CellPress
PARTNER JOURNAL

Molecular Plant
Review Article

A Pivotal Role of DELLAs in Regulating Multiple Hormone Signals

Jean-Michel Davière* and Patrick Achard

Institut de Biologie Moléculaire des Plantes (IBMP), UPR2357, associé avec l'Université de Strasbourg, 12, rue Général Zimmer, 67084 Strasbourg Cedex, France

*Correspondence: Jean-Michel Davière (jean-michel.daviere@ibmp-cnrs.unistra.fr)

http://dx.doi.org/10.1016/j.molp.2015.09.011

ABSTRACT

Plant phenotypic plasticity is controlled by diverse hormone pathways, which integrate and convey information from multiple developmental and environmental signals. Moreover, in plants many processes such as growth, development, and defense are regulated in similar ways by multiple hormones. Among them, gibberellins (GAs) are phytohormones with pleiotropic actions, regulating various growth processes throughout the plant life cycle. Previous work has revealed extensive interplay between GAs and other hormones, but the molecular mechanism became apparent only recently. Molecular and physiological studies have demonstrated that DELLA proteins, considered as master negative regulators of GA signaling, integrate multiple hormone signaling pathways through physical interactions with transcription factors or regulatory proteins from different families. In this review, we summarize the latest progress in GA signaling and its direct crosstalk with the main phytohormone signaling, emphasizing the multifaceted role of DELLA proteins with key components of major hormone signaling pathways.

Keywords: gibberellins, DELLAs, hormone crosstalk, plant development, phenotypic plasticity

Davière J.-M. and Achard P. (2016). A Pivotal Role of DELLAs in Regulating Multiple Hormone Signals. Mol. Plant. **9**, 10–20.

INTRODUCTION

Under natural conditions, as sessile organisms, plants have evolved the ability to adjust their architecture and physiology, in response to developmental cues and environmental challenges, thus favoring plant survival and ensuring species durability (Casal et al., 2004). During their lifespan, the modulation of plant developmental plasticity relies on the constant perception of external inputs such as changes in light quality and quantity, temperature, moisture, nutrient access, herbivorous feeding, and disease pressure. This external information must be integrated together with the intrinsic genetic program to adjust growth.

Phytohormones are small endogenous signaling molecules, such as gibberellin (GA), auxin (IAA), cytokinin (CK), brassinosteroid (BR), abscisic acid (ABA), ethylene (ET), jasmonic acid (JA), salicylic acid (SA), and strigolactone (SL), which orchestrate a dual function. Indeed, plant hormones are mediators that not only govern and coordinate endogenous developmental processes, but also convey environmental stimuli to drive adaptive responses to abiotic and biotic stresses. Genetic and pharmacological studies have unraveled most of the molecular components of metabolism, signal perception, and transduction of individual hormone pathways, which are specific and act in a non-redundant manner. However, over recent years, with the awareness of remarkable hormone-overlapping functions (in developmental processes and adaptive responses), it is noteworthy that the final outcome of the individual hormone effects is established from hormonal pathways that are interconnected through a complex network of interactions and feedback regulations (Kuppusamy et al., 2009; Vanstraelen and Benková, 2012). Hormone signaling pathways are known to interact at the level of gene expression, and the mechanisms of hormone crosstalk can be diverse. Accordingly, hormonal interplay regulates synthesis, sensitivity, and transport of other hormones, which modulates their levels, responses, and distributions, respectively (Santner and Estelle, 2009). As a result, hormonal interconnections have been functionally characterized in terms of additivity, synergism (when the output is enhanced compared with the individual inputs), or antagonism (when the resulting output is attenuated) (Chandler, 2009), whereas co-regulation refers to the modulation of outcomes for a determined developmental process, mediated through independent pathways.

Among these hormones, GAs are tetracyclic diterpenoids that play a major role in diverse key developmental processes in plants, encompassing seed germination, stem elongation, leaf expansion, trichome development, pollen maturation, and the induction of flowering (Fleet and Sun, 2005; Pimenta-Lange and Lange, 2006). Since their first discovery, 136 GAs have been

Published by the Molecular Plant Shanghai Editorial Office in association with Cell Press, an imprint of Elsevier Inc., on behalf of CSPB and IPPE, SIBS, CAS.

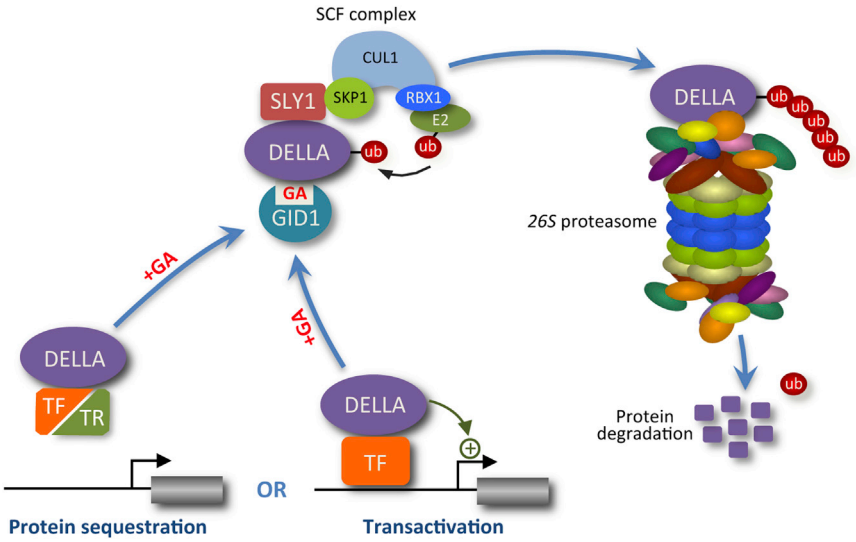

Figure 1. An Overview of the GA Signaling Pathway.
When GA concentrations are low, DELLAs repress GA responses by interacting with and inhibiting the activity of transcription factors (TF) or regulatory proteins (TR), or by activating the transcription of target genes associated with TF. When GA concentrations increase, GA binds to GID1 receptor, stimulating the interaction of DELLA with the SCF^{SLY1} complex. Once recruited to SCF^{SLY1} complex, DELLA is polyubiquitylated then subsequently degraded through the *26S* proteasome pathway, leading to the activation of GA responses.

identified in plants, fungi, and bacteria. Most of the GAs are precursors for the bioactive forms or deactivated metabolites, and only few (GA_1, GA_3, GA_4, and GA_7) have biological activity (Yamaguchi, 2008; Hedden and Thomas, 2012). During the past two decades, genetic studies and biochemical analyses of GA response mutants have gradually disclosed the molecular events that occur, from GA perception to the activation of transcriptional networks that regulate plant development (for review see Davière and Achard, 2013). These studies provided evidence of an undisputable individual function of GAs in different developmental processes, but have also demonstrated that GA activities overlap with all other hormones at different levels. In this review, we emphasize the recent findings, mainly obtained in *Arabidopsis*, on the direct crosstalk between GA and other hormone pathways. We focus on the key signaling component, the DELLA proteins, highlighting the molecular events that underlie their pivotal roles in major plant developmental processes and adaptive responses, in an integrated manner with other hormonal signaling pathways.

DELLA PROTEINS: REPRESSORS OF GA FUNCTIONS

Genetic screens both in *Arabidopsis* and rice have led to the identification of the key components of the GA perception and signaling pathway, extensively described in previous reviews (Gao et al., 2011; Sun, 2011; Wang and Deng, 2011; Hauvermale et al., 2012; Schwechheimer, 2012; Davière and Achard, 2013). The current model of GA action relies on the original observation that exogenous GA treatments were associated with DELLA protein destabilization to rescue dwarfism of a GA-deficient mutant (Silverstone et al., 2001). While DELLA proteins act as plant growth repressors, GAs trigger DELLA degradation and promote growth (Figure 1; Davière and Achard, 2013). *DELLA* genes are defined as repressors of GA signaling, due to the dwarfism observed in the gain-of-function mutants, whereas a slender or tall phenotype characterizes the loss-of-function mutants (Peng et al., 1997; Silverstone et al., 1998; Ikeda et al., 2001; Chandler et al., 2002; Cheng et al., 2004).

DELLA proteins are located in the nuclei, and represent a subset of the plant-specific GRAS family of transcription regulators (Bolle, 2004). Common to the GRAS proteins, DELLAs present a conserved C-terminal GRAS functional domain that is involved in protein–protein interaction and transcriptional regulation, and is characterized by two leucine heptad repeats (LHRI and LHRII) and three conserved motifs, VHIID, PFYRE, and SAW (Figure 2). In contrast to other GRAS proteins, DELLAs have a novel regulatory N terminus containing two conserved domains: the DELLA domain (with conserved amino acid sequence Asp-Glu-Leu-Leu-Ala, origin of the name DELLA) and the TVHYNP domain. Mutations in the DELLA or TVHYNP domains interfere with the ability of the protein to bind with the GA receptor GIBBERELLIN INSENSISTIVE 1 (GID1), which thereby stabilizes the DELLA repressor, resulting in a semi-dominant GA-insensitive dwarf phenotype (Ueguchi-Tanaka et al., 2005, 2007; Griffiths et al., 2006; Willige et al., 2007).

