DNA bordering the incorporated mutagen. Cloned plant DNA may be used as a hybridization probe to isolate a gene by screening a wild-type lambda or cosmid library. Final test includes transferring the cloned gene into vulnerable plants and analyzing whether they are disease-resistant. Transposons and T-DNA from the Ti plasmid are employed for insertional mutagenesis (Van Sluys & Tempé, 1989).

In map-based cloning, sometimes called positional cloning, the gene of interest must be mapped. RFLP is most often used to relate chromosomal location to a characteristic. Co-inheritance of disease resistance with a particular RFLP DNA probe determines the approximate site of the R gene in this case. Because the R gene is linked to multiple DNA probes, the probe may be used to find the R gene. After screening for coding sequences (e.g., cDNA) in a specified area using a YAC or BAC vector, the gene is discovered. After transferring suitable cDNA segments into susceptible plants, the last test is checking for disease resistance.

Plant resistance to pathogens needs the coordinated action of many gene products and gene expression modifications. In this way, transcription factors might be used to boost plant disease resistance. Instead of controlling a single gene, transcription factors govern a group. A single transcription factor may have the same impact as modifying a collection of plant genes. Transgenic plants enable targeted expression of pathogen-related genes in vivo, making them a good paradigm for assessing the function and tolerance of encoded proteins (Gachomo et al., 2003). Transgenic plants may also boost disease resistance in lucrative crops.

14. Conclusion and Future Directions

In the 21st century, due to advances in molecular tools and computer capacity, our understanding of plant-pathogen interactions is expanding rapidly. The study of plant diseases and their causes, known as phytopathology, is one of several disciplines that stand to benefit from the accumulation of knowledge on plant-pathogen interactions. Several causes will motivate research, including the rising need for long-lasting pathogen resistance in crops in response to disease challenges related to contemporary agricultural methods and climate change (Zhan et al., 2015). Research on plant immunity will continue, and attempts to improve crop resistance via genetic modification will proceed. The greatest way to create resistance is to keep tinkering with the receptors that set off defensive reactions. Since the CRISPR/Cas9 system's activity may be altered, NLRs may soon emerge as a pivotal biotechnology tool for the targeted creation of resistance to any pathogen. P. syringae protease AvrPphB cleaves PBS1 as a novel strategy for activating Arabidopsis NLR RPS5 (Qi et al., 2014; Shao et al., 2003). The PBS1 cleavage site, as shown by Kim et al., may be replaced with a cleavage site for other pathogen proteases, enabling other pathogens to elicit protective responses (Kim et al., 2016). While this technique is still in its infancy, it is expected that in the future, scientists will work to develop ways to create crops with new R-genes that have not been adopted from other species. Receptors must be paired with the appropriate kind of signal transduction to elicit the optimal defensive response when engineering new resistance pathways to varied illnesses (Sarma et al., 2016). A deeper understanding of disease resistance and plant defense will not only increase agricultural productivity by reducing crop loss, but also expand our understanding of the molecular relationships and coevolution that underlie this and many other fields.

The Review of Contemporary Scientific and Academic Studies
An International Multidisciplinary Online Journal
www.thercsas.com
ISSN: 2583-1380 Vol. 2 | Issue 10 | October 2022 Impact Factor: 4.736 (SJIF)

Reference

Ã, C. Z., & Felix, G. (n.d.). Plants and animals : a different taste for microbes ? https://doi.org/10.1016/j.pbi.2005.05.004

Abramovitch, R. B., Anderson, J. C., & Martin, G. B. (2006).Bacterial elicitation and evasion of plant innate immunity. Nature Reviews Molecular Cell Biology, 7(8), 601–611. https://doi.org/10.1038/nrm1984

Andersen, E. J., Ali, S., Byamukama, E., Yen, Y., & Nepal, M. P. (2018). Disease resistance mechanisms in plants.Genes, 9(7). https://doi.org/10.3390/genes9070339

Ausubel, F. M. (2005). Are innate immune signaling pathways in plants and animals conserved ? 6(10), 973–979. https://doi.org/10.1038/ni1253

