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Plant Hormone Signaling Systems in Plant Innate Immunity

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Chapter 1
Introduction

Abstract The plant hormones salicylic acid (SA), jasmonates (JA), ethylene (ET), abscisic acid (ABA), auxin (AUX), cytokinin (CK), gibberellin (GA), and brassinosteroid (BR) play an important role in intercellular and systemic signaling systems triggering expression of various defense-responsive genes. The SA–JA–ET signaling systems are considered as the backbone of the plant immune signaling system, while ABA, auxin, cytokinin, GA, and BR are involved in modulating plant immune responses by regulating host defense responses triggered by the SA–JA–ET signaling systems. SA signaling is required for the manifestation of systemic acquired resistance (SAR). Methyl salicylate, dehydroabietinal, pipecolic acid, azelaic acid, a lipid transfer protein (DIR1), a lipid-derived molecule (glycerol 3-phosphate), and a glycerol-3-phosphate-dependent factor have been reported as mobile signaling components in SA-induced SAR. Mediators MED16 and MED15 are involved in triggering SA-mediated SAR. SAR is associated with priming of defense responses, and the priming results in a faster and stronger induction of defense responses after pathogen attack. Histone modifications are systemically set during a priming event. The priming can be inherited epigenetically, and descendants of primed plants exhibit next-generation systemic acquired resistance. DNA methylation plays an important role in the transgenerational SAR. JA signaling triggers systemic immunity called "induced systemic resistance (ISR)." JA-Ile may be the mobile signal involved in the induction of ISR. The ISR involves priming of JA-dependent responses. MED25, MED16, and MED8 subunits of the Mediator complex interact with several transcription factors known to function in the control of JA-associated gene expression. Ethylene may act as a two-faceted player in the plant immune response network, triggering resistance or susceptibility against different pathogens. ABA signal perception and signal transduction pathway includes PYR/PYL/RCAR (an abscisic acid receptor), type 2C protein phosphatase (PP2C, a negative regulator), and SNF1-related protein kinase (SnRK2, a positive regulator). Auxin binds to TIR1/AFB nuclear receptors, which are F-box subunits of SCF ubiquitin ligase complex. The auxin signal is then modulated by the Aux/IAA repressors and the auxin response factor (ARF) transcription factors. Auxin signaling is also involved in triggering SAR. Auxin signaling increases SA levels, which trigger SAR. Cytokinins regulate the host defense responses either positively or negatively depending on the concentrations of cytokinins available at the infection site. Key components in the GA signaling pathway include the GA receptor GID1, the DELLA proteins, and the F-box proteins. GA regulates plant immune responses by

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modulating JA and SA signaling systems. Plant hormones act in concert. Plant hormone signaling pathways are not simple linear and isolated cascades, but can crosstalk with each other. Architecture of plant immune signaling networks may not be static and may vary with the invading pathogen genotype. Crosstalk between different hormone signaling pathways in the signaling network helps the plant to choose the effective defense strategy to follow, depending on the type of pathogen it is encountering. The crosstalk also allows the pathogens to manipulate plants to their own benefit by shutting down the specific hormone signaling pathway involved in triggering defense responses and hijacking the signaling pathway involved in induction of susceptibility.

1.1 Plant Innate Immunity

Plants are endowed with innate immune system, which has a high potential to detect and fight against viral, bacterial, oomycete, and fungal pathogens and protect the crop plants against a wide range of diseases (Vidhyasekaran 2004, 2007, 2014; Lacombe et al. 2010; Segonzac and Zipfel 2011; Alkan et al. 2012; Dubery et al. 2012; Denancé et al. 2013; Kim and Hwang 2014). The plant innate immune system is a sleeping system in unstressed healthy plants (Vidhyasekaran 2014). Specific signals are needed to activate the "sleeping" immune system. Pathogen-associated molecular patterns (PAMPs) of invading pathogens have been found to be potential signals to activate the plant innate immunity. These PAMP signals are perceived by the plant pattern recognition receptors (PRRs), and the PAMP–PRR signaling complex activates the plant immune system (Iriti and Faoro 2009; Nicaise et al. 2009; Petutschnig et al. 2010; Shinya et al. 2010; Schulze et al. 2010; Segonzac and Zipfel 2011; Yang et al. 2013). The plant immune system uses several second messengers to encode information generated by the PAMPs and deliver the information downstream of PRRs to proteins which decode/interpret signals and initiate defense gene expression (Mersmann et al. 2010; Boudsocq et al. 2010; Hwang and Hwang 2011). Plant hormones such as salicylic acid (SA), jasmonates (JA), ethylene (ET), abscisic acid (ABA), auxin (AUX), cytokinin (CK), gibberellin (GA), and brassinosteroid (BR) have been reported to play an important role in intercellular and systemic signaling systems triggering expression of various defense-responsive genes (Denancé et al. 2013; Yang et al. 2013; Alazem et al. 2014; Kim and Hwang 2014).

