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CURRENT REVIEW

Convergent and Divergent Signaling in PAMP-Triggered Immunity and Effector-Triggered Immunity

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Plants use diverse immune receptors to sense pathogen attacks. Recognition of pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors localized on the plasma membrane leads to PAMP-triggered immunity (PTI). Detection of pathogen effectors by intracellular or plasma membrane–localized immune receptors results in effector-triggered immunity (ETI). Despite the large variations in the magnitude and duration of immune responses triggered by different PAMPs or pathogen effectors during PTI and ETI, plasma membrane–localized immune receptors activate similar downstream molecular events such as mitogen-activated protein kinase activation, oxidative burst, ion influx, and increased biosynthesis of plant defense hormones, indicating that defense signals initiated at the plasma membrane converge at later points. On the other hand, activation of ETI by immune receptors localized to the nucleus appears to be more directly associated with transcriptional regulation of defense gene expression. Here, we review recent progress in signal transductions downstream of different groups of plant immune receptors, highlighting the converging and diverging molecular events.

In nature, plants live in an environment surrounded by diverse microbial pathogens. In response to pathogen attack, plants have evolved a sophisticated immune system to recognize pathogens and activate defense responses. Pattern recognition receptors (PRRs) localized on the plasma membrane are used to detect conserved molecular features of microbes collectively known as pathogen-associated molecular patterns (PAMPs) or microbe-associated molecular patterns (MAMPs) (Yu et al. 2017). All known PRRs fall into the receptor-like kinase (RLK) or receptor-like protein (RLP) families. Binding of PAMPs to PRRs triggers activation of PAMP-triggered immunity (PTI). In addition to PTI, plants use intracellular or transmembrane receptors known as resistance (R) proteins to detect specific effector proteins secreted by pathogens to promote their colonization of the host plants (Li et al. 2015b). Recognition of pathogen effectors by their cognate receptors leads to activation of effector-triggered immunity (ETI). Except for a number of R proteins in the RLK and RLP families, most R proteins belong to the nucleotide-binding site-leucine-rich repeat receptor (NLR) family. Typical NLRs are divided into two subgroups based on whether a Toll-interleukin 1-like receptor (TIR) domain or a coiled-coil (CC) domain is present at their N termini.

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Recognition of pathogens by immune receptors triggers a series of downstream defense responses including activation of mitogen-activated protein kinases (MAPKs), oxidative burst, ion influx, and increased biosynthesis of defense hormones in plants. Transcriptome analysis showed that there is substantial overlap between genes induced during PTI and ETI (Navarro et al. 2004) and similar genes are induced during *Arabidopsis* responses to virulent and avirulent *Pseudomonas syringae* pathogens but with quantitative difference in the magnitude of induction (Tao et al. 2003), suggesting that defense signaling converges in PTI and ETI. In this review, we focus on some of the convergent and divergent points in signal transduction downstream of plant immune receptor (Fig. 1).

PLANT IMMUNE RECEPTORS

Plants use a vast array of immune receptors for pathogen detection. A large number of RLKs and RLPs have been identified as receptors for different PAMPs from bacteria and fungi (Tang et al. 2017; Yu et al. 2017). Some of these receptors are conserved in higher plants, while others are unique to specific families of plants. Two conserved RLKs with short extracellular leucine-rich repeats (LRRs), BAK1 and SOBIR1, serve as adapter and signaling kinases for many of the PAMP receptors (Liebrand et al. 2014). Perception of PAMPs by different immune receptors triggers similar downstream defense responses, but the magnitude of these responses varies, depending on the concentration and nature of the PAMPs.

Plants also use a large family of NLRs to detect fast-evolving pathogen effectors (Jacob et al. 2013; Li et al. 2015b). Recognition of pathogen effectors by NLRs is highly specific and often leads to strong immune outcomes, such as activation of hypersensitive response (HR). Since pathogen effectors detected by NLRs evolve rapidly, most NLRs are highly divergent among different plant species. The best-known exceptions to this are two groups of CC-NLRs (CNLs), one represented by the tobacco NRG1 (N REQUIREMENT GENE 1) and the other represented by the *Arabidopsis* ADR1 (ACTIVATED DISEASE RESISTANCE 1) and the closely related ADR1-L1 (ADR1-LIKE 1) and ADR1-L2 (ADR1-LIKE 2), which are highly conserved in higher plants (Bonardi et al. 2011; Collier et al. 2011; Peart et al. 2005). They are required for resistance mediated by TIR-NLRs (TNLs) and may serve as adapter and signaling NLRs for TNLs (Bonardi et al. 2011; Peart et al. 2005).

