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MINI-REVIEW

Beyond proteolysis: the GA–GID1–DELLA module as a transcriptional control hub in plants

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ABSTRACT Gibberellins (GAs) promote growth and developmental transitions throughout the plant life cycle. A hallmark of GA action is the control of DELLA proteins, master repressors of GA responses. In the canonical pathway, bioactive GA binds the soluble receptor GID1, enabling formation of a GA–GID1–DELLA complex that recruits SCF-type E3 ubiquitin ligases (e.g., SLY1/SNE (SNEEZY; also called SLY2) in Arabidopsis and GID2 in rice) and triggers ubiquitination and 26S proteasome-mediated DELLA degradation (McGinnis et al. 2003; Dill et al. 2004; Gomi et al. 2004; Ariizumi et al. 2011). However, recent work shows that GA can neutralize DELLA output beyond simple proteolysis. Structural analyses reveal proteolysis-independent suppression of DELLA by GA–GID1 binding (Ariizumi et al. 2008; Dahal et al. 2025), chromatin studies show that phosphorylation can activate DELLA by promoting histone H2A binding at chromatin, and nutrient starvation studies identify ATG8-dependent autophagic DELLA degradation during dark skotomorphogenesis. Together, these findings support a hub model in which DELLA output depends on abundance, conformation, post-translational modifications, interaction partners, and chromatin engagement. We highlight how this expanded view of the GA–DELLA module informs precision strategies for crop improvement that tune growth–stress trade-offs with reduced pleiotropy.
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Introduction

Plants continuously balance growth with survival. Unlike motile organisms, plants must adjust development in place as light, temperature, water status, nutrient availability, and biotic pressure fluctuate. Gibberellins (GAs) are among the most potent growth-promoting phytohormones, controlling seed germination, cell expansion and division, organ elongation, phase transitions, and aspects of reproductive development (Olszewski et al. 2002; Sun 2011). GA biology is also inseparable from agricultural history: semi-dwarf "Green Revolution" alleles that alter GA metabolism or GA responsiveness increased lodging resistance and yield stability in cereals (Peng et al. 1999; Sasaki et al. 2002; Alabadi and Sun 2025).

A defining mechanistic feature of GA signaling is that it operates largely by de-repression. DELLA proteins—members of the GRAS family of nuclear regulators—act as central repressors of GA responses. When DELLA activity is high, growth-promoting transcriptional programs are restrained; when GA signaling is high, DELLA repression is relieved. In the canonical pathway, bioactive GA binds the soluble receptor Gibberellin Insensitive Dwarf1 (GID1), enabling formation of a GA–GID1–DELLA complex that recruits SCF-type ubiquitin ligases. DELLA proteins are ubiquitinated and degraded by the 26S proteasome, allowing GA-responsive growth programs to proceed (McGinnis et al. 2003; Dill et al. 2004; Murase et al. 2008).

Over the last decade, the simple "DELLA equals degradation" narrative has been refined in several ways. First, mechanistic interaction studies established that DELLAs are not sequence-specific DNA-binding factors. Instead, they act as transcriptional co-regulators that bind diverse transcription factors and signaling components, thereby reshaping gene regulatory networks (Davière and

Achard 2016; Alabadi and Sun 2025). Second, chromatin biology has entered the picture: DELLA proteins can influence promoter states by directly engaging chromatin components or recruiting chromatin regulators (Huang et al. 2024; Li et al. 2023). Third, non-canonical routes of DELLA neutralization and turnover have been discovered, including autophagic DELLA clearance under starvation and proteolysis-independent suppression of DELLA output by GA–GID1 binding (Zhang et al. 2025; Dahal et al. 2025).

A cluster of recent studies is particularly relevant for an updated mini-review. First, high-resolution structural work clarified how GA–GID1 assemblies can suppress DELLA output both by promoting ubiquitination and by directly reshaping DELLA interaction surfaces (Dahal et al. 2025). Second, chromatin mechanisms provide direct routes for tuning DELLA activity: phosphorylation can enhance DELLA binding to histone H2A and promoter regions (Huang et al. 2024), and in rice DELLA repression can be maintained through recruitment of chromatin modifiers that establish repressive chromatin states (Li et al. 2023). Third, alternative clearance routes have been discovered: under starvation in darkness, GA can drive ATG8-dependent autophagic DELLA degradation to enable skotomorphogenesis (Zhang et al. 2025). Together, these findings shift the emphasis from DELLA abundance alone to DELLA activity, interaction capacity, and context-specific clearance.

This focused mini-review summarizes (i) how GA availability is translated into DELLA control via GID1 and SCF machinery, (ii) how DELLA proteins regulate transcription through partner proteins and chromatin, (iii) mechanisms that modulate DELLA activity beyond canonical proteasomal turnover, and (iv) implications for crop improvement strategies that aim to tune growth–stress trade-offs with minimal pleiotropy.

The canonical GA–GID1–DELLA pathway

Bioactive GAs are produced and inactivated through a conserved enzymatic network. Key late biosynthetic steps include oxidation reactions catalyzed by GA20-oxidases and GA3-oxidases, whereas GA2-oxidases convert bioactive GAs to inactive forms (Olszewski et al. 2002). GA levels therefore reflect a balance between biosynthesis and catabolism, both of which are regulated developmentally and in response to environmental cues (Fig. 1).

GA metabolism is also embedded in feedback. When GA signaling is strong, transcriptional programs often reduce further GA accumulation by repressing biosynthetic genes and/or inducing catabolic genes; conversely, when GA signaling is low, biosynthesis can be upregulated. The net effect is homeostasis—stabilizing the growth state in fluctuating environments. For engineering, however, feedback means that interventions at a single enzymatic step can be partially compensated elsewhere. In practice, phenotypes can therefore be conditional, appearing strongly in one environment and weakly in another.

The identification of GID1 as a soluble GA receptor was a turning point for GA biology. In rice, gid1 mutants exhibit GA-insensitive dwarfism, and GID1 proteins bind GA and interact with DELLA proteins in a GA-dependent manner (Ueguchi-Tanaka et al. 2005). Structural studies revealed that GA binds in a pocket within GID1 and is covered by an N-terminal "lid" or switch region. Lid closure upon hormone binding exposes a surface that engages the conserved DELLA region of DELLA proteins, thereby coupling hormone binding to repressor recognition (Murase et al. 2008; Shimada et al. 2008).