1.2 Salicylic Acid Signaling

Salicylic acid (SA) is an important endogenous immune signal in the induction of disease resistance responses in plants (Anand et al. 2008; Fung et al. 2008; Garcion et al. 2008; Mukherjee et al. 2010; Dempsey et al. 2011; Liu et al. 2011a, b; Argueso

et al. 2012; Fu et al. 2012; Denancé et al. 2013; Gimenez-Ibanez and Solano 2013; Yang et al. 2013). Infection of plants by necrotizing pathogens, which induce the accumulation of SA, or treatment of plants with synthetic compounds, which are able to trigger SA signaling, induces systemic acquired resistance (SAR). SAR is a heightened state of defense against a broad spectrum of pathogens activated throughout a plant following a local infection (Liu et al. 2011a, b). SA signaling is required for the manifestation of SAR (Du et al. 2012; Návarová et al. 2012; Shah and Zeier 2013).

Methyl salicylate, dehydroabietinal, pipecolic acid, and azelaic acid are the systemic signal molecules involved in the activation of SAR (Jung et al. 2009; Manosalva et al. 2010; Chaturvedi et al. 2012; Návarová et al. 2012; Shah and Zeier 2013). A lipid transfer protein (DIR1), a lipid-derived molecule (glycerol 3-phosphate), and a glycerol-3-phosphate-dependent factor have been reported as lipid-based mobile signaling components in SA-induced SAR (Kachroo et al. 2001, 2004; Chaturvedi et al. 2008; Jung et al. 2009; Chanda et al. 2011). The mediators MED16 and MED15/NRB4 have been shown to be involved in triggering SA-mediated SAR. Mediator is a multiprotein complex that functions as a transcriptional coactivator (Conaway and Conaway 2011a, b; Kidd et al. 2011a; Canet et al. 2012; An and Mou 2013). MED16 may regulate the function of NPR1 in inducing SAR (Zhang et al. 2012).

SAR is associated with priming of defense (Kohler et al. 2002; Jung et al. 2009; Luna et al. 2012; Slaughter et al. 2012), and the priming results in a faster and stronger induction of defense mechanisms after pathogen attack (Conrath 2011). Jaskiewicz et al. (2011) showed that histone modifications are systemically set during a priming event. These modifications might create a memory of the primary infection that is associated with an amplified reaction to the second stress condition. The priming can be inherited epigenetically from disease-exposed plants, and descendants of primed plants exhibit next-generation systemic acquired resistance (Luna et al. 2012; Slaughter et al. 2012). The transgenerational SAR was found to be sustained over one stress-free generation, indicating an epigenetic basis of the phenomenon (Luna et al. 2012). DNA methylation may also play an important role in the transgenerational SAR (Luna et al. 2012).

NPR1 functions as a transcriptional co-activator in a TGA2–NPR1 complex after SA treatment. Binding of SA causes a conformational change in NPR1 that is accompanied by the release of the C-terminal transactivation domain from the N-terminal autoinhibitory BTB/POZ domain (Wu et al. 2012). Pathogen/PAMP exposure induces SA accumulation (Durrant and Dong 2004), and the induced SA controls the nuclear translocation of NPR1 through cellular redox changes (Spoel and Dong 2012). The SA-induced changes in gene expression have been found to have a link to chromatin remodeling, such as histone modifications and histone replacement. The recruitment of chromatin-modifying complexes to SA-responsive loci controls their basal and SA-induced expression (March-Diaz et al. 2008; van den Burg and Takken 2009, 2010; Jaskiewicz et al. 2011). SA signaling triggers transcription of a multitude of defense-related genes in plants (Krinke et al. 2007). Small RNA-directed RNA silencing is a potent immune surveillance system

targeting foreign nucleic acids of invading pathogens (Ding and Voinnet 2007; Jaubert et al. 2011). SA signaling may enhance the efficiency of RNA silencing pathway in triggering immune responses against viruses by activating RdRP/RDR (Diaz-Pendon et al. 2007).

