Plant Stress ©2013 Global Science Books

Signaling in Plant-Microbe Interactions

Alok Pandey[1] • Subhadeep Chaterjee[2*]

[1] Centre for Cellular and Molecular Biology, Council of Scientific and Industrial Research, Uppal Road, Hyderabad-500 007, Andhra Pradesh, India
[2] Centre for DNA Fingerprinting and Diagnostics, Nampally, Hyderabad-500001, India

Corresponding author: * **subhadeep@cdfd.org.in**

ABSTRACT

Plants are attacked by different kinds of pathogens; therefore plants have evolved defense mechanism to combat the pathogen attack and diseases. Many microbial signature molecules, which are known as microbe associated or pathogen associated molecular patterns (MAMPs/PAMPs) are recognized by a plant's primary layer of immune response, known as PAMP-triggered immunity (PTI). In the co-evolution of plant-microbe interactions, successful pathogens have acquired the ability to deliver effectors proteins directly inside plant cell to suppress PTI, allowing pathogen growth and disease. As a counter measure, plants have developed a second layer of defense system, by acquiring the ability to recognize these effector proteins via 'Resistance' (R) protein to trigger a defense response, known as effector triggered immunity (ETI). In this review, we discuss the developments that have taken place in understanding the PTI, effectors function, ETI and downstream signaling events. Understanding plant immune signaling pathways would be very helpful in controlling plant diseases.

Keywords: plant defense, receptor kinase, signal transduction, bacterial effectors
Abbreviations: CDPK, calcium dependent protein kinase; **ET**, ethylene; **ETI**, effector-triggered immunity; **HR**, hypersensitive response; **JA**, jasmonic acid; **MAPK**, mitogen activated protein kinase; **NB-LRR**, nucleotide binding-leucine rich repeat; **PAMPs/MAMPs/DAMP**, pathogen/microbe/damage associated molecular pattern; **PRR**, pattern recognition receptor; **PTI**, PAMP-triggered immunity; **RLK**, receptor like kinase; **ROS**, reactive oxygen species; **T2SS/T3SS**, type 2/3 secretion system; **SA**, salicylic acid; **T3Es**, type 3 effectors; **TAL**, transcription activator like

CONTENTS

INTRODUCTION

A number of plant diseases are caused by infectious agents including viruses, fungi and bacteria. Reducing yield losses due to plant diseases is necessary to secure sufficient food supply for a growing world population. Therefore, the study of plant-pathogen interactions is necessary to understand the molecular basis of plant diseases and its ultimate goal is to devise new strategies to protect crop plants against pathogen. Plants have the ability of recognizing and mounting defense responses against various kinds of pathogens. Plants have evolved to have two mechanisms of immunity to attain resistance against the pathogens. In this review, we outline our current knowledge of the signaling in plant-microbe interactions that have provided important insights to the mechanisms of activation of plant immunity and its suppression by successful pathogens's virulence functions.

PAMP-TRIGGERED IMMUNITY

The first mode of plant innate immunity is triggered upon the recognition of microbe-associated or pathogen-associated molecular patterns (MAMPs or PAMPs) or damage-associated molecular patterns (DAMPs) through plant receptor proteins called pattern recognition receptors (PRRs). This immune response is known as PAMP-triggered immunity (PTI) (**Fig. 1**) (Jones and Dangl 2006; Boller and Felix 2009). PTI represents immediate early and transient immune responses of plants against pathogens (Tsuda and Katagiri 2010).

Elicitors of PTI

PAMPs are essential components/structures or molecules that are conserved among diverse kind of species of pathogens. PAMPs play a critical role in the lifestyle of

Received: 27 February, 2012. Accepted: 25 December, 2012.

Invited Review

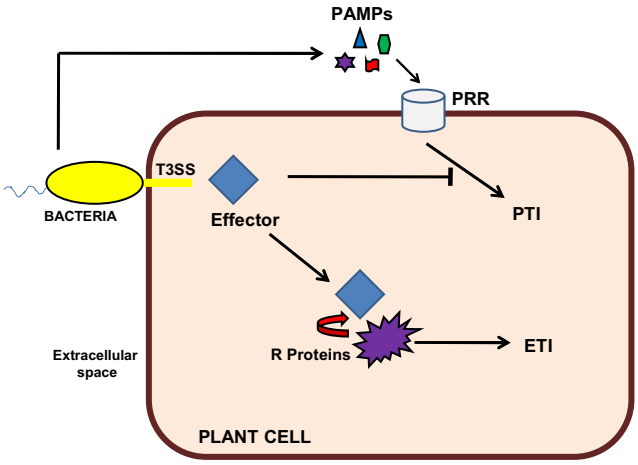

Fig. 1 Schematic representation of the signaling involved in plant immunity. Upon bacterial pathogen attack, the plant cell surface pattern recognition receptor (PRR) recognizes the PAMPs such as flagellin, EF-Tu, etc., and activates the PAMP-triggered immunity (PTI). However, a virulent pathogenic bacterium secretes effector proteins in to plant cell via a specialized structure, known as type 3 secretion system (T3SS). These effectors make the condition favorable for *in planta* growth by suppressing the PTI that leads to host susceptibility. In turn, plants have acquired a resistance (R) protein that recognizes effector protein that leads to effector-triggered immunity (ETI).

pathogens as well as are important for survival/pathogenesis. Therefore, pathogenic strains having defects or mutations in these conserved microbial signatures display impairment in causing disease on their respective hosts (Dodds and Rathjen 2010). Several PAMPs such as bacterial flagellin, elongation factor (EF-Tu), peptidoglycans (components of bacterial cell walls) have been shown to trigger PTI in *Arabidopsis* while chitin, flagellin peptides, a sulfated peptide Ax21 and lipopolysaccahride (LPS) were identified as PAMPs triggering PTI in rice (Boller and Felix 2009; Chen and Ronald 2011). Many plant pathogens secrete lytic enzymes to dissolve plant cell wall. The released cell wall fragments serve as an endogenous elicitors or DAMPs. Bacterial type 2 secretion system (T2SS) exports enzymes that are involved in degrading the plant cell wall such as pectinases, endoglucanases, cellulases, etc. These and other exoenzymes are believed to be responsible for causing the rotting and macerating phenotypes that are associated with these pathogens. Many of these T2SS enzymes are able to induce plant innate immunity by mediating damage to the cell wall and releasing DAMPs. For example, T2SS effectors from *Xanthomonas oryzae* pv. *oryzae* such as cellulase, lipase and xylanase act as a virulence factor and they are also capable of inducing the plant defense response (Jha *et al.* 2005, 2007). Some known DAMPs are produced under stress condition such as wound-induced *Arabidopsis* peptide Pep1 (see an excellent review on PAMPs/DAMPs by Boller and Felix 2009).

Perception of PAMPs by PRR

PRRs play a crucial role in initial pathogen perception and initiation of active defense responses. These plasma membrane localized receptors can be grouped into two classes-transmembrane receptor like kinase (RLKs) having a serine/threonine kinase domain and a transmembrane receptor like proteins (RLPs) lacking any apparent internal signaling domain. Their extracellular domains contain leucine-rich repeats (LRR) or LysM motifs. In *Arabidopsis*, more than 600 RLKs and more than 50 RLPs are present and several of them are responsive to various biotic stresses. PRRs display specificity for each kind of pathogen patterns (Zipfel 2008).