Several plant species harbor a single highly conserved *DELLA* gene, such as *PROCERA* in tomato (Martí et al., 2007), *VvGAI1* in grapevine (Zhong and Yang, 2012), and among cereals, *SLENDER RICE1* (*SLR1*) in rice (Ikeda et al., 2001), *SLENDER1* (*SLN1*) in barley (Chandler et al., 2002), *REDUCED HEIGHT-1* (*RHT-1*) in wheat (Peng et al., 1999), and *DWARF8* (*D8*) and *DWARF9* (*D9*) in maize (Winkler and Freeling, 1994; Lawit et al., 2010), while in *Arabidopsis* the *DELLA* gene has undergone amplification. Thus, the *Arabidopsis* genome encodes five DELLAs: GA-INSENSITIVE (GAI), REPRESSOR OF ga1-3 (RGA), RGA-LIKE1 (RGL1), RGL2, and RGL3 (Peng et al., 1997; Silverstone et al., 2001; Lee et al., 2002; Wen and Chang, 2002; Wild et al., 2012). Distinct but also overlapping functions of these DELLAs have been reported in repressing GA responses. Hence, RGA and GAI control cell expansion and cell division in hypocotyl, shoot and root, and floral induction (Dill and Sun, 2001; King et al., 2001; Feng et al., 2008; de Lucas et al., 2008; Davière et al., 2014), RGL2 is the major inhibitor of seed germination (Lee et al., 2002; Cao et al., 2005), RGA, RGL1, and RGL2 together modulate floral development (Cheng et al., 2004; Tyler et al., 2004), and RGL3 contributes to plant fitness during environmental stress (Achard et al., 2008; Wild et al., 2012). However, the relevant distinct DELLA functions might rely mainly on promoter-specific regulation and, therefore, tissue-specific gene expression, as suggested by promoter-swap experiments (Gallego-Bartolomé et al., 2010).

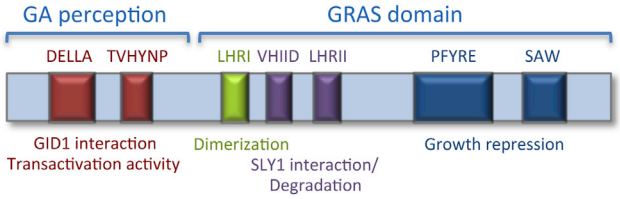

Figure 2. Domain Structure of a DELLA Protein.
Important motifs and associated functions are indicated with the same color code.

An important function of DELLAs relies on their ability to establish protein–protein interaction with diverse classes of regulatory proteins (Davière and Achard, 2013; Locascio et al., 2013). Through these interactions, DELLAs respectively inhibit the DNA-binding capacity of transcription factors (TF) or the activity of transcriptional regulators (TR) (Figure 1). Meanwhile, GAs relieve the repression of the DELLAs by promoting their degradation via the ubiquitin-proteasome pathway (McGinnis et al., 2003; Sasaki et al., 2003; Dill et al., 2004; Fu et al., 2004). Through the interactions with an ever-growing list of TF/TR from different families (Davière and Achard, 2013; Locascio et al., 2013), GA signaling controls the expression of a multitude of target genes functioning in distinct pathways. By doing so, DELLA proteins represent a central integrator of GA-dependent processes in a context-dependent manner.

An alternative mechanism of action arose from transcriptome analyses used to identify DELLA target genes, in transgenic plants expressing gain-of-function versions of DELLA (Zentella et al., 2007; Gallego-Bartolomé et al., 2011a, 2011b). Results from these studies suggested that DELLAs activate the transcription of target genes, despite there being no evidence for direct binding of DELLAs to DNA (Figure 1). Further work, using yeast one-hybrid experiments and transient expression assays in rice callus, has demonstrated that the N-terminal DELLA/TVHYNP domain of the rice DELLA, SLR1, possesses transactivation activity (Figure 2; Hirano et al., 2012). Moreover, it is only recently that DELLAs have been shown to associate with the promoter of target genes through the interaction with at least two families of TFs, INDETERMINATE DOMAIN (IDD) and type-B ARABIDOPSIS RESPONSE REGULATOR (ARR) factors (Yoshida et al., 2014; Marín-de la Rosa et al., 2015). These TFs serve as intermediate proteins between DELLA and DNA, which confers the ability of DELLAs to enhance the expression of target genes. On the other hand, DELLAs interact with the core subunit of the chromatin-remodeling factor SWI/SNF to increase the transcription of DELLA target genes (Sarnowska et al., 2013), which in turn modulates the GA responses and hormonal crosstalk in *Arabidopsis*.

DIRECT INTERACTIONS OF DELLAs WITH CORE COMPONENTS OF MULTIPLE HORMONE SIGNALING CASCADES

DELLA/ABI3/ABI5 Complexes Involved in Seed Germination

The decision for a seed to germinate is determined by the environment (light quality, temperature, and moisture) and by the internal growth regulators GA and ABA, which exert an antagonistic effect. While ABA is involved in the establishment and maintenance of seed dormancy, GAs promote the induction of germination (Koornneef et al., 2002). In the dry mature seed, ABA levels are high, which in turn activate downstream signaling components including the TFs ABSCISIC ACID INSENSITIVE 3 (ABI3) and ABI5, two key negative regulators of seed germination (Piskurewicz et al., 2008). By contrast, under favorable conditions ABA levels drop and GA synthesis begins, promoting seed germination by enhancing the degradation of RGL2 (Lee et al., 2002; Piskurewicz et al., 2008). Previous studies suggested that RGL2 represses seed germination through the induction of *XERICO*, a gene encoding a RING-H2 zinc factor promoting ABA synthesis (Ko et al., 2006; Zentella et al., 2007; Piskurewicz et al., 2008). More recently, the interaction of DELLA proteins with ABI3 and ABI5 led to the discovery of the regulatory mechanism (Figure 3A; Lim et al., 2013). DELLA, ABI3, and ABI5 form a protein complex that binds the promoter and activates the transcription of target genes, such as *SOMNUS* (*SOM*), a C3H-type zinc finger that negatively regulates seed germination (Kim et al., 2008; Park et al., 2011; Lim et al., 2013). According to the current model, unfavorable conditions (e.g. high temperature, darkness) both increase ABA levels and decrease GA levels, which thereby enhance the accumulation of DELLA/ABI3/ABI5 complexes on *SOM* promoter and activate its transcription (Oh et al., 2006; Lim et al., 2013). Interestingly, because SOM also activates ABA biosynthesis and represses GA biosynthesis (Kim et al., 2008), SOM might form a positive feedback loop to strongly inhibit seed germination under unfavorable conditions (Lim et al., 2013).

DELLA/BZR1/ARF6/PIF4 Interactions Control Light- and Temperature-Mediated Seedling Development

Seedling hypocotyl growth relies on coordinated regulation of cell elongation by many hormonal and environmental signals, including BR, auxin, GA, light, and temperature. Although these signals have synergistic effects on growth, the molecular mechanism ensuring coordinated cellular responses remained unknown until recently. BRs are steroid hormones that play a key role in light and temperature regulation of seedling growth, as exemplified by BR biosynthetic and signaling mutants exhibiting de-etiolated phenotypes (inhibition of hypocotyl elongation and opening of the cotyledons) in the dark (Li et al., 1996). Upon binding to BR, BRASSINOSTEROID INSENSITIVE1 (BRI1) receptor kinase is activated and initiates a downstream signaling cascade, which leads to the dephosphorylation and the nuclear localization of BRI1-EMS-SUPPRESSOR1/BRASSINAZOLE-RESISTANT2 (BES1/BZR2) and BZR1 TFs (Li and Chory, 1997; Vert et al., 2005; Wang et al., 2012). Thus, in the presence of BRs, BES1 and BZR1 move into the nucleus and regulate the expression of target genes, including the PACLOBUTRAZOL-RESISTANT (PRE) family of helix-loop-helix factors implicated in cell elongation (Lee et al., 2006; Bai et al., 2012a, 2012b). Moreover, genetic studies indicate that BZR1 may interact with PHYTOCHROME-INTERACTING FACTOR4 (PIF4), a light-/temperature-regulated TF controlling the expression of cell wall- and auxin-related genes (Huq and Quail, 2002; Koini et al., 2009), thus ensuring coordinate growth by BRs and environmental signals (Oh et al., 2012).

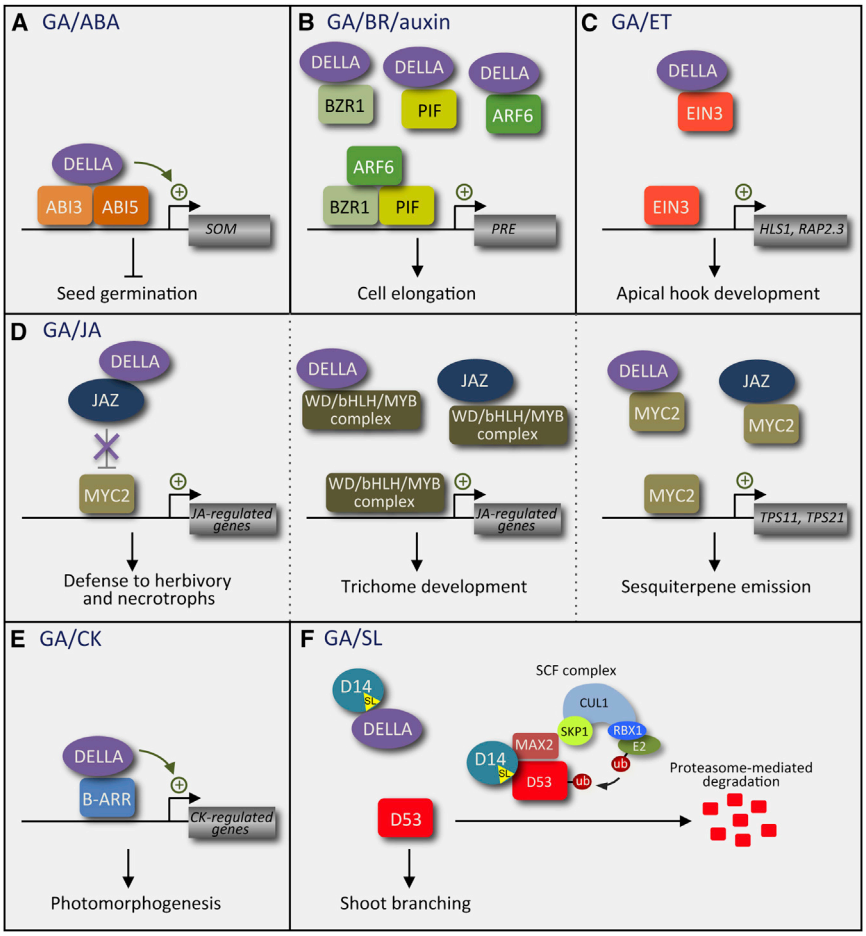

Figure 3. A Pivotal Role of DELLAs in Regulating Multiple Hormone Signals.

