Chapter 8
Interactions of Ethylene and Other Signals

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Abstract As sessile organisms, plants utilize a wise strategy for adapting to the environment. The strategy involves the integration of its internal hormone signaling variations with exogenous environmental changes to coordinate plant growth and development. Like other phytohormones, ethylene plays a key role in these integration processes. In this chapter, we will discuss the interactions of ethylene with environmental signal (light) and several internal hormones (auxin, jasmonate, and gibberellins) in the regulation of plant growth, and highlight the recent advances in understanding their associated molecular mechanisms.

Keywords Ethylene · Light · Auxin · Jasmonate · Gibberellins · EIN3

8.1 Interaction with Light

Light is more than a source of energy for plants. It is the most important environmental cue for plants because it tells plants time, geographic location, and growth directions. Seedlings grown in dark exhibit long hypocotyls and closed yellow cotyledons (skotomorphogenesis); while seedlings grown in light exhibit short hypocotyls and opened green cotyledons (photomorphogenesis) (Nemhauser and Chory 2002). Consistent with these massive morphological differences, light

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regulates nearly 30 % of the global mRNA transcripts in the genomes of both monocots and dicots (Jiao et al. 2005; Ma et al. 2001).

As described in the previous chapter, all the typical ethylene seedling triple responses (i.e., a short/swollen root and hypocotyl, and an exaggerated apical hook) are observed under dark conditions (Guzman and Ecker 1990); however, light reverses the ethylene-triggered exaggerated hook and ethylene promotes hypocotyl growth instead of inhibition in light. According to a very recent study, germinated seeds sense the soil cover conditions (soil depth and texture) by producing different concentrations of ethylene (Zhong et al. 2014). In other words, germinated seeds can "see" their surrounding environment by sensing different ethylene quantities. It is hypothesized that ethylene promotes the exaggerated hook formation to protect the shoot apical meristem that resides between the two cotyledons when protruding through the soil. After seedlings penetrate the soil cover, light rapidly reverses the apical hook (reducing the hook angle) and induces chlorophyll synthesis and cotyledon opening. This dramatic morphological change during the transition from dark to light prepares cotyledons for photosynthesis.

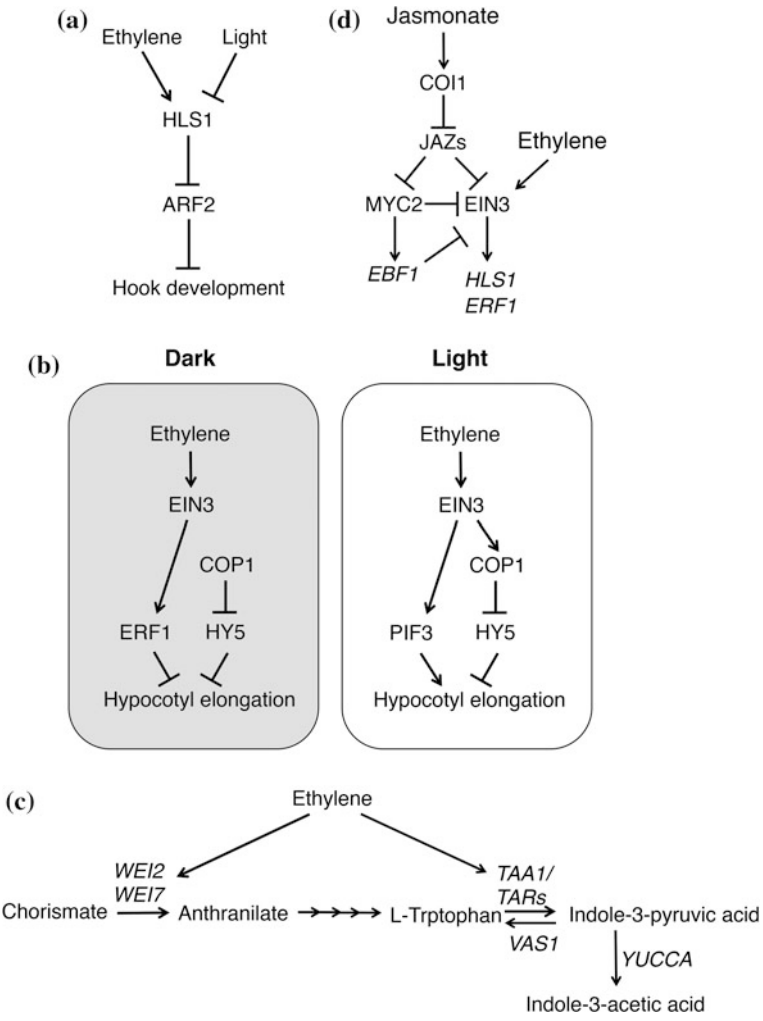
Hook development is caused by the differential elongation of hypocotyl cells (Silk and Erickson 1978), which is governed by another crucial phytohormone auxin. Auxin is synthesized in meristematic tissues and transported in a basipetal direction to fulfill its physiological functions. Blocking auxin transport by N-1-naphthylphthalamic acid (NPA) treatment or treating seedlings with exogenous auxin prohibits hook formation (Lehman et al. 1996). In the early screening for ethylene-insensitive mutants, dozens of *hookless* mutants were identified and the mutated genes were further cloned (Guzman and Ecker 1990; Lehman et al. 1996). Among them, *HOOKLESS1*, which encodes a protein similar to N-acetyltransferase, is a major player in determining apical hook angle. The strong allele of *hookless1* mutant (i.e., *hls1-1*) shows opened cotyledons in dark (no hook angles in the apical area) regardless in the presence or absence of ethylene. On the other hand, weak *hookless1* allele (i.e., *hls1-10*) does not form hook angles in the absence of ethylene and could bend to some extent (average hook angle is 6.5°) in the presence of ethylene, but this response is quite mild comparing with the wild-type controls (average hook angle is 298°). Further observations show that the *hls1* mutation suppresses the constitutively exaggerated-hook phenotype in *ctr1* or *EIN3ox* (a transgenic plant overexpressing EIN3), both of which exhibit constitutive ethylene responses, suggesting that HLS1 acts downstream of CTR1 and EIN3. Ethylene-activated EIN3 directly binds to the *HLS1* promoter to induce *HLS1* expression (An et al. 2012; Chang et al. 2013; Lehman et al. 1996). Expression profiles of several auxin-regulated genes are altered in *hls1* mutant, implying that HLS1 controls auxin activities (Lehman et al. 1996). It is further reported that one auxin responsive transcription factor AUXIN RESPONSE FACTOR2 (ARF2) acts downstream of HLS1, as *arf2* mutation suppresses *hls1* (Li et al. 2004). Overexpression of *ARF2* plants is less sensitive to ethylene in hook development, which indicates that ARF2 is a negative regulator in the hook development process. In contrast with the increase of HLS1 protein, ethylene destabilizes the ARF2 protein in a HLS1 dependent manner (Li et al. 2004). Inhibiting the 26S proteasome by treatment with chemical