Most angiosperms encode multiple GID1 paralogs. In *Arabidopsis*, GID1A, GID1B, and GID1C act partially redundantly but show distinct expression patterns and ligand affinity profiles. Receptor diversity provides a plausible route for tissue-specific sensitivity: different cell types can display different GA thresholds for DELLA neutralization, depending on which receptor paralogs are expressed and how strongly they bind bioactive GA. This concept is useful for translational work because it suggests that receptor tuning can shift growth decisions without necessarily changing GA pools (Griffiths et al. 2006).

After GA–GID1 binds DELLA, the complex becomes a preferred substrate for SCF-type ubiquitin ligases. In *Arabidopsis*, SLEEPY1 (SLY1) encodes an F-box protein that acts as the substrate recognition subunit of an SCF complex promoting DELLA ubiquitination (McGinnis et al. 2003). Loss-of-function sly1 mutants are GA-insensitive because DELLA repressors persist. Conversely, biochemical and genetic evidence showed that SLY1 targets DELLA proteins such as RGA and GAI for GA-stimulated ubiquitination and 26S proteasome degradation (Dill et al. 2004). In rice, GID2 plays an analogous role (Gomi et al. 2004).

Mechanistically, the requirement for GA–GID1 binding provides specificity. DELLA proteins are not constitutive SCF substrates; rather, GA–GID1 binding changes DELLA conformation and/or exposes surfaces that facilitate productive recognition by the ubiquitination machinery. This coupling helps prevent inappropriate DELLA destruction when GA levels are low, preserving the ability to restrain growth. It also explains why mutations that impair GA–GID1 binding stabilize DELLAs and cause GA-insensitive dwarf phenotypes across species (Murase et al. 2008; Alabadi and Sun 2025).

The "inhibitor of an inhibitor" logic of GA–DELLA signaling has two practical consequences. First, GA responses can be rapid: the pathway removes a pre-

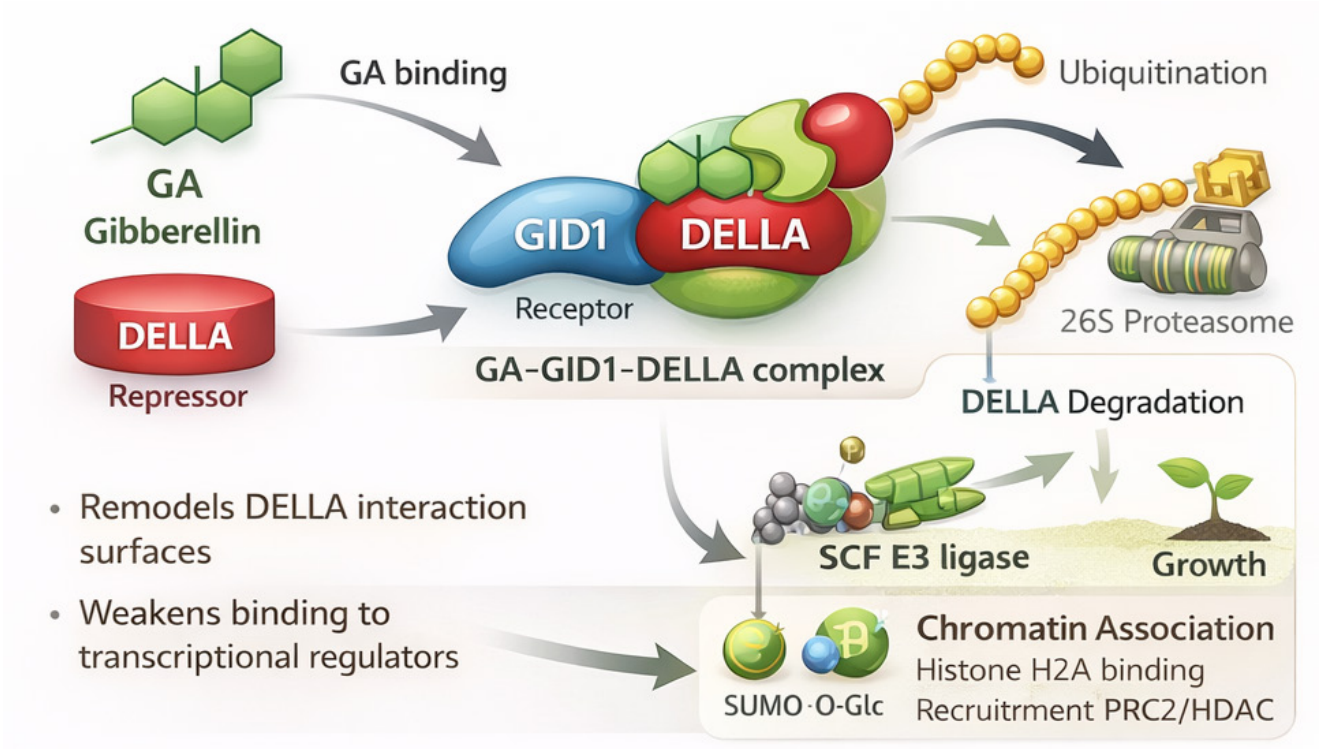

Figure 1. Canonical GA–GID1–DELLA signaling and dual modes of DELLA suppression. Bioactive GA binds the soluble receptor GID1, enabling GA–GID1 association with DELLA proteins. The complex recruits SCF E3 ligases (e.g., SLY1/GID2), promoting DELLA ubiquitination and 26S proteasome degradation. Recent structural data also support a proteolysis-independent mechanism in which GA–GID1 binding remodels DELLA interaction surfaces and weakens binding to downstream transcriptional regulators.

existing repressor rather than waiting for synthesis of new transcription factors (Harberd et al. 2009). Second, the system is readily reversible: when GA levels fall, DELLA synthesis and reduced turnover allow repressors to accumulate again, re-establishing growth restraint. These properties make the GA–GID1–DELLA module an effective controller of growth plasticity.