(A) DELLA, ABI3, and ABI5 proteins mediate GA and ABA signaling to activate *SOM* expression, a key repressor of seed germination.

(B) BZR1, ARF6, and PIF4 form a functional complex to regulate a large number of genes contributing to hypocotyl cell elongation, such as *PRE*. DELLA interacts with BZR1, ARF6, and PIF4 to inhibit their DNA-binding ability, thereby modulating GA, BR, and light/temperature signaling.

(C) DELLA interacts with EIN3 and inhibits its function. GAs enhance ET-mediated apical hook formation by inducing the expression of *HLS1* and *RAP2.3*, via derepression of EIN3 function.

(D) On the left, DELLA positively regulates JA-mediated resistance to herbivory and necrotrophic pathogens by sequestering JAZ into inactive complexes, unable to inhibit MYC2 transcriptional activity. In the middle, both DELLA and JAZ interact with and inhibit WD-repeat/bHLH/MYB complex to inactivate downstream genes and repress trichome development. On the right, DELLA inhibits sesquiterpene synthase gene expression, including *TPS11* and *TSP22*, in *Arabidopsis* inflorescences, through interaction with the DNA-binding domain of MYC2.

(E) DELLA enhances the transactivation ability of type-B ARR TF onto CK-regulated genes, thereby mediating GA- and CK-dependent regulation of photomorphogenesis.

(F) SL inhibit axillary bud outgrowth by stimulating D14 receptor–SCF^{MAX2}-dependent degradation of D53 repressor by the *26S* proteasome. DELLA–D14 interaction restrains SL-induced signal transduction by D14.

Auxin, another important plant growth hormone, promotes hypocotyl cell elongation in a context-dependent manner (Stewart and Nemhauser, 2010; Del Bianco and Kepinski, 2011). Auxin signaling induces ubiquitylation and proteasome-mediated degradation of AUX/IAA family proteins to release their inhibition on the auxin response factors (ARFs), TFs that directly activate or repress the expression of auxin response genes (Chapman and Estelle, 2009). Indirect cross-regulation between auxin and BR has been shown at several levels, but the large number of common target genes shared by ARF6, BZR1, and PIF4 raised the possibility of direct interactions among these TFs (Oh et al., 2014). Indeed, ARF6, BZR1, and PIF4 interact with each other and interdependently activate a common set of target genes involved in cell expansion (Oh et al., 2014). Strikingly, DELLAs also interact with ARF6, BZR1, and PIF4 and inhibit their transcriptional activity (Figure 3B; de Lucas et al., 2008; Feng et al., 2008; Bai et al., 2012a, 2012b; Gallego-Bartolomé et al., 2012; Li et al., 2012; Oh et al., 2014). Accordingly, *della* loss-of-function mutants are hyper-responsive to BR treatments, whereas the gain-of-function *gai* mutant responds weakly to exogenous BR (Lilley et al., 2013). On the other hand, auxin promotion of hypocotyl elongation is abolished in *gai* mutant or in paclobutrazol-treated seedlings (PAC, an inhibitor of GA biosynthesis), but not in PAC-treated *della* mutants, indicating that DELLA accumulation inhibits both BR and auxin sensitivity (Lilley et al., 2013; Oh et al., 2014). Thus, these results are in agreement with the model that GA-induced degradation of DELLAs allows ARF6/BZR1/PIF4 complex to bind to promoters of target genes and activate hypocotyl cell elongation (Figure 3B).

An additional layer of regulation involves PICKLE/ENHANCED PHOTOMORPHOGENIC1 (PKL/EPP1), a chromatin-remodeling factor involved in the repression of the trimethylation of histone H3 Lys-27 (H3K27me3) on target promoters (Ogas et al., 1999). PKL/EPP1 directly interacts with PIF3 and BZR1 (individually and in complex) to promote hypocotyl growth by repressing the H3K27me3 modifications on cell elongation-related promoter genes (Zhang et al., 2014). Interestingly, DELLAs physically interact with PKL/EPP1 and negatively regulate its activity, offering an additional level of control in restraining cell elongation (Zhang et al., 2014).

Altogether, these results demonstrate that GAs release DELLA-mediated inhibition of BZR1 and ARF6, and that DELLA-BZR1-ARF6-PIF-PKL interaction defines a core transcription module that mediates coordinated growth regulation by integrating GA, BR, auxin, and light/temperature environmental stimuli. DELLA control of BZR1-ARF-PIF transcription module is unlikely to be limited to the regulation of hypocotyl length, as GAs and BRs, for example, also control root growth, even though they act in different tissues: GAs in the endodermis and BRs in the epidermis (Ubeda-Tomás et al., 2008; Hacham et al., 2011).

DELLA/EIN3 Interaction Regulates Seedling Apical Hook Development in the Dark

When dicotyledonous seedlings face germination in darkness, the upper part of the hypocotyl forms a transient developmental structure known as the apical hook, thought to protect the shoot apical meristem (SAM) from damage during growth through the soil. This curvature is caused by asymmetric growth of the inner and outer sides of the hypocotyl, due to differential cell expansion and division rates (Raz and Ecker, 1999). This process is coordinated by several plant hormones, including ET and GAs, which modulate auxin distribution across the curvature (Achard et al., 2003; Vandenbussche et al., 2010; Zádníková et al., 2010; Gallego-Bartolomé et al., 2011a, 2011b). ET activates a downstream signaling cascade by stimulating the accumulation of ETHYLENE INSENSITIVE3 (EIN3) and EIN3-like (EIL), a family of TFs that activate ET responses (Chao et al., 1997; Potuschak et al., 2003; Guo and Ecker, 2003). Accordingly, exogenous treatment with ET or its precursor 1-aminocyclopropane-1-carboxylic acid leads to the development of exaggerated apical hook, while *ein3* mutants exhibit reduced curvature of etiolated seedlings (Chao et al., 1997). GAs also perform a prominent role for the establishment and maintenance of the apical hook, in particular in preventing premature apical hook opening in darkness (Achard et al., 2003; Vriezen et al., 2003; Gallego-Bartolomé et al., 2011a, 2011b). In this scenario, *della* loss-of-function mutant seedlings develop a hook with exaggerated curvature, whereas seedlings proceed directly to the opening phase when DELLA proteins accumulate (Achard et al., 2003). Recently, two reports have revealed the molecular mechanism by which ET and GAs coordinately regulate apical hook development (An et al., 2012; Marín-de la Rosa et al., 2014). Whereas EIN3/EILs proteins bind the promoter and activate the expression of *HOOKLESS1* (*HLS1*; an *N*-acetyltransferase) and *RELATED TO APETALA2.3* (*RAPT2.3*; a TF belonging to the group VII ETHYLENE RESPONSE FACTOR), both essential for hook formation (Lehman et al., 1996; Marín-de la Rosa et al., 2014), DELLAs counteract the effect of ET by inhibiting the activity of EIN3/EILs through physical interaction (Figure 3C; An et al., 2012). Since GAs and ET regulate a number of similar growth processes throughout plant development, it is tempting to speculate that DELLA–EIN3 interaction plays a part in the coordinated action of the two hormones.

DELLA Interaction with JAZ and MYC2 Fine-Tunes Plant Defense over Growth

In response to multiple developmental signals and environmental challenges, plants constantly fine-tune their transcriptional programming to optimize the tradeoff between growth and defense, in a dynamic process, which involves various plant hormones. Among these, JAs are a class of lipid-derived small molecules that regulate multiple plant growth responses, including the defense against pathogens and insects, and the adaptation to abiotic stresses such as wounding and drought. JAs are also involved in developmental processes such as root growth and stamen development (Wasternack and Hause, 2013). Upon elicitation by exogenous or endogenous signals, bioactive jasmonyl-L-isoleucine (JA-Ile) is synthesized by JASMONATE RESISTANT1 (JAR1; Fonseca et al., 2009) and sensed by CORONATINE INSENSITIVE1-JASMONATE ZIM DOMAIN (COI1-JAZ) receptor complexes (Xie et al., 1998; Chini et al., 2007; Thines et al., 2007), and this leads to the degradation of JAZ proteins acting as repressors of TFs such as MYC2, a pivotal transcriptional activator that regulates JA responses (Lorenzo et al., 2004). Recent findings have emphasized a role of GAs in compromising JA-mediated stress and defense mechanisms. For example, flagellin, a microbe-associated molecular pattern, enhances the stability of DELLAs, resulting in a growth arrest associated with increased JA-dependent defenses and elevated resistance against necrotrophic pathogens (Navarro et al., 2008). Accordingly, *della* loss-of-function mutants are partially insensitive to gene induction by JA, whereas the constitutively active dominant *della* mutant *gai* is hypersensitive for JA-responsive gene induction, implicating DELLAs in JA signaling (Navarro et al., 2008). Moreover, DELLAs have been reported to interact with JAZs, thereby competing with their cognate MYC2 TF and thus modulating JA responses (Figure 3D; Chini et al., 2007; Hou et al., 2010, 2013; Fernández-Calvo et al., 2011; Wild et al., 2012). These results provide a mechanistic understanding on how JA signaling could be fine-tuned by other signaling pathways through the DELLAs.

