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New mechanistic links between sugar and hormone signalling networks

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Plant growth and development must be coordinated with metabolism, notably with the efficiency of photosynthesis and the uptake of nutrients. This coordination requires local connections between hormonal response and metabolic state, as well as long-distance connections between shoot and root tissues. Recently, several molecular mechanisms have been proposed to explain the integration of sugar signalling with hormone pathways. In this work, DELLA and PIF proteins have emerged as hubs in sugar-hormone cross-regulation networks.

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Introduction

Plants are autotrophic organisms that rely on light to produce sugars. Not surprisingly, in addition to acting as an essential source for carbon metabolism in plants, sugars also act as signalling molecules that modulate a vast array of plant developmental processes [1]. In both of these contexts, plants must manage their carbon resources carefully. The amount of carbon that will be fixed the next day is largely unpredictable at dusk, yet, during the night, starch degradation is tightly controlled so that it is almost but not totally exhausted at dawn [2].

Environmental stresses further challenge energy balance. With growth itself consuming energy, trade-offs exist between growth and adaptation to unfavourable environmental conditions. Plant hormones play an essential role in plant growth and development. Multiple mechanisms exist to coordinate hormone-driven processes so that they are energetically compatible with the carbon status of the plant. These mechanisms may act by modulating hormone synthesis, transport and signalling, so that the hormonal responses promoting growth are dampened in conditions of limited carbon resources. Sugar-sensing as a mechanism for fine-tuning of the hormonal response is of critical importance [3]. Feedback mechanisms that connect back in the opposite direction are also likely, although mechanisms for controlling hormone production and response are more straightforward to regulate than the often unpredictable light-driven production of sugar. Here, we will focus on the ways plants adapt their hormone-dependent processes on the metabolic status of the plant, and how this interaction shapes the plant to improve its overall fitness in a given environment.

Metabolic interactions, long-range signalling and hormones

Light is the most powerful environmental cue for a photosynthetic organism. Alongside the advantages of using light to produce your own food supply, photoautotrophy brings a number of significant regulatory challenges. These challenges are especially acute in multicellular plants, where carbon fixation is restricted to a subset of cells (a population that changes in number and location over developmental time), and these cells need to then share their metabolic products with cells at a distance. To compound this problem, cellular life requires a sensitive balancing between the amount of fixed carbon and other raw materials, like nitrogen and water. Functional equilibrium is a term that has been used to describe the way plants promote growth in above- or belowground tissues to constantly correct metabolic imbalances [4]. For example, in bright light where fixed carbon might be accumulating at a rapid rate, the plant devotes energy to increase the uptake of nitrogen through induction of nitrogen transporters and increased production of lateral roots [5].

The plant must balance metabolic demands across the plant, while also managing dramatic daily fluctuations in carbon fixation rates. During the day, growth is fuelled by sugars produced by photosynthesis, while at night growth relies on starch [6]. *Arabidopsis* mutants defective in either starch synthesis or degradation are smaller than wild-type plants, indicating that starch metabolism at night is required for growth [7•,8]. Many genes involved in hormone synthesis and signalling are expressed at dawn, coincident with the maximal rate of growth in the same experimental conditions [9]. The peak of growth at dawn requires light [10], but it does not correlate with maximum sugar availability, which occurs later in the day. This result leaves open the precise relationship between growth

stimulated by sugars and growth stimulated by hormones. Any organ-specific responses to daily fluctuations in carbon metabolism are also largely unknown.

Understanding how plants communicate carbon status over long distances is critical for increasing our knowledge of plants as integrated systems. Plant hormones and sugars themselves are obvious candidates for this job. The glucose 'sensor' hexokinase HXK1 has been shown to be important for nutrient, light and hormone signalling in *Arabidopsis*, and the HKX1 mutant *glucose insensitive2* (*gin2*) is insensitive to auxin and hypersensitive to cytokinins [11]. Glucose downstream signalling also involves the target-of-rapamycin (TOR) signalling pathway that controls meristem activation via different transcriptional activators [12]. Anthocyanin biosynthesis is induced by sugars, and cytokinins can enhance this induction via the cytokinin response regulators ARR1, ARR10 and ARR12, [13]. This signalling cascade involves transcriptional activation of MYB75/PAP1 by LONG HYPOCOTYL 5 (HY5) [14].