MG132 can suppress ARF2 degradation, suggesting that the ubiquitin-mediated protein degradation pathway facilitates the degradation of ARF2 (Li et al. 2004).

Although for decades, it had been documented that light is able to reverse the apical hook in many plant species even in the presence of ethylene (Liscum and Hangarter 1993; Rubinstein 1971), the underlying molecular basis was uncovered only after the characterization of HLS1 and ARF2. Light treatment dramatically reduces HLS1 protein levels but increases ARF2 protein accumulation, wherein the modulation of ARF2 protein level is dependent on the presence of HLS1 (Li et al. 2004). This opposite regulation of HLS1 and ARF2 protein accumulation by light and ethylene explains how light antagonizes ethylene's physiological function with regard to hook development (Fig. 8.1a).

Although a molecular framework of light–ethylene antagonistic regulation on hook development has been established, there are still some questions that need to be explored in the future: (1) The biochemical nature of HLS1 is a mystery, especially whether or how its putative N-acetyltransferase activity regulates ARF2 and controls its downstream event; (2) Which E3 ubiquitin ligase control HLS1 or ARF2 protein degradation as their protein degradation is 26S proteasome-dependent? And (3) what is the link between light-activated photoreceptors to the downstream protein degradation events?

The regulation of hypocotyls elongation presents another interesting observation for light and ethylene interaction. Ethylene inhibits hypocotyl elongation in dark, but promotes it in light (Alonso et al. 1999; Guzman and Ecker 1990; Smalle et al. 1997). The elongation of hypocotyl cells causes ethylene-stimulated hypocotyl elongation in light. It is reported that one basic-helix-loop-helix (bHLH) transcription factor PHYTOCHROME-INTERACTING FACTROR3 (PIF3) is required for this process. Loss-of-function mutant *pif3* is insensitive to the ethylene-stimulated hypocotyl elongation upon light exposure. Given the evidence that *pif3* suppresses the long hypocotyl phenotype of *ctr1* or *EIN3ox*, and that overexpression of *PIF3* rescues the short hypocotyl phenotype of *ein3 eil1*, it is concluded that PIF3 acts downstream of EIN3/EIL1 in the regulation of hypocotyl elongation in light (Zhong et al. 2012). However, *pif3* mutant does not show any remarkable ethylene-related hypocotyl phenotype in dark, suggesting that PIF3 functions specifically in light. Further results show that no matter in light or dark, ethylene treatment induces *PIF3* expression and EIN3 directly associates with *PIF3* promoter to activate its transcription. Although *PIF3* transcript is induced by ethylene in both light and dark conditions, light rapidly promotes PIF3 protein degradation through LIGHT-RESPONSE BRIC-A-BRACK/TRAMTRACK/BROAD (LRB) E3 ubiquitin ligases (Al-Sady et al. 2006; Ni et al. 2013, 2014; Zhong et al. 2012). In other words, PIF3 protein accumulation is abundant in dark but limited in light. It is thus hypothesized that ethylene-induced *PIF3* transcription cannot exert an additive effect in dark but can only contribute to the hypocotyl elongation in light. On the other hand, ethylene-induced AP2-type transcription factor ETHYLENE RESPONSE FACTOR1 (ERF1) controls the ethylene-promoted hypocotyl growth inhibition in dark. Similar to PIF3, *ERF1* is another EIN3/EIL1 target gene.