RECEPTOR-LIKE CYTOPLASMIC KINASES (RLCKS) IN PLANT IMMUNITY

RLCKs contain a Ser/Thr-special cytoplasmic kinase domain similar to RLKs but lack an extracellular domain or transmembrane domain. They could be anchored to the plasma membrane through N-terminal myristoylation or palmitoylation. RLCKs have emerged as direct targets and immediate downstream signaling components of RLKs (Lin et al. 2013). In *Arabidopsis*, several RLCKs are involved in the activation of different downstream defense responses during PTI. These RLCKs may represent critical divergent points of signal transduction downstream of PRRs.

The *Arabidopsis* RLCK BIK1 interacts with FLS2 and is rapidly phosphorylated in a FLS2-dependent manner upon perception of the bacterial flagellin peptide flg22 (Lu et al. 2010; Zhang et al. 2010a). BIK1 is required for the induction of reactive oxygen species (ROS) production by different PAMPs. Another *Arabidopsis* RLCK, BSK1, also interacts with FLS2 and contributes to flg22-induced ROS production (Shi et al. 2013). In contrast, the *Arabidopsis* RLCK PBL13 is involved in the negative regulation of flg22-induced ROS production (Lin et al. 2015). In rice, OsRLCK185 associates with chitin receptor OsCERK1 and is phosphorylated by OsCERK1 after chitin treatment (Yamaguchi et al. 2013). OsRLCK185 and its *Arabidopsis* homolog PBL27 are involved in chitin-induced ROS production and MAPK activation (Shinya et al. 2014; Yamada et al. 2016; Yamaguchi et al. 2013).

Two other *Arabidopsis* RLCKs, PCRK1 and PCRK2, also interact with FLS2 and are rapidly phosphorylated following treatment with flg22 (Kong et al. 2016). PCRK1 and PCRK2 function redundantly to promote pathogen-induced salicylic acid (SA) biosynthesis. Loss of PCRK1 and PCRK2 leads to compromised PTI and reduced resistance against pathogens (Kong et al. 2016; Sreekanta et al. 2015). Another *Arabidopsis* RLCK, PBL1, together with its closely related BIK1 is required for PAMP-induced Ca^{2+} elevation (Li et al. 2014; Ranf et al. 2014),