To survive in nature, effective plant defense against biotic and abiotic stresses has a cost and is often concomitant with a significant growth inhibition. For example, wound-induced endogenous JA synthesis, mimicking herbivory, stunts plant growth while also activating plant immunity (Zhang and Turner, 2008). A recent report proposed that JA prioritizes defense over growth by interfering with GA signaling (Yang et al., 2012). In this work, the authors demonstrated that DELLA–JAZ interaction releases PIF TFs to enhance cell elongation. Consistent with this, the growth of *della* loss-of-function mutants is partially insensitive to JAs (Hou et al., 2010; Yang et al., 2012). Moreover, a *pif* quadruple mutant is no longer able to respond to JA-mediated inhibition of hypocotyl growth, whereas overexpression of *PIF3* substantially overcomes JA-induced growth inhibition (Yang et al., 2012). These findings unravel the pivotal function of the core DELLA/JAZ/PIF complex in modulating plant defense over growth when facing environmental stresses and pathogen attacks. It is noteworthy that this crosstalk may be impaired when plants suffer from light-restrictive conditions (low-red/far-red ratios). In this situation, the tradeoff defense growth is unbalanced due to a rapid turnover of DELLA proteins and differential regulation of JAZ and MYC2 protein stability, leading to a repression of the JA responses (Djakovic-Petrovic et al., 2007; de Wit et al., 2013; Chico et al., 2014; Leone et al., 2014).

In contrast to their antagonistic roles in modulating growth and defense, recent works revealed that GA and JA signaling also synergistically regulate plant development. First, both DELLA and JAZ proteins directly interact with major components of the WD-repeat/bHLH/MYB complex to modulate trichome development (Figure 3D; Qi et al., 2014). Second, GAs and JAs synergistically promote stamen filament growth and fertility by activating the expression of the R2R3-MYB TFs *MYB21*, *MYB24*, and *MYB57*, involved in anther and stamen development (Cheng et al., 2009). In this context, GA signaling upregulates the expression of *DEFECTIVE ANTHER DEHISCENCE1* (*DAD1*) and *LIPOXYGENASE1* (*LOX1*) (two key JA biosynthesis genes) to promote JA production, which in turn releases the repressive activity of JAZs onto MYB TFs (Cheng et al., 2009; Song et al.,

2011). The latter situation, illustrating an integrative role of GAs and JAs, refers to the regulation of the production of floral volatile terpenes. GAs and JAs jointly activate the expression of two sesquiterpene synthase genes (*TPS21* and *TPS11*) in a MYC2-dependent manner (Figure 3D; Hong et al., 2012). By interacting with DELLA and JAZ proteins, MYC2 integrates both GA and JA signals into the induction of sesquiterpene production in flowers. Noteworthy, because DELLA and JAZ proteins also interact with each other (Hou et al., 2010), it is likely that these competitive interactions between DELLA, JAZ, and MYC2 result in dynamic and localized expression of target genes involved in various processes.

DELLA/Type-B ARR Complexes Activate CK-Regulated Gene Expression

GAs and CKs are known to exert antagonistic regulation of multiple developmental processes (Weiss and Ori, 2007). In agreement with this line of reasoning, SAM activity is enhanced by CKs and restricted by GAs (Sakamoto et al., 2001; Jasinski et al., 2005; Yanai et al., 2005). Moreover, studies have shown that KNOTTED1-like homeobox KNOX1 proteins orchestrate, in part, the balance between CKs and GAs in the SAM by inducing CK synthesis, and directly inhibiting GA production, or indirectly promoting GA deactivation (Sakamoto et al., 2001; Hay et al., 2002; Jasinski et al., 2005; Yanai et al., 2005). Whereas SAM activities require high CK and low GA signals, later stages of cell maturation and elongation (away from SAM) imply the opposite: low CK and high GA signals (Weiss and Ori, 2007). Similarly, root growth and hypocotyl elongation of etiolated seedlings are promoted by GAs and repressed by CKs, respectively (Chory et al., 1994; Alabadí et al., 2004; Argyros et al., 2008; Achard et al., 2009; Ubeda-Tomás et al., 2009).

Until now, all data have shown a development-dependent reciprocal negative interaction between CKs and GAs, suggesting a transcriptional crosstalk, mainly affecting the availability of both hormones in a particular plant tissue and developing stage of the plant (Greenboim-Wainberg et al., 2005; Jasinski et al., 2005; Weiss and Ori, 2007). Nevertheless, more recent work has underpinned relevant regulation of root meristem maintenance and photomorphogenesis that requires both DELLA proteins and type-B ARABIDOPSIS RESPONSE REGULATORS (ARRs), the DNA-binding TFs that mediate CK signaling (Moubayidin et al., 2010; Marín-de la Rosa et al., 2015). This study has unraveled a physical interaction between DELLAs and type-B ARRs, in which ARR1 mediates the presence of DELLA proteins at target promoters and DELLAs, in turn, enhance the transcription ability of ARR1 (Figure 3E; Marín-de la Rosa et al., 2015). Thereby, DELLA/ARR heterodimers represent a novel co-regulatory module at the interface of GA and CK signals, which transcriptionally activates target genes similarly to the DELLA/IDD complex previously described (Yoshida et al., 2014).

DELLA/D14 Interaction Controls Axillary Bud Outgrowth

Shoot branching is a major determinant of plant architecture and crop yield, which is under integrated control of multiple hormones and environmental signals (Domagalska and Leyser, 2011; Ruyter-Spira et al., 2011; Rameau et al., 2015). Among the phytohormones, SLs are terpenoid lactones that have recently been identified to inhibit axillary bud outgrowth (Gomez-Roldan et al., 2008; Umehara et al., 2008). Studies with branching mutants insensitive to SLs have determined the key components in the SL signaling pathway: the putative SL receptor DWARF14 (D14), the F-box protein DWARF3/MAX2/RMS4, and the TF DWARF53 (D53). According to the model, SL binding by D14 promotes polyubiquitylation of D53 by the D14-$SCF^{D3/MAX2/RMS4}$ ubiquitin ligase complex, and subsequent degradation by the proteasome pathway, leading to the activation of SL responses (Figure 3F; Stirnberg et al., 2007; Arite et al., 2009; Nakamura et al., 2013; Jiang et al., 2013; Zhou et al., 2013). For a long time, GAs have been identified to also control shoot branching, as exemplified by GA-deficient mutants, which all exhibit higher shoot branching than wild-type (Murfet and Reid, 1993; Silverstone et al., 1997; Agharkar et al., 2007; Lo et al., 2008). Conversely, *della* mutants display reduced shoot branching and/or altered branching patterns (Cheng et al., 2004). Although genetic studies in pea suggest that GAs act independently of SLs to repress axillary bud outgrowth (de Saint Germain et al., 2013), a recent study reported that the rice DELLA SLR1 was able to interact with D14 in an SL-dependent manner and to modulate downstream SL signaling (Figure 3F; Nakamura et al., 2013). Further investigations will be crucial to provide clearer insights into GA and SL signaling interplay.

Another point of integration might occur at the level of the class II TEOSINTE BRANCHED1, CYCLOIDEA, and PCF (TCP) TFs. *TEOSINTE BRANCHED1* (*TB1*) from maize, the orthologs *OsTB1* from rice, and *BRANCHED1* (*BRC1*/*TCP18*) from *Arabidopsis* play a central role in the control of axillary bud development (Doebley et al., 1997; Takeda et al., 2003; Aguilar-Martínez et al., 2007; Braun et al., 2012). *TB1*/*BRC1* are expressed in axillary meristems, and their mutations cause enhanced shoot branching (Doebley et al., 1997; Aguilar-Martínez et al., 2007). These TCPs represent a point convergence of both CK and SL signals to control bud outgrowth (Ferguson and Beveridge, 2009), and might also be under GA regulation. Indeed, recent work has shown that DELLAs interact with several members of the class I TCP proteins, regulating cell proliferation at the embryonic root tip and shoot apex, and hence controlling seed germination and plant height, respectively (Davière et al., 2014; Resentini et al., 2015). Further analysis should investigate a possible interaction between DELLA and TB1/BRC1 and its contribution on the GA and SL interplay in controlling axillary bud outgrowth.

CONCLUSIONS

The rapidly expanding information on the mechanisms of DELLA actions is providing novel insights into how DELLAs may function as a central hub, integrating signals from multiple hormone pathways and environmental cues (Achard et al., 2006). Studies reviewed here have reported direct connections between DELLAs and key components of almost all hormone pathways. For example, DELLA interaction with ARF6/BZR1/PIF4 TFs defines a central growth regulation circuit that integrates GA, auxin, BR, and light/temperature signaling in a simple network controlling the expression of hundreds of genes regulating hypocotyl cell elongation (Oh et al., 2014). Moreover, these interconnections, acting spatially and temporally, allow

fine-tuning of the tradeoff growth/defense and, thus, phenotypic plasticity, as illustrated by the role of DELLA–JAZ interactions. Under favorable growth conditions, GAs trigger the degradation of DELLAs, which allows the accumulation of free PIF and TCP TFs controlling growth (Yang et al., 2012; Hou et al., 2013; Davière et al., 2014), but also liberates excess of JAZs to inhibit JA/MYC2- and ET/EIN3-mediated defense responses (Hou et al., 2010; Zhu et al., 2011; Wild et al., 2012). On the contrary, stress-induced production of JA stimulates JAZ degradation, which in turn promotes defense and releases DELLAs to inhibit GA-mediated growth responses, allowing land plants to adapt their life cycle to the continuously fluctuating environment (Yang et al., 2012; Hou et al., 2013).

It is noteworthy that many other indirect interconnections (not reviewed here) have been reported between GAs and other hormone pathways, in processes that involve intertwined feedback loops, connecting either hormone biosynthesis, distribution, or signaling. For example, GA activities modulate auxin distribution by stabilizing the PIN FORMED (PIN) auxin efflux facilitators along the lower side of gravistimulated roots (Willige et al., 2011; Löfke et al., 2013). Furthermore, for many other developmental processes, notably axillary bud outgrowth and shade-avoidance responses, the knowledge of molecular mechanisms that integrate environmental signals and endogenous cues is still fragmented. Further elucidation of molecular interactions among known key players and identification of novel components in phytohormone networks will extend our understanding of the molecular mechanisms underlying the coordinate growth of the different plant organs, which certainly is an important challenge for the future.

FUNDING

This work was supported by the Centre National de la Recherche Scientifique, the French Ministry of Research and Higher Education, and Initiative d'Excellence (IDEX) grant from the University of Strasbourg.

ACKNOWLEDGMENTS

We apologize to colleagues whose work or original publications could not be included owing to space constraints. No conflict of interest declared.

