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A Pivotal Role of DELLAs in Regulating Multiple Hormone Signals

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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

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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

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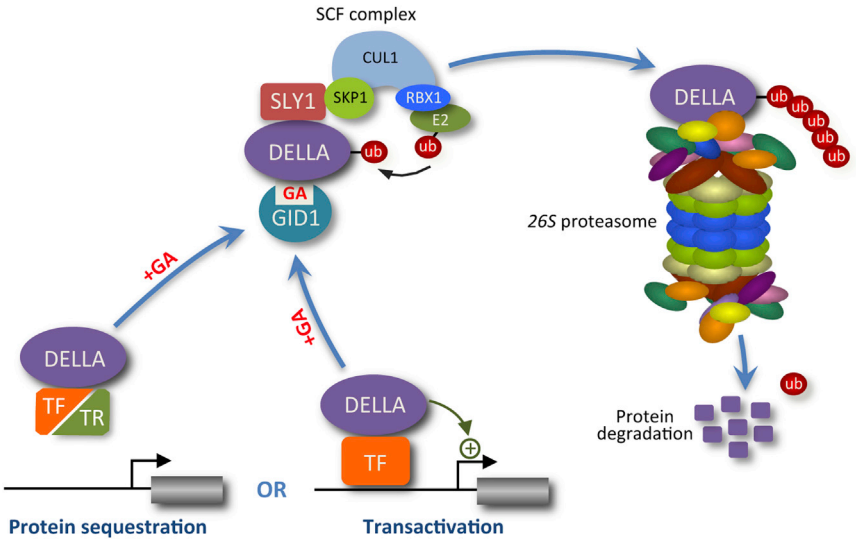

Figure 1. An Overview of the GA Signaling Pathway.
When GA concentrations are low, DELLAs repress GA responses by interacting with and inhibiting the activity of transcription factors (TF) or regulatory proteins (TR), or by activating the transcription of target genes associated with TF. When GA concentrations 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).