The well-characterized PRR of *Arabidopsis* that recognizes the bacterial flagellin is leucine rich repeat-receptor like kinase (LRR-RLK) FLAGELLIN SENSING 2 (FLS2). The FLS2 directly binds flagellin and forms an active signaling complex. A 22-amino acid epitope (flg22) present in the flagellin N-terminus is enough to activate the *Arabidopsis* FLS2 receptor (Chinchilla *et al.* 2006). The *Arabidopsis* plants lacking FLS2 are insensitive to flagellin/flg22 and these plants display more susceptibility towards pathogenic bacterium *Pseudomonas syringae* pv. *tomato* DC3000 (Zipfel *et al.* 2004). Also, in *Nicotiana benthamiana*, silencing of *NbFLS2* leads to increased growth of various kinds of compatible, non-host and non-pathogenic strains of *P. syringae* (Hann and Rathjen 2007). However, PAMPs-treated *Arabidopsis fls2* mutants treated with crude bacterial extracts display resistance indicating that multiple PRRs do exist for PAMPs other than flagellin and they ensure the restriction of *in planta* microbial growth (Zipfel *et al.* 2004). EF-Tu as a PAMP is perceived in *Arabidopsis* and some other plants of family Brassicaceae. The elf18, a highly conserved N-acetylated 18-amino acid peptide, is sufficient to trigger PTI. *Arabidopsis* PRR that recognizes EF-Tu, is the LRR-RLK EF-TU RECEPTOR (EFR) (Kunze *et al.* 2004; Zipfel *et al.* 2006). *Arabidopsis efr* mutants show more susceptibility towards *Agrobacterium tumefaciens* as well as some weak strains of *P. syringae* pv. *tomato*, indicating the importance of EF-Tu recognition driven plant defense against bacterial attack (Zipfel *et al.* 2006). The rice *Xa21* (which encodes for a LRR-RLK) (Song *et al.* 1995) is a PRR, which confers resistance to multiple *X. oryzae* pv. *oryzae* strains (Wang *et al.* 1996) producing Ax21 (Activator of XA21-mediated immunity) molecules (Shen *et al.* 2002; Lee *et al.* 2009). The *X. oryzae* pv. *oryzae* genetic locus encoding for Ax21 has been identified and the Ax21 molecule was characterized as a sulfated 194 aa long protein, which triggers XA21-mediated immunity in rice towards *X. oryzae* pv. *oryzae* (Lee *et al.* 2009). A sulfated 17 amino acids peptide ($AxY^{S}22$) derived from N-terminal region of Ax21 can directly bind to XA21 and is sufficient for activation of XA21-mediated immunity. The PRR for DAMP AtPep1 has also been identified. The AtPep1 represents C-terminal part of a small protein encoded by *PROPEP1*, a gene induced by wounding. In *Arabidopsis*, a LRR-RLK, PEPR1 acts as PRR for AtPep1 peptide (Yamaguchi *et al.* 2006).

Regulators of PTI

The establishment of PTI depends on the rapid recruitment of multiple SERKs (SOMATIC EMBYROGENESIS RECEPTOR LIKE KINASE) members within PRR complex. Most PRRs require the LRR-RK BRASSINOSTEROID INSENSITIVE-1-ASSOCIATED KINASE/SERK3 (BAK1/SERK3) for their activity (Chinchilla *et al.* 2007; Heese *et al.* 2007; Roux *et al.* 2011). The PRRs such as EFR and FLS2 rapidly forms complex with BAK1 upon treatment of EF-Tu and flg22. This interaction leads to phosphorylation of both PRR and BAK1 proteins. *Arabidopsis* plants having *bak1* mutations show decreased response to either flg22/elf18 (Chinchilla *et al.* 2007; Heese *et al.* 2007). Furthermore, a cytoplasmic protein kinase, BIK1 (BOTRYTIS-INDUCED KINASE 1) has been identified as a regulator of FLS2-BAK1 interaction. Up-regulation of the *bik1* gene as well as rapid phophorylation of BIK1 upon flagellin perception has been observed. *In vivo*, BIK1 interacts with FLS2 and BAK1 transphosphorylates both FLS2 and BAK1 to propagate flagellin mediated PTI signaling. The *bik1* mutants are reduced for flagellin mediated response as well as immunity to the nonpathogenic bacterial infection. This indicates that BIK1 is an important component in PTI signaling (Lu *et al.* 2010). Recently, it has been shown that flagellin also recruit two closely related U-box E3 ubiquitin ligases, PUB12 and PUB13, to FLS2 receptor complex in *Arabidopsis*. BAK1 is required for FLS2-PUB12/PUB13 association. PUB12 /PUB13 attenuate the activity of FLS2 by polyubiquitination and subsequent degradation. *Arabidopsis* plants lacking PUB12 and PUB13 display increased

level of resistance against *Pseudomonas spp*. These suggest that PUB12/PUB13 are negative regulators of flagellin signaling. It also indicates that PUB12/PUB13 can be genetically manipulated to enhance the disease resistance in plants (Lu *et al.* 2011).

Understanding of PAMPs induced PRRs signaling in plants can provide novel strategies to control the plant disease. It has been shown that PRR retains its activity when it is transferred between two plant families. For example, transgenic expression of *Arabidopsis* EFR provides responsiveness to EF-Tu in *N. benthamiana* and tomato plants and also confers broad-spectrum bacterial resistance (Lacombe *et al.* 2010). These results indicate that signaling pathways downstream of PRRs are well conserved across plants species and interfamily PRRs transfer could provide durable resistance against economically important bacterial pathogens.

PATHOGEN EFFECTORS

Successful pathogens suppress PAMP-triggered immunity and therefore, are able to cause a disease on respective host (**Fig. 1**). Bacterial pathogens employ a variety of virulence factors that facilitate their growth and disease-causing capabilities in plant tissues. An important step of bacterial pathogenesis is the delivery of virulence proteins from the bacterium into the plant's apoplast or cytoplasm. Indeed, in many early genetic screens for mutants of bacterial pathogenesis, mutations that disrupted for the function of protein-secretion systems were identified rather than effector proteins and enzymes that are direct modulators of plant biology (Preston *et al.* 2005). The well characterized secretion system in plant pathogens is the type 3 secretion system (T3SS). The T3SS is related to the bacterial flagellin, and forms a pilus that injects effectors into the plant cell. Inside the plant cell, these effectors modulate the plant's physiology to benefit the pathogen (Alfano and Collmer 1997; Buttner and Bonas 2002). Bacteria of different lifestyles, including pathogenic as well as symbiotic, depends on the T3SS to successfully interact with their hosts. Many plant-pathogenic bacteria such as *Xanthomonas spp.* inject more than 25 different kinds of type 3 effectors (T3Es) proteins directly into plant cells using T3SS (Kay and Bonas 2009). These T3Es promote pathogenicity by modulating host defense signaling and suppressing PTI (Alfano and Collmer 2004; Jones and Dangl 2006; Boller and He 2009). In phytopathogenic bacteria, the components of T3SS are encoded by *hrp* (hypersensitive response and pathogenicity) genes. Mutations in these genes result in loss of pathogenicity on susceptible host plants and inability to elicit the HR on non-host or resistant host plants (Alfano and Collmer 1997). For example, mutations in the *hrp* region of *X. oryzae* pv. *oryzae* result in the loss of pathogenicity on rice and loss of elicitation of the HR on either non-host plants such as tomato or resistant rice cultivars (Zhu *et al.* 2000). Mutations in genes for individual T3E often have less or no significant effect on the virulence phenotype indicating functional redundancy among T3Es (Roden *et al.* 2004; Castaneda *et al.* 2005). Although few T3Es have been shown to be important for virulence of plant pathogenic bacteria, various studies indicate that individual T3Es participate in suppression of plant innate immune responses that are triggered by PAMPs (Espinosa and Alfano 2004; Keshavarzi *et al.* 2004; Grant *et al.* 2006; Jha *et al.* 2007).