During germination and early seedling growth, there is strong evidence that sugars and hormones interact closely. The sucrose non-fermenting kinase 1 (SnRK1) is under control of hormones (auxin, CKs, ABA) and sugars, and has a role in coordinating signals during cotyledon growth and differentiation [15]. Two recent reports suggest that sucrose itself, rather than auxin, is acting as a long-distance signal in promoting root growth [16] and bud dormancy [17]. Both of these studies have strong evidence that sucrose is getting to the target tissues, but current methodologies make it difficult to get the needed temporal and spatial resolution to be sure that the sucrose effect is fully independent of auxin. New technologies like fluorescent-labeled auxin [18], sugar sensors [19,20] and methods to quantify auxin at the tissue-level [21] may resolve the extent to which these signals act in sequence, act independently or some synergistic combination of the two possibilities.

Dealing with high sugar levels: the sugar-ABA connection

Arabidopsis seedlings cannot survive growth on high sugar-containing media (e.g. 6% glucose). This phenotype led to elegant screens for mutants that are insensitive to sugars. Interestingly, many of these mutants have defects in ABA synthesis or signalling (see [22] for a review). Although this might suggest that the use of high sugar levels selected for mutants tolerant to osmotic stress, insensitivity to sugars in these mutants is uncoupled from the role of carbohydrates as an osmoticum. Two models are possible for explaining the overlap between sugar and ABA signalling. High sugar levels may trigger enhanced ABA synthesis and this in turn activates ABA signalling [23] or ABA signalling activates shared targets of a separate sugar signalling pathway [24]. A synergistic interaction between ABA and sugar signalling is supported by the fact that ABA alone cannot regulate some sugar-dependent genes, although it has a clear enhancing effect when provided with sucrose [25]. A key-element in the ABA-sugar connection is the transcription factor ABI4 [26]. Several sugar-insensitive mutants are allelic to *abi4*, and ABI4 is proposed to regulate sugar-responsive genes by binding directly to their promoters (reviewed by [22]). While high sugar induces *ABI4* expression, this may be a consequence of the developmental arrest triggered by high sugar [24].

A new component of the sugar-ABA signalling pathway was recently identified using natural variation analysis in Arabidopsis [27•]. The Col-0 and C24 accessions in Arabidopsis differ in their sensitivity to high (5.5%) glucose. It was discovered that the QTL responsible for this difference coincides with the *ANAC60* gene, which displays distinct splicing variants in C24 and Col-0. The Col-0 variant is localized in the nucleus, while the C24 variant is membrane-localized. *ANAC60* induction by glucose requires ABA signalling and ABI4 activates the ANAC60 promoter, thus placing *ANAC60* in the sugar-ABA signalling pathway. Localization of ANAC60 in the nucleus attenuates ABA signalling and results in sugar insensitivity, thus providing a potential negative feedback mechanism on ABI4 action. The involvement of ABI4 linking sugar and ABA signalling has been studied mostly during germination, and it would be interesting to know if it plays a role also in other environmental conditions affecting sugar and ABA, such as during stress conditions.

Auxin, cytokinins, sugars and growth

Auxin and cytokinins are additional hormones with clear links to sucrose sensing and signalling, and all three compounds can function as short- and long-distance signalling molecules. This feature has led to the suggestion that all three play a role in integration of growth and development between shoots and roots. The multi-level interactions between auxins, cytokinins and sucrose are highly complex and not well understood, even in the model *Arabidopsis*. Further complicating matters, many studies involve manipulation of hormone and sugar levels, and, although this has given very valuable information, it may not accurately reflect *in vivo* conditions.