Baker, C. M., Chitrakar, R., Obulareddy, N., Panchal, S., Williams, P., &Melotto, M. (2010). Molecular battles between plant and pathogenic bacteria in the phyllosphere. Brazilian Journal of Medical and Biological Research, 43(8), 698–704. https://doi.org/10.1590/S0100-879X2010007500060

Bhattacharjee, S., Hiller, N. L., Liolios, K., Win, J., Kanneganti, T., Young, C., Kamoun, S., &Haldar, K. (2006). The Malarial Host-Targeting Signal Is Conserved in the Irish Potato Famine Pathogen. 2(5). https://doi.org/10.1371/journal.ppat.0020050

Boch, J., &Bonas, U. (2010).Xanthomonas AvrBs3 Family-Type III Effectors : Discovery and Function. https://doi.org/10.1146/annurev-phyto-080508-081936

Boller, T., Miescher-institut, F., & Box, P. O. (2000). FLS2 : An LRR Receptor – like Kinase Involved in the Perception of the Bacterial Elicitor Flagellin in Arabidopsis. 5, 1003–1011.

Brueggeman, R., Rostoks, N., Kudrna, D., Kilian, A., Han, F., Chen, J., Druka, A., Steffenson, B., &Kleinhofs, A. (2002). The barley stem rust-resistance gene Rpg1 is a novel disease-resistance gene with homology to receptor kinases. Proceedings of the National Academy of Sciences of the United States of America, 99(14), 9328–9333. https://doi.org/10.1073/pnas.142284999

Centre, J. I., Lane, C., Proteins, a P., & Protein, C. a V. L. R. R. (1997). The Role of Leucine-Rich Repeat Proteins in Plant Defences Interleukin-1 Receptor .....ExtracytoplasmicLRRs .....A . The AWJL Proteins of Wheat .....Advances in Botanical Research, 24.

Chisholm, S. T., Coaker, G., Day, B., &Staskawicz, B. J. (2006). Host-microbe interactions: Shaping the evolution of the plant immune response. Cell, 124(4), 803–814. https://doi.org/10.1016/j.cell.2006.02.008

Chon, W., Provart, N. J., Glazebrook, J., Katagiri, F., Chang, H. S., Eulgem, T., Mauch, F., Luan, S., Zou, G., Whitham, S. A., Budworth, P. R., Tao, Y., Xie, Z., Chen, X., Lam, S., Kreps, J. A., Harper, J. F., Si-Ammour, A., Mauch-Mani, B., … Zhu, T. (2002). Expression profile matrix of Arabidopsis transcription factor genes suggests their putative functions in response to environmental stresses. Plant Cell, 14(3), 559–574. https://doi.org/10.1105/tpc.010410

Dangl, J. L. (2013). Pivoting the Plant Immune System. 746. https://doi.org/10.1126/science.1236011

De Wit, P. J. G. M. (2007). How plants recognize pathogens and defend themselves. Cellular and Molecular Life Sciences, 64(21), 2726–2732. https://doi.org/10.1007/s00018-007-7284-7

Defense, P., Alfano, J. R., &Collmer, A. (2004). T YPE III S ECRETION S YSTEM E FFECTOR P ROTEINS : Double Agents in Bacterial Disease. 385–414. https://doi.org/10.1146/annurev.phyto.42.040103.110731

Deslandes, L., Olivier, J., Peeters, N., Feng, D. X., Khounlotham, M., Boucher, C., Marco, Y., &Somssich, I. (2003). Physical interaction between RRS1-R , a protein conferring resistance to bacterial wilt , and PopP2 , a type III effector targeted to the plant nucleus.

Feuillet, C., &Schachermayr, G. (1997). Molecular cloning of a new receptor-like kinase gene encoded at the LrlO disease resistance locus of wheat. 11(September 1996), 45–52.

Flor, H. H. (1971). Current status of the gene-fob-gene concept.275–296.