Bacterial effectors functions

There is a great diversity of effectors among bacterial species based on sequence level comparisons within different strains of plant pathogenic bacteria. In the past few years, genome sequences of many plant pathogenic bacteria have revealed that the type and variety of repertoire of T3SS effectors is very large and not much is known about the function of these effectors. These effectors have diverse enzymatic activities, such as cysteine protease (Shao *et al.* 2002; Lopez-Solanilla *et al.* 2004; Mudgett 2005), SUMO protease, ubiquitin E3 ligase and protein phosphatase activity, mono-ADP-ribosyltransferase, and studies of subcellular localization and host-mediated post-translational modifications have provided further clues regarding effector function (Gohre and Robatzek 2008).

P. syringae effectors such as AvrPto and AvrPtoB, target the FLS2–BAK1 complex (Gohre *et al.* 2008; Shan *et al.* 2008). The N-terminal kinase-targeting domain of AvrPtoB is sufficient to suppress flagellin responses while its C-terminal E3 ligase domain promote the degradation of FLS2 complex (Xiang *et al.* 2008). As a kinase inhibitor, AvrPto suppresses activity of various PRR receptor kinases. *Arabidopsis* resistance regulator RIN4 (RPM1-INTERACTING PROTEIN 4) is targeted by the *P. syringae* effectors AvrB, AvrRPM1 and AvrRpt2 through various molecular mechanisms (Mackey *et al.* 2002; Axtell *et al.* 2003; Mackey *et al.* 2003).

Interestingly, not all T3Es suppress PTI, but some bacterial effectors acts as transcription factors, which induce the expression of some specific host susceptible gene required for disease development and *in planta* growth. These T3Es are called TAL (transcription activator like) belonging to conserved AvrBs3/PthA effector family (Boch *et al.* 2009; Moscou and Bogdanove 2009). The presence of TAL-T3Es representing major virulence factor is restricted to *Xanthomonas* spp., but less conserved relatives have been also identified in *Ralstonia solanacearum* (Gurlebeck *et al.* 2006). They share features of eukaryotic transcription factors and are characterized by the presence of a central domain of tandem repeats, nuclear localization signals and an acidic transcriptional activation domain at their C-terminal region (Zhu *et al.* 1998; Szurek *et al.* 2001; Schornack *et al.* 2006).

X. campestris pv. *vesicatoria* AvrBs3 causes hypertrophy in mesophyll cells of susceptible pepper hosts. This helps in pathogen release to the plant surface during the late infective phase and also helps in pathogen spread in the field (Marois *et al.* 2002; Wichmann and Bergelson 2004). Several host (pepper) target genes of *X. campestris* pv. *vesicatoria* have been identified and are known as *UPA* (Up regulated by AvrBs3). The expression of a transcription factor *UPA20*, key regulator of cell hypertrophy, is up regulated by AvrBs3 (Kay *et al.* 2007; Kay and Bonas 2009). Promoter analysis of *UPA* genes revealed the presence of a UPA box, at which AvrBs3 binds directly and modulates host gene expression (Romer *et al.* 2007). The role of TAL-T3Es in the elicitation of citrus canker by *X. axonopodis* pv. *citri* and in the formation of water soaked lesion in leaves by the cotton pathogen *X. campestris* pv. *malvacearum*, have been demonstrated (Yang *et al.* 1996; Al-Saadi *et al.* 2007).

The AvrXa7, PthXo1, PthXo2 and PthXo3 proteins are the major virulence T3Es of this family in *X. oryzae* pv. *oryzae* (White and Yang 2009). *X. oryzae* pv. *oryzae* strains disrupted for TAL-T3Es exhibit severe virulence deficiency (Yang and White 2004). The PthXo1 protein induces the expression of a dominant allele *OsSWEET11* [also known as *Os8N3*; corresponding recessive allele (*xa13* or *ossweet11*) is promoter mutant of *OsSWEET11* (*Xa13*) and it encodes a protein belonging to class of sugar transporters, called SWEETs] (Yang *et al.* 2006; Chen *et al.* 2010). The gene *pthXo1* was identified from PXO99^{A} strain of *X. oryzae* pv. *oryzae*. PthXo1 cannot up regulate expression of *OsSWEET11* in rice lines homozygous for *xa13* allele. Promoter sequence variation leads to loss of *xa13* inducibility and consequently loss of susceptibility towards *X. oryzae* pv. *oryzae* strain PXO99^{A}. Hence, *OsSWEET11*, a target of PthXo1, is classified as host susceptibility (S) gene (Yang *et al.* 2006). *OsSWEET11* is a plasma membrane localized protein and PthXo1 activates transcription of *OsSWEET11* to induce the efflux of sugar to feed the *X. oryzae* pv. *oryzae* in the xylem (Chen *et al.* 2010). Knockdown of *OsSWEET11* via RNAi in susceptible rice line leads to resistance, but unlike rice plants having *xa13* allele, these

silenced plants exhibit low pollen viability and reduced seed set (Chu *et al.* 2006, 2010). Rice plants have evolved to have the *xa13* allele, which eliminates the disease susceptibility without affecting the normal developmental process. However, *xa13*-mediated resistance can be defeated by *X. oryzae* pv. *oryzae* strain PXO99^{A} having the alternative TAL effector AvrXa7, which activates the another sugar transporter *OsSWEET14* for sugar efflux to support the pathogen growth (Chen *et al.* 2010).

X. oryzae pv. *oryzae* strain PXO99^{A} also induces the expression of two other rice genes in a T3SS dependent manner. These are, *OsTFX1* (encodes a member of bZIP transcription family, present on chromosome 9) and *OsTFIIAγ1* (encodes a small subunit of the transcription factor IIA). The *OsTFX1* and *OsTFIIAγ1* genes are induced by TAL-T3Es PthXo6 and PthXo7, respectively. The loss of *pthXo6* results in reduced virulence of *X. oryzae* pv. *oryzae* and ectopic expression of *OsTFX1* (its function in normal plant is unknown) abrogates the requirement for *pthXo6* for full virulence (Sugio *et al.* 2007). In rice, there are two loci for the γ subunit of the TFIIA, one on chromosome 1 (*OsTFIIAγ1*) and another on chromosome 5 [two alleles, *OsTFIIAγ5* and *xa5* (encodes for TFIIA^{xa5})]. The PthXo7 induces the expression of *OsTFIIAγ1* and contributes to virulence on rice containing *xa5* the resistance gene [a recessive allele (missense mutant) of *OsTFIIAγ5* encoding a second form of the TFIIA small subunit on chromosome 5 of rice] (Sugio *et al.* 2007). TFIIAγ5 has been shown to be the predominant form of protein in rice while TFIIAγ1 may have a role in some specific, but as yet unknown stages. The *xa5* gene provides resistance to plants while maintaining the functionality of the protein, which is required for normal gene expression. It has been suggested that TFIIA^{xa5} may not interact with TAL-T3Es. Therefore, the PXO99^{A} strain of *X. oryzae* pv. *oryzae* may have evolved to have a *pthXo7* gene, which elevates the level of TFIIAγ1 (White and Yang 2009), to compensate for an inability to upregulate expression of this gene in rice plants homozygous for the *xa5* allele. *X. oryzae* pv. *oryzae* therefore alters the expression of multiple genes of host using TAL-T3Es supporting the hypothesis that the expression of cognate target genes results in host susceptibility, which brings about a favorable host environment for the pathogen to cause disease.

There are also examples in which bacteria can manipulate hormone pathways of host plant. Plant hormones can quickly and potently affect plant physiology; therefore it is not surprising that pathogens manipulate plant hormone signaling to promote disease. The *P syringae* pv. *tomato* toxin coronatine functions as a methyl jasmonate homologue to alter jasmonic acid (JA)-dependent plant responses. Microarray experiments show that coronatine dramatically reprogrammes host gene expression, causing altered expression of many genes (Uppalapati *et al.* 2005), including the upregulation of genes that are involved in the synthesis of endogenous JA. Coronatine-dependent reprogramming of plant gene expression has been shown to induce systemic susceptibility to bacterial pathogens, demonstrating that effector-mediated hormone regulation can broadly function as a virulence mechanism. T3Es have also been shown to modulate JA signaling to inhibit plant defence (He *et al.* 2004). Further understanding of the functions of the T3Es from plant pathogenic bacteria will help in understanding of pathogenicity strategies employed by plant pathogenic bacteria.