1.3 Jasmonate Signaling

Several metabolites of jasmonates (JA) have been reported to act as signal molecules in triggering plant immunity. Among them, (+)-7-iso-jasmonoyl-L-isoleucine (JA-Ile) is the major bioactive form of the hormone JA (Kombrink 2012; Wasternack and Hause 2013). JA signaling systems modulate plant immune responses and confer resistance or susceptibility against different pathogens (Méndez-Bravo et al. 2011; Moffat et al. 2012). JA receptor is a three-molecule co-receptor complex, consisting of COI1, JAZ, and inositol pentakisphosphate, all of which are indispensable for high-affinity hormone binding (Sheard et al. 2010). The JA receptor JAZ proteins are suppressors of jasmonate signaling (Chini et al. 2007; Howe 2010; Wasternack and Hause 2013). Repression of JA response genes involves binding of JAZ to NINJA, which contains an EAR motif that recruits the corepressor TPL, which may silence gene expression. COI1 is involved in the degradation of the repressors of the JA signaling pathway through SCF^{COI1}-dependent ubiquitin (Thines et al. 2007). In response to stress cues that activate JA-Ile synthesis, high levels of JA-Ile promote SCF^{COI1}-mediated ubiquitination and subsequent degradation of JAZs by the 26S proteasome. JAZ degradation relieves TPL-mediated repression of gene expression (Howe 2010; Wasternack and Hause 2013). Acetylation of the core histones in nucleosomes plays an important role in gene regulation (Wu et al. 2008), and histone deacetylation has been shown to be involved in COI1-mediated activation of JA-inducible transcription factors (Wang et al. 2008b). MED25, MED16, and MED8 subunits of the Mediator complex interact with several transcription factors (TFs) known to function in the control of JA-associated gene expression (Kidd et al. 2009; Cevik et al. 2012; Iñigo et al. 2012; Wathugala et al. 2012; Zhang et al. 2012). MYC2 is a master regulator of the JA signaling pathway. Several ERF, bHLH, WRKY, MYB, NAC, and bZIP transcription factors have been shown to act downstream of JA signaling system triggering expression of JA-responsive defense genes (Nurmberg et al. 2007; Wasternack 2007; Zander et al. 2010; Cheng et al. 2011; Le Hénanff et al. 2013).

JA signaling triggers systemic immunity conferring resistance against a wide range of pathogens, and the systemic immunity triggered by JA is called "induced systemic resistance (ISR)" as against "systemic acquired resistance (SAR)" induced by SA. ISR is dependent mostly on jasmonic acid (Kravchuk et al. 2011; Niu et al. 2011; Weller et al. 2012; Zamioudis and Peterse 2012; Bakker et al. 2013; Martinez-Medina et al. 2013). ISR is triggered mostly by biocontrol agents (BCAs) and necrotrophic fungi. Several chemicals and PAMPs/MAMPs have also been reported to trigger ISR (Kravchuk et al. 2011). JA-Ile may be the mobile signal involved in

the induction of ISR (Sato et al. 2011; Matsuura et al. 2012). JA-Ile may be synthesized de novo and transported into systemic tissues (Matsuura et al. 2012). The ISR has been shown to be mainly based on priming JA-dependent responses (Martinez-Medina et al. 2013). Treatment with *Trichoderma hamatum* T382 primes the plant (ISR-prime), resulting in an accelerated activation of defense responses against *B. cinerea* during ISR-boost in *Arabidopsis thaliana* (Mathys et al. 2012). Hexanoic acid-treated plants infected with the necrotrophic pathogen *Botrytis cinerea* showed priming in the expression of the JA-responsive genes *PDF1.2*, *PR-4*, and *VSP1* in *Arabidopsis* (Kravchuk et al. 2011).

1.4 Ethylene Signaling

Ethylene (ET) signaling system is an important component in plant innate immune system (Berr et al. 2010; Nie et al. 2011; Shakeel et al. 2013). Pathogen invasion or PAMP application results in enhanced expression of ET biosynthetic genes leading to enhanced ET biosynthesis (Qutob et al. 2006; Denoux et al. 2008; Mur et al. 2008; Zhu et al. 2011a; Nambeesan et al. 2012; Vidhyasekaran 2014). Ethylene signal transduction is initiated by the binding of ethylene to its membrane-bound receptors ETR1, ERS1, ETR2, EIN4, and ERS2 (Grefen et al. 2008; Zhao and Guo 2011; Shakeel et al. 2013). The five-member family of ethylene receptors act as negative regulators in the ethylene signaling pathway (Qu and Schaller 2004; Gao and Schaller 2009). CTR1 functions as a key mediator of ethylene signal transduction, acting just downstream of the receptors. It negatively regulates ET signaling (Guo et al. 2004; Yoo et al. 2008). All the five ethylene receptors physically interact with CTR1 (Gao et al. 2003). EIN2 is a positive regulator of the ethylene signaling pathway and acts downstream of CTR1 (Ju et al. 2012; Qiao et al. 2012; Shakeel et al. 2013). Upon ethylene binding to the ethylene receptors, the ethylene receptors inactivate CTR1, potentially through propagation of conformational changes in the receptor–CTR1 protein complex. EIN2 becomes dephosphorylated and this results in proteolytic cleavage and release of C-terminal domain of EIN2 (Ju and Chang 2012; Ju et al. 2012; Qiao et al. 2012; Wen et al. 2012; Shakeel et al. 2013). The C-terminal domain of EIN2 translocates to the nucleus. In the nucleus, EIN2 either directly or indirectly activates the transcription factors EIN3 and EIN3-like1 (EIL1) to initiate the transcriptional response to ethylene (Qiao et al. 2012; Wen et al. 2012; Shakeel et al. 2013). EIN3 binds to the promoter sequence of the ethylene-inducible transcription factor ERF1 (Solano et al. 1998). ERFs contain a single DNA-binding domain. ERFs have been shown to bind specifically to the GCC-box that is found in several promoters of the pathogenesis-related (PR) genes as well as ethylene- and jasmonate-inducible defense genes (Yamamoto et al. 1999; Gutterson and Reuber 2004). ERF2 might play a major role in the elicitor-induced GCC-box-mediated transcription of defense genes (Yamamoto et al. 1999). The transcription factor ERF1 has been shown to induce transcription of several defense-related *PR* genes (Zhou et al. 2005; Johansson et al. 2006; Jung et al. 2007; Oñate-Sánchez et al. 2007).