Early structural work established the basic recognition mechanism by solving the crystal structure of a GA–GID1–DELLA ternary complex, revealing how the GID1 lid covers the hormone and how DELLA motifs are presented to the receptor (Murase et al. 2008; Shimada et al. 2008). More recent structural analyses have begun to explain why DELLA inactivation is not always equivalent to DELLA destruction. A 2025 study reported cryo-EM structures of GA-bound GID1A with full-length *Arabidopsis* RGA, including a complex containing the SCF substrate adaptor SLY1 and ASK1, and showed that GA–GID1 binding can suppress DELLA output through both proteolysis-dependent and proteolysis-independent mechanisms (Dahal et al. 2025). An earlier study also reported proteolysis-independent downregulation of DELLA output by GA without immediate DELLA destruction (Ariizumi et al. 2008).

These findings support a broadened view: GA can neutralize DELLA output through multiple routes, including destabilization (canonical), conformational masking/competition (proteolysis-independent), and in specific contexts, alternative clearance pathways such as autophagy (Zhang et al. 2025). In other words, GA is not merely a trigger for DELLA destruction; it can be a trigger for DELLA disengagement from downstream regulators, which may precede or even substitute for degradation in some cellular contexts (Fig. 1).

DELLA proteins as transcriptional control hubs

DELLAs are GRAS family regulators with two broad functional regions. The N-terminal region contains conserved motifs (including the DELLA and TVHYNP motifs) required for GA–GID1 interaction, as revealed by structural studies (Murase et al. 2008). The C-terminal GRAS domain provides multiple protein–protein interaction surfaces that support binding to transcription factors, co-regulators, and chromatin modifiers. Because DELLA proteins possess several interaction interfaces and can bind many partners, they behave as hubs that translate

GA status into shifts in transcriptional network behavior (Davière and Achard 2016; Alabadi and Sun 2025).

A hub architecture also explains pleiotropy. If a protein interacts with many regulators, altering its abundance or activity can produce broad phenotypic effects. The agricultural success of semi-dwarfing alleles illustrates that pleiotropy can be beneficial when it shifts plant architecture toward lodging resistance and yield stability (Peng et al. 1999), but it also underscores the need for precise tuning in modern breeding where target environments and management practices are diverse (Fig. 2).

Because DELLAs do not bind DNA in a sequence-specific manner, they regulate transcription by influencing other DNA-binding proteins and chromatin states. Four non-exclusive mechanisms are frequently invoked. First, DELLAs can sequester transcription factors away from DNA. Second, DELLA binding can inhibit transcription factor activation domains or interfere with recruitment of co-activators. Third, DELLAs can reshape multi-protein complexes on promoters, changing transcriptional potency without fully removing the factors. Fourth, DELLAs can recruit chromatin regulators to impose (or maintain) repressive promoter states, effectively "locking" some gene expression programs until DELLA output is neutralized.

At the transcriptome level, DELLA output is often reflected in coordinated changes in genes involved in cell wall remodeling, cell cycle control, and hormone metabolism, consistent with the central growth role of GA. Because DELLAs participate in feedback on GA metabolism, DELLA-dependent transcription can both interpret and reshape GA status. Quantitative aspects of DELLA action—how strongly a DELLA constrains transcription factor function, how long it remains bound at chromatin, and how it competes with other co-regulators—are therefore likely to be as important as simple presence or absence (Alabadi and Sun 2025; Davière and Achard 2016). Early genome-wide analyses defined DELLA-dependent GA transcriptional targets and feedback regulation of GA metabolism (Zentella et al. 2007).

It is therefore useful to distinguish DELLA abundance from DELLA output. Protein abundance is an important determinant of output, but so are partner availability, post-translational modifications, and chromatin context. This distinction becomes particularly important when interpreting experiments or breeding phenotypes where DELLA levels change only modestly but downstream transcription changes substantially (Huang et al. 2024; Dahal et al. 2025).

The integration of GA with light signaling is one of the best-studied examples of DELLA hub function. PHYTO-