EFFECTOR-TRIGGERED IMMUNITY

Plants have evolved to have a second layer of immunity, which is mediated by Resistance (R) proteins that specifically recognize cognate pathogens effectors to induce effector-triggered immunity (ETI) or *R* gene-mediated disease resistance (**Fig. 1**) (Dodds and Rathjen 2010). Recognition of specific bacterial T3Es by plants carrying the cognate resistance (*R*) gene leads to start of a programmed cell death called hypersensitive response (HR), which limits the proliferation of the pathogen (Chisholm *et al.* 2006; Jones and Dangl 2006). Although ETI and PTI both give similar kind of response, ETI provides qualitatively prolonged and faster response (Tsuda and Katagiri 2010). In the absence of this interaction, pathogen escapes detection from plant and cause disease.

Mostly, resistance genes belong to a family of intracellular proteins having a nucleotide- binding (NB) site and leucine rich repeat (LRR) domain (Dangle and Jones 2001). Based on N-terminal domain, the NB-LRR class of *R* genes can be divided into coiled-coil (CC) NB-LRR and Toll-Interleukin-1 receptor (TIR) NB-LRR. For example, among the TIR-NB-LRR class of cytoplasmic R proteins are RPP5 and RPS4, which confer resistance to downy mildew pathogen *Peronospora parasitica* and bacterium *P. syringae*, respectively (Gassmann *et al.* 1999; Nöel *et al.* 1999). RPM1 and RPS2 are of the CC-NB-LRR-type of R-proteins that provide plant a resistant to *P. syringae* strains expressing the cognate effector genes (Holub 2001). Few components of ETI signaling have been identified. For example, EDS1 (ENHANCED DISEASE SUSCEPTIBILITY 1) of *Arabidopsis* is required for TIR-NB-LRR mediated signaling (Wiermer *et al.* 2005) whereas NDR1 (NONRACE-SPECIFIC DISEASE RESISTANCE 1) is required for some of the CC-NB-LRR mediated signaling (Day *et al.* 2006).

NB-LRR proteins can recognize pathogen effectors via two ways either 1) directly by physical interaction or 2) indirectly through an accessory protein that is part of an NB-LRR protein complex. In indirect mode, the pathogens effectors modifies the accessory proteins as a virulence target and this leads to recognition of modified accessory proteins by the NB-LRR protein. According to guard hypothesis (Dangl and Jones 2001), R protein does not interact directly with a pathogen effector but rather with another plant protein (the guard). The attempt of the pathogen to modify the guard activates the R protein, and plant resistance is triggered (Dangl and Jones 2001). *Arabidopsis* RIN4 is an example of a guard protein. Two *P. syringae* effector proteins, AvrRpm1 and AvrRpt2, manipulate RIN4, a regulator of PAMP signaling, and thus, interfere with the activation of basal defences (Cui *et al.* 2009).

The tomato plants carrying the NB-LRR protein Prf trigger resistance against *P. syringae* expressing effectors AvrPto and AvrPtoB whereas *P. syringae* strains having effectors AvrB or AvrRpm1, AvrRpt2 and AvrPphB trigger resistance in *Arabidopsis* plants carrying NB-LRR proteins RPM1, RPS2 and RPS5, respectively (Chisholm *et al.* 2006). In tomato, the NB-LRR protein Prf forms a complex with the accessory protein Pto kinase, which is target of AvrPto and AvrPtoB effectors of *P. syingae* pv. *tomato* (Mucyn *et al*. 2006). AvrPto does not have any catalytic activity; however it targets Pto as a kinase inhibitor and triggers disease resistance in tomato by interacting with Pto directly (Tang *et al*. 1996; Mucyn *et al*. 2006; Xing *et al.* 2007). Pto and its homologue Fen interact, AvrPtoB, to trigger resistance (Kim *et al*. 2002; Rosebrock *et al*. 2007). N-terminus of AvrPtoB inhibits Pto kinase activity whereas its C-terminus displays homology to eukaryotic E3 ubiquitin ligase (Abramovitch *et al*. 2006; Janjusevic *et al*. 2006). By ubiquitin ligase activity, AvrPtoB degrades Fen to destabilize Fen-Prf complex (Rosebrock *et al*. 2007), thereby pathogen escapes recognition of AvrPtoB by Fen-Prf complex (Ntoukakis *et al*. 2009). In contrast, AvrPtoB does not ubiquitinate Pto because Pto kinase phosphorylate C-terminus of AvrPtoB to inhibit its intrinsic ubiquitin E3 ligase activity (Ntoukakis *et al*. 2009). That prevents the degradation of resistance Pto-Prf complex. This interaction between AvrPtoB and Pto-Prf/Fen-Prf represent a fine example of evolutionary race between pathogen effectors mediated pathogenesis and R-gene mediated resistance in plants.

AvrPphB is a cysteins protease that target and cleaves the protein kinase PBS1 of *Arabidopsis*. The PBS1 is associated with RPS5 (RESISTANCE TO PSEUDOMONAS SYRINGAE 5). The cleavage of PBS1 in the PBS1-RPS5

complex leads to RPS5 conformational changes, which trigger resistance (Shao *et al.* 2003). In *Arabidopsis*, a key regulator of plant immunity, RIN4 (a membrane localized protein) is monitored by two R proteins, namely, RPM1 and RPS2. *P. syringae* effectors, AvrB and AvrRpm1 are recognized by RPM1. AvrB and AvrRpm1 directed phosphorylation of RIN4 activates RPM1, which in turn activates resistance signaling (Mackey *et al.* 2002). Kim *et al.* (2005) have shown that by modifying RIN4, AvrRpm1 suppress PTI. Another *P. syrinage* protease effector AvrRpt2 degrades RIN4 that leads to activation of RPS2 protein mediated resistance signaling pathways (Kim *et al.* 2005). The AvrRpt2 also suppresses the PTI by degrading RIN4 protein (Axtell and Stasskawicz 2003; Mackey *et al*. 2003). Overall, this indicates that a single R protein can recognize more than one effector via monitoring modifications in a common accessory protein, RIN4. It is highly like that pathogen effectors, AvrB and AvrRpm1 are evolved to inhibit PTI by targeting RIN4. In turn, plant evolved to have RPM1 to detect these effectors. Subsequently, pathogen evolved to have AvrRpt2 that deactivates the RPM1 mediated resistance in plants. However, in this evolutionary race, finally plants have evolved to have RPS2 to detect the presence of AvrRpt2, keeping resistance intact and inhibiting pathogen growth. This R protein-effector interaction is a remarkable example of evolutionary tussle between pathogen effectors and host resistance signaling pathways. This also indicates that acquisition of effectors by pathogen to suppress PAMP-triggered immunity led to evolution of R protein mediated ETI in plants. However, pathogens often evade recognition by plant by a loss of *avr* genes that lead to breakdown of *R*-gene mediated resistance in crops. R-protein-mediated recognition of basal defence suppressing effectors presents a strong selective challenge to the invading pathogen because loss of the recognized effector might also cause a significant decrease in pathogens fitness.