Ethylene may act as a two-faceted player in the plant immune response network, triggering resistance or susceptibility against different pathogens (De Vleesschauwer et al. 2008, 2010; Gaige et al. 2010; Akagi et al. 2011; Son et al. 2012). ET has also been reported to be involved in systemic immunity (Zhu et al. 2011a). Ethylene has been shown to be an integral part of PAMP-triggered immunity. Ethylene perception and signaling are crucial for the PRR *FLS2* gene transcription (Boutrot et al. 2010). FLS2 promoter revealed the presence of nine potential EIN3/EIL-binding sites (Boutrot et al. 2010), suggesting that EIN3 may bind to the promoter of the *FLS2* gene to influence its transcription. Plants mutated in the key ethylene signaling protein EIN2 are impaired in all the PRR FLS2-mediated responses. The EIN3 and EIN3-like transcription factors, which depend on EIN2 activity for their accumulation, directly controlled the transcription of the PRR *FLS2* gene transcription (Boutrot et al. 2010).

1.5 Abscisic Acid Signaling

The phytohormone abscisic acid (ABA) plays a multifaceted role in plant immunity (Cao et al. 2011; Alazem et al. 2014). ABA induces defense responses (Asselbergh et al. 2008; Fan et al. 2009; Garcia-Andrade et al. 2011) or suppresses the immune responses depending upon the type of plant–pathogen interactions (Feng et al. 2012; Sánchez-Vallet et al. 2012; Yazawa et al. 2012). Pathogen/pathogen-associated molecular patterns (PAMPs) induce increase in ABA accumulation triggering disease resistance (Whenham et al. 1986) or susceptibility (Mohr and Cahill 2003; Koga et al. 2004; Schmidt et al. 2008). ABA signal perception and signal transduction pathway includes PYR/PYL/RCAR (an abscisic acid receptor), type 2C protein phosphatase (PP2C, a negative regulator), and SNF1-related protein kinase (SnRK2, a positive regulator) (Umezawa et al. 2010, 2013). In the presence of accumulated ABA, the PYR/PYL/RCAR receptor proteins disrupt the interaction between the SnRK2s and PP2Cs, thus preventing the PP2C-mediated dephosphorylation of the SnRK2s and resulting in the activation of the SnRK2 kinases (Fujii et al. 2009; Miyazono et al. 2009; Umezawa et al. 2009; Vlad et al. 2009; Raghavendra et al. 2010). The SnRK2 kinases phosphorylate and activate downstream transcription factors, which initiate transcription at ABA-responsive promoter elements (Sheard and Zheng 2009). The *cis*-regulatory elements responsible for the ABA regulation of gene expression share a conserved motif, ACGTGGC, which is known as ABA-responsive element (ABRE). ABRE appears in the promoters of many defense genes (Adie et al. 2007). The ABA-induced gene regulation is mediated by a subfamily of basic leucine zipper class transcription factors referred to as ABRE-binding factors (ABFs, also referred to as AREBs) (Choi et al. 2005; Furihata et al. 2006). The bZIP-type transcription factors AREBs/ABFs bind ABRE and transactivate downstream gene expression in *Arabidopsis* (Furihata et al. 2006). MYC2, MYB2, BOS1, and WRKY transcription factors are also involved in ABA-inducible gene expression (Abe et al. 2003; Mengiste et al. 2003; Anderson et al. 2004; Xie