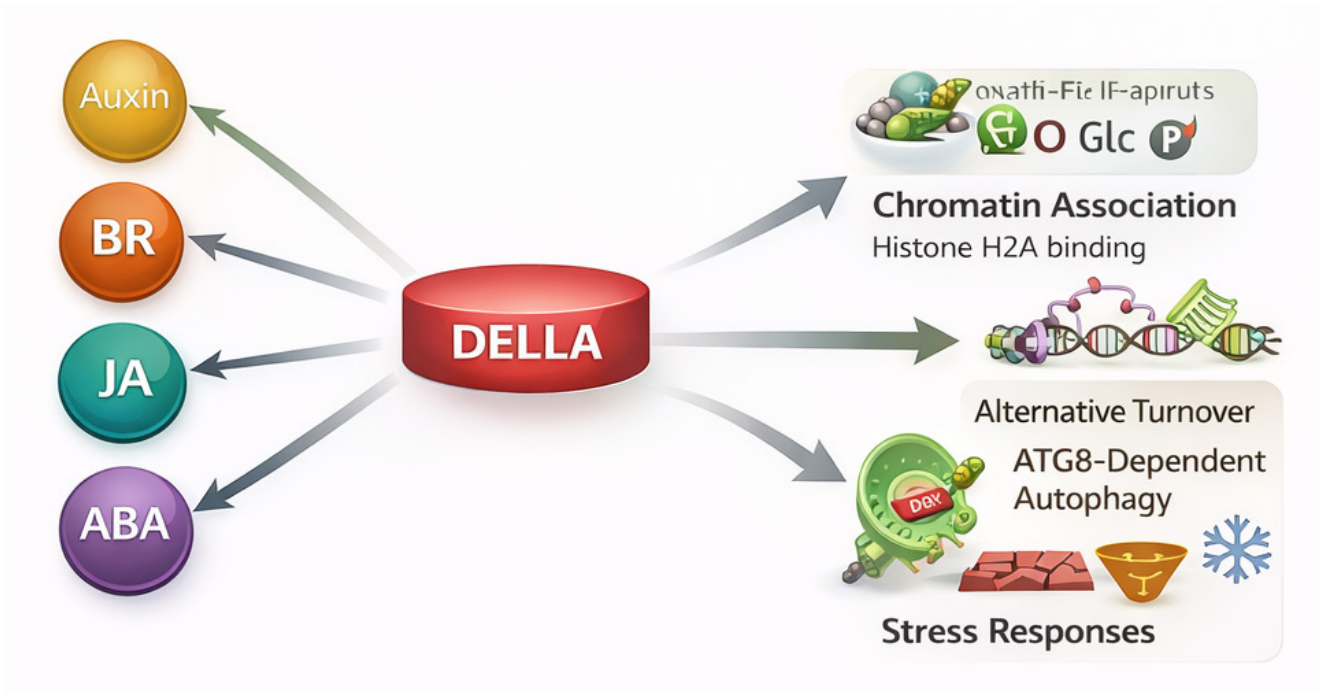

Figure 2. DELLA as an integrative transcriptional control hub. DELLA proteins interact with multiple regulatory modules, including light/PIF, BR/BZR1, and JA/JAZ–MYC networks. DELLA output can also be tuned by post-translational modifications, chromatin association (e.g., histone H2A binding; recruitment of PRC2/HDAC), and alternative turnover such as ATG8-dependent autophagy. The combined network implements context-dependent growth–stress trade-offs.

CHROME INTERACTING FACTORs (PIFs) are bHLH transcription factors that promote elongation growth and shade avoidance. DELLAs interact directly with PIFs and antagonize their ability to promote elongation. The coordinated regulation of *Arabidopsis* development by light and GA provided early evidence that DELLA–PIF interactions are a core mechanism for gating elongation (Feng et al. 2008; de Lucas et al. 2008).

DELLA–PIF regulation is not limited to sequestration. DELLAs can also reduce PIF protein abundance through the ubiquitin–proteasome system, providing an additional layer of repression beyond direct inhibition of transcriptional activity (Li et al. 2016). The existence of both activity inhibition and protein abundance control at the PIF node illustrates a broader point: DELLA hubs can impose multi-layer control on key transcriptional regulators, thereby sharpening growth decisions in response to GA status.

Brassinosteroids (BRs) promote cell expansion and organ elongation, and BR and GA outputs are often synergistic. Molecular crosstalk occurs directly at the level of transcriptional regulators. The BR-responsive transcription factor BZR1 interacts with DELLAs, and this interaction mediates direct signaling crosstalk between BR and GA pathways (Li et al. 2012). A practical interpretation is that BR can drive a growth transcriptional program, while GA reduces DELLA constraint to allow BZR1 and related factors to execute that program. A shared transcription module integrating BR, GA, and light has been described, linking BR/GA signals with phytochrome inputs (Bai et al. 2012). Consistent with this view, GA–BR crosstalk at the DELLA–BZR1 node can tune growth and stress-response outputs in a context-dependent manner (Gallego-Bartolomé et al. 2012).

For systems thinking, DELLA–BZR1 crosstalk demonstrates how a single hub can harmonize multiple growth signals. If BR is high but GA is low, DELLA repression can prevent costly elongation. If both hormones are high, repression is relieved and growth proceeds. Such gating prevents incoherent outputs in a fluctuating environment and contributes to the robustness of growth control.

Defense signaling frequently antagonizes growth. Jasmonates (JAs) are central regulators of defense and wound responses, with JAZ proteins acting as repressors and MYC transcription factors acting as activators of JA responses. DELLA proteins can bind JAZ proteins, enabling GA status to modulate JA signaling outputs. In *Arabidopsis*, DELLAs were shown to bind JAZ and to promote a transcriptional module involving WD-repeat/bHLH/MYB complexes, linking growth and defense regulation (Qi et al. 2014). JA signaling can also interfere with the GA–DELLA–PIF growth cascade and prioritize defense over growth (Yang et al. 2012).

DELLAs also intersect with MYC2, a key JA-responsive transcription factor. DELLA–MYC2 interaction contributes to regulation of specialized metabolism; for example, DELLA interaction with MYC2 influences sesquiterpene synthase gene expression in *Arabidopsis* (Hong et al. 2012). These examples support the view that DELLAs do not simply suppress growth; they re-prioritize transcriptional programs based on hormone context, potentially shifting investment toward defense-associated outputs when GA is low.

Beyond transcription factor binding, recent evidence supports direct chromatin engagement by DELLAs. In *Arabidopsis*, phosphorylation of the DELLA protein RGA was shown to activate DELLA output by promoting binding to histone H2A at chromatin and increasing association with target promoters (Huang et al. 2024). This mechanism provides a clear example of how DELLA activity can increase without a corresponding increase in protein abundance. In principle, phosphorylation-dependent chromatin binding couples external cues (for example, stress-activated kinase pathways) to GA output by tuning promoter residence time of DELLAs.

In rice, DELLA-mediated repression can be maintained through chromatin modification. The rice DELLA protein SLR1 was shown to form a tripartite complex with Polycomb-repressive complex 2 and a histone deacetylase, which together establish a silent chromatin state at GA-inducible genes; GA signaling and SLR1 loss disrupt this state, enabling gene induction (Li et al. 2023). This finding is important for crops because it suggests that DELLA output can include a memory-like chromatin component, potentially making GA responses more switch-like in certain tissues.

The interaction and chromatin mechanisms described above converge on a unifying concept: DELLA proteins function as context-dependent gates that raise or lower the probability that growth-promoting transcriptional states will be adopted. When DELLA output is high, multiple growth regulators (e.g., PIFs, BZR1-associated factors) are constrained, and chromatin at GA-inducible loci may remain in repressive states. When GA neutralizes DELLA output, these constraints are removed, and transcription factor networks can shift rapidly toward growth. Because the set of DELLA partners differs between tissues and developmental stages, the same change in GA can yield different transcriptional outcomes in different contexts.

Beyond canonical SCF-proteasome degradation: tuning DELLA output

Most plants encode multiple DELLA paralogs that act redundantly to some extent, but can show specialization

in expression and partner interactions. This architecture increases robustness, yet it also implies that global manipulation of GA signaling often produces pleiotropy. Tissue-specific or stage-specific modulation of particular DELLA paralogs is therefore an appealing strategy for tailoring phenotypes.