(a)
Ethylene
Light
HLS1
ARF2
Hook development
(d)
Jasmonate
COI1
JAZs
Ethylene
MYC2
EIN3
EBF1
HLS1
ERF1
(b)
Dark
Light
Ethylene
EIN3
COP1
ERF1
HY5
Hypocotyl elongation
Ethylene
EIN3
COP1
PIF3
HY5
Hypocotyl elongation
(c)
Ethylene
WEI2
WEI7
Chorismate
Anthranilate
L-Trptophan
TAA1/
TARs
VAS1
Indole-3-pyruvic acid
YUCCA
Indole-3-acetic acid

◀ **Fig. 8.1** **a** Light antagonizes ethylene-induced apical hook formation. Ethylene promotes HLS1 expression and ARF2 degradation to induce hook formation, while light represses HLS1 expression and accumulates ARF2 to inhibit hook development. **b** A simplified illustration depicting the opposite ethylene responses under *dark* and *light* conditions. In *dark*, ethylene-activated EIN3 induces ERF1 expression, which inhibits hypocotyl elongation. Although COP1 targets HY5 for degradation and promotes hypocotyl elongation, enhanced ERF1 expression overrides the loss of HY5 effect to ultimately suppress hypocotyl elongation. In *light*, EIN3-induced PIF3 expression plays a predominant role and COP1 is restrained in the nucleus wherein degrading HY5, so the combination of these two pathways leads to hypocotyl elongation. **c** Ethylene induces auxin biosynthesis. WEI2 and WEI7 catalyze the production of anthranilate, which is further converted to L-tryptophan by several steps. TAA1/TARs convert L-tryptophan to indole-3-pyruvic acid, while VAS1 converts indole-3-pyruvic acid to L-tryptophan. Indole-3-pyruvic acid is then converted to indole-3-acetic acid by YUCCA enzymes. Ethylene induces WEI2, WEI7, and TAA1 expression for promoting auxin synthesis. **d** Jasmonate–ethylene interactions. Jasmonate activates MYC2 and EIN3 transcription factors through the removal of JAZ repressors by promoting COI1–JAZ interactions, while ethylene activates EIN3 via enhancing EIN3 protein accumulation. EIN3 induces HLS1 or ERF1 expression for diverse responses. MYC2 induces EBF1 expression to promote EIN3 turn over and physically interacts with EIN3 to further inhibit its activity

Ethylene induces *ERF1* expression in both light and dark conditions as well. Overexpression of *ERF1* causes short hypocotyl phenotype in dark but not in light (Solano et al. 1998; Zhong et al. 2012). In contrast to PIF3, light stabilizes ERF1 protein, while dark triggers its degradation, which makes ERF1 protein level limited in dark but abundant in light. The effect of ethylene-induced *ERF1* expression is masked in light condition but prominent in dark (Zhong et al. 2012). Taken together, ethylene induces *ERF1* and *PIF3* expression in both dark and light; however, the fate of their encoded proteins is totally opposite under different light conditions. In dark, PIF3 is stabilized and saturated, while ERF1 is degraded and limited, so the ethylene-induced *ERF1* expression contributes to the observed phenotype (short hypocotyl). In contrast to dark, ERF1 is saturated and PIF3 is limited in light, so the consequence of ethylene-induced *PIF3* expression is evident (long hypocotyl). These PIF3-ERF1 and HLS1-ARF2 modules suggest that protein degradation plays a vital role in the control of light–ethylene interactions (Lorrain and Fankhauser 2012; Wang et al. 2013).

In addition to this PIF3-ERF1 module in the controlling of hypocotyl elongation in light and dark conditions, it is reported that one basic leucine zipper (bZIP) transcription factor LONG HYPOCOTYL5 (HY5) is also necessary for ethylene-promoted hypocotyl elongation in light (Yu et al. 2013). HY5 positively regulates plant photomorphogenesis through directly controlling expression of thousands of genes (Lee et al. 2007; Zhang et al. 2011). E3 ubiquitin ligase CONSTITUTIVE PHOTOMORPHOGENESIS1 (COP1) interacts with HY5 and promotes its degradation in dark, whereas light triggers COP1 movement from the nucleus to cytoplasm to relieve its inhibition on HY5 (Ang et al. 1998; Hardtke et al. 2000; Osterlund et al. 2000; von Arnim and Deng 1994).