Received: July 21, 2015
Revised: September 17, 2015
Accepted: September 21, 2015
Published: September 25, 2015

REFERENCES

Achard, P., Vriezen, W.H., Van Der Straeten, D., and Harberd, N.P. (2003). Ethylene regulates *Arabidopsis* development via the modulation of DELLA protein growth repressor function. Plant Cell **15**:2816–2825.

Achard, P., Cheng, H., De Grauwe, L., Decat, J., Schoutteten, H., Moritz, T., Van Der Straeten, D., Peng, J., and Harberd, N.P. (2006). Integration of plant responses to environmentally activated phytohormonal signals. Science **311**:91–94.

Achard, P., Renou, J.P., Berthomé, R., Harberd, N.P., and Genschik, P. (2008). Plant DELLAs restrain growth and promote survival of adversity by reducing the levels of reactive oxygen species. Curr. Biol. **18**:656–660.

Achard, P., Gusti, A., Cheminant, S., Alioua, M., Dhondt, S., Coppens, F., Beemster, G.T., and Genschik, P. (2009). Gibberellin signaling controls cell proliferation rate in *Arabidopsis*. Curr. Biol. **19**:1188–1193.

Agharkar, M., Lomba, P., Altpeter, F., Zhang, H., Kenworthy, K., and Lange, T. (2007). Stable expression of AtGA2ox1 in a low-input turfgrass (*Paspalum notatum* Flugge) reduces bioactive gibberellin levels and improves turf quality under field conditions. Plant Biotechnol. J **5**:791–801.

Aguilar-Martínez, J.A., Poza-Carrión, C., and Cubas, P. (2007). *Arabidopsis* BRANCHED1 acts as an integrator of branching signals within axillary buds. Plant Cell **19**:458–472.

Alabadí, D., Gil, J., Blázquez, M.A., and García-Martínez, J.L. (2004). Gibberellins repress photomorphogenesis in darkness. Plant Physiol. **134**:1050–1057.

An, F., Zhang, X., Zhu, Z., Ji, Y., He, W., Jiang, Z., Li, M., and Guo, H. (2012). Coordinated regulation of apical hook development by gibberellins and ethylene in etiolated *Arabidopsis* seedlings. Cell Res. **22**:915–927.

Argyros, R.D., Mathews, D.E., Chiang, Y.H., Palmer, C.M., Thibault, D.M., Etheridge, N., Argyros, D.A., Mason, M.G., Kieber, J.J., and Schaller, G.E. (2008). Type B response regulators of *Arabidopsis* play key roles in cytokinin signaling and plant development. Plant Cell **20**:2102–2116.

Arite, T., Umehara, M., Ishikawa, S., Hanada, A., Maekawa, M., Yamaguchi, S., and Kyozuka, J. (2009). d14, a strigolactone-insensitive mutant of rice, shows an accelerated outgrowth of tillers. Plant Cell Physiol **50**:1416–1424.

Bai, M.Y., Shang, J.X., Oh, E., Fan, M., Bai, Y., Zentella, R., Sun, T.P., and Wang, Z.Y. (2012a). Brassinosteroid, gibberellin and phytochrome impinge on a common transcription module in *Arabidopsis*. Nat. Cell Biol. **14**:810–817.

Bai, M.Y., Fan, M., Oh, E., and Wang, Z.Y. (2012b). A triple helix-loop-helix/basic helix-loop-helix cascade controls cell elongation downstream of multiple hormonal and environmental signaling pathways in *Arabidopsis*. Plant Cell **24**:4917–4929.

Bolle, C. (2004). The role of GRAS proteins in plant signal transduction and development. Planta **218**:683–692.

Braun, N., de Saint Germain, A., Pillot, J.P., Boutet-Mercey, S., Dalmais, M., Antoniadi, I., Li, X., Maia-Grondard, A., Le Signor, C., Bouteiller, N., et al. (2012). The pea TCP transcription factor PsBRC1 acts downstream of strigolactones to control shoot branching. Plant Physiol. **158**:225–238.

Casal, J.J., Fankhauser, C., Coupland, G., and Blázquez, M.A. (2004). Signalling for developmental plasticity. Trends Plant Sci. **9**:309–314.

Cao, D., Hussain, A., Cheng, H., and Peng, J. (2005). Loss of function of four DELLA genes leads to light- and gibberellin-independent seed germination in *Arabidopsis*. Planta **223**:105–113.

Chandler, J.W. (2009). Auxin as compère in plant hormone crosstalk. Planta **231**:1–12.

Chandler, P.M., Marion-Poll, A., Ellis, M., and Gubler, F. (2002). Mutants at the Slender1 locus of barley cv Himalaya. Molecular and physiological characterization. Plant Physiol. **129**:181–190.

Chao, Q., Rothenberg, M., Solano, R., Roman, G., Terzaghi, W., and Ecker, J.R. (1997). Activation of the ethylene gas response pathway in *Arabidopsis* by the nuclear protein ETHYLENE-INSENSITIVE3 and related proteins. Cell **89**:1133–1144.

Chapman, E.J., and Estelle, M. (2009). Mechanism of auxin-regulated gene expression in plants. Annu. Rev. Genet. **43**:265–285.

Cheng, H., Qin, L., Lee, S., Fu, X., Richards, D.E., Cao, D., Luo, D., Harberd, N.P., and Peng, J. (2004). Gibberellin regulates *Arabidopsis* floral development via suppression of DELLA protein function. Development **131**:1055–1164.

Cheng, H., Song, S., Xiao, L., Soo, H.M., Cheng, Z., Xie, D., and Peng, J. (2009). Gibberellin acts through jasmonate to control the expression

of MYB21, MYB24, and MYB57 to promote stamen filament growth in *Arabidopsis*. PLoS Genet. **5**:e1000440.

Chico, J.M., Fernández-Barbero, G., Chini, A., Fernández-Calvo, P., Díez-Díaz, M., and Solano, R. (2014). Repression of jasmonate-dependent defenses by shade involves differential regulation of protein stability of MYC transcription factors and their JAZ repressors in *Arabidopsis*. Plant Cell **26**:1967–1980.

Chini, A., Fonseca, S., Fernández, G., Adie, B., Chico, J.M., Lorenzo, O., García-Casado, G., López-Vidriero, I., Lozano, F.M., Ponce, M.R., et al. (2007). The JAZ family of repressors is the missing link in jasmonate signalling. Nature **448**:666–671.

Chory, J., Reinecke, D., Sim, S., Washburn, T., and Brenner, M. (1994). A Role for cytokinins in de-etiolation in *Arabidopsis* (det mutants have an altered response to cytokinins). Plant Physiol. **104**:339–347.

Davière, J.M., and Achard, P. (2013). Gibberellin signaling in plants. Development **140**:1147–1151.

Davière, J.M., Wild, M., Regnault, T., Baumberger, N., Eisler, H., Genschik, P., and Achard, P. (2014). Class I TCP-DELLA interactions in inflorescence shoot apex determine plant height. Curr. Biol. **24**:1923–1928.

Del Bianco, M., and Kepinski, S. (2011). Context, specificity, and self-organization in auxin response. Cold Spring Harb. Perspect. Biol. **3**:a001578.

de Lucas, M., Davière, J.M., Rodríguez-Falcón, M., Pontin, M., Iglesias-Pedraz, J.M., Lorrain, S., Fankhauser, C., Blázquez, M.A., Titarenko, E., and Prat, S. (2008). A molecular framework for light and gibberellin control of cell elongation. Nature **451**:480–484.

de Saint Germain, A., Ligerot, Y., Dun, E.A., Pillot, J.P., Ross, J.J., Beveridge, C.A., and Rameau, C. (2013). Strigolactones stimulate internode elongation independently of gibberellins. Plant Physiol. **163**:1012–1025.

de Wit, M., Spoel, S.H., Sanchez-Perez, G.F., Gommers, C.M., Pieterse, C.M., Voesenek, L.A., and Pierik, R. (2013). Perception of low red:far-red ratio compromises both salicylic acid- and jasmonic acid-dependent pathogen defences in *Arabidopsis*. Plant J. **75**:90–103.

Dill, A., and Sun, T. (2001). Synergistic derepression of gibberellin signaling by removing RGA and GAI function in *Arabidopsis thaliana*. Genetics **159**:777–785.

Dill, A., Thomas, S.G., Hu, J., Steber, C.M., and Sun, T.P. (2004). The *Arabidopsis* F-box protein SLEEPY1 targets gibberellin signaling repressors for gibberellin-induced degradation. Plant Cell **16**:1392–1405.

Djakovic-Petrovic, T., de Wit, M., Voesenek, L.A., and Pierik, R. (2007). DELLA protein function in growth responses to canopy signals. Plant J. **51**:117–126.

Doebley, J., Stec, A., and Hubbard, L. (1997). The evolution of apical dominance in maize. Nature **386**:485–488.

Domagalska, M.A., and Leyser, O. (2011). Signal integration in the control of shoot branching. Nat. Rev. Mol. Cell Biol. **12**:211–221.

Feng, S., Martinez, C., Gusmaroli, G., Wang, Y., Zhou, J., Wang, F., Chen, L., Yu, L., Iglesias-Pedraz, J.M., Kircher, S., et al. (2008). Coordinated regulation of *Arabidopsis thaliana* development by light and gibberellins. Nature **451**:475–479.

Ferguson, B.J., and Beveridge, C.A. (2009). Roles for auxin, cytokinin, and strigolactone in regulating shoot branching. Plant Physiol. **150**:482–493.

Fernández-Calvo, P., Chini, A., Fernández-Barbero, G., Chico, J.M., Gimenez-Ibanez, S., Geerinck, J., Eeckhout, D., Schweizer, F., Godoy, M., Franco-Zorrilla, J.M., et al. (2011). The *Arabidopsis* bHLH transcription factors MYC3 and MYC4 are targets of JAZ repressors and act additively with MYC2 in the activation of jasmonate responses. Plant Cell **23**:701–715.