et al. 2005). ABA signaling system is involved in the induction of callose (β-1,3-glucan) deposition (Yazawa et al. 2012), which is involved in conferring disease resistance. Stomatal closure is an innate immune response involved in bacterial disease resistance (Hettenhausen et al. 2012). ABA induces stomatal closure immune response (Saito et al. 2008; Hossain et al. 2011; Munemasa et al. 2011; Hubbard et al. 2012; Sugiyama et al. 2012; Uraji et al. 2012). ABA regulates plant immune responses mostly by modulating other plant hormone signaling systems involved in the immune signaling systems. Antagonistic interaction between ABA and JA signaling pathways modulates defense gene expression and disease resistance (Anderson et al. 2004; Chen et al. 2012). ABA negatively regulates SA-dependent immune responses (Sánchez-Vallet et al. 2012). ABA signaling system suppresses SA signaling system and vice versa (Alazem et al. 2014). ABA signaling may also act synergistically with SA signaling in triggering plant immune responses (Seo and Park 2010). Ethylene signaling pathway triggers ABA biosynthesis pathway (Wasilewska et al. 2008; Hauser et al. 2011; Liu et al. 2012). ABA-induced resistance against the brown spot pathogen *Cochliobolus miyabeanus* in rice involves repression of ethylene signaling (De Vleesschauwer et al. 2010) Synergistic interaction between ABA and ethylene signaling systems has also been reported (Sánchez-Vallet et al. 2012).

1.6 Auxin Signaling

The plant hormones SA, JA, and ET signaling systems are considered as the backbone of the plant immune signaling system. In contrast, the plant hormone auxin is considered as a simple signaling molecule involved in modulation of those hormone signaling pathways activating or suppressing the plant defense responses (Hayashi 2012; Peer et al. 2013; Sauer et al. 2013; Tatsuki et al. 2013). Auxin binds to TIR1/AFB nuclear receptors, which are F-box subunits of SCF ubiquitin ligase complex (Dharmasiri et al. 2005; Mockaitis and Estelle 2008; Parry et al. 2009; Calderon-Villalobos et al. 2010). The auxin signal is then modulated by the Aux/IAA repressors and the auxin response factor (ARF) transcription factors (Hayashi 2012). The specificity of the auxin-regulated gene expression is regulated by the expression of these regulatory proteins (Hayashi 2012). Auxin signaling appears to be mostly involved in disease susceptibility rather than in disease resistance (O'Donnell et al. 2003; Kidd et al. 2011b). Elevated levels of endogenous plant IAA have been observed during pathogen infection, and the susceptible reaction seems to be associated with rapidly increased endogenous biosynthesis of IAA (Fu et al. 2011). Auxins may induce susceptibility by inducing the formation of the conjugated forms of auxin through the action of GH3 proteins (Fu and Wang 2011; González-Lamothe et al. 2012). Fungal and bacterial pathogens hijack the host auxin metabolism in *Arabidopsis thaliana*, leading to the accumulation of a conjugated form of the hormone, indole-3-acetic acid (IAA)–Asp, to promote disease development. IAA–Asp increases pathogen progression in the plant by regulating the transcription of

virulence genes (González-Lamothe et al. 2012). Auxin may suppress the induction of SA signaling and induce susceptibility (Robert-Seilaniantz et al. 2011).

Auxin also induces resistance against some pathogens, probably modulating auxin homeostasis, polar auxin transport, and expression of ARF transcription factors (Robert-Seilaniantz et al. 2011; Mah et al. 2012). Auxin signaling has been reported to be involved in triggering systemic acquired resistance (SAR). Auxin signaling increases SA levels, which trigger SAR (Rock and Sun 2005). Auxin is highly mobile and is involved in SA-triggered SAR (Truman et al. 2010). Auxin signaling induces disease resistance by triggering accumulation of SA, which positively regulates defense responses, and by suppressing both JA and ABA signaling systems, which negatively regulate defense responses (Truman et al. 2010). Auxin triggers biosynthesis of ethylene (Tatsuki et al. 2013). Application of ethylene biosynthetic precursor ACC triggers an increase in the rate of IAA biosynthesis (Swarup et al. 2007), and ACC treatments also increase IAA transport (Negi et al. 2008). Ethylene has been shown to induce susceptibility (De Vleesschauwer et al. 2010; Pantelides et al. 2013) or resistance (De Vleesschauwer et al. 2008; Gaige et al. 2010; Zhu et al. 2011a; Nambeesan et al. 2012) against various pathogens.