It is shown that *hy5* mutant is insensitive to ethylene-promoted hypocotyl elongation in light, but its response in dark is indistinguishable to the wild type,

which implies that HY5 is involved in the ethylene-promoted hypocotyl elongation in light. Immunoblot results show that ethylene promotes HY5 protein degradation specifically in light but not in dark and this degradation process is dependent on EIN3 and COP1. Further analysis demonstrates that COP1 acts downstream of EIN3 in control of HY5 stability. Moreover, ethylene stimulates the nuclear localization of COP1 in light but not in dark, and in the absence of EIN3, this effect is absent, suggesting that ethylene facilitates COP1 movement in an EIN3 dependent manner. This ethylene-promoted COP1 nuclear localization causes the degradation of HY5, which ultimately induces the hypocotyl elongation (Fig. 8.1b) (Yu et al. 2013).

These two separate mechanical studies shed new light on the understanding of how light regulates ethylene-triggered hypocotyl elongation and lead to a new question: how can these two seemly unrelated mechanisms be reconciled? One possible explanation is that both of them may regulate auxin biosynthesis or distribution to eventually regulate hypocotyl cell elongation, given the evidence that auxin determines the hypocotyl cell elongation (Chapman et al. 2012). It is reported that auxin biosynthesis mutants or signaling mutants are insensitive to the ethylene-promoted hypocotyl elongation in light and that HY5 regulates auxin synthesis gene expression and auxin transporter localization (Cluis et al. 2004; Liang et al. 2012). Because *PIF3* related genes (*PIF4*, *PIF5* and *PIF7*) directly regulate auxin biosynthesis (Franklin et al. 2011; Hornitschek et al. 2012; Li et al. 2012; Nozue et al. 2011; Sun et al. 2012), it is speculated that *PIF3* may also contribute to affect auxin levels.

Besides regulating hook development and hypocotyl elongation, ethylene coordinates with light to properly synthesize chlorophyll. In etiolated seedlings, chlorophyll precursors (protochlorophyllide) accumulate in the etioplasts, while upon light exposure three isoforms of protochlorophyllide oxidoreductase (POR) are photoactivated and further catalyze the conversion from protochlorophyllide to chlorophyll. However, if the activity of PORs is inadequate upon light exposure, accumulated protochlorophyllide will produce large amounts of reactive oxygen species (ROS) that will cause cellular damage. The amount of protochlorophyllide is positively correlated with the dark incubation time. When seedlings are incubated in dark for 3–4 days and then exposed to light for 2 days, the average greening rate in wild type is more than 90 %. However, when seedlings are incubated in dark for an extended number of days, such as 9 days, followed by light illumination for 2 days, their greening rate decreases to less than 20 %. Ethylene supplement greatly rescues this reduction of greening rate. In the presence of ethylene, although seedlings are still kept in dark for 9 days and then exposed to light for 2 days, the greening rate is improved from 20 to 80 %. Further results show that EIN3/EIL1 are required for this regulation and they directly bind to the *PORA* and *PORB* (two major isoforms of POR genes) promoters to induce their mRNA expression and catalyze the protochlorophyllide conversion (Zhong et al. 2009). In addition, ethylene-induced PIF3 binds to the promoters of *HEMA1*, *GUN4* and *GUN5* genes and represses their expression. HEMA1, GUN4, and GUN5 proteins are essential for the production of protochlorophyllide (Zhong et al. 2014). In conclusion, ethylene-activated EIN3/

EIL1 directly induce *PORA*/*PORB* expression to promote protochlorophyllide conversion and induce *PIF3* expression to further block protochlorophyllide accumulation to prevent light-induced photo-oxidative damage.

8.2 Interaction with Auxin

Without a doubt, auxin is one of the most extensively studied plant hormone in the phytohormone field during the past several decades. The interactions between ethylene and auxin are broadly investigated from earlier physiological studies to the current genomic studies. Due to limited space in this chapter, we could not include most of the early literature regarding exciting discoveries in the field. Instead, we will mainly point out the molecular mechanisms of ethylene–auxin interactions, particularly the interesting discoveries reported recently. There are several specific detailed reviews discussing the findings in the ethylene–auxin interactions (Lee and Cho 2013; Robles et al. 2013; Vanstraelen and Benkova 2012; Zhao and Guo 2011), readers who want to know more are encouraged to further refer to those reviews. Details about the integration of ethylene and auxin signaling can be found in Chap. 10.

Apical hook formation of etiolated seedlings by ethylene is a result of asymmetric auxin distribution, which causes the differential cell elongation. Auxin and ethylene act synergistically to inhibit root elongation and promote root hair initiation, but antagonistically in other growth events, such as lateral root development and root gravitropism. The general concept for the underlying mechanism is that ethylene modulates auxin biosynthesis and/or polar transport, especially in a cell-type-specific manner, which eventually causes the redistribution of auxin in different cells and alters the growth patterns. On the other hand, auxin also regulates ethylene biosynthesis through inducing the expression of several key enzymes in the ethylene biosynthesis pathway. In order to illustrate the molecular mechanisms more clearly, we first introduce the basic auxin biology in the following paragraphs.