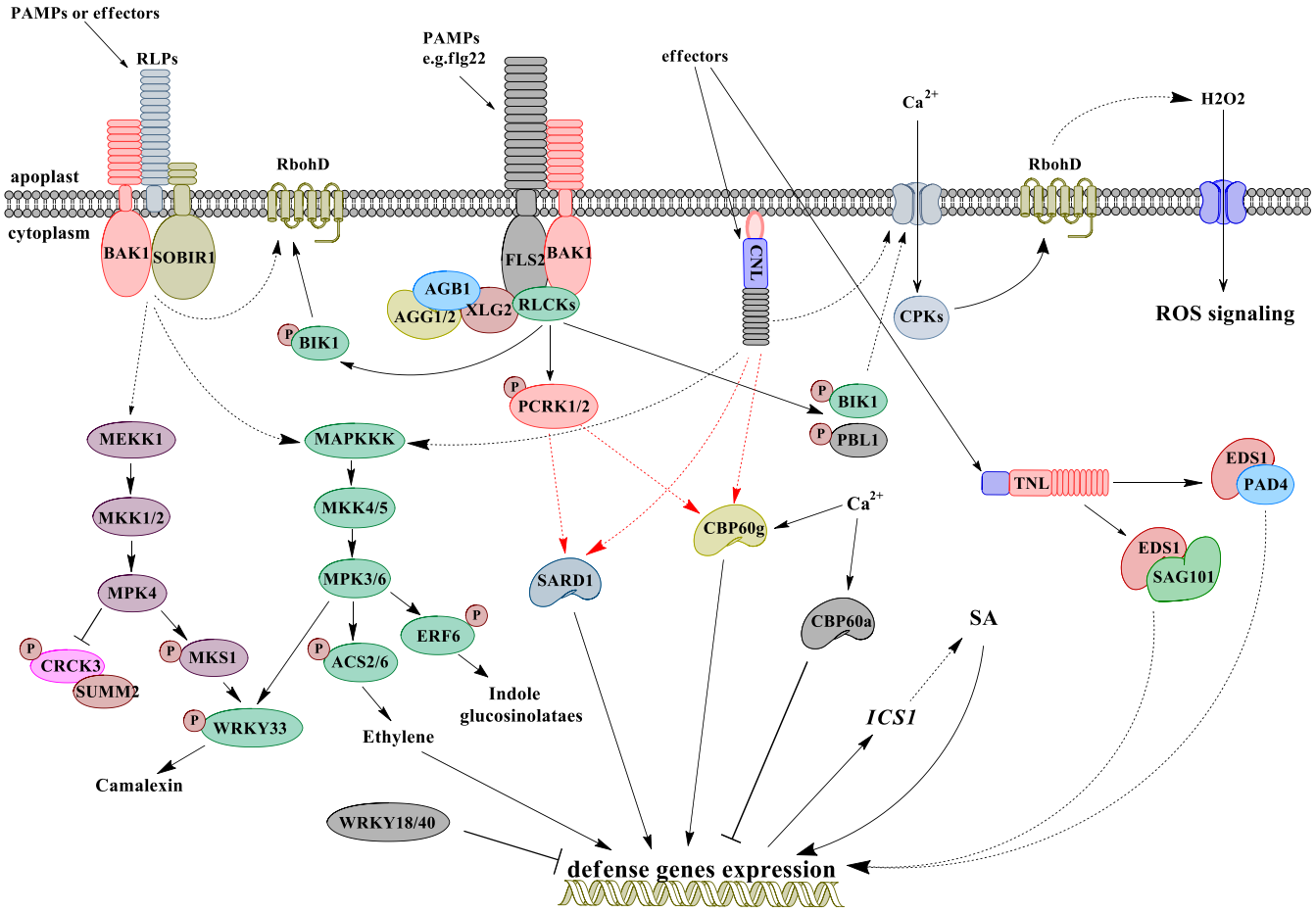

Fig. 1. Overview of defense signaling downstream of plant immune receptors. Perception of pathogen-associated molecular patterns (PAMPs) or pathogen effectors triggers activation of membrane receptors in the receptor-like kinase or receptor-like protein family and coiled coil-nucleotide binding-leucine rich repeat (CNL) families, leading to calcium influx, activation of mitogen-activated protein kinases (MAPKs or MPKs) and reactive oxygen species (ROS) production. Multiple receptor-like cytoplasmic kinases (RLCKs) associate with pattern recognition receptors such as FLS2. Among them, BIK1 and PBL1 contribute to the activation of calcium influx. BIK1 also contributes to the activation of ROS production by phosphorylating RbohD. Two RLCKs, PCRK1 and PCRK2, contribute to activation of the expression of SARD1 and CBP60g. Calcium influx contributes to activation of RbohD and ROS production through phosphorylation of RbohD by calcium-dependent protein kinases (CPKs). Activation of MPKs induced the biosynthesis of ET, camalexin and indole glucosinolates. Activation of defense responses by TNLs is facilitated the EDS1/PAD4 and EDS1/SAG101 complexes. BAK1 = BRI1-associated receptor kinase1, SOBIR1 = suppressor of bir1 1, MKK = MAPK kinase, MEKK = MAPK/ERK kinase kinase, MAPKKK = MAPK kinase kinase, CRCK3 = calmodulin-binding RLCK3, SUMM2 = Suppressor of mkk1 mkk2 2, MKS1 = MAP kinase substrate 1, WRKY = WRKY DNA-binding protein, BIK1 = *Botrytis*-induced kinase 1, PBL1 = PBS1-like 1, ACS = 1-AMINO-CYCLOPROPANE-1-CARBOXYLATE SYNTHASE, ERF6 = ethylene response factor 6, FLS2 = flagellin-sensitive2, AGB1 = *Arabidopsis* G protein β-subunit 1, AGG1/2 = *Arabidopsis* G protein γ-subunits 1 and 2, XLG2 = extra-large GTP-binding protein 2, PCRK1/2 = pattern-triggered immunity compromised receptor-like cytoplasmic kinase 1 and 2, TNL = Toll-interleukin 1-like receptor-nucleotide binding-leucine rich repeat, SARD1 = SAR deficient 1, CBP60 = calmodulin-binding protein 60, RhohD = respiratory burst oxidase protein D, SA = salicylic acid, ICS1 = isochorismate synthase 1, EDS1 = enhanced disease susceptibility 1, PAD4 = phytoalexin deficient 4, SAG101 = senescence-associated gene 101. The red lines indicate regulation through transcriptional control.

suggesting that they are involved in activation of Ca^{2+} signaling in PTI.