Several recent studies have connected sucrose to the production of auxin [28,29,30•], a strong candidate for a long-distance signal promoting lateral root production. Auxin biosynthesis is induced by soluble sugars, and daily fluctuations in sugar content are correlated with fluctuations in auxin levels [30•]. The circadian clock also gates sensitivity to auxin treatment [31]. Glucose treatment of *Arabidopsis* seedlings induces expression of multiple genes encoding auxin biosynthetic enzymes, including *YUCCA8* and *YUCCA9* [30•], consistent with an earlier report that a putative maize *YUCCA* gene is strongly

induced by glucose [28]. Sucrose supplementation, required for rhythmic hypocotyl elongation, induces *YUCCA9* in shoots but not roots, a similar pattern seen for several other auxin-induced genes [29,32]. Interestingly, sucrose effects on auxin levels are more pronounced in roots than in shoots, suggesting sugars may impact auxin transport and/or conjugation pathways as well. The growth promoting effect of sucrose is likely through its effect on auxin, as it can be partially mimicked by directly adding auxin and can be blocked by adding polar auxin inhibitors [29]. This mechanism is reminiscent of shade avoidance syndrome, where shade detected primarily in the cotyledons is transmitted by induction of auxin biosynthesis and increased rootward auxin transport [33•,34]. Auxin signalling has also been linked to sugar metabolism. For example, down-regulation of the tomato auxin response repressor *SlARF4* led to a dramatic increase in chloroplast number and an increase in sugar and starch content in the fruit [35].

Cytokinin is also critical for growth, senescence and stress tolerance, and regulation of cytokinin levels has been used to engineer important crop species (reviewed in [36]). Overexpression of the cytokinin biosynthetic gene *ISOPENTENYLTRANSFERASE* (*IPT*) gene under a stress-induced promoter increased drought stress tolerance in rice [37]. The transgenic plants showed increased sucrose content in source tissues and maintained nitrate acquisition in the root system. In *Arabidopsis* seedlings, high CO_2 levels increased root growth, especially under abiotic stress conditions [38]. Low pH and high CO_2 led to an accumulation of glucose, sucrose and starch, as well as an increase in auxin and a decrease in cytokinin levels. These conditions were associated with an increase in lateral root number. A role for cytokinin biosynthesis in storage-organ formation was recently discovered [39•]. Overexpression of the *LONELY GUY 1* (*LOG1*) gene in tomato induced tuber-like organs from the axillary meristems. This indicates that cytokinins play an important role in storage-organ formation and in the regulation of source/sink relationships.

Sugars and cytokinins interact during plant growth and development, and these interactions can be both direct and indirect, and involve cell-specific and long-distance interactions. Transcript profiling of *Arabidopsis* seedlings after glucose and cytokinin treatment showed that many genes involved in stress responses and developmental pathways were affected [40]. Glucose and cytokinins acted both agonistically and antagonistically on gene expression, and glucose had a strong effect on genes involved in cytokinin metabolism and signalling. Cytokinin deficiency, caused by constitutive overexpression of cytokinin oxidase (*CKX*) genes, leads to drastic changes in root and shoot growth [41]. The molecular mechanisms are only partly known, and involve changes in the cell cycle and in photosynthetic activity, altered carbohydrate distribution and source/sink relations.

Gibberellins, jasmonates, brassinosteroids, sugars, and growth

Daily fluctuations in gibberellin (GA) sensitivity track the fluctuations in sugar levels and are regulated by the circadian clock [31,42]. The growth-repressing, GA-regulated DELLA proteins are more stable during the day, consistent with higher sensitivity to gibberellins at night [42]. This is in agreement with the evidence in rice and *Arabidopsis* of higher GA content at dusk [7•,43], possibly inducing the destabilization of DELLAs at night. The higher GA level detected in the late afternoon correlates well with the diurnal fluctuations in expression of GA biosynthetic genes, peaking in the afternoon [7•]. Mutants defective in starch metabolism suffer from starvation at night and this negatively affects their growth at night [6]. Additionally, it was shown that starvation at night represses the mRNA level of kaurene synthase, leading to low level of kaurene, a precursor of GA [7•]. Thus, it seems that the level of GA is regulated so that growth is reduced when plants are suffering from carbon starvation.