Friedman, A. R., & Baker, B. J. (2007).The evolution of resistance genes in multi-protein plant resistance systems. Current Opinion in Genetics and Development, 17(6), 493–499. https://doi.org/10.1016/j.gde.2007.08.014

Friesen, T. L., Stukenbrock, E. H., Liu, Z., Meinhardt, S., Ling, H., Faris, J. D., Rasmussen, J. B., Solomon, P. S., Mcdonald, B. A., & Oliver, R. P. (2006). Emergence of a new disease as a result of interspecific virulence gene transfer. 38(8), 953–956. https://doi.org/10.1038/ng1839

Gachomo, E. W., Shonukan, O. O., &Kotchoni, S. O. (2003).The molecular initiation and subsequent acquisition of disease resistance in plants. African Journal of Biotechnology, 2(2), 26–36. https://doi.org/10.5897/ajb2003.000-1005

Gardiner, D. M., Upadhyaya, N. M., Stiller, J., Ellis, J. G., Dodds, P. N., Kazan, K., & Manners, J. M. (2014). Genomic Analysis of Xanthomonastranslucens Pathogenic on Wheat and Barley Reveals Cross-Kingdom Gene Transfer Events and Diverse Protein Delivery Systems.9(1). https://doi.org/10.1371/journal.pone.0084995

Glazebrook, J. (2005). A GAINST B IOTROPHIC AND N ECROTROPHIC. https://doi.org/10.1146/annurev.phyto.43.040204.135923

Grant, M., & Lamb, C. (2006).Systemic immunity. Current Opinion in Plant Biology, 9(4), 414–420. https://doi.org/10.1016/j.pbi.2006.05.013

Gururani, M. A., Venkatesh, J., Upadhyaya, C. P., Nookaraju, A., Pandey, S. K., & Park, S. W. (2012a). Plant disease resistance genes: Current status and future directions. Physiological and Molecular Plant Pathology, 78(October), 51–65. https://doi.org/10.1016/j.pmpp.2012.01.002

Gururani, M. A., Venkatesh, J., Upadhyaya, C. P., Nookaraju, A., Pandey, S. K., & Park, S. W. (2012b). Plant disease resistance genes: Current status and future directions. Physiological and Molecular Plant Pathology, 78(January 2012), 51–65. https://doi.org/10.1016/j.pmpp.2012.01.002

H. H. Flor. (1942). Host-Parasite Interaction in Flax Rust- Its Genetics and Other Implications.In Phytopathology (Vol. 45, pp. 680–685).

Halterman, D. A., Wei, F., & Wise, R. P. (2003). Powdery mildew-induced Mla mRNAs are alternatively spliced and contain multiple upstream open reading frames. Plant Physiology, 131(2), 558–567. https://doi.org/10.1104/pp.014407

Hauck, P., Thilmony, R., & He, S. Y. (2003). A Pseudomonas syringae type III effector suppresses cell wall-based extracellular defense in susceptible Arabidopsis plants. 100(14).

Hefetz, A., Keeling, C. I., Winston, M. L., Slessor, K. N., Nielsen, J., Lanfear, R., Liebig, J., Millar, J. G., Hanks, L. M., Suarez, A. V, Ecology, C., Blomquist, G. J., Woodard, S. H., Robinson, G. E., Forister, M. L., Pitts, J. P., Vogt, R. G., Pheromone, I., & Volatiles, P. (2014). Identification of a Plant Receptor for. January, 290–294.

Johal, G. S., & Briggs, S. P. (1992).Reductase activity encoded by the HM1 disease resistance gene in maize. Science, 258(5084), 985–987. https://doi.org/10.1126/science.1359642

Jones, D. A., &Takemoto, D. (2004). Plant innate immunity - Direct and indirect recognition of general and specific pathogen-associated molecules. Current Opinion in Immunology, 16(1), 48–62. https://doi.org/10.1016/j.coi.2003.11.016

Jones, J. D. G. (2001). Putting knowledge of plant disease resistance genes to work. Current Opinion in Plant Biology, 4(4), 281–287. https://doi.org/10.1016/S1369-5266(00)00174-6

Jones, J. D. G., &Dangl, J. L. (2006).The plant immune system. Nature, 444(7117), 323–329. https://doi.org/10.1038/nature05286

Kim, S. H., Qi, D., & Helm, M. (2016).Disease Resistance Protein. Science, 351(November 2015), 684–687.