Auxin synthesis is complicated and has been studied for a relatively long time. Only recently has the main auxin synthesis route been convincingly elucidated through comprehensive genetic analysis and chemical quantification methods. Indole-3-acetic acid (IAA) is the most common form of auxin in planta. L-tryptophan (Trp) is recognized as the main precursor for auxin synthesis, which is then converted to indole-3-pyruvic acid (3-IPA) by a family of tryptophan aminotransferase named TRYPTOPHAN AMINOTRANSFERASE OF ARABIDOPSIS 1 (TAA1) and TAA1-related 1–4 (TARs). TAA1 is identified by several individual research groups, and also named WEAK ETHYLENE INSENSITIVE8 (WEI8), SHADE AVOIDANCE3 (SAV3), or TRANSPORTER INHIBITOR RESISTANT2 (TIR2) in their reports (Stepanova et al. 2008; Tao et al. 2008; Yamada et al. 2009). Flavin-containing monooxygenase family proteins (called YUCCA) convert 3-IPA to IAA (Mashiguchi et al. 2011; Stepanova et al. 2011; Won et al. 2011). Auxin transporters are required for auxin distribution into different cells.

AUXIN RESISTANT1 (AUX1) and LIKE AUX1 (LAX1) are auxin influx carriers, whereas PIN-FORMED (PIN) proteins and ATP BINDING CASSETTE TYPE B/P-GLYCOPROTEIN/MULTIDRUG RESISTANCE (ABCB/PGP/MDR) proteins are auxin efflux carriers (Benjamins and Scheres 2008).

Auxin signaling comprises two different pathways, one acts inside the nucleus and the other one acts on the cell surface. TRANSPROT INHIBITOR1 (TIR1) and its interacting AUXIN/INDOLE-3-ACETIC ACID (AUX/IAA) proteins are the co-receptors for auxin perception in the nucleus (Dharmasiri et al. 2005; Kepinski and Leyser 2005). Crystallography studies show that auxin functions like "molecular glue" to promote TIR1-AUX/IAA protein–protein interaction (Tan et al. 2007). TIR1 is an F-box protein, which forms an SCF^{TIR1} E3 ubiquitin ligase and directly targets AUX/IAA degradation through 26S proteasome pathway (Gray et al. 2001). In the absence of auxin, AUX/IAA proteins recruit the Groucho/Tup1 co-repressor protein TOPLESS and interact with the downstream AUXIN RESPONSE FACTOR (ARFs) transcription factors to repress their transcriptional activities (Szemenyei et al. 2008). After auxin perception, AUX/IAA proteins are degraded by SCF^{TIR1} to release their repression of ARFs. ARFs then elicit the downstream gene expression and regulate a variety of auxin responses. Besides these TIR1-AUX/IAA receptors, cell-surface localized AUXIN BINDING PROTEIN1 (ABP1) was proposed to be an auxin receptor for a long time. ABP1 was found to be involved in cell morphogenesis, root development, and the endocytosis regulation of PIN efflux carriers (Robert et al. 2010; Xu et al. 2010). Further studies reveal that cytoplasm membrane localized ABP1 activates ROPs (Rho-like guanosine triphosphatases from plants) in an auxin-dependent manner to regulate cytoskeleton reorientation and PIN protein endocytosis (Robert et al. 2010; Xu et al. 2010). Very recently, it was reported that auxin promotes the membrane localized TRANSMEMBRANE KINASE (TMK) members of the receptor-like kinase family proteins interact with ABP1, which are required for the activation of ROPs (Xu et al. 2014). The auxin-promoted ABP1–TMK interaction on the cell surface implies that auxin tends to function as "molecular glue" regardless its cellular localizations.

Returning to the ethylene–auxin interactions, ethylene was reported to modulate the auxin action via the regulation of its biosynthesis. It is shown that ethylene promotes auxin biosynthesis through upregulation of *WEAK ETHYLENE INSENSITIVE2* (*WEI2*) and *WEI7* transcription. *WEI2* and *WEI7* each encode a subunit of anthranilate synthase, which is a rate-limiting enzyme for the auxin precursor Trp synthesis (Stepanova et al. 2005). Both *wei2* and *wei7* mutants are insensitive to ethylene in the aspect of root growth inhibition but not in hypocotyl or hook, which suggests that auxin is necessary for the ethylene-triggered root growth inhibition. Ethylene induces the auxin reporter *DR5*::*GUS* expression in root tips, while this induction is diminished in *wei2* or *wei7* mutants, further supporting that ethylene induces auxin synthesis through WEI2 and WEI7. Similar to WEI2 and WEI7, ethylene also induces *WEI8* (*TAA1*) expression and promotes auxin production to inhibit root elongation (Stepanova et al. 2008). Taken together, these two studies demonstrate that ethylene upregulates at least two consecutive catalytic steps to promote auxin biosynthesis for root growth inhibition (Fig. 8.1c).