1.7 Cytokinins

Cytokinins act as both long-range and local signals (Hwang and Sakakibara 2006) and play an important role in modulation of plant innate immunity (Choi et al. 2010; Grosskinsky et al. 2011; Naseem et al. 2012; Pieterse et al. 2012). Cytokinin signaling system may regulate positively or negatively the plant defense responses (Choi et al. 2010; Argueso et al. 2012). Cytokinins may regulate the host defense responses either positively or negatively depending on the concentrations of cytokinins available at the infection site (Babosha 2009; Argueso et al. 2012). Cytokinin may modulate SA signaling system to trigger immune responses (De Vleesschauwer et al. 2010; Pantelides et al. 2013). ABA treatment decreases the expression of several genes involved in cytokinin biosynthesis and degradation (Tsai et al. 2012) Cytokinin antagonistically impacts the signaling of auxin (Stepanova and Alonso 2011). Synergism between auxin and cytokinin signaling has also been reported (Hwang et al. 2012). Elevated plant auxin levels enhance susceptibility by repressing the defense-related *PR1* gene expression (Kazan and Manners 2009), while elevated cytokinin levels mediate resistance and induction of *PR1* (Choi et al. 2011; Naseem et al. 2012).

1.8 Gibberellins

Gibberellins (GA) are important plant growth hormones involved in plant innate immunity. GA modulates plant defense responses, mostly by regulating SA–JA–ET signaling systems. Key components in the GA signaling pathway include the GA

receptor GID1, the DELLA proteins, and the F-box proteins (Hauvermale et al. 2012; Daviére and Achard 2013). Upon GA binding, the GA-dependent conformational change causes the GID1 N-terminal helical lid domain to behave like "molecular glue" to form the GA–GID1–DELLA complex. DELLAs repress GA-dependent defense responses, whereas GA relieves their repressive activity (Achard and Genschik 2009). GA lifts DELLA repression by targeting DELLA for destruction via the ubiquitin–proteasome pathway. GA regulates the plant innate immune responses either positively or negatively. It induces susceptibility or resistance against different fungal and bacterial pathogens (Navarro et al. 2008; Yang et al. 2008; De Vleesschauwer et al. 2012; Qin et al. 2013). GA modulates plant disease resistance or susceptibility by inducing the degradation of DELLA proteins (Hauvermale et al. 2012). GA regulates plant immune responses by modulating JA and SA signaling systems (Navarro et al. 2006; Yang et al. 2008; Qi et al. 2014). It also enhances SAR against pathogens (Xia et al. 2010). GA expedites SA accumulation (Navarro et al. 2008; Alonso-Ramirez et al. 2009) and promotes resistance against pathogens by degrading DELLA proteins (Navarro et al. 2008). Loss-of-function mutants in DELLAs, the suppressors of GA signaling up-regulate the SA-mediated defense and down-regulate JA/ET-mediated defense in *Arabidopsis* (Robert-Seilaniantz et al. 2007). GA interacts antagonistically with JA signaling (Yang et al. 2013), while GA attenuates the JA-induced expression of a number of JA-responsive genes (Cao et al. 2006; Hou et al. 2008, 2010). Both JA and GA signaling systems modulate plant immune responses. JA interferes with gibberellin signaling cascade. JA delays GA-mediated DELLA protein degradation. The JAZ protein JAZ9 inhibits RGA (a DELLA protein) interaction with the transcription factor PIF3 (phytochrome-interacting factor 3) (Yang et al. 2012). JA signaling has been shown to activate expression of DELLA genes involved in GA signaling pathway. JA-induced *RGL3* expression works via the COI1/MYC2-dependent signaling pathway. JA-mediated induction of RGL3 expression was abolished in the *coi1-1* mutant, indicating that *RGL3* is downstream of COI1 (Wild et al. 2012). Brassinosteroids (BR) negatively regulate innate immune responses induced by GAs. BR and GA cause cross-inhibitory effects on the reciprocal hormone biosynthesis pathways to interact in a mutually antagonistic manner (De Vleesschauwer et al. 2012). Pathogen triggers overexpression of DELLA proteins to suppress GA-regulated defense responses (De Vleesschauwer et al. 2012).

1.9 Brassinosteroids

Brassinosteroids (BRs) are growth-promoting steroidal hormones in plants, and they are also involved in plant innate immunity (Nakashita et al. 2003; Bajguz and Hayat 2009; Divi et al. 2010; Jaillais et al. 2011; Albrecht et al. 2012; Owens et al. 2012; Wang 2012; Vriet et al. 2012). BR signals are perceived by the plasma membrane receptor BRI1 and co-receptor BAK1. Several positive (BSK1, BSU1, PP2A, CDG1) and negative (BKI1, BIN2, MSBP1, and 14-3-3) regulators of BR