Kutschera, U., &Hossfeld, U. (2012). Physiological phytopathology: Origin and evolution of a scientific discipline. Journal of Applied Botany and Food Quality, 85(1), 1–5.

Lawrence, G. J., Finnegan, E. J., Ayliffe, M. A., & Ellis, J. G. (1995). The L6 gene for flax rust resistance is related to the arabidopsis bacterial resistance gene RPS2 and the tobacco viral resistance gene N. Plant Cell, 7(8), 1195–1206. https://doi.org/10.2307/3870095

Loon, L. C. Van, Rep, M., &Pieterse, C. M. J. (2006).Significance of Inducible Defense-related Proteins in Infected Plants. https://doi.org/10.1146/annurev.phyto.44.070505.143425

Martinon, F. (2005). NLRs join TLRs as innate sensors of pathogens. 26(8). https://doi.org/10.1016/j.it.2005.06.004

Niehl, A., Wyrsch, I., Boller, T., & Heinlein, M. (2016). Double-stranded RNAs induce a pattern-triggered immune signaling pathway in plants. 4.

Oerke, E. C., &Dehne, H. W. (2004).Safeguarding production - Losses in major crops and the role of crop protection. Crop Protection, 23(4), 275–285. https://doi.org/10.1016/j.cropro.2003.10.001

Park, C., & Ronald, P. C. (2012).immune receptor. Nature Communications, 3(May), 1–6. https://doi.org/10.1038/ncomms1932

Presti, L. Lo, Lanver, D., Schweizer, G., Tanaka, S., Liang, L., Tollot, M., Zuccaro, A., Reissmann, S., &Kahmann, R. (2015).Fungal Effectors and Plant Susceptibility. https://doi.org/10.1146/annurev-arplant-043014-114623

Prince, D. C., Drurey, C., Zipfel, C., &Hogenhout, S. A. (2014). The Leucine-Rich Repeat Receptor-Like Kinase BRASSINOSTEROID INSENSITIVE1-ASSOCIATED KINASE1 and the Cytochrome P450 PHYTOALEXIN DEFICIENT3 Contribute to Innate Immunity to. 164(April), 2207–2219. https://doi.org/10.1104/pp.114.235598

Qi, D., Dubiella, U., Kim, S. H., Isaiah Sloss, D., Dowen, R. H., Dixon, J. E., & Innes, R. W. (2014). Recognition of the protein kinase AVRPPHB SUSCEPTIBLE1 by the disease resistance protein RESISTANCE TO PSEUDOMONAS SYRINGAE5 Is dependent on S-acylation and an exposed loop in AVRPPHB SUSCEPTIBLE. Plant Physiology, 164(1), 340–351. https://doi.org/10.1104/pp.113.227686

Qiu, J. L., Zhou, L., Yun, B. W., Nielsen, H. B., Fiil, B. K., Petersen, K., MacKinlay, J., Loake, G. J., Mundy, J., & Morris, P. C. (2008). Arabidopsis mitogen-activated protein kinase kinases MKK1 and MKK2 have overlapping functions in defense signaling mediated by MEKK1, MPK4, and MKS1. Plant Physiology, 148(1), 212–222. https://doi.org/10.1104/pp.108.120006

Ramonell, K. M., & Somerville, S. (2002). The genomics parade of defense responses: To infinity and beyond. Current Opinion in Plant Biology, 5(4), 291–294. https://doi.org/10.1016/S1369-5266(02)00266-2

Rhoades, B. Y. V. H. (2000). Genetically By. 21, 243–246.

Rooney, H. C. E., Van'tKlooster, J. W., Van Der Hoorn, R. A. L., Joosten, M. H. A. J., Jones, J. D. G., & De Wit, P. J. G. M. (2005). Plant science: Cladosporium Avr2 inhibits tomato Rcr3 protease required for Cf-2-dependent disease resistance. Science, 308(5729), 1783–1786. https://doi.org/10.1126/science.1111404

Rushton, P. J., Reinstädler, A., Lipka, V., Lippok, B., &Somssich, I. E. (2002). Synthetic plant promoters containing defined regulatory elements provide novel insights into pathogen- and wound-induced signaling. Plant Cell, 14(4), 749–762. https://doi.org/10.1105/tpc.010412