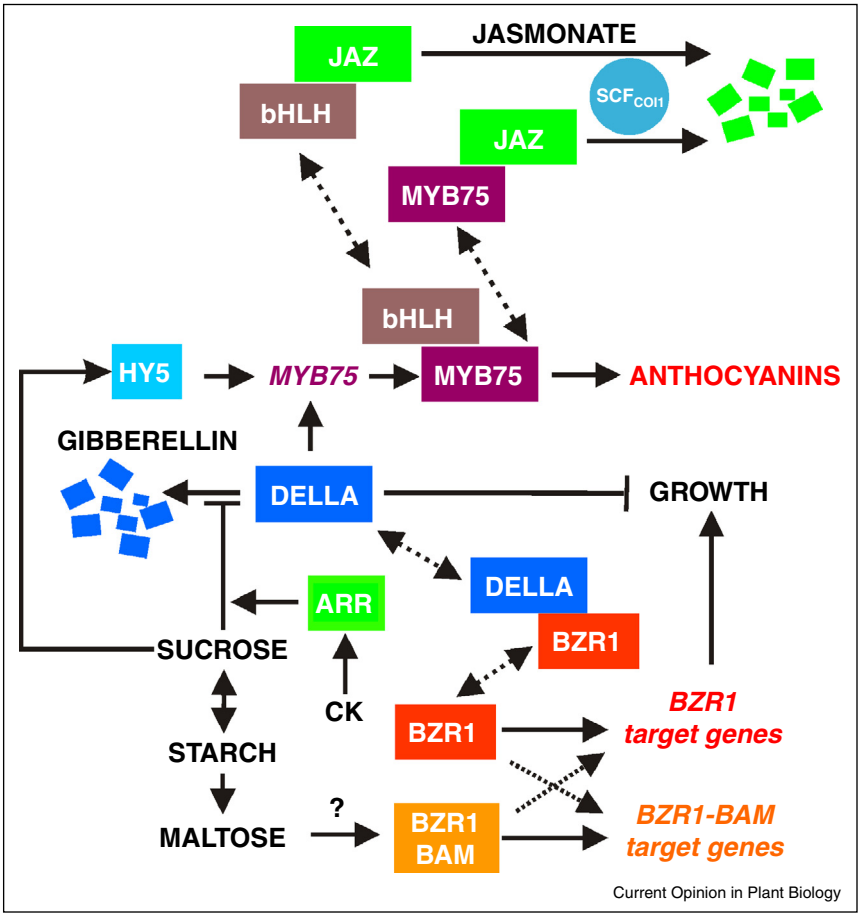
Recent evidence showing that sucrose stabilizes DELLA proteins [44] provides an explanation for the negative effect of GA [45] on the sucrose-dependent induction of the anthocyanin biosynthetic pathway [46,47]. Loreti *et al.* showed that GA repress the expression of several sucrose-induced genes involved in anthocyanin synthesis [45]. This repressive effect was strongly reduced in *gai*, a mutant expressing a stabilized DELLA protein, thus indicating that DELLAs are involved in the sucrose-GA interaction [45]. Li *et al.* showed that sucrose, but not glucose, stabilizes the DELLA protein REPRESSOR OF GA (RGA) [44]. Given that DELLA proteins are stabilized by sucrose [44], it would be tempting to speculate that the increased DELLA level during the day [42] is due to the increased sucrose level during the day. However, a higher growth rate during the day was observed in a starchless mutant that displays much higher sucrose levels during the light period [6]. This increase in growth during the day would be in disagreement with a higher DELLA protein level. The slower growth at night in the starchless mutants [6] is likely due to the lack of starch to fuel growth, together with the adjustment of the GA level to match the lower growth potential deriving from the lack of sugars at night [7•]. The dwarfism of GA-deficient mutants is, instead, uncoupled from carbon availability [48] indicating that GA is primarily required for growth.

The importance of DELLAs in the regulation of a very large number of plant developmental and stress response programmes [49] suggests that they represent a point of convergence for the hormonal and sucrose-dependent

regulatory networks (Figure 1). The induction of anthocyanin synthesis is a sucrose-specific phenomena [46], and sucrose-dependent stabilization of DELLAs provides a relatively simple mechanism to connect sugars with other signalling pathways. DELLAs activate transcription of PAP1/MYB75 [50], the sucrose-induced transcription factor required for anthocyanin synthesis [47]. Anthocyanin biosynthesis is positively regulated by jasmonate, and this activation can be synergistically enhanced by sucrose [45]. Jasmonates act by releasing the bHLH and MYB factors required for anthocyanin synthesis from repression by JASMONATE-ZIM-DOMAIN PROTEIN (JAZ) proteins [51].