signaling control the activities of BZR1 and BES1 family of transcription factors, which regulate the expression of hundreds to thousands of genes for various BR responses (Wang et al. 2008a; Kim et al. 2009; Li et al. 2010). BRs either positively (Khripach et al. 2000; Nakashita et al. 2003) or negatively (Albrecht et al. 2012; Belkhadir et al. 2012; De Vleesschauwer et al. 2012; Nahar et al. 2013) regulate plant innate immunity. BAK1, a key component in BR signaling pathway (Schwessinger et al. 2011), is involved in triggering plant disease resistance by modulating JA signaling system (Yang et al. 2011). BR may also induce susceptibility to pathogens (De Vleesschauwer et al. 2012). BR negates disease resistance conferred by the SA synthetic analog benzothiadiazole, suggesting negative crosstalk between BR and SA signaling pathways. BR-mediated suppression of SA defenses occurs downstream of SA biosynthesis, but upstream of NPR1 and OsWRKY45 in the SA signaling pathway (De Vleesschauwer et al. 2012). BR triggers the expression of GA repressor proteins and suppresses GA-induced defense responses (De Vleesschauwer et al. 2012). Crosstalk between PAMP–PRR signaling and BR synthesis pathway has been reported (Albrecht et al. 2012). Increasing the endogenous pool of bioactive BR antagonizes flg22-induced responses (Belkhadir et al. 2012). BRI1–BAK signaling modulates PAMP–PRR signaling pathway. BAK1 is a common co-receptor for the PRRs activated by various PAMPs. Similarly BAK1 is a co-receptor for the BR receptor, BRI1. Signaling downstream of BAK1 differs between BRI1 and FLS2 (PRR for flg22) pathways (Lu et al. 2010). Pathogen infection results in elevation of BR signal processing (De Vleesschauwer et al. 2012). Pathogens may exploit BRs as virulence factors and hijack the plant BR machinery to cause disease (De Vleesschauwer et al. 2012).

1.10 Plant Hormone Signaling Network

Plant hormones activate different signaling pathways inducing distinctly different defense genes (Liu et al. 2007; Spoel et al. 2007; Mitsuhara et al. 2008; van Verk et al. 2008; Cevik et al. 2012). These signaling pathways are not simple linear and isolated cascades, but can crosstalk with each other (Tsuda et al. 2009; Verhage et al. 2010; Yang et al. 2013). Architecture of plant immune signaling networks may not be static and may vary with the pathogen genotype invasion. Both antagonism and synergism between SA and JA signaling systems have been widely reported in plants (Robert-Seilaniantz et al. 2011; El Rahman et al. 2012; Pieterse et al. 2012; Thaler et al. 2012; Zander et al. 2012; Zheng et al. 2012; Gimenez-Ibanez and Solano 2013; Van der Does et al. 2013). Crosstalk between JA and ET (Melotto et al. 2008; Pré et al. 2008; Bari and Jones 2009; Grant and Jones 2009; Pauwels and Goossens 2011; Robert-Seilaniantz et al. 2011; Zhu et al. 2011b), SA and ET (Leon-Reyes et al. 2010), JA and GA (Yang et al. 2013), SA and auxin (Robert-Seilaniantz et al. 2011), and SA and ABA (Xu et al. 2013) has been reported. The DELLA protein RGL3 in the GA pathway represses the SA pathway (Wild et al. 2012). In contrast, the DELLA protein enhances the expression of JA-dependent expression

(Wild et al. 2012). The interplay between SA, JA, and GA signaling pathways has been reported in *Arabidopsis* (Wild et al. 2012). Synergism between ABA and SA signaling systems has also been reported in *Arabidopsis* (Chen et al. 2013). Mutual interactions between stress-specific hormones such as SA and JA/ET are regarded as the central backbone of the immunity (Pieterse et al. 2012). However, the growth-promoting hormones (auxin, cytokinins, gibberellic acid, and abscisic acid) either inhibit or potentiate this balance in mediating the protection or susceptibility of the plant against the invading pathogen (Pieterse et al. 2012; Naseem et al. 2012; Naseem and Dandekar 2012).

Plant hormones act in concert (Naseem et al. 2012; Naseem and Dandekar 2012). Crosstalk between defense signaling pathways may provide the plant with a powerful regulatory potential, which helps the plant to "decide" which defensive strategy to follow, depending on the type of attacker it is encountering (De Vos et al. 2005). Plants modulate the relative abundance of SA, JA, and ET levels; modify the expression of defense-related genes; and coordinate complex interactions between defense signaling pathways to activate an effective defense response against attack by various types of pathogens (Bari and Jones 2009). Crosstalk between the hormone signaling systems fine-tunes the defense responses in the plant immune system (Grant and Jones 2009; El Rahman et al. 2012; Pieterse et al. 2009, 2012). Argueso et al. (2012) showed that cytokinin up-regulates plant immunity via an elevation of SA-dependent defense responses and SA in turn feedback inhibits cytokinin signaling. The crosstalk between cytokinin and SA signaling networks may help plants to fine-tune defense responses against pathogens (Argueso et al. 2012). DELLAs, the repressors of GA signaling, promote susceptibility to virulent biotrophs and resistance to necrotrophs, partly by altering the relative strength of salicylic acid and jasmonic acid (Navarro et al. 2008).