Sanseverino, W., Roma, G., De Simone, M., Faino, L., Melito, S., Stupka, E., Frusciante, L., &Ercolano, M. R. (2009). PRGdb: A bioinformatics platform for plant resistance gene analysis. Nucleic Acids Research, 38(SUPPL.1), 814–821. https://doi.org/10.1093/nar/gkp978

Sarma, B. K., Singh, H. B., Fernando, D., Silva, R. N., & Gupta, V. K. (2016). Enhancing Plant Disease Resistance without R Genes. Trends in Biotechnology, 34(7), 523–525. https://doi.org/10.1016/j.tibtech.2016.04.002

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(5637), 1230–1233. https://doi.org/10.1126/science.1085671

Shiu, S., &Bleecker, A. B. (2014). Expansion of the Receptor-Like Kinase / Pelle Gene Family and Receptor-Like Proteins in Arabidopsis 1 [w]. 132, 530–543. https://doi.org/10.1104/pp.103.021964.tochaud

Smith, K. D., Andersen-nissen, E., Hayashi, F., Strobe, K., Bergman, M. A., Barrett, S. L. R., Cookson, B. T., &Aderem, A. (2020). Toll-like receptor 5 recognizes a conserved site on flagellin required for protofilament formation and bacterial motility. 4(12), 1247–1254. https://doi.org/10.1038/ni1011

Stergiopoulos, I., De Kock, M. J. D., Lindhout, P., & De Wit, P. J. G. M. (2007). Allelic variation in the effector genes of the tomato pathogen Cladosporiumfulvum reveals different modes of adaptive evolution. Molecular Plant-Microbe Interactions, 20(10), 1271–1283. https://doi.org/10.1094/MPMI-20-10-1271

Toru, T. Y., &Stergiopoulos, I. (2016). Plant Pathogen Effectors : Cellular Probes Interfering with Plant Defenses in a Spatial and Temporal Manner. June, 1–23. https://doi.org/10.1146/annurev-phyto-080615-100204

Van Der Hoorn, R. A. L., &Kamoun, S. (2008). From guard to decoy: A new model for perception of plant pathogen effectors. Plant Cell, 20(8), 2009–2017. https://doi.org/10.1105/tpc.108.060194

Van Sluys, M. A., &Tempé, J. (1989).Behavior of the maize transposable element Activator in Daucuscarota. MGG Molecular & General Genetics, 219(1–2), 313–319. https://doi.org/10.1007/BF00261193

Vivier, E., &Malissen, B. (2005). Innate and adaptive immunity : specificities and signaling hierarchies revisited. 6(1), 17–22. https://doi.org/10.1038/ni1153

Voegele, R. T., Voegele, R. T., &Mendgen, K. (2003). Rust haustoria : nutrient uptake and beyond. 93–100. https://doi.org/10.1046/j.1469-8137.2003.00761.x

Xue, J. Y., Takken, F. L. W., Nepal, M. P., Maekawa, T., & Shao, Z. Q. (2020). Editorial: Evolution and Functional Mechanisms of Plant Disease Resistance. Frontiers in Genetics, 11(October), 10–12. https://doi.org/10.3389/fgene.2020.593240

Zhan, J., Thrall, P. H., Papaïx, J., Xie, L., & Burdon, J. J. (2015).Playing on a Pathogen's Weakness: Using Evolution to Guide Sustainable Plant Disease Control Strategies. Annual Review of Phytopathology, 53(April), 19–43. https://doi.org/10.1146/annurev-phyto-080614-120040

Zicola, J. (2016). Functional analysis of Ecp6 : The LysM effector from the tomato pathogenic fungus Cladosporiumfulvum. January, 5–8. https://doi.org/10.13140/RG.2.1.3186.1846

Zipfel, C. (2014). Plant pattern-recognition receptors.Trends in Immunology, 1(Figure 1), 1–7. https://doi.org/10.1016/j.it.2014.05.004

Zipfel, C., Robatzek, S., Navarro, L., Oakeley, E. J., Jones, J. D. G., Felix, G., &Boller, T. (2004).Bacterial disease resistance in Arabidopsis through flagellin perception. 428(April), 15–18.