Fleet, C.M., and Sun, T.P. (2005). A DELLAcate balance: the role of gibberellin in plant morphogenesis. Curr. Opin. Plant Biol. **8**:77–85.

Fonseca, S., Chini, A., Hamberg, M., Adie, B., Porzel, A., Kramell, R., Miersch, O., Wasternack, C., and Solano, R. (2009). (+)-7-iso-Jasmonoyl-L-isoleucine is the endogenous bioactive jasmonate. Nat. Chem. Biol. **5**:344–350.

Fu, X., Richards, D.E., Fleck, B., Xie, D., Burton, N., and Harberd, N.P. (2004). The *Arabidopsis* mutant sleepy1gar2-1 protein promotes plant growth by increasing the affinity of the SCFSLY1 E3 ubiquitin ligase for DELLA protein substrates. Plant Cell **16**:1406–1418.

Gallego-Bartolomé, J., Minguet, E.G., Marín, J.A., Prat, S., Blázquez, M.A., and Alabadí, D. (2010). Transcriptional diversification and functional conservation between DELLA proteins in *Arabidopsis*. Mol. Biol. Evol. **27**:1247–1256.

Gallego-Bartolomé, J., Alabadí, D., and Blázquez, M.A. (2011a). DELLA-induced early transcriptional changes during etiolated development in *Arabidopsis thaliana*. PLoS One **6**:e23918.

Gallego-Bartolomé, J., Arana, M.V., Vandenbussche, F., Zádníková, P., Minguet, E.G., Guardiola, V., Van Der Straeten, D., Benkova, E., Alabadí, D., and Blázquez, M.A. (2011b). Hierarchy of hormone action controlling apical hook development in *Arabidopsis*. Plant J. **67**:622–634.

Gallego-Bartolomé, J., Minguet, E.G., Grau-Enguix, F., Abbas, M., Locascio, A., Thomas, S.G., Alabadí, D., and Blázquez, M.A. (2012). Molecular mechanism for the interaction between gibberellin and brassinosteroid signaling pathways in *Arabidopsis*. Proc. Natl. Acad. Sci. USA **109**:13446–13451.

Gao, X.H., Xiao, S.L., Yao, Q.F., Wang, Y.J., and Fu, X.D. (2011). An updated GA signaling 'relief of repression' regulatory model. Mol. Plant **4**:601–606.

Greenboim-Wainberg, Y., Maymon, I., Borochov, R., Alvarez, J., Olszewski, N., Ori, N., Eshed, Y., and Weiss, D. (2005). Cross talk between gibberellin and cytokinin: the *Arabidopsis* GA response inhibitor SPINDLY plays a positive role in cytokinin signaling. Plant Cell **17**:92–102.

Gomez-Roldan, V., Fermas, S., Brewer, P.B., Puech-Pagès, V., Dun, E.A., Pillot, J.P., Letisse, F., Matusova, R., Danoun, S., Portais, J.C., et al. (2008). Strigolactone inhibition of shoot branching. Nature **455**:189–194.

Griffiths, J., Murase, K., Rieu, I., Zentella, R., Zhang, Z.L., Powers, S.J., Gong, F., Phillips, A.L., Hedden, P., Sun, T.P., et al. (2006). Genetic characterization and functional analysis of the GID1 gibberellin receptors in *Arabidopsis*. Plant Cell **18**:3399–3414.

Guo, H., and Ecker, J.R. (2003). Plant responses to ethylene gas are mediated by SCF(EBF1/EBF2)-dependent proteolysis of EIN3 transcription factor. Cell **115**:667–677.

Hacham, Y., Holland, N., Butterfield, C., Ubeda-Tomas, S., Bennett, M.J., Chory, J., and Savaldi-Goldstein, S. (2011). Brassinosteroid perception in the epidermis controls root meristem size. Development **138**:839–848.

Hauvermale, A.L., Ariizumi, T., and Steber, C.M. (2012). Gibberellin signaling: a theme and variations on DELLA repression. Plant Physiol. **160**:83–92.

Hay, A., Kaur, H., Phillips, A., Hedden, P., Hake, S., and Tsiantis, M. (2002). The gibberellin pathway mediates KNOTTED1-type homeobox function in plants with different body plans. Curr. Biol. **12**:1557–1565.

Hedden, P., and Thomas, S.G. (2012). Gibberellin biosynthesis and its regulation. Biochem. J. **444**:11–25.

Hirano, K., Kouketu, E., Katoh, H., Aya, K., Ueguchi-Tanaka, M., and Matsuoka, M. (2012). The suppressive function of the rice DELLA protein SLR1 is dependent on its transcriptional activation activity. Plant J. **71**:443–453.

Hong, G.J., Xue, X.Y., Mao, Y.B., Wang, L.J., and Chen, X.Y. (2012). *Arabidopsis* MYC2 interacts with DELLA proteins in regulating sesquiterpene synthase gene expression. Plant Cell **24**:2635–2648.

Hou, X., Lee, L.Y., Xia, K., Yan, Y., and Yu, H. (2010). DELLAs modulate jasmonate signaling via competitive binding to JAZs. Dev. Cell **19**:884–894.

Hou, X., Ding, L., and Yu, H. (2013). Crosstalk between GA and JA signaling mediates plant growth and defense. Plant Cell Rep. **32**:1067–1074.

Huq, E., and Quail, P.H. (2002). PIF4, a phytochrome-interacting bHLH factor, functions as a negative regulator of phytochrome B signaling in *Arabidopsis*. EMBO J. **21**:2441–2450.

Ikeda, A., Ueguchi-Tanaka, M., Sonoda, Y., Kitano, H., Koshioka, M., Futsuhara, Y., Matsuoka, M., and Yamaguchi, J. (2001). Slender rice, a constitutive gibberellin response mutant, is caused by a null mutation of the SLR1 gene, an ortholog of the height-regulating gene GAI/RGA/RHT/D8. Plant Cell **13**:999–1010.

Jasinski, S., Piazza, P., Craft, J., Hay, A., Woolley, L., Rieu, I., Phillips, A., Hedden, P., and Tsiantis, M. (2005). KNOX action in *Arabidopsis* is mediated by coordinate regulation of cytokinin and gibberellin activities. Curr. Biol. **15**:1560–1565.

Jiang, L., Liu, X., Xiong, G., Liu, H., Chen, F., Wang, L., Meng, X., Liu, G., Yu, H., Yuan, Y., et al. (2013). DWARF 53 acts as a repressor of strigolactone signalling in rice. Nature **504**:401–405.

Kim, D.H., Yamaguchi, S., Lim, S., Oh, E., Park, J., Hanada, A., Kamiya, Y., and Choi, G. (2008). SOMNUS, a CCCH-type zinc finger protein in *Arabidopsis*, negatively regulates light-dependent seed germination downstream of PIL5. Plant Cell **20**:1260–1277.

King, K.E., Moritz, T., and Harberd, N.P. (2001). Gibberellins are not required for normal stem growth in *Arabidopsis thaliana* in the absence of GAI and RGA. Genetics **159**:767–776.

Ko, J.-H., Yang, S.H., and Han, K.-H. (2006). Upregulation of an *Arabidopsis* RING-H2 gene, XERICO, confers drought tolerance through increased abscisic acid biosynthesis. Plant J. **47**:343–355.

Koini, M.A., Alvey, L., Allen, T., Tilley, C.A., Harberd, N.P., Whitelam, G.C., and Franklin, K.A. (2009). High temperature-mediated adaptations in plant architecture require the bHLH transcription factor PIF4. Curr. Biol. **19**:408–413.

Koornneef, M., Bentsink, L., and Hilhorst, H. (2002). Seed dormancy and germination. Curr. Opin. Plant Biol. **5**:33–36.

Kuppusamy, K.T., Walcher, C.L., and Nemhauser, J.L. (2009). Cross-regulatory mechanisms in hormone signaling. Plant Mol. Biol. **69**:375–381.

Lawit, S.J., Wych, H.M., Xu, D., Kundu, S., and Tomes, D.T. (2010). Maize DELLA proteins dwarf plant8 and dwarf plant9 as modulators of plant development. Plant Cell Physiol. **51**:1854–1868.

Lee, S., Cheng, H., King, K.E., Wang, W., He, Y., Hussain, A., Lo, J., Harberd, N.P., and Peng, J. (2002). Gibberellin regulates *Arabidopsis* seed germination via RGL2, a GAI/RGA-like gene whose expression is up-regulated following imbibition. Genes Dev. **16**:646–658.

Lee, S., Lee, S., Yang, K.Y., Kim, Y.M., Park, S.Y., Kim, S.Y., and Soh, M.S. (2006). Overexpression of PRE1 and its homologous genes activates Gibberellin-dependent responses in *Arabidopsis thaliana*. Plant Cell Physiol. **47**:591–600.

Lehman, A., Black, R., and Ecker, J.R. (1996). HOOKLESS1, an ethylene response gene, is required for differential cell elongation in the *Arabidopsis* hypocotyl. Cell **85**:183–194.

Leone, M., Keller, M.M., Cerrudo, I., and Ballaré, C.L. (2014). To grow or defend? Low red : far-red ratios reduce jasmonate sensitivity in *Arabidopsis* seedlings by promoting DELLA degradation and increasing JAZ10 stability. New Phytol. **204**:355–367.

Li, J., and Chory, J. (1997). A putative leucine-rich repeat receptor kinase involved in brassinosteroid signal transduction. Cell **90**:929–938.

Li, J., Nagpal, P., Vitart, V., McMorris, T.C., and Chory, J. (1996). A role for brassinosteroids in light-dependent development of *Arabidopsis*. Science **272**:398–401.

Li, Q.F., Wang, C., Jiang, L., Li, S., Sun, S.S., and He, J.X. (2012). An interaction between BZR1 and DELLAs mediates direct signaling crosstalk between brassinosteroids and gibberellins in *Arabidopsis*. Sci. Signal. **5**:ra72.

Lilley, S.J.L., Gan, Y., Graham, I.A., and Nemhauser, J.L. (2013). The effects of DELLAs on growth change with developmental stage and brassinosteroid levels. Plant J. **76**:165–173.