HETEROTRIMERIC G PROTEINS IN PLANT IMMUNITY

In metazoans and fungi, heterotrimeric G proteins consisting of Gα, Gβ, and Gγ subunits serve as physical couplers that connect G protein–coupled receptors (GPCR) to downstream enzymes in signal transduction (Oldham and Hamm 2008). While there is no bona fide GPCR in plants, heterotrimeric G proteins have been shown to function as a convergent point for RLK-mediated immune signaling (Liu et al. 2013). Loss of the Gβ subunit AGB1 or the Gγ subunits AGG1 and AGG2 leads to reduced ROS production triggered by different elicitors, including elf18, flg22, and chitin, compromising PTI (Ishikawa 2009; Liu et al. 2013; Lorek et al. 2013; Torres et al. 2013). AGB1, AGG1, and AGG2 are also required for the cell death and autoimmunity of the *bir1-1* mutant (Liu et al. 2013), which is mediated by the RLK SOBIR1 and BAK1 (Gao et al. 2009; Liu et al. 2016). Analysis of knockout mutants of the Gα subunit XLG2 revealed that XLG2 is also required for flg22-induced ROS production and activation of cell death in the *bir1-1* mutant (Maruta et al. 2015). Recently XLG2 was shown to directly interact with FLS2 and BIK1 and it functions together with AGB1, AGG1, and AGG2 to attenuate proteasome-mediated degradation of BIK1 (Liang et al. 2016). The mechanism of how XLG2, AGB1, AGG1, and AGG2 affect the accumulation of BIK1 is currently unclear. It remains to be seen whether it is related to CPK28, which serves as a negative regulator of BIK1 accumulation (Monaghan et al. 2014).

MAPK SIGNALING

MAPK cascades are conserved pathways used for signal transduction in eukaryotes. Perception of PAMPs by PRRs leads to rapid activation of MAPKs. At least six *Arabidopsis* MAPKs, including MPK1, MPK3, MPK4, MPK6, MPK11, and MPK13, are activated by flg22 treatment (Asai et al. 2002; Bethke et al. 2012; Droillard et al. 2004; Nitta et al. 2014; Nühse et al. 2000; Teige et al. 2004). Activation of MPK3 and MPK6 relies on the upstream MKK4 and MKK5 (Asai et al. 2002). The identity of the MAPKKK functioning upstream of MKK4 and MKK5 in flg22-induced MAPK activation is still unknown. Activation of MPK4 by flg22 is dependent on the upstream MEKK1 and MKK1 and MKK2 (Gao et al. 2008; Ichimura et al. 2006; Nakagami et al. 2006; Qiu et al. 2008a; Suarez-Rodriguez et al. 2007). MAPKs phosphorylate a wild range of target proteins with different roles in plant immunity (Meng and Zhang 2013), which serve as divergent points of signaling downstream of immune receptors.

Arabidopsis MPK3 and MPK6 are involved in the activation of a variety of immune responses. They promote ethylene biosynthesis by phosphorylating the ethylene biosynthesis enzymes ACS2 and ACS6 (Liu and Zhang 2004). Phosphorylation of ACS2 and ACS6 results in their stabilization and increased ethylene production. MPK3 and MPK6 also regulate camalexin biosynthesis through their target protein WRKY33 (Mao et al. 2011; Ren et al. 2008). Phosphorylation of WRKY33 by MPK3 and MPK6 is required for its function in promoting pathogen-induced camalexin biosynthesis. ETHYLENE RESPONSE FACTOR6 (ERF6) is another substrate of MPK3 and MPK6 (Meng et al. 2013). MPK3 and MPK6 promote biosynthesis of indole glucosinolates in plant immunity via ERF6 (Xu et al. 2016). Recently MPK3 and MPK6 were also shown to promote stomatal immunity by modulating malate metabolism during pathogen infection (Su et al. 2017).