GA signaling is embedded in feedback loops that regulate GA biosynthesis and catabolism, contributing to homeostasis (Olszewski et al. 2002; Gao et al. 2011). From an applied perspective, feedback means that phenotypes can drift across environments or developmental stages. For example, a genotype with increased GA sensitivity might compensate by inducing GA catabolism, reducing the net effect under certain conditions. Designing durable traits therefore benefits from measuring both GA levels and DELLA output in relevant environments.

In addition to ubiquitination, DELLA proteins are regulated by post-translational modifications (PTMs) that can affect stability, localization, partner binding, and chromatin association. A synthesis of PTM mechanisms and concepts is provided by Blanco-Touriñán and colleagues (Blanco-Touriñán et al. 2020). PTMs enable graded control: rather than switching DELLA fully "on" or "off" by changing abundance, cells can modulate DELLA potency through modifications that change how strongly DELLAs bind partners or chromatin. For example, SUMO conjugation of DELLAs can restrain growth in a GA-independent manner under stress (Conti et al. 2014). In addition, O-fucosylation by SPINDLY can enhance DELLA activity and modulate interactions with other growth regulators (Zentella et al. 2017).

From a network perspective, PTMs are attractive because they provide a route for other signaling pathways (e.g., stress-activated kinases or nutrient-responsive modification enzymes) to tune GA responsiveness without changing GA concentration. This can generate rapid, reversible modulation of growth restraint. For example, if a stress cue increases a modification that strengthens DELLA–chromatin binding or DELLA–partner binding, growth can be restrained even if GA levels are not drastically reduced. Conversely, removing such modifications could enable rapid growth recovery. These concepts suggest that PTM enzymes and their upstream regulators may be underappreciated breeding targets for context-specific control (Blanco-Touriñán et al. 2020).

Phosphorylation-dependent activation of RGA via histone H2A binding is a concrete example of this rheostat model (Huang et al. 2024). Mechanistically, phosphorylation may expose or stabilize chromatin-binding interfaces, increasing promoter residence time. Conceptually, PTM-based control offers a rapid route for integrating stress signaling with GA responses because PTMs can change on timescales faster than transcriptional reprogramming of GA metabolism.

A striking recent advance is the demonstration that GA can promote DELLA clearance via autophagy in a specific physiological setting. Under nutrient starvation in darkness, GA-induced seed germination and skotomorphogenesis were shown to depend in part on ATG8-dependent autophagic degradation of DELLA proteins in *Arabidopsis* (Zhang et al. 2025). GA promoted nuclear export of DELLA proteins and ATG8, increased their co-localization in autophagosomes, and stimulated autophagosome formation. These data support a non-canonical route for DELLA turnover that complements SCF-proteasome degradation.

Autophagic DELLA degradation is conceptually informative because it couples hormone signaling to a major cellular recycling pathway. During early growth in darkness, seedlings depend on internal reserves. Autophagy recycles macromolecules and supports energy homeostasis, while GA drives developmental progression. Linking GA signaling to autophagic removal of a growth repressor may ensure that developmental transitions proceed even under resource limitation, while simultaneously mobilizing resources to support growth.

The existence of alternative degradation routes also has methodological implications. Experiments that infer GA signaling solely from proteasome inhibitors or ubiquitination assays may miss context-specific autophagic contributions. Conversely, breeding and engineering strategies that target ubiquitination components may not fully control DELLA output in conditions where autophagy participates. Future work defining when autophagy dominates, and how it interacts with SCF-proteasome turnover, will be important for a unified quantitative model of DELLA regulation.

Structural and biochemical work indicates that GA-bound GID1 can suppress DELLA output without immediate destruction by reshaping DELLA interaction surfaces and weakening binding to downstream regulators (Dahal et al. 2025). This mechanism implies that DELLA abundance is not always a faithful proxy for DELLA activity. From a practical standpoint, interpreting phenotypes may require functional readouts such as transcriptional targets, partner occupancy, or chromatin association, especially in cases where GA levels change rapidly or where DELLA PTMs tune activity.

Network integration: environment-dependent outputs of the GA–DELLA hub

Many environmental stresses reduce growth. GA–DELLA signaling provides an efficient mechanism to implement this: stresses frequently reduce bioactive GA levels, in-

crease DELLA abundance or activity, and restrain elongation and other growth outputs. This restraint conserves resources and can improve survival. Conversely, when conditions are favorable, GA-mediated suppression of DELLA output enables rapid growth and developmental progression.

DELLAs also integrate multiple hormone and environmental signals beyond GA itself. A foundational study demonstrated that DELLAs integrate environmentally activated phytohormonal signals, helping explain how diverse inputs converge on growth restraint (Achard et al. 2006). Subsequent work provided mechanistic bases for this integration at the interaction level: DELLAs bind regulators from multiple hormone pathways and environmental signaling circuits (Davière and Achard 2016; Harberd et al. 2009). Thus, GA can be viewed as a controller that adjusts the effective strength of other pathways by modulating a shared transcriptional gate.

Light quality and photoperiod shape GA metabolism and responsiveness, and DELLA–PIF interactions gate light-regulated elongation programs (Feng et al. 2008; Li et al. 2016). In shade avoidance, increased GA signaling can amplify elongation, whereas DELLA accumulation can prevent elongation when resources are limiting. This gating is important because uncontrolled elongation can reduce mechanical stability and divert resources from reproduction.

Temperature also influences elongation and developmental timing. Although a full thermomorphogenesis review is outside the scope of this mini-review, the central idea is that GA–DELLA outputs depend on temperature-sensitive networks and that DELLA hubs are positioned to translate these networks into growth decisions. In practical terms, this means that GA-related traits selected in one climate may behave differently in another, emphasizing the importance of multi-environment phenotyping.

Abscisic acid (ABA) promotes stress tolerance and often suppresses growth. GA and ABA frequently act antagonistically, particularly during germination. Under water deficit, reduced GA levels and enhanced DELLA output contribute to growth restraint and can support stress-adaptive transcription. From a breeding perspective, this creates a trade-off: genotypes with strong GA responsiveness may perform well under irrigation, whereas genotypes with higher DELLA restraint may better tolerate drought at the cost of maximal growth.