Lim, S., Park, J., Lee, N., Jeong, J., Toh, S., Watanabe, A., Kim, J., Kang, H., Kim, D.H., Kawakami, N., et al. (2013). ABA-insensitive3, ABA-insensitive5, and DELLAs interact to activate the expression of SOMNUS and other high-temperature-inducible genes in imbibed seeds in *Arabidopsis*. Plant Cell **25**:4863–4878.

Lo, S.F., Yang, S.Y., Chen, K.T., Hsing, Y.I., Zeevaart, J.A., Chen, L.J., and Yu, S.M. (2008). A novel class of gibberellin 2-oxidases control semidwarfism, tillering, and root development in rice. Plant Cell **20**:2603–2618.

Locascio, A., Blázquez, M.A., and Alabadí, D. (2013). Genomic analysis of DELLA protein activity. Plant Cell Physiol. **54**:1229–1237.

Löfke, C., Zwiewka, M., Heilmann, I., Van Montagu, M.C., Teichmann, T., and Friml, J. (2013). Asymmetric gibberellin signaling regulates vacuolar trafficking of PIN auxin transporters during root gravitropism. Proc. Natl. Acad. Sci. USA **110**:3627–3632.

Lorenzo, O., Chico, J.M., Sánchez-Serrano, J.J., and Solano, R. (2004). JASMONATE-INSENSITIVE1 encodes a MYC transcription factor essential to discriminate between different jasmonate-regulated defense responses in *Arabidopsis*. Plant Cell **16**:1938–1950.

Marín-de la Rosa, N., Sotillo, B., Miskolczi, P., Gibbs, D.J., Vicente, J., Carbonero, P., Oñate-Sánchez, L., Holdsworth, M.J., Bhalerao, R., Alabadí, D., et al. (2014). Large-scale identification of gibberellin-related transcription factors defines group VII ETHYLENE RESPONSE FACTORS as functional DELLA partners. Plant Physiol. **166**:1022–1032.

Marín-de la Rosa, N., Pfeiffer, A., Hill, K., Locascio, A., Bhalerao, R.P., Miskolczi, P., Grønlund, A.L., Wanchoo-Kohli, A., Thomas, S.G., Bennett, M.J., et al. (2015). Genome wide binding site analysis reveals transcriptional coactivation of cytokinin-responsive genes by DELLA proteins. PLoS Genet. **11**:e1005337.

Martí, C., Orzáez, D., Ellul, P., Moreno, V., Carbonell, J., and Granell, A. (2007). Silencing of DELLA induces facultative parthenocarpy in tomato fruits. Plant J. **52**:865–876.

McGinnis, K.M., Thomas, S.G., Soule, J.D., Strader, L.C., Zale, J.M., Sun, T.P., and Steber, C.M. (2003). The *Arabidopsis* SLEEPY1 gene encodes a putative F-box subunit of an SCF E3 ubiquitin ligase. Plant Cell **15**:1120–1130.

Moubayidin, L., Perilli, S., Dello Ioio, R., Di Mambro, R., Costantino, P., and Sabatini, S. (2010). The rate of cell differentiation controls the *Arabidopsis* root meristem growth phase. Curr. Biol. **20**:1138–1143.

Murfet, I.C., and Reid, J.B. (1993). Developmental mutants. In Peas: Genetics, Molecular Biology and Biotechnology, R. Casey and D.R. Davies, eds. (Wallingford: CAB), pp. 165–216.

Nakamura, H., Xue, Y.L., Miyakawa, T., Hou, F., Qin, H.M., Fukui, K., Shi, X., Ito, E., Ito, S., Park, S.H., et al. (2013). Molecular mechanism of strigolactone perception by DWARF14. Nat. Commun. **4**:2613.

Navarro, L., Bari, R., Achard, P., Lisón, P., Nemri, A., Harberd, N.P., and Jones, J.D. (2008). DELLAs control plant immune responses by modulating the balance of jasmonic acid and salicylic acid signaling. Curr. Biol. **18**:650–655.

Ogas, J., Kaufmann, S., Henderson, J., and Somerville, C. (1999). PICKLE is a CHD3 chromatin-remodeling factor that regulates the transition from embryonic to vegetative development in *Arabidopsis*. Proc. Natl. Acad. Sci. USA **96**:13839–13844.

Oh, E., Yamaguchi, S., Kamiya, Y., Bae, G., Chung, W.-I., and Choi, G. (2006). Light activates the degradation of PIL5 protein to promote seed germination through gibberellin in *Arabidopsis*. Plant J. **47**:124–139.

Oh, E., Zhu, J.Y., and Wang, Z.Y. (2012). Interaction between BZR1 and PIF4 integrates brassinosteroid and environmental responses. Nat. Cell Biol. **14**:802–809.

Oh, E., Zhu, J.Y., Bai, M.Y., Arenhart, R.A., Sun, Y., and Wang, Z.Y. (2014). Cell elongation is regulated through a central circuit of interacting transcription factors in the *Arabidopsis* hypocotyl. eLife **3**:e03031.

Park, J., Lee, N., Kim, W., Lim, S., and Choi, G. (2011). ABI3 and PIL5 collaboratively activate the expression of SOMNUS by directly binding to its promoter in imbibed *Arabidopsis* seeds. Plant Cell **23**:1404–1415.

Peng, J., Carol, P., Richards, D.E., King, K.E., Cowling, R.J., Murphy, G.P., and Harberd, N.P. (1997). The *Arabidopsis* GAI gene defines a signaling pathway that negatively regulates gibberellin responses. Genes Dev. **11**:3194–3205.

Peng, J., Richards, D.E., Hartley, N.M., Murphy, G.P., Devos, K.M., Flintham, J.E., Beales, J., Fish, L.J., Worland, A.J., Pelica, F., et al. (1999). 'Green revolution' genes encode mutant gibberellin response modulators. Nature **400**:256–261.

Pimenta-Lange, M.J., and Lange, T. (2006). Gibberellin biosynthesis and the regulation of plant development. Plant Biol. **8**:281–290.

Piskurewicz, U., Jikumaru, Y., Kinoshita, N., Nambara, E., Kamiya, Y., and Lopez-Molina, L. (2008). The gibberellic acid signaling repressor RGL2 inhibits *Arabidopsis* seed germination by stimulating abscisic acid synthesis and ABI5 activity. Plant Cell **20**:2729–2745.

Potuschak, T., Lechner, E., Parmentier, Y., Yanagisawa, S., Grava, S., Koncz, C., and Genschik, P. (2003). EIN3-dependent regulation of plant ethylene hormone signaling by two *Arabidopsis* F box proteins: EBF1 and EBF2. Cell **115**:679–689.

Qi, T., Huang, H., Wu, D., Yan, J., Qi, Y., Song, S., and Xie, D. (2014). *Arabidopsis* DELLA and JAZ proteins bind the WD-repeat/bHLH/MYB complex to modulate gibberellin and jasmonate signaling synergy. Plant Cell **26**:1118–1133.

Rameau, C., Bertheloot, J., Leduc, N., Andrieu, B., Foucher, F., and Sakr, S. (2015). Multiple pathways regulate shoot branching. Front. Plant Sci. **5**:741.

Raz, V., and Ecker, J.R. (1999). Regulation of differential growth in the apical hook of *Arabidopsis*. Development **126**:3661–3668.

Resentini, F., Felipo-Benavent, A., Colombo, L., Blázquez, M.A., Alabadí, D., and Masiero, S. (2015). TCP14 and TCP15 mediate the promotion of seed germination by gibberellins in *Arabidopsis thaliana*. Mol. Plant **8**:482–485.

Ruyter-Spira, C., Kohlen, W., Charnikhova, T., van Zeijl, A., van Bezouwen, L., de Ruijter, N., Cardoso, C., Lopez-Raez, J.A., Matusova, R., Bours, R., et al. (2011). Physiological effects of the synthetic strigolactone analog GR24 on root system architecture in *Arabidopsis*: another belowground role for strigolactones? Plant Physiol. **155**:721–734.

Sakamoto, T., Kamiya, N., Ueguchi-Tanaka, M., Iwahori, S., and Matsuoka, M. (2001). KNOX homeodomain protein directly suppresses the expression of a gibberellin biosynthetic gene in the tobacco shoot apical meristem. Genes Dev. **15**:581–590.

Santner, A., and Estelle, M. (2009). Recent advances and emerging trends in plant hormone signalling. Nature **459**:1071–1078.

Sarnowska, E.A., Rolicka, A.T., Bucior, E., Cwiek, P., Tohge, T., Fernie, A.R., Jikumaru, Y., Kamiya, Y., Franzen, R., Schmelzer, E., et al. (2013). DELLA-interacting SWI3C core subunit of switch/sucrose nonfermenting chromatin remodeling complex modulates gibberellin responses and hormonal cross talk in *Arabidopsis*. Plant Physiol. **163**:305–317.

Sasaki, A., Itoh, H., Gomi, K., Ueguchi-Tanaka, M., Ishiyama, K., Kobayashi, M., Jeong, D.H., An, G., Kitano, H., Ashikari, M., et al. (2003). Accumulation of phosphorylated repressor for gibberellin signaling in an F-box mutant. Science **299**:1896–1898.

Schwechheimer, C. (2012). Gibberellin signaling in plants - the extended version. Front. Plant Sci. **2**:107.

Silverstone, A.L., Mak, P.Y., Martínez, E.C., and Sun, T.P. (1997). The new RGA locus encodes a negative regulator of gibberellin response in *Arabidopsis thaliana*. Genetics **146**:1087–1099.

Silverstone, A.L., Ciampaglio, C.N., and Sun, T. (1998). The *Arabidopsis* RGA gene encodes a transcriptional regulator repressing the gibberellin signal transduction pathway. Plant Cell **10**:155–169.

Silverstone, A.L., Jung, H.S., Dill, A., Kawaide, H., Kamiya, Y., and Sun, T.P. (2001). Repressing a repressor: gibberellin-induced rapid reduction of the RGA protein in *Arabidopsis*. Plant Cell **13**:1555–1566.