DELLAs also connect sucrose and GA to brassinosteroids (BR). The BR and GA pathways closely interact through direct interaction of DELLA proteins with the BRASSINAZOLE-RESISTANT 1 (BZR1) transcription factor [52]. In this context, stabilization of DELLAs by sucrose [44] would result in a higher DELLA level, sequestering BRZ1 and thus contributing to repressed growth. The situation *in vivo* may be more complicated, as DELLAs effect on growth changes during development [53•]. The recent evidence showing that two β-amylases (BAM7 and BAM8) possess BZR1-type DNA binding domains raise the exciting hypothesis that BAM7 and BAM8 could represent maltose sensors linking starch metabolism to BR signalling [54]. The *bam7 bam8* mutant is dwarf, and this is indeed suggestive of a role of these nuclear-localized β-amylases in regulating growth, probably by competing with BZR1 activity. The BZR1-BAM regulated gene expression does not appear to correlate with maltose

Figure 1



Schematic representation of hormone-sugar interactions for the regulation of plant growth and anthocyanin synthesis. Sucrose influences anthocyanin synthesis by activating the transcription factor MYB75 through HY5 [14]. Sucrose also affects DELLA protein stability [44] positively influencing MYB75 transcription and, as a consequence, anthocyanin synthesis. Stabilization of DELLAs by sucrose [44] would result in a higher DELLA level, sequestering BRZ1 and thus contributing to repressed growth. Gibberellins antagonize anthocyanin synthesis by triggering the degradation of DELLA proteins. Jasmonates act by releasing the bHLH and MYB factors required for anthocyanin synthesis from repression by JAZ proteins [51]. CK enhance the sucrose-dependent pathway trough the action of ARR proteins. Two β-amylases (BAM7 and BAM8) possess BZR1-type DNA binding domains and thus could represent maltose sensors linking starch metabolism to BR signalling [54]. See text for additional details.

level; however, BAM8's function as a transcriptional activator, although independent of catalysis, requires an intact substrate-binding site (Figure 1; [55•]).

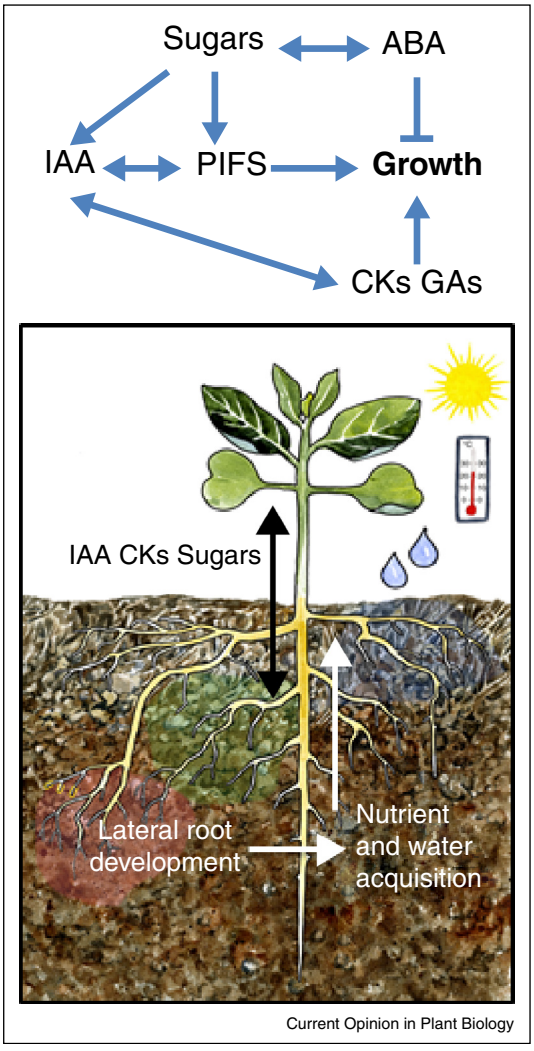
PIFs connect sucrose to hormones and environmental signals