MPK4 is a multifunctional protein involved in both positive and negative regulation of plant immunity. It contributes to the upregulation of about 50% of flg22-induced genes (Frei dit Frey et al. 2014). The MEKK1-MKK1/MKK2-MPK4 cascade promotes basal resistance against pathogens and is protected by the CNL SUMM2 (Zhang et al. 2012). SUMM2 monitors the phosphorylation status of CRCK3, a substrate of MPK4 (Zhang et al. 2016). MPK4 promotes camalexin biosynthesis through its substrate protein MKS1 and WRKY33 (Qiu et al. 2008b). MPK4 also negatively regulates flg22-induced gene expression by modulating the activity of the transcriptional repressor ASR3 (Li et al. 2015a). Transgenic plants expressing a constitutively active MPK4 mutant accumulate less SA following pathogen infection and display enhanced susceptibility to pathogens, suggesting that MPK4 may be involved in the negative regulation of SA biosynthesis (Berriri et al. 2012).

In tomato, silencing of MAPKKKα leads to reduced AvrPto-induced HR, suggesting that MAPKKKα is involved in immunity mediated by the CNL Prf (del Pozo et al. 2004). In *Arabidopsis*, perception of the bacteria effector AvrRpt2 by the plasma membrane–localized CNL RPS2 results in activation of MPK3 and MPK6 (Tsuda et al. 2013). Unlike MAPK activation in PTI, which usually lasts less than 1 h, activation of MAK3 and MPK6 by RPS2 persists for several hours. The sustained activation of MPK3 and MPK6 contributes to activation of SA-independent gene expression and resistance against pathogens (Tsuda et al. 2013). How RPS2 activates MAPK signaling and whether activation of MPK3 and MPK6 is a general defense response downstream of CNLs remains to be determined. Currently, there is no evidence that MAPK signaling is involved in immunity mediated by TNLs.

CA^{2+} SIGNALING IN PTI AND ETI

Ca^{2+} serves as a secondary messenger in many signaling processes. Recognition of PAMP elicitors by PRRs immediately triggers Ca^{2+} influx at the plasma membrane (Ranf et al. 2011). Similarly, recognition of pathogen effectors by the CNL RPM1 also triggers Ca^{2+} influx during ETI (Grant et al. 2000). Even though several groups of proteins, such as ionotropic glutamate receptor-like channels, cyclic nucleotide gated channels, and mechanosensitive MCA-like channels, have been implicated as potential Ca^{2+} channels in plants, the identity of plasma membrane Ca^{2+} channels responsible for the Ca^{2+} influx in PTI and ETI is still unknown (Seybold et al. 2014). However, many Ca^{2+}-responsive proteins have been identified as critical regulators of plant immunity.

In *Arabidopsis*, four closely related calcium-dependent protein kinases (CPKs), namely, CPK4, CPK5, CPK6, and CPK11, are involved in promoting flg22-induced ROS production and transcriptional reprograming (Boudsocq et al. 2010). Overexpression of CPK5 causes autoimmunity (Dubiella et al. 2013), which was recently shown to be dependent on the truncated TIR-NB protein TN2 (Liu et al. 2017). CPK5 and CPK6 were also implicated in the positive regulation of ETI, as loss of CPK5 and CPK6 leads to compromised resistance mediated by the CNLs RPS2 and RPM1 (Gao et al. 2013). CPK4, CPK5, and CPK11 can phosphorylate several WRKY transcription factors in vitro and phosphorylation of these transcription factors enhances their DNA-binding activity. Two other closely related CPKs, CPK1 and CPK2, promote ROS production following activation of RPS2 and RPM1-mediated immunity (Gao et al. 2013). In rice, the calcineurin B-like interacting protein kinases OsCIPK14 and OsCIPK15 are involved in PAMP-induced ROS production and the induction of HR during pathogen attack (Kurusu et al. 2010a and b).

Several calmodulin (CaM)-binding transcription factors including CAMTA3, CBP60g, and CBP60a have been identified as critical regulators of plant defense responses in *Arabidopsis*. Loss of CAMTA3 results in autoimmunity (Du et al. 2009),

which is partially due to activation of defense responses mediated by the TNLs DSC1 and DSC2 (Lolle et al. 2017). On the other hand, a gain-of-function mutation in CAMTA3 causes compromised resistance to pathogens, suggesting CAMTA3 as an authentic negative regulator of immunity (Jing et al. 2011; Nie et al. 2012). Loss of CBP60a results in increased basal defense gene expression and enhanced pathogen resistance (Truman et al. 2013). In contrast, loss of CBP60g leads to reduced flg22-induced SA accumulation and enhanced susceptibility to the bacterial pathogen *P. syringae* (Wang et al. 2009). The mechanism for the antagonism between these two closely related proteins remains unclear.