SIGNALING MECHANISM AND DOWNSTREAM RESPONSES IN PTI AND ETI

During both PTI and ETI, plant display various responses that include localized cell death (hypertensive response), stomata closure, deposition of callose to strengthen the plant cell wall at sites of infection, production of reactive oxygen species (ROS), rapid ion fluxes across the plasma membrane, accumulation of anti-microbial compounds, hormonal changes, activation of signaling cascades and change in gene expression, all of which ensures the prevention of pathogen growth (Chrisholm *et al.* 2006; Tsuda and Katagiri 2010). Transcriptome studies have shown that set of genes induced during PTI and ETI are overlapping in nature (Navaro *et al.* 2004). This suggests that plants use common downstream signaling pathways in response to various pathogens stimuli. Several studies have indicated that a successful pathogen interfere PTI signaling pathways by using various effectors, however they do not interfere ETI signaling pathways. Pathogen can escape from ETI by evading plant recognition mechanism. Additionally, genetic screens to get components of ETI signaling resulted in only inactivation of genes encoding for *R*-genes. Taken together, this suggests that ETI signaling pathways are robust than PTI signaling pathways against plant pathogens.

Ion fluxes, reactive oxygen species production and plant cell death

Recognition of PAMPs/DAMPs causes rapid influx of H^+ and Ca^{2+} and efflux of K^+ and anions such as nitrate (Wendehenne *et al.* 2002; Boller and Felix 2009). Increased cytoplasmic Ca^{2+} acts as secondary messenger and activates calcium-dependent protein kinases (CDPKs) (Ludwig *et al.* 2005; Ma 2011). Plants also respond to pathogens by producing reactive oxygen species (ROS) (Torres *et al*. 2006) that can act as stress signals or as an antibacterial agent. ROS production is dependent on NADPH oxidase AtRbohD in *Arabidopsis*. Zhang *et al*. (2007) has shown that *Arabidopsis atrbohD* mutants are deficient for flg-22 induced PTI. Generally, PAMPs induce transient/low amplitude of ROS production, however R-protein directed pathogen effector recognition leads to sustained and high amplitude of ROS production (Torres *et al.* 2006; Tsuda and Katagiri 2010).

In ETI, recognition of effector protein by R-protein leads to a form of rapid plant cell death known as hypersensitive response (HR), which may have role in preventing pathogen growth (Jones and Dangle 2006). In a study, it has been shown that AvrRps4-triggered (RPS4-mediated ETI) HR involves autophagy while AvrRpt2-triggered (RPS2-mediated ETI) HR does not involve autophagy. This indicates that pathways leading to HR are different in different R-protein mediated ETI events (Hofius *et al.* 2009). The *P. syringae* pv. *tabaci* 6605 flagellin induces cell death, indicating that HR and cell death can occur in PTI as well as ETI (Naito *et al.* 2008).

Gene expression changes and various host kinase signaling

In several studies, it has been found that upon PAMP treatment, a large number of host plant genes are differentially expressed. Treatment with PAMPs such as flg22, elf26, and chitin leads to up regulation of large subset of common genes at early time points (Tsuda and Katagiri 2010). This suggests that PTI signaling triggered by various kinds of PAMPs have common downstream signaling components. Denoux *et al.* (2008) showed that oligogalacturonides (oligosaccharides derived from the plant cell wall produced by a fungal pathogen) and flg22 induces similar transcriptional changes at early time points of treatments but the response of later time points differs. This suggest that, although host plants can use common components in early PTI signaling, but host plants may use entirely different components in late PTI signaling depending on the type of PAMPs to ensure the potent immune response against pathogen. Furthermore, it has been found that significant common genes are induced by PMAP and effector recognition (Navarro *et al.* 2004). This suggests that overlapping gene expression changes are observed in downstream responses during both PTI and ETI.

The involvement of mitogen activated protein kinase (MAPK) signaling cascade in *Arabidopsis* innate immunity have been studied well (Asai *et al.* 2002). In eukaryotic systems, components of MAPK signaling cascade transfer the signals from extracellular receptors to cell for providing the appropriate cellular responses. A MAPK cascade consists of a complex consisting of MAPK kinase kinase (MAPKKK), which phosphorylates a MAPK kinase (MAPKK), which phosphorylates MAPK. MAPK cascade regulates and modulates the activity of variety of substrates including transcription factors. The crucial role of MAPK cascade has been established in both PTI and ETI (Pitzschke *et al.* 2009; Tsuda and Katagiri 2010). Recognition of flg-22 triggers the activation of MAPKKs MKK4/5 and MAPKs MPK3/6. This causes further activation of WRKY transcription factors, which in turn, activates the expression of several plant defense related genes (Asai *et al.* 2002). Asai *et al.* (2002) also demonstrated that constitutive activation of MAPK cascade provides resistance against both bacterial and fungal pathogens. PAMPs induced MAPK activation takes place at very early time points and its activation is transient in nature. MPK3/6 are activated by other PAMPs such as elf18, chitin, etc (Tsuda and Katagiri 2010). MPK3/6 are also activated upon infection of *P. syringae*, but prolonged activation of MPK3/6 has been observed if *Arabidopsis* plants are infected with *P. syringae* strains carrying effector, AvrRpt2 (Underwood *et al.* 2007). Other than MAPK signaling cascade, activation of CDPKs is also important in achieving FLS2-mediated immunity (Boudsocq *et al.* 2010).

Plant hormone signaling

Plant hormones such as salicylic acid (SA), jasmonic acid (JA), ethylene (ET) play important role in regulation of defense gene expression and plant innate immunity (Bari and Jones 2009). SA and JA-ET signaling pathways work antagonistically. SA signaling pathway provides resistance against biotrophs/hemibiotrophs such as *P. syringae*, whereas JA-ET signaling pathway provides immunity against necrotrophs such as fungal pathogen *Alternaria* spp. (Bari and Jones 2009; Tsuda and Katagiri 2010). PAMPs such as flg22 induce the production of SA. Tsuda *et al.* (2008) demonstrated that SA deficient mutant was compromised for flg22 triggered PTI against *P. syringae* pv. *tomato* DC3000. Moreover, PAMPs also triggers the ET and JA production (Halim *et al.* 2009). This suggests that both SA and JA-ET signaling pathways act synergistically in PTI to achieve immunity. The AvrRpt2 triggered immunity via RPS2 display dependency on SA accumulation. Production of JA and ET has also been observed during ETI (Tsuda and Katagiri 2010). Besides, SA, JA and ET, the plant hormones such as auxin, abscisic acid, gibberllin, cytokinin, brassinosteroids play an important role in plant-pathogen interactions (Robert-Seilaniantz *et al.* 2011).

CONCLUSION

The research reviewed indicates that both plant and pathogen have co-evolved to possess various mechanisms for survival. These studies have provided important insights into the molecular signaling in plant-microbe interactions and are indicative of the ongoing evolutionary tussle between the pathogen and its host plant. A better understanding of the mechanisms underlying this interplay might lead to effective strategies for preventing yield losses due to plant pathogens.

ACKNOWLEDGEMENTS

Alok Pandey was supported by research fellowships from the Council of Scientific and Industrial Research (CSIR) and Department of Biotechnology, Government of India. This work was supported by funding from Department of Biotechnology, Government of India and CDFD to SC. We also want to acknowledge DBT-IYBA (Innovative Young Biotechnologist) award grant to SC.