The Phytochrome-Interacting Factor (PIF) family of transcription factors seem to have their basic helix-loop-helices in every process involving light, temperature and growth [56]. As their family name implies, they were originally identified through their direct interaction with phytochromes [57]. Activated phytochromes target PIFs for destruction, yet their relationship is far from a linear hierarchy of action [58]. PIFs attenuate the light signal through negative feedback on phytochrome transcription, as well as by bringing them along when they are targeted for proteasome-mediated degradation [59]. A combination of circadian clock and light regulation control the activity of PIF4 and PIF5, leading to predictable daily oscillations in seedling growth rates [60]. These PIF-driven growth cycles depend on supplying seedlings with exogenous sucrose [32,61]. PIFs, working in an antagonistic regulatory circuit with HY5, integrate light and temperature cues to regulate photosynthetic genes [62]. Consistent with this central role at the crossroads of environment and growth responses, the activity of PIF4 and PIF5 have also recently been linked to dark-induced senescence [63]. Evolution may be using the PIF subnetwork to optimize growth responses in new environments, as a recent study of natural variation in 77 *Arabidopsis* accessions revealed a clear link between variation in clock-regulated expression of *PIF4* and growth rate [64].

Complexity can also be found in the relationship of PIFs and auxin. Work on temperature and shade avoidance have placed PIFs upstream of *YUCCA* genes and auxin biosynthesis [33•,65,66,67], yet auxin response requires PIF function [29,68] placing them downstream of auxin as well (Figure 2). It is equally challenging to draw a linear network between sugar, PIFs and auxin. Glucose induction of auxin biosynthesis was strongly enhanced in a *pif1 pif3 pif4 pif5* (*pifQ*) mutant background and strongly repressed in plants overexpressing *PIF5* [30•]. In contrast, the higher levels of auxin promoted by sucrose supplementation were lost in *pifQ* mutants, although the induction of *YUCCA8* expression was enhanced [29].

PIFs directly target a number of genes involved in chloroplast development and optimal function [69,70,71], providing an additional connection between PIFs and carbon metabolism. In addition, PIFs interact with a number of other transcription factors, including key regulators of the auxin, gibberellins and brassinosteroid response pathways [72]. While it is unlikely that all of these factors are interacting in all tissues at all times, and there is evidence that composition and function of growth promoting complexes are dynamic [53•], a refined spatial and temporal PIF interaction map may provide critical clues about cellular state. A multiscale mathematical model of growth offers great promise for eventually

Figure 2



Sugars and plant hormones are key components in growth regulation. Light, temperature and other environmental factors are sensed by the aerial parts of the plant. This will affect photosynthesis and the production of sugars, in turn regulating the levels of IAA and PIF function. CKs, GAs and ABA also affect growth, and these signalling pathways are linked with sugar and nutrient status. CKs, IAA and sugars function as long-distance signals, affecting e.g. lateral root development and shoot branching. IAA and sugars can be transported from shoot to root, inducing lateral root development in order to increase the uptake of water and nutrients from the soil, in turn increasing the growth capacity of the shoot. Signalling from root to shoot is also important for coordination of growth and development of the whole plant. We are just starting to untangle these pathways, discovering interacting partners and regulatory loops. In the future, multiscale modeling of these pathways will be very helpful to integrate all the information in order to get a better understanding of the regulation of plant growth.

synthesizing metabolic and gene regulatory networks into tools able to predict plant performance in new environments [73•], as well as highlighting the most functionally important of the potential high-order protein complexes.

Concluding remarks

Sugars have long been appreciated as building blocks required for plant growth. Their regulatory roles are just beginning to be fully acknowledged. Not surprisingly, hormonal signalling pathways are major targets for sugar regulation: survival depends on integration of growth and development with the metabolic status of the plant. Sugar levels fluctuate depending on the efficiency of photosynthesis, as well as on energy and growth requirements. Furthermore, the spatiotemporal map of sugar status is highly dynamic. Sugars are translocated from source to sink tissues, making carbohydrates very interesting as potential long-range signalling molecules. The recent report indicating that sucrose rather than auxin is possibly responsible for apical dominance [17] suggests that sugars can indeed exert an important differentiation role. Despite rapid, exciting new evidences of sugar-hormone cross-regulation, the identity of the molecular points of convergence of these signalling pathways is still quite limited, although DELLA and PIF proteins are good candidates for molecular hubs operating at the crossroads of many pathways. The regulatory network, is, however, probably more complex and must include a role for sugars in the regulation of hormone synthesis as well as hormone signalling. A representation that is possibly closer to reality is that of a interaction network of the hormonal signalling pathways with an array of signalling pathways related to the nutrient and energy status of the plants.