In an attempt to screen for *sav3*/*wei8*/*taa1* suppressors, *vas1* (for reversal of *sav3* phenotype) mutant was identified and further investigated. *VAS1* encodes a pyridoxal-phosphate-dependent aminotransferase, which converts 3-IPA to Trp (Zheng et al. 2013). More interesting, this reaction relies on methionine (Met) as an amino donor and 3-IPA as an amino acceptor. Of note, Met is the precursor for ACC synthesis. That is to say, VAS1 suppresses both Met and 3-IPA accumulation by catalyzing their conversion to Trp and 2-oxo-4-methylthiobutyric acid. Experimental evidence indicates that both IAA and ACC concentrations in *vas1* mutant are higher than the wild-type control, suggesting that auxin biosynthesis and ethylene biosynthesis are linked by VAS1, a metabolic enzyme (Fig. 8.1c). This study provides a new view on the understanding of the complex interactions between auxin and ethylene.

Another level of ethylene–auxin interactions is ethylene's modulation of auxin distribution because polar auxin transport is necessary for generating proper ethylene responses. Several independent ethylene-insensitive mutant screening experiments (including our unpublished results) have demonstrated that *aux1* and *pin2,* both of which are defective in polar auxin transport, are insensitive to ethylene in root growth inhibition or *DR5*::*GFP* reporter expression (Luschnig et al. 1998; Negi et al. 2008; Pickett et al. 1990). It is further reported that ethylene promotes *AUX1* or *PIN2* transcription to elevate the auxin transport (Lewis et al. 2011; Ruzicka et al. 2007).

The auxin- and ethylene-regulated gene expression profiles at the genomic scale have also been investigated. Including *aux1* (impaired in auxin transport in certain cell types) and *ein2* (blocking ethylene signaling) mutants in their experimental design, Jose Alonso's group found that nearly a quarter of auxin-regulated gene expression is dependent on ethylene and vice versa, suggesting that auxin and ethylene regulate gene expression in a largely independent manner (Stepanova et al. 2007). Revealing the direct gene targets for EIN3, the recent EIN3 chromatin immunoprecipitation sequencing (ChIP-seq) results show that EIN3 can directly target *AUX1*, *IAA29* and several *ARF* genes to modulate auxin responses (Chang et al. 2013), supporting the complicated ethylene-triggered transcriptional control of auxin signaling.

Additional level of the interactions between ethylene and auxin occurs at the protein level, among proteins involved in their signaling. A number of studies demonstrate that ethylene stimulates AUX1 protein degradation on the inner side of apical hook and auxin stabilizes EIN3 protein through $SCF^{EBF1/2}$ in root tips (He et al. 2011; Vandenbussche et al. 2010). Although the E3 ubiquitin ligase that targets AUX1 and how auxin modulates $SCF^{EBF1/2}$ functions are unknown, these reports indicate that the interactions of auxin and ethylene occur both at the transcriptional and posttranscriptional levels.

It can be concluded that the crosstalk between ethylene and auxin exist almost everywhere from their biosynthesis to their posttranscriptional events. With further studies and the advance of research tools, it can be expected that the studies of ethylene and auxin interactions will be more fruitful in the future, especially for the

purposes of identifying different action modes in different cell types and investigating whether ethylene modulates the recently identified ABP1-TMK-ROP cell-surface auxin signaling.

8.3 Interaction with Jasmonate

Ethylene and jasmonate are recognized as two types of crucial defense hormones for against necrotrophic fungi infections (Dong 1998). After pathogen infection, a subset of pathogen responsive genes (such as *ERF1*, *ORA59*, and *PDF1.2*) are quickly induced and to help plants resistant to infections. Both intact ethylene and jasmonate signaling are required for upregulating those gene expressions and enhancing plant resistance to infections. It has been reported that ethylene and jasmonate signaling mutants are more susceptible to *Botrytis cinerea* infections. Both jasmonate and ethylene treatment induce those gene expressions in a synergistic manner. Because jasmonate treatment cannot induce those gene expressions in ethylene insensitive mutants and similarly ethylene cannot induce them in jasmonate insensitive mutants, it suggests that ethylene and jasmonate act interdependently in controlling those gene expressions. (Lorenzo et al. 2003; Penninckx et al. 1996). In addition to their coactions in plant defense, ethylene and jasmonate are also reported to be two necessary hormones for regulating plant root hair development (Zhu et al. 2006). However, signal interactions in plants are more complicated and elaborate than one can imagine. Besides those synergistic interactions, ethylene and jasmonate act antagonistically in many other aspects. Jasmonate inhibits the ethylene-promoted apical hook formation, while ethylene represses the jasmonate-induced wounding responses (Memelink 2009; Turner et al. 2002). Here, we will focus on the recent progresses in understanding those two facets of ethylene and jasmonate interactions.