REFERENCES

Abramovitch RB, Janjusevic R, Stebbins CE, Martin GB (2006) Type III effector AvrPtoB requires intrinsic E3 ubiquitin ligase activity to suppress plant cell death and immunity. *Proceedings of the National Academy of Sciences USA* **103**, 2851-2856

Alfano JR, Collmer A (1997) The type III (Hrp) secretion pathway of plant pathogenic bacteria: trafficking harpins, Avr proteins, and death. *Journal of Bacteriology* **179**, 5655-5662

Alfano JR, Collmer A (2004) Type III secretion system effector proteins: Double agents in bacterial disease and plant defense. *Annual Review of Phytopathology* **42**, 385-414

Al-Saadi A, Reddy JD, Duan YP, Brunings AM, Yuan Q, Gabriel DW (2007) All five host-range variants of *Xanthomonas citri* carry one *pthA* homolog with 17.5 repeats that determines pathogenicity on citrus, but none determine host-range variation. *Molecular Plant-Microbe Interactions* **20**, 934-943

Asai T, Tena G, Plotnikova J, Willmann MR, Chiu WL, Gomez-Gomez L, Boller T, Ausubel FM, Sheen J (2002) MAP kinase signaling cascade in *Arabidopsis* innate immunity. *Nature* **415**, 977-983

Axtell MJ, Staskawicz BJ (2003) Initiation of RPS2-specified disease resistance in *Arabidopsis* is coupled to the AvrRpt2-directed elimination of RIN4. *Cell* **112**, 369-377

Bari R, Jones JD (2009) Role of plant hormones in plant defense responses. *Plant Molecular Biology* **69**, 473-488

Boch J, Scholze H, Schornack S, Landgraf A, Hahn S, Kay S, Lahaye T, Nickstadt A, Bonas U (2009) Breaking the code of DNA binding specificity of TAL-type III effectors. *Science* **326**, 1509-1512

Boller T, Felix G (2009) A renaissance of elicitors: perception of microbe-associated molecular patterns and danger signals by pattern-recognition receptors. *Annual Review of Plant Biology* **60**, 379-406

Boller T, He SY (2009) Innate immunity in plants: An arms race between pattern recognition receptors in plants and effectors in microbial pathogens. *Science* **324**, 742-744

Boudsocq M, Willmann MR, McCormack M, Lee H, Shan L, He P, Bush J, Cheng SH, Sheen J (2010) Differential innate immune signaling via Ca^{2+} sensor protein kinases. *Nature* **464**, 418-422

Buttner D, Bonas U (2002) Getting across-bacterial type III effector proteins on their way to the plant cell. *EMBO Journal* **21**, 5313-5322

Castaneda A, Reddy JD, El-Yacoubi B, Gabriel DW (2005) Mutagenesis of all eight *avr* genes in *Xanthomonas campestris* pv. *campestris* had no detected effect on pathogenicity, but one *avr* gene affected race specificity. *Molecular Plant-Microbe Interactions* **18**, 1306-1317

Chen LQ, Hou BH, Lalonde S, Takanaga H, Hartung ML, Qu X, Guo W, Kim J, Underwood W, Chaudhri B, Chermak D, Aantony G, White FF, Somerville SC, Mudgett MB, Frommer WB (2010) Sugar transporters for intercellular exchange and nutrition of pathogens. *Nature* **468**, 527-532

Chen X, Ronald P (2011) Innate immunity in rice. *Trends in Plant Science* **16**, 451-459

Chinchilla D, Bauer Z, Regenass M, Boller T, Felix G (2006) The *Arabidopsis* receptor kinase FLS2 binds flg22 and determines the specificity of flagellin perception. *Plant Cell* **18**, 465-476

Chinchilla D, Zipfel C, Robatzek S, Kemmerling B, Nurnberger T, Jones JD, Felix G, Boller T (2007) A flagellin-induced complex of the receptor FLS2 and BAK1 initiates plant defence. *Nature* **448**, 497-500

Chisholm ST, Coaker G, Day B, Staskawicz BJ (2006) Host-microbe interactions: Shaping the evolution of the plant immune response. *Cell* **124**, 803-814

Chu Z, Yuan M, Yao J, Ge, X, Yuan, B., Xu, C, Li X, Fu B, Li H, Bennetzen JL, Zhang Q, Wang S (2006) Promoter mutations of an essential gene for pollen development result in disease resistance in rice. *Genes and Development* **20**, 1250-1255

Cui H, Xiang T, Zhou JM (2009) Plant immunity: A lesson from pathogenic bacterial effector proteins. *Cellular Microbiology* **11**, 1453-1461

Dangl JL, Jones JD (2001) Plant pathogens and integrated defence responses to infection. *Nature* **411**, 826-833

Day B, Dahlbeck D, Staskawicz BJ (2006) NDR1 interaction with RIN4 mediates the differential activation of multiple disease resistance pathways in *Arabidopsis. Plant Cell* **18**, 2782-2791

Denoux C, Galletti R, Mammarella N, Gopalan S, Werck D, De Lorenzo G, Ferrari S, Ausubel FM, Dewdney J (2008) Activation of defense response pathways by OGs and Flg22 elicitors in *Arabidopsis* seedlings. *Molecular Plant* **1**, 423-445

Dodds PN, Rathjen JP (2010) Plant immunity: Towards an integrated view of plant-pathogen interactions. *Nature Review Genetics* **11**, 539-548

Espinosa A, Alfano JR (2004) Disabling surveillance: Bacterial type III secretion system effectors that suppress innate immunity. *Cellular Microbiology* **6**, 1027-1040

Gassmann W, Hinsch ME, Staskawicz BJ (1999) The *Arabidopsis* RPS4 bacterial-resistance gene is a member of the TIR-NBS-LRR family of disease-resistance genes. *Plant Journal* **20**, 265-277

Gohre V, Robatzek S (2008) Breaking the barriers: Microbial effector molecules subvert plant immunity. *Annual Review of Phytopathol*ogy **46**, 189-215

Gohre V, Spallek T, Haweker H, Mersmann S, Mentzel T, Boller T, de Torres M, Mansfield JM, Robatzek KS (2008) Plant pattern-recognition receptor FLS2 is directed for degradation by the bacterial ubiquitin ligase AvrPtoB. *Current Biology* **18**, 1824-1832

Grant SR, Fisher EJ, Chang JH, Mole BM, Dangl JL (2006) Subterfuge and manipulation: type III effector proteins of phytopathogenic bacteria. *Annual Review of Microbiology* **60**, 425-449

Gurlebeck D, Thieme F, Bonas U (2006) Type III effector proteins from the plant pathogen *Xanthomonas* and their role in the interaction with the host plant. *Journal of Plant Physiology* **163**, 233-255

Halim VA, Altmann S, Ellinger D, Eschen-Lippold L, Miersch O, Scheel D, Rosahl S (2009) PAMP-induced defense responses in potato require both salicylic acid and jasmonic acid. *Plant Journal* **57**, 230-242

Hann DR, Rathjen JP (2007) Early events in the pathogenicity of *Pseudomonas syringae* on *Nicotiana benthamiana*. *Plant Journal* **49**, 607-618

Heese A, Hann DR, Gimenez-Ibanez S, Jones AME, He K, Li J, Schroeder JI, Peck SC, Rathjen JP (2007) The receptor-like kinase SERK3/BAK1 is a central regulator of innate immunity in plants. *Proceedings of the National Academy of Sciences USA* **104**, 12217-12222

He P, Chintamanani S, Chen Z, Zhu L, Kunkel BN, Alfano JR, Tang X, Zhou JM (2004) Activation of a COI1-dependent pathway in *Arabidopsis* by *Pseudomonas syringae* type III effectors and coronatine. *Plant Journal* **37**, 589-602

Hofius D, Schultz-Larsen T, Joensen J, Tsitsigiannis DI, Petersen NH, Mattsson O, Jorgensen LB, Jones JD, Mundy J, Petersen M (2009) Autophagic components contribute to hypersensitive cell death in *Arabidopsis*. *Cell* **137**, 773-783

Holub EB (2001) The arms race is ancient history in *Arabidopsis*, the wildflower. *Nature Review Genetics* **2**, 516-527

Janjusevic R, Abramovitch RB, Martin GB, Stebbins CE (2006) A bacterial inhibitor of host programmed cell death defenses is an E3 ubiquitin ligase. *Science* **311**, 222-226