The hub view offers a route to reconcile this trade-off. Rather than globally increasing DELLA output, one can aim to increase DELLA-mediated restraint only under stress or in specific tissues. For example, modulating DELLA chromatin association (Huang et al. 2024) or using stress-responsive promoters for DELLA expression could, in principle, restrain growth during drought while permitting growth recovery after stress release.

Nutrient limitation constrains growth and can shift hormone signaling priorities. The discovery of GA-triggered autophagic DELLA degradation under starvation suggests that plants can reconfigure DELLA control depending on physiological state (Zhang et al. 2025). In some contexts, retaining DELLA repression may conserve resources; in others, especially during germination or establishment, removing DELLA may be required for developmental progression.

This context dependence implies that GA sensitivity should be evaluated not only under optimal nutrition but also under nutrient-limited conditions that resemble field realities. It also suggests that breeding for nutrient use efficiency may inadvertently select for altered GA–DELLA behavior, because growth rate, resource allocation, and hormone regulation are tightly coupled.

Biotic stress responses often antagonize growth, and DELLA hubs can contribute to this antagonism by interacting with defense regulators. DELLA interaction with JAZ proteins and with MYC2 provides routes for coordinating growth and jasmonate-dependent programs (Qi et al. 2014; Hong et al. 2012). Whether DELLA stabilization improves resistance depends on the pathosystem and the environment, but the mechanistic principle is that DELLA-dependent constraint on growth can accompany re-prioritization toward defense-associated transcription.

For crop systems, the key metric is frequently yield stability rather than maximal resistance. Semi-dwarfing alleles already illustrate that increased DELLA restraint can stabilize performance by preventing lodging. In a similar way, moderate DELLA-based restraint might stabilize yield under combined stresses by preventing excessively aggressive growth that becomes unsustainable under pathogen pressure or resource limitation. Testing this idea requires integrated phenotyping that measures both defense outcomes and yield components across environments.

Translational relevance: crop improvement through DELLA tuning

The Green Revolution demonstrated that GA pathways are high-leverage targets for plant architecture. In rice, the semi-dwarf sd1 allele corresponds to a defect in GA biosynthesis that lowers GA levels and reduces plant height (Sasaki et al. 2002). In wheat, Reduced height (Rht) alleles encode DELLA variants that reduce GA responsiveness, leading to semi-dwarfism and improved lodging resistance under high input agriculture (Peng et al. 1999; Alabadi and Sun 2025). These examples illustrate two major intervention strategies: reduce GA input (biosynthesis) or reduce

GA signal output (DELLA responsiveness).

Importantly, these alleles are not simply "growth reducing." By shifting biomass allocation and increasing harvest index, they improved yield stability and allowed crops to exploit fertilizer inputs without lodging. However, their pleiotropic effects can be context dependent. For example, altered emergence traits or seedling vigor can be problematic in some environments. This underscores why modern DELLA engineering should aim for precision rather than maximal stabilization.

Beyond height, GA–DELLA signaling influences branching/tillering, root system architecture, flowering time, seed germination and dormancy, and responses to abiotic stress. Because DELLAs are hubs, modifying their output can affect multiple traits simultaneously. For example, semi-dwarfing alleles that stabilize DELLA activity can change seedling vigor, canopy architecture, and resource allocation, which may in turn influence root development and stress resilience. This breadth can be exploited, but it also demands careful multi-trait evaluation.

This breadth can be exploited, but it also demands careful evaluation. A DELLA intervention that improves lodging resistance may inadvertently alter flowering time or seedling emergence. Conversely, modest changes in root architecture may have large effects on water and nutrient acquisition, which can feed back to hormone levels and further modify growth. Therefore, trait-based design should be supported by mechanistic knowledge of which DELLA paralogs and partners dominate in the tissues of interest.

Genome editing expands the design space for GA–DELLA manipulation. One strategy is cis-regulatory tuning: editing promoters or enhancers to adjust expression of DELLA genes, GID1 receptors, or GA metabolism genes in specific tissues or developmental stages. Because coding sequences remain intact, native interaction specificity is preserved while dosage changes shift the growth–restraint balance. Tissue-specific promoters can, in principle, reduce GA responsiveness in stems while preserving GA functions needed in reproductive tissues or germination.

A second strategy is to tune receptor sensitivity. Because GID1 receptors set the coupling between GA and DELLA neutralization, altering receptor dosage or ligand affinity could shift the GA concentration needed to suppress DELLA output. Receptor tuning may be particularly useful where GA metabolism is constrained by other developmental processes.

A third, more ambitious strategy is interface engineering guided by structural insight. Recent structures show that GA–GID1 can suppress DELLA in proteolysis-independent ways by remodeling DELLA interaction surfaces (Dahal et al. 2025). In principle, modifying DELLA or GID1 interfaces could decouple some outputs from others—for example, retaining enough DELLA function to restrain stem elongation while allowing adequate GA responsiveness in seeds or roots. However, because DELLAs interact with many partners, interface changes can have unpredictable network effects and must be validated across multiple tissues and environments.

Chromatin mechanisms suggest additional intervention points. In rice, DELLA-mediated repression can be maintained via recruitment of chromatin modifiers (Li et al. 2023). In *Arabidopsis*, phosphorylation increased DELLA–chromatin binding (Huang et al. 2024). These results imply that manipulating chromatin regulators that collaborate with DELLAs could tune GA responsiveness without altering GA levels or DELLA abundance directly. Such strategies might be attractive when breeders wish to preserve hormone homeostasis while adjusting transcriptional thresholds.

Because GA–DELLA outputs are environment dependent, any DELLA-based trait should be tested across representative climates, nutrient regimes, and stress combinations. Second, partial and tissue-specific perturbations are usually more robust than strong constitutive changes. Third, feedback on GA metabolism can attenuate interventions, so measuring GA levels, receptor expression, and DELLA activity can help diagnose why a genotype behaves differently across environments (Olszewski et al. 2002; Gao et al. 2011). Fourth, phenotyping should include traits beyond height. Seedling emergence, root architecture, phenology, and stress recovery dynamics often determine yield stability.