Song, S., Qi, T., Huang, H., Ren, Q., Wu, D., Chang, C., Peng, W., Liu, Y., Peng, J., and Xie, D. (2011). The Jasmonate-ZIM domain proteins interact with the R2R3-MYB transcription factors MYB21 and MYB24 to affect jasmonate-regulated stamen development in *Arabidopsis*. Plant Cell **23**:1000–1013.

Stewart, J.L., and Nemhauser, J.L. (2010). Do trees grow on money? Auxin as the currency of the cellular economy. Cold Spring Harb. Perspect. Biol. **2**:a001420.

Stirnberg, P., Furner, I.J., and Leyser, O. (2007). MAX2 participates in an SCF complex which acts locally at the node to suppress shoot branching. Plant J. **50**:80–94.

Sun, T.P. (2011). The molecular mechanism and evolution of the GA-GID1-DELLA signaling module in plants. Curr. Biol. **21**:R338–R345.

Takeda, T., Suwa, Y., Suzuki, M., Kitano, H., Ueguchi-Tanaka, M., Ashikari, M., Matsuoka, M., and Ueguchi, C. (2003). The OsTB1 gene negatively regulates lateral branching in rice. Plant J. **33**:513–520.

Thines, B., Katsir, L., Melotto, M., Niu, Y., Mandaokar, A., Liu, G., Nomura, K., He, S.Y., Howe, G.A., and Browse, J. (2007). JAZ repressor proteins are targets of the SCF(COI1) complex during jasmonate signalling. Nature **448**:661–665.

Tyler, L., Thomas, S.G., Hu, J., Dill, A., Alonso, J.M., Ecker, J.R., and Sun, T.P. (2004). Della proteins and gibberellin-regulated seed germination and floral development in *Arabidopsis*. Plant Physiol. **135**:1008–1019.

Ubeda-Tomás, S., Swarup, R., Coates, J., Swarup, K., Laplaze, L., Beemster, G.T., Hedden, P., Bhalerao, R., and Bennett, M.J. (2008). Root growth in *Arabidopsis* requires gibberellin/DELLA signalling in the endodermis. Nat. Cell Biol. **10**:625–628.

Ubeda-Tomás, S., Federici, F., Casimiro, I., Beemster, G.T., Bhalerao, R., Swarup, R., Doerner, P., Haseloff, J., and Bennett, M.J. (2009). Gibberellin signaling in the endodermis controls *Arabidopsis* root meristem size. Curr. Biol. **19**:1194–1199.

Ueguchi-Tanaka, M., Ashikari, M., Nakajima, M., Itoh, H., Katoh, E., Kobayashi, M., Chow, T.Y., Hsing, Y.I., Kitano, H., Yamaguchi, I., et al. (2005). GIBBERELLIN INSENSITIVE DWARF1 encodes a soluble receptor for gibberellin. Nature **437**:693–698.

Ueguchi-Tanaka, M., Nakajima, M., Katoh, E., Ohmiya, H., Asano, K., Saji, S., Hongyu, X., Ashikari, M., Kitano, H., Yamaguchi, I., et al. (2007). Molecular interactions of a soluble gibberellin receptor, GID1, with a rice DELLA protein, SLR1, and gibberellin. Plant Cell. **19**:2140–2155.

Umehara, M., Hanada, A., Yoshida, S., Akiyama, K., Arite, T., Takeda-Kamiya, N., Magome, H., Kamiya, Y., Shirasu, K., Yoneyama, K., et al. (2008). Inhibition of shoot branching by new terpenoid plant hormones. Nature **455**:195–200.

Vandenbussche, F., Petrásek, J., Zádníková, P., Hoyerová, K., Pesek, B., Raz, V., Swarup, R., Bennett, M., Zazímalová, E., Benková, E., et al. (2010). The auxin influx carriers AUX1 and LAX3 are involved in auxin-ethylene interactions during apical hook development in *Arabidopsis thaliana* seedlings. Development **137**:597–606.

Vanstraelen, M., and Benková, E. (2012). Hormonal interactions in the regulation of plant development. Annu. Rev. Cell Dev. Biol. **28**:463–487.

Vert, G., Nemhauser, J.L., Geldner, N., Hong, F., and Chory, J. (2005). Molecular mechanisms of steroid hormone signaling in plants. Annu. Rev. Cell Dev. Biol. **21**:177–201.

Vriezen, W.H., Zhou, Z., and Van Der Straeten, D. (2003). Regulation of submergence-induced enhanced shoot elongation in *Oryza sativa* L. Ann. Bot. **91**:263–270.

Wang, F., and Deng, X.W. (2011). Plant ubiquitin-proteasome pathway and its role in gibberellin signaling. Cell Res. **21**:1286–1294.

Wang, Z.Y., Bai, M.Y., Oh, E., and Zhu, J.Y. (2012). Brassinosteroid signaling network and regulation of photomorphogenesis. Annu. Rev. Genet. **46**:701–724.

Wasternack, C., and Hause, B. (2013). Jasmonates: biosynthesis, perception, signal transduction and action in plant stress response, growth and development. An update to the 2007 review in Annals of Botany. Ann. Bot. **111**:1021–1058.

Weiss, D., and Ori, N. (2007). Mechanisms of cross talk between gibberellin and other hormones. Plant Physiol. **144**:1240–1246.

Wen, C.K., and Chang, C. (2002). *Arabidopsis* RGL1 encodes a negative regulator of gibberellin responses. Plant Cell **14**:87–100.

Wild, M., Davière, J.M., Cheminant, S., Regnault, T., Baumberger, N., Heintz, D., Baltz, R., Genschik, P., and Achard, P. (2012). The *Arabidopsis* DELLA RGA-LIKE3 is a direct target of MYC2 and modulates jasmonate signaling responses. Plant Cell **24**:3307–3319.

Willige, B.C., Ghosh, S., Nill, C., Zourelidou, M., Dohmann, E.M., Maier, A., and Schwechheimer, C. (2007). The DELLA domain of GA INSENSITIVE mediates the interaction with the GA INSENSITIVE DWARF1A gibberellin receptor of *Arabidopsis*. Plant Cell **19**:1209–1220.

Willige, B.C., Isono, E., Richter, R., Zourelidou, M., and Schwechheimer, C. (2011). Gibberellin regulates PIN-FORMED abundance and is required for auxin transport-dependent growth and development in *Arabidopsis thaliana*. Plant Cell **23**:2184–2195.

Winkler, R.G., and Freeling, M. (1994). Physiological genetics of the dominant gibberellin-nonresponsive maize dwarfs, Dwarf8 and Dwarf9. Planta **193**:341–348.

Xie, D.X., Feys, B.F., James, S., Nieto-Rostro, M., and Turner, J.G. (1998). COI1: an *Arabidopsis* gene required for jasmonate-regulated defense and fertility. Science **280**:1091–1094.

Yamaguchi, S. (2008). Gibberellin metabolism and its regulation. Annu. Rev. Plant Biol. **59**:225–251.

Yanai, O., Shani, E., Dolezal, K., Tarkowski, P., Sablowski, R., Sandberg, G., Samach, A., and Ori, N. (2005). *Arabidopsis* KNOXI proteins activate cytokinin biosynthesis. Curr. Biol. **15**:1566–1571.

Yang, D.L., Yao, J., Mei, C.S., Tong, X.H., Zeng, L.J., Li, Q., Xiao, L.T., Sun, T.P., Li, J., Deng, X.W., et al. (2012). Plant hormone jasmonate prioritizes defense over growth by interfering with gibberellin signaling cascade. Proc. Natl. Acad. Sci. USA **109**:1192–1200.

Yoshida, H., Hirano, K., Sato, T., Mitsuda, N., Nomoto, M., Maeo, K., Koketsu, E., Mitani, R., Kawamura, M., Ishiguro, S., et al. (2014). DELLA protein functions as a transcriptional activator through the DNA binding of the indeterminate domain family proteins. Proc. Natl. Acad. Sci. USA **111**:7861–7866.

Zádníková, P., Petrásek, J., Marhavy, P., Raz, V., Vandenbussche, F., Ding, Z., Schwarzerová, K., Morita, M.T., Tasaka, M., Hejátko, J., et al. (2010). Role of PIN-mediated auxin efflux in apical hook development of *Arabidopsis thaliana*. Development **137**:607–617.

Zentella, R., Zhang, Z.L., Park, M., Thomas, S.G., Endo, A., Murase, K., Fleet, C.M., Jikumaru, Y., Nambara, E., Kamiya, Y., et al. (2007). Global analysis of Della direct targets in early gibberellin signaling in *Arabidopsis*. Plant Cell **19**:3037–3057.

Zhang, D., Jing, Y., Jiang, Z., and Lin, R. (2014). The chromatin-remodeling factor PICKLE integrates brassinosteroid and gibberellin signaling during Skotomorphogenic growth in *Arabidopsis*. Plant Cell **26**:2472–2485.

Zhang, Y., and Turner, J.G. (2008). Wound-induced endogenous jasmonates stunt plant growth by inhibiting mitosis. PLoS One **3**:e3699.

Zhong, G.Y., and Yang, Y. (2012). Characterization of grape Gibberellin Insensitive1 mutant alleles in transgenic *Arabidopsis*. Transgenic Res. **21**:725–741.

Zhou, F., Lin, Q., Zhu, L., Ren, Y., Zhou, K., Shabek, N., Wu, F., Mao, H., Dong, W., Gan, L., et al. (2013). D14-SCF(D3)-dependent degradation of D53 regulates strigolactone signalling. Nature **504**:406–410.

Zhu, Z., An, F., Feng, Y., Li, P., Xue, L., A, M., Jiang, Z., Kim, J.M., To, T.K., Li, W., Zhang, et al. (2011). Derepression of ethylene-stabilized transcription factors (EIN3/EIL1) mediates jasmonate and ethylene signaling synergy in *Arabidopsis*. Proc. Natl. Acad. Sci. USA **108**:12539–12544.