Jha G, Rajeshwari R, Sonti RV (2005) Bacterial type two secretion system secreted proteins: Double-edged swords for plant pathogens. *Molecular Plant-Microbe Interaction* **19**, 891-898

Jha G, Rajeshwari R, Sonti RV (2007) Functional interplay between two *Xanthomonas oryzae* pv. *oryzae* secretion systems in modulating virulence on rice. *Molecular Plant-Microbe Interactions* **20**, 31-40

Jones JD, Dangl JL (2006) The plant immune system. *Nature* **444**, 323-329

Kay S, Hahn S, Marois E, Hause G, Bonas U (2007) A bacterial effector acts as a plant transcription factor and induces a cell size regulator. *Science* **318**, 648-651

Kay S, Bonas U (2009) How *Xanthomonas* type III effectors manipulate the host plant. *Current Opinion in Microbiology* **12**, 37-43

Keshavarzi M, Soylu S, Brown I, Bonas U, Nicole M, Rossiter J, Mansfield J (2004) Basal defenses induced in pepper by lipopolysaccharides are suppressed by *Xanthomonas campestris* pv. *vesicatoria*. *Molecular Plant-Microbe Interaction* **17**, 805-815

Kim MG, da Cunha L, McFall AJ, Belkhadir Y, DebRoy S, Dangl JL, Mackey D (2005) Two *Pseudomonas syringae* type III effectors inhibit RIN4-regulated basal defense in *Arabidopsis*. *Cell* **121**, 749-759

Kim YJ, Lin NC, Martin GB (2002) Two distinct *Pseudomonas* effector proteins interact with the Pto kinase and activate plant immunity. *Cell* **109**, 589-598

Kunze G, Zipfel C, Robatzek S, Niehaus K, Boller T, Felix G (2004) The N terminus of bacterial elongation factor Tu elicits innate immunity in *Arabidopsis* plants. *Plant Cell* **16**, 3496-3507

Lacombe S, Rougon-Cardoso A, Sherwood E, Peeters N, Dahlbeck D, van Esse HP, Smoker M, Rallapalli G, Thomma BP, Staskawicz B, Jones JD, Zipfel C (2010) Interfamily transfer of a plant pattern-recognition receptor confers broad-spectrum bacterial resistance. *Nature Biotechnology* **28**, 365-369

Lee SW, Han SW, Sririyanum M, Park CJ, Seo YS, Ronald PC (2009) A type I-secreted, sulfated peptide triggers XA21-mediated innate immunity. *Science* **326**, 850-853

Lopez-Solanilla E, Bronstein PA, Schneider A, Collmer A (2004) HopPtoN is a *Pseudomonas syringae* Hrp (type III secretion system) cysteine protease effector that suppresses pathogen-induced necrosis associated with both compatible and incompatible plant interactions. *Molecular Microbiology* **54**, 353-365

Lu D, Wu S, Gao X, Zhang Y, Shan L, 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 USA* **107**, 496-501

Lu D, Lin W, Gao X, Wu S, Cheng C, Avila J, Heese A, Devarenne TP, He P, Shan L (2011) Direct ubiquitination of pattern recognition receptor FLS2 attenuates plant innate immunity. *Science* **332**, 1439-1442

Ludwig AA, Saitoh H, Felix G, Freymark G, Miersch O, Wasternack C, Boller T, Jones JD, Romeis T (2005) Ethylene-mediated cross-talk between calcium-dependent protein kinase and MAPK signaling controls stress responses in plants. *Proceedings of the National Academy of Sciences USA* **102**, 10736-10741

Ma W (2011) Roles of Ca^{2+} and cyclic nucleotide gated channel in plant innate immunity. *Plant Science* **181**, 342-346

Mackey D, Holt BF 3rd, Wiig A, Dangl JL (2002) RIN4 interacts with *Pseudomonas syringae* type III effector molecules and is required for RPM1-mediated disease resistance in *Arabidopsis*. *Cell* **108**, 743-754

Mackey D, Belkhadir Y, Alonso JM, Ecker JR, Dangl JL (2003) *Arabidopsis* RIN4 is a target of the type III virulence effector AvrRpt2 and modulates RPS2-mediated resistance. *Cell* **112**, 379-389

Marois E, Van den Ackerveken G, Bonas U (2002) The *Xanthomonas* type III effector protein AvrBs3 modulates plant gene expression and induces cell hypertrophy in the susceptible host. *Molecular Plant-Microbe Interaction* **15**, 637-646

Moscou MJ, Bogdanove AJ (2009) A simple cipher governs DNA recognition by TAL effectors. *Science* **326**, 1501

Mucyn TS, Clemente A, Andriotis VM, Balmuth AL, Oldroyd GE, Staskawicz BJ, Rathjen JP (2006) The tomato NBARC-LRR protein Prf interacts with Pto kinase *in vivo* to regulate specific plant immunity. *Plant Cell* **18**, 2792-2806

Mudgett MB (2005) New insights to the function of phytopathogenic bacterial type III effectors in plants. *Annual Review of Plant Biology* **56**, 509-531

Naito K, Taguchi F, Suzuki T, Inagaki Y, Toyoda K, Shiraishi T, Ichinose Y (2008) Amino acid sequence of bacterial microbe associated molecular pattern flg22 is required for virulence. *Molecular Plant-Microbe Interactions* **21**, 1165-1174

Navarro L, Zipfel C, Rowland O, Keller I, Robatzek S, Boller T, Jones JD (2004) The transcriptional innate immune response to flg22, Interplay and overlap with *Avr* gene-dependent defense responses and bacterial pathogenesis. *Plant Physiol*ogy **135**, 1113-1128

Noël L, Moores TL, Van der Biezen EA, Parniske M, Daniels MJ, Parker JE, Jones JDG (1999) Pronounced intra specific haplotype divergence at the RPP5 complex disease resistance locus of *Arabidopsis*. *Plant Cell* **11**, 2099-2111

Ntoukakis V, Mucyn TS, Gimenez-Ibanez S, Chapman HC, Gutierrez JR, Balmuth AL, Jones AM, Rathjen JP (2009) Host inhibition of a bacterial virulence effector triggers immunity to infection. *Science* **324**, 784-787

Pitzschke A, Schikora A, Hirt H (2009) MAPK cascade signalling networks in plant defence. *Current Opinion in Plant Biology* **12**, 421-426

Preston GM, Studholme DJ, Caldelari I (2005) Profiling the secretomes of plant pathogenic Proteobacteria. *FEMS Microbiological Review* **29**, 331-360

Robert-Seilaniantz A, Grant M, Jones JD (2011) Hormone crosstalk in plant disease and defense: More than just JASMONATE-SALICYLATE antagonism. *Annual Review of Phytopathology* **49**, 317-343

Roden JA, Belt B, Ross JB, Tachibana T, Vargas J, Mudgett MB (2004) A genetic screen to isolate type III effectors translocated into pepper cells during *Xanthomonas* infection. *Proceedings of the National Academy of Sciences USA* **101**, 16624-16629

Romer P, Hahn S, Jordan T, Strauss T, Bonas U, Lahaye T (2007) Plant pathogen recognition mediated by promoter activation of the pepper *Bs3* resistance gene. *Science* **318**, 645-648

Rosebrock TR, Zeng L, Brady JJ, Abramovitch RB, Xiao F, Martin GB (2007) A bacterial E3 ubiquitin ligase targets a host protein kinase to disrupt plant immunity. *Nature* **448**, 370-374

Roux M, Schwessinger B, Albrecht C, Chinchilla D, Jones A, Holton N, Malinovsky FG, Tör M, de Vries S, Zipfel C (2011) The *Arabidopsis* leucine -rich repeat receptor-like kinases BAK1/SERK3 and BKK1/SERK4 are required for innate immunity to hemibiotrophic and biotrophic pathogens. *Plant Cell* **23**, 2440-2455