Where possible, it is valuable to monitor transcriptional or biochemical markers of GA–DELLA output (for example, expression of GA-responsive genes or DELLA-regulated modules) to connect genotype to mechanism. Such mechanistic phenotyping can shorten breeding cycles by revealing whether a candidate allele shifts GA input (hormone levels), signal perception (receptor sensitivity), or transcriptional gating (DELLA output).

Conclusions and outlook

The GA–GID1–DELLA module is a prototypical plant hormone signaling system built on de-repression. Canonically, GA binding to GID1 enables DELLA recognition by SCF ubiquitin ligases and 26S proteasome degradation, thereby derepressing growth (McGinnis et al. 2003; Dill et al. 2004; Murase et al. 2008; Harberd et al. 2009). This logic explains how plants can rapidly shift gene expression and growth in response to changes in GA levels.

Recent work broadens this canonical view. GA–GID1 can suppress DELLA output in a proteolysis-independent

manner (Ariizumi et al. 2008; Dahal et al. 2025), DELLA activity can be tuned via chromatin association and phosphorylation (Huang et al. 2024), DELLA repression can be maintained through recruitment of chromatin modifiers (Li et al. 2023), and in specific physiological settings GA can promote DELLA degradation via autophagy (Zhang et al. 2025). Together, these findings strengthen the view that DELLA proteins are integrative hubs whose output depends on abundance, conformation, modifications, interaction partners, and chromatin engagement.

For crop improvement, the hub view suggests that precision tuning will outperform blunt stabilization. The most promising interventions are likely to be those that adjust DELLA output in the right tissue, at the right time, and under the right environmental conditions. With expanding structural insight, chromatin mechanisms, and genome editing capacity, the GA–DELLA module remains a compelling target for rational design of growth and yield stability traits.

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References

Achard P, Cheng H, De Grauwe L, Decat J, Schoutteten H, Moritz T, Van Der Straeten D, Peng J, Harberd NP (2006) Integration of plant responses to environmentally activated phytohormonal signals. Science 311(5757):91-94. doi:10.1126/science.1118642.

Alabadi D, Sun TP (2025) Green Revolution DELLA proteins: functional analysis and regulatory mechanisms. Annu Rev Plant Biol 76(1):373-400. doi:10.1146/annurev-arplant-053124-050732.

Ariizumi T, Lawrence PK, Steber CM (2011) SNEEZY and SLEEPY1 control the DNA-binding activity of E2F and the DELLA proteins in Arabidopsis. Plant Physiol 155(2):765-775. doi:10.1104/pp.110.166272.

Ariizumi T, Murase K, Sun TP, Steber CM (2008) Proteolysis-independent downregulation of DELLA repression in Arabidopsis by the gibberellin receptor GID1. Plant Cell 20(9):2447-2459. doi:10.1105/tpc.108.058487.

Bai MY, Shang JX, Oh E, Fan M, Bai Y, Zentella R, Sun TP, Wang ZY (2012) Brassinosteroid, gibberellin and phytochrome signals integrate to regulate a transcription module in Arabidopsis. Nat Cell Biol 14(8):810-817. doi:10.1038/ncb2546.

Blanco-Touriñán N, Serrano-Mislata A, Alabadí D (2020) Regulation of DELLA proteins by post-translational modifications. Plant Cell Physiol 61(11):1891-1901. doi:10.1093/pcp/pcaa113.

Conti L, Nelis S, Zhang C, Woodcock A, Swarup R, Galbiati M, Tonelli C, Napier R, Hedden P, Bennett M, Sadanandom A (2014) Small ubiquitin-like modifier protein SUMO enables plants to control growth independently of the phytohormone gibberellin. Dev Cell 28(1):102-110. doi:10.1016/j.devcel.2013.12.004.

Dahal P, Wang Y, Hu J, Park J, Forker K, Zhang ZL, Sharma K, Borgnia MJ, Sun TP, Zhou P (2025) Structural insights into proteolysis-dependent and -independent suppression of the master regulator DELLA by the gibberellin receptor. Proc Natl Acad Sci U S A 122(32):e2511012122. doi:10.1073/pnas.2511012122.

Davière JM, Achard P (2016) A pivotal role of DELLAs in regulating multiple hormone signals. Mol Plant 9(1):10-20. doi:10.1016/j.molp.2015.09.011.

de Lucas M, Davière JM, Rodríguez-Falcón M, Pontin M, Iglesias-Pedraz JM, Lorrain S, Fankhauser C, Blázquez MA, Titarenko E, Prat S (2008) A molecular framework for light and gibberellin control of cell elongation. Nature 451(7177):480-484. doi:10.1038/nature06520.

Dill A, Thomas SG, Hu JH, Steber CM, Sun TP (2004) The Arabidopsis F-box protein SLEEPY1 targets gibberellin signaling repressors for gibberellin-induced degradation. Plant Cell 16(6):1392-1405. doi:10.1105/tpc.020958.

Feng S, Martinez C, Gusmaroli G, Wang Y, Zhou J, Wang F, Chen L, Yu L, Iglesias-Pedraz JM, Kircher S, Schäfer E, Fu X, Fan LM, Deng XW (2008) Coordinated regulation of Arabidopsis thaliana development by light and gibberellins. Nature 451(7177):475-479. doi:10.1038/nature06448.

Gallego-Bartolomé J, Minguet EG, Grau-Enguix F, Abbas M, Locascio A, Thomas SG, Alabadí D, Blázquez MA (2012) Molecular mechanism for the interaction between gibberellin and brassinosteroid signaling pathways in Arabidopsis. Proc Natl Acad Sci U S A 109(33):13446-13451. doi:10.1073/pnas.1119992109.

Gao XH, Xiao SL, Yao QF, Wang YJ, Fu XD (2011) An updated GA signaling 'relief of repression' regulatory model. Mol Plant 4(4):601-606. doi:10.1093/mp/ssr046.

Gomi K, Sasaki A, Itoh H, Ueguchi-Tanaka M, Ashikari M, Kitano H, Matsuoka M (2004) GID2, an F-box subunit of the SCF E3 complex, specifically interacts with phosphorylated SLR1 protein and regulates the gibberellin response in rice. Plant J 37(4):626-634. doi:10.1111/j.1365-313X.2003.01990.x.