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References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

1. Lastdrager J, Hanson J, Smeekens S: **Sugar signals and the control of plant growth and development**. *J Exp Bot* 2014, **65**:799-807.

2. Graf A, Schlereth A, Stitt M, Smith AM: **Circadian control of carbohydrate availability for growth in Arabidopsis plants at night**. *Proc Natl Acad Sci U S A* 2010, **107**:9458-9463.

3. Ruan YL: **Sucrose metabolism: gateway to diverse carbon use and sugar signaling**. *Annu Rev Plant Biol* 2014, **65**:33-67.

4. Poorter H, Niklas KJ, Reich PB, Oleksyn J, Poot P, Mommer L: **Biomass allocation to leaves, stems and roots: meta-analyses of interspecific variation and environmental control**. *New Phytol* 2012, **193**:30-50.

5. Forde BG: **Local and long-range signaling pathways regulating plant responses to nitrate**. *Annu Rev Plant Biol* 2002, **53**:203-224.

6. Wiese A, Christ MM, Virnich O, Schurr U, Walter A: **Spatio-temporal leaf growth patterns of *Arabidopsis thaliana* and evidence for sugar control of the diel leaf growth cycle**. *New Phytol* 2007, **174**:752-761.

7. • Paparelli E, Parlanti S, Gonzali S, Novi G, Mariotti L, Ceccarelli N, van Dongen JT, Kolling K, Zeeman SC, Perata P: **Nighttime sugar starvation orchestrates gibberellin biosynthesis and plant growth in Arabidopsis**. *Plant Cell* 2013, **25**:3760-3769.
Arabidopsis mutants defective in starch synthesis or degradation are dwarf because they synthesize a lower level of gibberellins. These mutants experience sugar starvation at night, which represses gibberellin synthesis by down-regulating the kaurene synthase gene.

8. Stitt M, Zeeman SC: **Starch turnover: pathways, regulation and role in growth**. *Curr Opin Plant Biol* 2012, **15**:282-292.

9. Michael TP, Breton G, Hazen SP, Priest H, Mockler TC, Kay SA, Chory J: **A morning-specific phytohormone gene expression program underlying rhythmic plant growth**. *PLoS Biol* 2008, **6**:e225.

10. Dornbusch T, Michaud O, Xenarios I, Fankhauser C: **Differentially phased leaf growth and movements in Arabidopsis depend on coordinated circadian and light regulation**. *Plant Cell* 2014.

11. Moore B, Zhou L, Rolland F, Hall Q, Cheng WH, Liu YX, Hwang I, Jones T, Sheen J: **Role of the Arabidopsis glucose sensor HXK1 in nutrient, light, and hormonal signaling**. *Science* 2003, **300**:332-336.

12. Xiong Y, McCormack M, Li L, Hall Q, Xiang C, Sheen J: **Glucose-TOR signalling reprograms the transcriptome and activates meristems**. *Nature* 2013, **496**:181-186.

13. Das PK, Shin DH, Choi SB, Yoo SD, Choi G, Park YI: **Cytokinins enhance sugar-induced anthocyanin biosynthesis in Arabidopsis**. *Mol Cells* 2012, **34**:93-101.

14. Shin DH, Choi M, Kim K, Bang G, Cho M, Choi SB, Choi G, Park YI: **HY5 regulates anthocyanin biosynthesis by inducing the transcriptional activation of the MYB75/PAP1 transcription factor in Arabidopsis**. *FEBS Lett* 2013, **587**:1543-1547.

15. Radchuk R, Emery RJ, Weier D, Vigeolas H, Geigenberger P, Lunn JE, Feil R, Weschke W, Weber H: **Sucrose non-fermenting kinase 1 (SnRK1) coordinates metabolic and hormonal signals during pea cotyledon growth and differentiation**. *Plant J* 2009, **61**:324-338.

16. Kircher S, Schopfer P: **Photosynthetic sucrose acts as cotyledon-derived long-distance signal to control root growth during early seedling development in Arabidopsis**. *Proc Natl Acad Sci U S A* 2012, **109**:11217-11221.

17. Mason MG, Ross JJ, Babst BA, Wienclaw BN, Beveridge CA: **Sugar demand, not auxin, is the initial regulator of apical dominance**. *Proc Natl Acad Sci U S A* 2014, **111**:6092-6097.