Schornack S, Meyer A, Romer P, Jordan T, Lahaye T (2006) Gene-for-gene-mediated recognition of nuclear-targeted AvrBs3-like bacterial effector proteins. *Journal of Plant Physiology* **163**, 256-272

Shan L, He P, Li J, Heese A, Peck SC, Nurnberger T, Martin GB, Sheen J (2008) Bacterial effectors target the common signaling partner BAK1 to disrupt multiple MAMP receptor signaling complexes and impede plant immunity. *Cell Host and Microbe* **4**, 17-27

Shao F, Merritt PM, Bao Z, Innes RW, Dixon JE (2002) A *Yersinia* effector and a *Pseudomonas* avirulence protein define a family of cysteine proteases functioning in bacterial pathogenesis. *Cell* **109**, 575-588

Shao F, Golstein C, Ade J, Stoutemyer M, Dixon JE, Innes RW (2003) Cleavage of *Arabidopsis* PBS1 by a bacterial type III effector. *Science* **301**, 1230-1233

Shen Y, Sharma P, da Silva FG, Ronald P (2002) The *Xanthomonas oryzae* pv. *lozengeoryzae raxP* and *raxQ* genes encode an ATP sulphurylase and adenosine-5'-phosphosulphate kinase that are required for AvrXa21 avirulence activity. *Molecular Microbiology* **44**, 37-48

Song WY, Wang GL, Chen LL, Kim HS, Pi LY, Holsten T, Gardner J, Wang B, Zhai WX, Zhu LH, Fauquet C, Ronald P (1995) A receptor kinase-like protein encoded by the rice disease resistance gene, *Xa21*. *Science* **270**, 1804-1806

Sugio A, Yang B, Zhu T, White FF (2007) Two type III effector genes of *Xanthomonas oryzae* pv. *oryzae* control the induction of the host genes *OsTFIIAγ1* and *OsTFX1* during bacterial blight of rice. *Proceedings of the National Academy of Sciences USA* **104**, 10720-10725

Szurek B, Marois E, Bonas U, Van den Ackerveken G (2001) Eukaryotic features of the *Xanthomonas* type III effector AvrBs3: Protein domains involved in transcriptional activation and the interaction with nuclear import receptors from pepper. *Plant Journal* **26**, 523-534

Tang X, Frederick RD, Zhou J, Halterman DA, Jia Y, Martin GB (1996) Initiation of plant disease resistance by physical interaction of AvrPto and Pto kinase. *Science* **274**, 2060-2063

Torres MA, Jones JD, Dangl JL (2006) Reactive oxygen species signaling in response to pathogens. *Plant Physiology* **141**, 373-378

Tsuda K, Sato M, Glazebrook J, Cohen JD, Katagiri F (2008) Interplay between MAMP-triggered and SA-mediated defense responses. *Plant Journal* **53**, 763-775

Tsuda K, Katagiri F (2010) Comparing signaling mechanisms engaged in pattern-triggered and effector-triggered immunity. *Current Opinion in Plant Biology* **13**, 459-465

Underwood W, Zhang S, He SY (2007) The *Pseudomonas syringae* type III effector tyrosine phosphatase HopAO1 suppresses innate immunity in *Arabidopsis thaliana*. *Plant Journal* **52**, 658-672

Uppalapati SR, Ayoubi P, Weng H, Palmer DA, Mitchell RE, Jones W, Bender CL (2005) The phytotoxin coronatine and methyl jasmonate impact multiple phytohormone pathways in tomato. *Plant Journal* **42**, 201-217

Wang GL, Song WY, Ruan DL, Sideris S, Ronald PC (1996) The cloned gene, *Xa21*, confers resistance to multiple *Xanthomonas oryzae* pv. *oryzae* isolates in transgenic plants. *Molecular Plant-Microbe Interactions* **9**, 850-855

Wendehenne D, Lamotte O, Frachisse JM, Barbier-Brygoo H, Pugin A (2002) Nitrate efflux is an essential component of the cryptogein signaling pathway leading to defense responses and hypersensitive cell death in tobacco. *Plant Cell* **14**, 1937-1951

Wichmann G, Bergelson J (2004) Effector genes of *Xanthomonas axonopodis* pv. *vesicatoria* promote transmission and enhance other fitness traits in the field. *Genetics* **166**, 693-706

Wiermer M, Feys BJ, Parker JE (2005) Plant immunity: The EDS1 regulatory node. *Current Opinion in Plant Biology* **8**, 383-389

White FF, Yang B (2009) Host and pathogen factors controlling the rice-*Xanthomonas oryzae* interaction. *Plant Physiology* **150**, 1677-1686

Xiang T, Zong N, Zou Y, Wu Y, Zhang J, Xing W, Li Y, Tang X, Zhu L, Chai J, Zhou JM (2008) *Pseudomonas syringae* effector AvrPto blocks innate immunity by targeting receptor kinases. *Current Biology* **18,** 74-80

Xing W, Zou Y, Liu Q, Liu J, Luo X, Huang Q, Chen S, Zhu L, Bi R, Hao Q, Wu JW, Zhou JM, Chai J (2007) The structural basis for activation of plant immunity by bacterial effector protein AvrPto. *Nature* **449,** 243-247

Yamaguchi Y, Pearce G, Ryan CA (2006) The cell surface leucine-rich repeat receptor for AtPep1, an endogenous peptide elicitor in *Arabidopsis*, is functional in transgenic tobacco cells. *Proceedings of the National Academy of Sciences USA* **103**, 10104-10109

Yang B, White FF (2004) Diverse members of the AvrBs3/PthA family of type III effectors are major virulence determinants in bacterial blight disease of rice. *Molecular Plant-Microbe Interaction* **17**, 1192-1200

Yang B, Sugio A, White FF (2006) *Os8N3* is a host disease-susceptibility gene for bacterial blight of rice. *Proceedings of the National Academy of Sciences USA* **103**, 10503-10508

Yang YN, Yuan QP, Gabriel DW (1996) Watersoaking function(s) of XcmH1005 are redundantly encoded by members of the *Xanthomonas avr/pth* gene family. *Molecular Plant-Microbe Interaction* **9**, 105-113

Zhang J, Shao F, Li Y, Cui H, Chen L, Li H, Zou Y, Long C, Lan L, Chai J, Chen S, Tang X, Zhou JM (2007) A *Pseudomonas syringae* effector inactivates MAPKs to suppress PAMP-induced immunity in plants. *Cell Host and Microbe* **1**, 175-185

Zhu W, MaGbanua MM, White FF (2000) Identification of two novel *hrp*-associated genes in the *hrp* gene cluster of *Xanthomonas oryzae* pv. *oryzae*. *Journal of Bacteriology* **182**, 1844-1853

Zhu W, Yang B, Chittoor JM, Johnson LB, White FF (1998) AvrXa10 contains an acidic transcriptional activation domain in the functionally conserved C terminus. *Molecular Plant- Microbe Interaction* **11**, 824-832

Zipfel C (2008) Pattern-recognition receptors in plant innate immunity. *Current Opinion in Immunology* **20**, 10-16

Zipfel C, Kunze G, Chinchilla D, Caniard A, Jones JD, Boller T, Felix G (2006) Perception of the bacterial PAMP EF-Tu by the receptor EFR restricts *Agrobacterium*-mediated transformation. *Cell* **125**, 749-760

Zipfel C, Robatzek S, Navarro L, Oakeley EJ, Jones JD, Felix G, Boller T (2004) Bacterial disease resistance in *Arabidopsis* through flagellin perception. *Nature* **428**, 764-767