Without jasmonate perception, bHLH transcription factor MYC2 is repressed by the direct interaction with a family of proteins, named JASMONATE ZIM-DOMAIN (JAZ) proteins (Chini et al. 2007; Thines et al. 2007). JAZ proteins associate with NOVEL INTERACTOR of JAZ (NINJA) adapter protein, which interacts with TOPLESS co-repressors to fulfill the repression on MYC2 (Pauwels et al. 2010). After jasmonate synthesis is induced by pathogen infection or wounding, the bioactive form of jasmonate facilitates the interaction between JAZs and an F-box protein CORONATINE INSENSITIVE1 (COI1), which assembles in SCF^{COI1} E3 ligase and directly targets JAZs degradation (Chini et al. 2007; Devoto et al. 2002; Katsir et al. 2008; Sheard et al. 2010; Thines et al. 2007; Xie et al. 1998; Xu et al. 2002). The degradation of JAZs relieves their repression on MYC2 or other JAZ-interacting transcription factors to activate jasmonate signaling.

As described before, *ERF1* is a direct target gene of EIN3/EIL1 and ERF1, then activates its target genes like *PDF1.2* (Solano et al. 1998). It is thus speculated that EIN3/EIL1 are integration nodes for the interdependent coaction of ethylene and jasmonate. Ethylene activates EIN3/EIL1 by stabilizing EIN3/EIL1 protein

abundance, while jasmonate activates EIN3/EIL1 in an unknown manner. Further experimental results show that JAZ proteins directly interact with EIN3/EIL1 and repress EIN3/EIL1 functions. It is also reported that JAZ proteins interact with HISTONE DEACETYLASE6 (HDA6) as a co-repressor to suppress EIN3/EIL1 functions through histone deacetylation, which suggest that there is an alternative mechanism for JAZ repression other than the NINJA-TOPLESS model. Jasmonate treatment weakens the interaction between HDA6 and EIN3/EIL1 due to the degradation of JAZs, suggesting that jasmonate activates EIN3/EIL1 through a derepression mechanism. In support of this conclusion, *hda6* mutants are hypersensitive to jasmonate treatment (Zhu et al. 2011). Taken together, EIN3/EIL1 integrate jasmonate and ethylene signaling synergy through different mechanisms. Jasmonate activates EIN3/EIL1 through promoting JAZ degradation to release their repression on EIN3/EIL1, while ethylene stabilizes EIN3/EIL1 via the repression on $SCF^{EBF1/2}$ (Fig. 8.1d) (An et al. 2010).

In addition to the synergistic and interdependent interactions, jasmonate antagonizes ethylene-induced hook formation. It is recently reported that jasmonate reduces *HLS1* expression even in the presence of ethylene. Further studies show that jasmonate-activated transcription factor MYC2 directly binds *EBF1* promoter and induces *EBF1* expression. The induction of *EBF1* then promotes EIN3/EIL1 turnover, which suppresses EIN3/EIL1 functions and their downstream *HLS1* expression to fulfill this inhibition effect (Zhang et al. 2014). Moreover, MYC2 physically interacts with EIN3/EIL1 and abrogates EIN3/EIL1 DNA binding ability, which provides another mechanistic illustration for jasmonate-ethylene antagonism (Fig. 8.1d) (Song et al. 2014; Zhang et al. 2014).

The antagonistic interaction between jasmonate and ethylene ensures that their biological effects can be fine-tuned. Because jasmonate- and ethylene-activated downstream defense genes are usually associated with cell death, how to shut down their signal transduction is equivalently important as how to turn it on. Ethylene-stabilized EIN3/EIL1 directly induces *EBF2* expression as a negative feedback regulation (Konishi and Yanagisawa 2008), while jasmonate activates MYC2 to suppress EIN3/EIL1 DNA binding ability and also induce *EBF1* to promote EIN3/EIL1 degradation.

8.4 Interaction with Gibberellins

Gibberellins are a type of growth-promoting hormones, which positively regulate seed germination, apical hook development, hypocotyl elongation, flowering time, and root elongation (Daviere and Achard 2013; Fu and Harberd 2003). It has been reported that ethylene coordinates with gibberellins at least in regulating apical hook development, root elongation, and flowering initiation.

Ethylene promotes apical hook development. However, blocking gibberellins biosynthesis by paclobutrazol (PAC) inhibits hook formation, while treatment with gibberellins induce hook formation (An et al. 2012). It suggests that adequate