ROS SIGNALING

Perception of PAMPs by PRRs triggers rapid production of H_2O_2 (Zipfel 2009). Activation of ETI also leads to early ROS production (Torres et al. 2006). Most of the apoplastic ROS in early PTI and ETI responses is produced via the respiratory burst oxidase homolog D (RbohD). RbohD is phosphorylated by BIK1 upon perception of flg22 and phosphorylation of RbohD is required for flg22-induced ROS production (Kadota et al. 2014; Li et al. 2014). RbohD is also phosphorylated by various CPKs, as discussed above, which contributes to activation of ROS production in both PTI and ETI (Boudsocq et al. 2010; Gao et al. 2013). In addition to activation of RbohD by protein kinases, the small G protein OsRac1 plays an important role, as well, in promoting ROS production during ETI and PTI in rice (Akamatsu et al. 2013; Kawano et al. 2010).

ROS produced by RbohD contributes to resistance against pathogens (Kadota et al. 2014; Zhang et al. 2007). It is also involved in promoting cell death in RPM1-mediated immunity (Torres et al. 2002). Whether ROS has additional roles in plant defense signaling and how apoplastic ROS is perceived by plants remains to be determined. Identifying signaling components downstream of ROS will greatly help us understand the biological functions of ROS in PTI and ETI.

SIGNALING COMPONENTS DOWNSTREAM OF NLRS

Immunity specified by CNLs such as *Arabidopsis* RPS2, RPM1, and RPS5 is dependent on the plasma membrane–localized NDR1 protein (Century et al. 1995). However, NDR1 is not required for resistance mediated by TNLs (Aarts et al. 1998). Interestingly, loss of NDR1 also leads to compromised PTI responses and basal resistance against virulent pathogens (Century et al. 1995; Knepper et al. 2011), suggesting that NDR1 may have a more general role in plant immunity. NDR1 is predicted to be an integrin-like protein (Knepper et al. 2011). The molecular mechanism of how NDR1 regulates plant immune responses remains to be determined.

Three lipase-like proteins, EDS1, PAD4, and SAG101, function downstream of TNLs (Wiermer et al. 2005). EDS1 is localized in both the cytoplasm and nucleus (García et al. 2010). It has been shown to interact with TNLs (Bhattacharjee et al. 2011; Heidrich et al. 2011) and functions as a convergent point for immunity specified by TNLs. TNL-mediated immunity seems fully dependent on EDS1, whereas contributions of PAD4 and SAG101 vary depending on the specific TNLs (Wiermer et al. 2005). Surprisingly, EDS1 also contributes to CNL RPS2-mediated immunity when pathogen-induced SA biosynthesis is blocked (Cui et al. 2017). PAD4 and SAG101 associate with EDS1 in separate complexes (Feys et al. 2005; Wagner et al. 2013). Interestingly, overexpression of EDS1 and PAD4 together in plants is sufficient to activate defense gene expression (Cui et al. 2017). Although several transcriptional regulators including tobacco SPL6 and *Arabidopsis* TPR1 (TOPLESS-RELATED 1), TCP, and the bHLH84 family transcription factors have been shown to contribute to TNL-mediated immunity (Kim et al. 2014; Padmanabhan et al. 2013; Xu et al. 2014; Zhu et al. 2010), their exact relationships with EDS1 and PAD4 remain to be determined.

Two groups of conserved CNLs are involved in immunity specified by TNLs. Tobacco NRG1 is required for immunity mediated by the TNL N protein (Peart et al. 2005). *Arabidopsis* ADR1, ADR1-L1, and ADR1-L2 are redundantly required for immunity specified by multiple TNLs (Bonardi et al. 2011; Dong et al. 2016). These CNLs most likely function as helper NLRs in TNL-mediated immune signaling. The contribution of ADR1, ADR1-L1, and ADR1-L2 to TNL-mediated resistance varies, depending on individual TNLs (Dong et al. 2016). Whether NRG1 serves as a general signaling component for TNL-mediated immunity remains to be determined.