Crosstalk between defense signaling pathways may also allow pathogens to manipulate plants to their own benefit by shutting down induced defense through influences on the signaling network. Infection with biotrophic *Pseudomonas syringae*, which induces SA-mediated defense, renders plants more susceptible to the necrotrophic pathogen *Alternaria brassicicola* by suppressing JA signaling pathway (Spoel et al. 2007). *Botrytis cinerea* manipulates the antagonistic effects between immune pathways to promote disease development in tomato (El Oirdi et al. 2011). The rice bacterial blight pathogen *Xanthomonas oryzae* pv. *oryzae* has been shown to hijack the rice ABA machinery to cause disease (Xu et al. 2013). This immune-suppressive effect of ABA may be due to suppression of SA-mediated defenses that normally serve to limit pathogen growth (Xu et al. 2013).

Concentration of the plant hormones in the signaling network may also alter the immune responses. Treatment of rice plants with increasing concentrations of gibberellic acid (GA) enhanced resistance to *Pythium graminicola* in a concentration-dependent manner. Conversely, depletion of endogenous GA levels using the GA biosynthesis inhibitor uniconazole promoted disease susceptibility (De Vleesschauwer et al. 2012). Enhanced biosynthesis of ethylene induced by ACC treatment decreases SA- and JA-associated defense signaling (Shen et al. 2011). A transient synergistic enhancement in the expression of genes associated with

either JA or SA signaling was observed when both jasmonic acid and salicylic acid were applied at low concentrations. However, antagonism was observed at more prolonged treatment times or at higher concentrations. Similar results were also observed when adding the jasmonate precursor α-linolenic acid with salicylic acid (Mur et al. 2006). These results suggest that the outcomes of JA–SA interactions depend on the relative concentration of JA and SA.

Activation of multiple hormone signaling pathways may induce resistance against a wide range of pathogens (Hénanff et al. 2013). JA signaling system triggers resistance against necrotrophic pathogens (McGrath et al. 2005; Zheng et al. 2006; Méndez-Bravo et al. 2011; El Rahman et al. 2012), while SA signaling is involved in triggering resistance against biotrophic and hemibiotrophic pathogens (Thaler et al. 2004; Nie 2006; De Vos et al. 2006; Spoel et al. 2007; Jelenska et al. 2007; El Oirdi et al. 2011). By contrast, the SA–JA–ET–ABA signaling network triggers expression of several defense genes and confers resistance to both necrotrophic and biotrophic pathogens (Hénanff et al. 2013). *Bacillus cereus* induces systemic resistance against pathogens by simultaneously activating SA-, JA-, and ET-dependent signaling pathways (Niu et al. 2011).

1.11 Can Molecular Manipulation of Plant Hormone Signaling Network Help the Plant to Win the War Against Pathogens?

Crosstalk between the different hormone signaling systems fine-tunes the defense responses against biotrophic and necrotrophic fungal, oomycete, bacterial, and viral pathogens (Pieterse et al. 2009; Méndez-Bravo et al. 2011; El Rahman et al. 2012; Pieterse et al. 2012; Xu et al. 2013). Crosstalk between different hormone signaling pathways in the hormone signaling network helps the plant to choose the effective defense strategy to follow depending on the type of pathogen it is encountering (De Vos et al. 2005; Niu et al. 2011; Nambeesan et al. 2012; Wang et al. 2012; Hénanff et al. 2013). The crosstalk also allows the pathogens to manipulate plants to their own benefit by shutting down the specific hormone signaling pathway involved in triggering defense responses and hijacking the signaling pathway involved in induction of susceptibility (de Torres-Zabala et al. 2007; Katsir et al. 2008; Xu et al. 2013). Can we manipulate specific signaling system to activate defense responses and suppress the action of pathogens in hijacking the signaling pathway triggering susceptibility? It has been reported that concentration of the plant hormones in the signaling network can alter the strong and fast expression of specific hormones (Mur et al. 2006; Shen et al. 2011; De Vleesschauwer et al. 2012). Manipulation of the signaling network may be a potential strategy to enhance activation and improvement of plant immunity for crop disease management. This book describes the molecular basis of plant hormone-induced immune responses in plants to develop technologies for effective management of crop diseases. Enhancing disease resistance through altered regulation of plant immunity systems would be durable and