Griffiths J, Murase K, Rieu I, Zentella R, Zhang ZL, Powers SJ, Gong F, Phillips AL, Hedden P, Sun TP, Thomas SG (2006) Genetic characterization and functional analysis of the GID1 gibberellin receptors in Arabidopsis. Plant Cell 18(12):3399-3414. doi:10.1105/tpc.106.047415.

Harberd NP, Belfield E, Yasumura Y (2009) The angiosperm gibberellin–GID1–DELLA growth regulatory mechanism: how an 'inhibitor of an inhibitor' enables flexible response to fluctuating environments. Plant Cell 21(5):1328-1339. doi:10.1105/tpc.109.066969.

Hong GJ, Xue XY, Mao YB, Wang LJ, Chen XY (2012) Arabidopsis MYC2 interacts with DELLA proteins in regulating sesquiterpene synthase gene expression. Plant Cell 24(6):2635-2648. doi:10.1105/tpc.112.098749.

Huang X, Zentella R, Park J, Reser L, Bai DL, Ross MM, Shabanowitz J, Hunt DF, Sun TP (2024) Phosphorylation activates master growth regulator DELLA by promoting histone H2A binding at chromatin in Arabidopsis. Nat Commun 15(1):7694. doi:10.1038/s41467-024-52033-x.

Li J, Li Q, Wang W, Zhang X, Chu C, Tang X, Zhu B, Xiong L, Zhao Y, Zhou DX (2023) DELLA-mediated gene repression is maintained by chromatin modification in rice. EMBO J 42(21):e114220. doi:10.15252/embj.2023114220.

Li K, Yu R, Fan LM, Wei N, Chen H, Deng XW (2016) DELLA-mediated PIF degradation contributes to coordination of light and gibberellin signalling in Arabidopsis. Nat Commun 7:11868. doi:10.1038/ncomms11868.

Li QF, Wang C, Jiang L, Li S, Sun SS, He JX (2012) An interaction between BZR1 and DELLAs mediates direct signaling crosstalk between brassinosteroids and gibberellins in Arabidopsis. Plant Cell 24(7):2859-2874. doi:10.1105/tpc.112.098004.

McGinnis KM, Thomas SG, Soule JD, Strader LC, Zale JM, Sun TP, Steber CM (2003) The Arabidopsis SLEEPY1 gene encodes a putative F-box subunit of an SCF E3 ubiquitin ligase. Plant Cell 15(5):1120-1130. doi:10.1105/tpc.010827.

Murase K, Hirano Y, Sun TP, Hakoshima T (2008) Gibberellin-induced DELLA recognition by the gibberellin receptor GID1. Nature 456(7221):459-463. doi:10.1038/nature07519.

Olszewski N, Sun TP, Gubler F (2002) Gibberellin signaling: biosynthesis, catabolism, and response pathways. Plant Cell 14(suppl 1):S61-S80. doi:10.1105/tpc.010476.

Peng J, Richards DE, Hartley NM, Murphy GP, Devos KM, Flintham JE, Beales J, Fish LJ, Worland AJ, Pelica F, Sudhakar D, Christou P, Snape JW, Gale MD, Harberd NP (1999) 'Green revolution' genes encode mutant gibberellin response modulators. Nature 400(6741):256-261. doi:10.1038/22307.

Qi T, Huang H, Wu D, Yan J, Qi Y, Song S, 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(3):1118-1133. doi:10.1105/tpc.113.121731.

Sasaki A, Ashikari M, Ueguchi-Tanaka M, Itoh H, Nishimura A, Swapan D, Ishiyama K, Saito T, Kobayashi M, Khush GS, Kitano H, Matsuoka M (2002) Green revolution: a mutant gibberellin-synthesis gene in rice. Nature 416(6882):701-702. doi:10.1038/416701a.

Shimada A, Ueguchi-Tanaka M, Nakatsu T, Nakajima M, Naoe Y, Ohmiya H, Kato H, Matsuoka M (2008) Structural basis for gibberellin recognition by its receptor GID1. Nature 456(7221):520-523. doi:10.1038/nature07546.

Sun TP (2011) The molecular mechanism and evolution of the GA–GID1–DELLA signaling module in plants. Curr Biol 21(9):R338-R345. doi:10.1016/j.cub.2011.02.036.

Ueguchi-Tanaka M, Ashikari M, Nakajima M, Itoh H, Katoh E, Kobayashi M, Chow TY, Hsing YI, Kitano H, Yamaguchi I, Matsuoka M (2005) Gibberellin Insensitive Dwarf1 encodes a soluble receptor for gibberellin. Nature 437(7059):693-698. doi:10.1038/nature04028.

Yang DL, Yao J, Mei CS, Tong XH, Zeng LJ, Li Q, Xiao LT, Sun TP, Li J, Deng XW, Lee CM, Thomashow MF, Yang Y, He ZH (2012) Plant hormone jasmonate prioritizes defense over growth by interfering with gibberellin signaling cascade. Proc Natl Acad Sci U S A 109(19):E1192-E1200. doi:10.1073/pnas.1201616109.

Zentella R, Zhang ZL, Park M, Thomas SG, Endo A, Murase K, Fleet CM, Jikumaru Y, Nambara E, Kamiya Y, Sun TP (2007) Global analysis of DELLA direct targets in early gibberellin signaling in Arabidopsis. Plant Cell 19(10):3037-3057. doi:10.1105/tpc.107.054999.

Zentella R, Sui N, Barnhill B, Hsieh WP, Hu J, Shabanowitz J, Boyce M, Olszewski NE, Zhou P, Hunt DF, Sun TP (2017) The O-fucosyltransferase SPINDLY activates nuclear growth repressor DELLA. Nat Chem Biol 13(5):479-485. doi:10.1038/nchembio.2320.

Zhang S, Jiang L, Chen H, Liu H, Xiong M, Niu Y, Xie L, Wang L, Mao Z, Guo T, Wang W, Yang HQ (2025) Gibberellin triggers ATG8-dependent autophagic degradation of DELLA proteins to promote seed germination and skotomorphogenesis under nutrient starvation in Arabidopsis. Mol Plant 18(12):2101-2118. doi:10.1016/j.molp.2025.10.011.