HORMONE SIGNALING IN PTI AND ETI

Several plant hormones including SA, ethylene (ET), and jasmonic acid (JA) are involved in plant defense against pathogens. SA is a major contributor to resistance against biotrophic pathogens, whereas both ethylene and JA play critical roles in immunity against necrotrophic pathogens (Glazebrook 2005). Activation of PTI or ETI triggers a dramatic increase in SA levels (Dempsey et al. 2011). Activation of PTI also triggers a transient increase in ethylene production facilitated by MPK3 and MPK6 (Liu and Zhang 2004). SA has been shown to contribute to pathogen resistance mediated by NLRs such as SNC1, RPP4, and RPS2 (Nawrath and Metraux 1999; van der Biezen et al. 2002; Zhang et al. 2003). It also contributes to flg22-induced resistance against *P. syringae* (Tsuda et al. 2008). Analysis of the *Arabidopsis dde2 ein2 pad4 sid2* quadruple mutant revealed that SA, ET, and JA signaling have additive effects on flg22-triggered immunity and RPS2-triggered immunity against *P. syringae* (Tsuda et al. 2009).

MASTER TRANSCRIPTION FACTORS IN PTI AND ETI

Two pathogen-induced transcription factors, SARD1 and CBP60g, serve as a convergent point in PTI and ETI signaling. Treatment with flg22 or a *P. syringae* strain deficient in the type III secretion system results in rapid induction of *SARD1* and *CBP60g* (Kong et al. 2016; Wang et al. 2009, 2011). Activation of ETI also leads to upregulation of *SARD1* and *CBP60g* (Zhang et al. 2010b). Overexpression of SARD1 but not CBP60g is sufficient to activate a plant defense against pathogens (Zhang et al. 2010b), likely because it is regulated at both transcriptional and posttranscriptional levels as a CaM-binding protein.

SARD1 and CBP60g were originally shown to promote SA biosynthesis during PTI and ETI (Wang et al. 2009, 2011; Zhang et al. 2010b). They directly regulate the expression of *SID2* and *EDS5*, which encode two critical components for pathogen-induced SA accumulation (Sun et al. 2015; Zhang et al. 2010b). SARD1 and CBP60g are also involved in the induction of genes encoding SA receptors during pathogen infection (Sun et al. 2015), suggesting that they serve as positive regulators of both biosynthesis and perception of SA. Chromatin-immunoprecipitation-sequencing (ChIP-seq) analysis further revealed that SARD1 and CBP60g directly regulate the expression of many other signaling components in plant immunity, such as BAK1, AGB1, BIK1, MEKK1, MKK4, MPK3, and CPK4 in PTI and EDS1, PAD4, ADR1, ADR-L1, and ADR-L2 in ETI, indicating that they play critical roles in positive feedback regulation of plant immunity (Sun et al. 2015). In addition, a number of negative regulators of plant immunity were also identified as target genes of SARD1 and

CBP60g, suggesting that SARD1 and CBP60g likely also contribute to the negative feedback regulation of plant defense responses.

Many WRKY transcription factors are involved in the regulation of defense gene expression in plant immunity (Birkenbihl et al. 2017). Among them, *Arabidopsis* WRKY33 functions as a key positive regulator of immunity against necrotrophic pathogens (Zheng et al. 2006), whereas WRKY18 and WRKY40 serve as critical negative regulators of resistance against biotrophic pathogens (Xu et al. 2006). ChIP-seq analysis revealed that WRKY33, WRKY18, and WRKY40 each target more than 1,000 genes following treatment with flg22 (Birkenbihl et al. 2016). Many of these target genes are involved in pathogen perception or signal transduction during PTI, suggesting that WRKY33, WRKY18, and WRKY40 function as master regulators in plant immunity.

CONCLUDING REMARKS

Forward and reverse genetic analyses have identified many important regulatory components involved in PTI and ETI signaling. Some of these components represent convergent or divergent points in signal transduction downstream of different groups of immune receptors. There are still many big gaps in our understanding of the plant immune signaling network. Major questions, such as how immune signaling is initiated by NLRs, which $Ca2^{+}$ channels are responsible for the $Ca2^{+}$ influx following activation of membrane-localized immune receptors, and how ROS is perceived and how it contributes to plant immunity, remain to be addressed in the future.

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