gibberellins are required for ethylene function in the regulation of hook development. DELLA proteins are crucial GRAS (for GAI, RGA, SCARECROW) family transcriptional repressors in gibberellin signaling, which include REPRESSOR OF *ga1-3* (RGA), GA-INSENSITIVE (GAI), RGA-LIKE1 (RGL1), RGL2, and RGL3. In the absence of gibberellins, DELLA proteins directly interact with their downstream transcription factors and inhibit or modulate their transcriptional activity. In the presence of gibberellins, gibberellins bind with its receptor GA-INSENSITIVE DWARF1 (GID1) to promote GID1-DELLA interactions, which in turn facilitate the binding of an F-box protein SLEEPY1 (SLY1) to DELLA proteins and then cause DELLA proteins degradation to relieve repressions (Hauvermale et al. 2012; Sun 2008; Sun and Gubler 2004). Further genetic studies demonstrate that *della* mutant (with all five DELLA gene mutations) shows exaggerate hook, but *ein3 eil1* or *ein2* can fully suppress *della* hook phenotype (An et al. 2012). In addition to the phenotypic observations, *HLS1* mRNA expression is also examined under gibberellins treatment. Gibberellins induce *HLS1* expression in the wild type but not in *ein3 eil1*. These results imply that gibberellins positively regulate hook development through ethylene-activated EIN3/EIL1 pathway. Two members of DELLA proteins, GAI and RGA physically interact with EIN3/EIL1. Although there seems to be a lack of biochemical experiments to determine how DELLA-EIN3/EIL1 interactions affect EIN3/EIL1 functions, it is deduced that DELLAs inhibit EIN3/EIL1 transcriptional activities with the help of a reporter line, which carries EIN3-Binding Site driven glucuronidase (*EBS*::*GUS*) to specifically reflect EIN3/EIL1 functions. Ethylene stimulates *GUS* expression, as a consequence of the activation of EIN3/EIL1, but PAC treatment strongly represses *GUS* expression even in the presence of ethylene. PAC treatment is a commonly used experimental strategy for upregulating in vivo DELLA protein levels because blocking gibberellin synthesis inhibits DELLA degradation (Feng et al. 2008; Wang et al. 2009). In conclusion, DELLA proteins directly interact with EIN3/EIL1 and inhibit *HLS1* expression for repressing hook development. Gibberellin treatment leads to the degradation of DELLA and releases their repression of EIN3/EIL1, which activates *HLS1* expression and promotes hook formation.

Ethylene inhibits root elongation, which is largely dependent on auxin as discussed in Sect. 8.2. However, it is reported that gibberellin signaling is also involved in ethylene-induced root growth inhibition. DELLA mutants are less sensitive to ethylene in the aspect of root growth inhibition, while application of gibberellins suppresses ethylene's effect on the root growth inhibition (Achard et al. 2003). These results suggest that gibberellins antagonize ethylene in root growth. Previous report has shown that the degradation of DELLA is required for root elongation (Fu and Harberd 2003). Gibberellin-triggered nuclear GFP-RGA disappearance degradation is slower when ethylene is applied simultaneously, which suggests that ethylene inhibits DELLA degradation. Consistent with this ethylene treatment, GFP-RGA is more stable in the constitutive ethylene responsive mutant *ctr1* than in wild-type background (Achard et al. 2003). Taken together, it is concluded that ethylene modulates DELLA protein stabilities for the regulation of root elongation.

Gibberellins are positive regulators in flowering time control, but how ethylene regulates flowering initiation is not fully understood. It is shown that application of ethylene or activation of ethylene signaling (*ctr1* mutants or *ebf1 ebf2* mutants) delays flowering time (Achard et al. 2007). Consistent with this observation, the bioactive gibberellin contents in *ctr1* are much lower than in wild-type controls. Furthermore, DELLA mutants suppress *ctr1* late flowering phenotype, suggesting that DELLA proteins are downstream factors in the ethylene-regulated flowering time control. Experimental results show that lower bioactive gibberellin contents cause the accumulation of DELLA proteins in *ctr1*, which inhibits floral meristem identity genes like *LEAFY* (*LFY*) and *SUPRESSOR OF OVEREXPRESSION CONSTANS1* (*SOC1*) and causes late flowering (Achard et al. 2007; Blazquez and Weigel 2000).

The promotion of hypocotyl elongation is one of the most remarkable functions of gibberellin. It has been demonstrated that DELLA proteins interact with PIF3 and PIF4 to repress their DNA binding abilities. Gibberellin treatment induces DELLA degradation so as to activate PIF3 and PIF4 and then promotes cell elongation (de Lucas et al. 2008; Feng et al. 2008). Since ethylene promoted cell elongation in light is archived by EIN3-activated *PIF3* mRNA expression and EIN3 physically interacts with DELLA proteins (An et al. 2012; Zhong et al. 2012), it is plausible to further investigate if EIN3 affects PIF3 DNA binding ability by modulating DELLA-PIF3 interactions.

8.5 Concluding Remarks

In conclusion, interactions between ethylene and other plant growth signals exist, from the biosynthesis pathway to the signal transduction pathway. Notably, protein–protein interactions and protein–DNA associations are major connections for integrating different signal interactions. Although there are plenty of achievements in the field of ethylene, the current understanding is still just the tip of iceberg. With the improvement of single cell detection methods and next-generation sequencing techniques, it will be very intriguing to dissect signal interactions in different cell types and take advantage of systems biology approaches to generate signal networks to fully understand signal interactions not only at the static whole plant level, but also at the dynamic single cell level.

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