18. Hayashi K, Nakamura S, Fukunaga S, Nishimura T, Jenness MK, Murphy AS, Motose H, Nozaki H, Furutani M, Aoyama T: **Auxin transport sites are visualized in planta using fluorescent auxin analogs**. *Proc Natl Acad Sci U S A* 2014, **111**:11557-11562.

19. Chaudhuri B, Hormann F, Frommer WB: **Dynamic imaging of glucose flux impedance using FRET sensors in wild-type Arabidopsis plants**. *J Exp Bot* 2011, **62**:2411-2417.

20. Lager I, Looger LL, Hilpert M, Lalonde S, Frommer WB: **Conversion of a putative Agrobacterium sugar-binding protein into a FRET sensor with high selectivity for sucrose**. *J Biol Chem* 2006, **281**:30875-30883.

21. Novak O, Henykova E, Sairanen I, Kowalczyk M, Pospisil T, Ljung K: **Tissue-specific profiling of the *Arabidopsis thaliana* auxin metabolome**. *Plant J* 2012, **72**:523-536.

22. Rook F, Hadingham SA, Li Y, Bevan MW: **Sugar and ABA response pathways and the control of gene expression**. *Plant Cell Environ* 2006, **29**:426-434.

23. Arenas-Huertero F, Arroyo A, Zhou L, Sheen J, Leon P: **Analysis of Arabidopsis glucose insensitive mutants, gin5 and gin6,**

reveals a central role of the plant hormone ABA in the regulation of plant vegetative development by sugar. *Genes Dev* 2000, **14**:2085-2096.

24. Rook F, Corke F, Card R, Munz G, Smith C, Bevan MW: **Impaired sucrose-induction mutants reveal the modulation of sugar-induced starch biosynthetic gene expression by abscisic acid signalling**. *Plant J* 2001, **26**:421-433.

25. Yoshida KT, Fujiwara T, Naito S: **The synergistic effects of sugar and abscisic acid on myo-inositol-1-phosphate synthase expression**. *Physiol Plant* 2002, **114**:581-587.

26. Wind JJ, Peviani A, Snel B, Hanson J, Smeekens SC: **ABI4: versatile activator and repressor**. *Trends Plant Sci* 2013, **18**:125-132.

27. • Li P, Zhou H, Shi X, Yu B, Zhou Y, Chen S, Wang Y, Peng Y, Meyer RC, Smeekens SC *et al.*: **The ABI4-induced Arabidopsis ANAC060 transcription factor attenuates ABA signaling and renders seedlings sugar insensitive when present in the nucleus**. *PLoS Genet* 2014, **10**:e 1004213.
The authors identify ANAC060 as a new component of the sugar-ABA signalling pathway. They demonstrate that nuclear localization of ANAC060 is required for inducing an ABI4-dependent feed-back mechanism inducing sugar insensitivity.

28. Le CS, Schmelz EA, Chourey PS: **Sugar levels regulate tryptophan-dependent auxin biosynthesis in developing maize kernels**. *Plant Physiol* 2010, **153**:306-318.

29. Lilley JL, Gee CW, Sairanen I, Ljung K, Nemhauser JL: **An endogenous carbon-sensing pathway triggers increased auxin flux and hypocotyl elongation**. *Plant Physiol* 2012, **160**:2261-2270.

30. • Sairanen I, Novak O, Pencik A, Ikeda Y, Jones B, Sandberg G, Ljung K: **Soluble carbohydrates regulate auxin biosynthesis via PIF proteins in Arabidopsis**. *Plant Cell* 2012, **24**:4907-4916.
The authors demonstrate a direct link between sugar status and auxin biosynthesis, involving the PIF transcriptional regulators.

31. Covington MF, Harmer SL: **The circadian clock regulates auxin signaling and responses in Arabidopsis**. *PLoS Biol* 2007, **5**:e222.

32. Stewart JL, Maloof JN, Nemhauser JL: **PIF genes mediate the effect of sucrose on seedling growth dynamics**. *PLoS ONE* 2011, **6**:e19894.

33. • Hornitschek P, Kohnen MV, Lorrain S, Rougemont J, Ljung K, Lopez-Vidriero I, Franco-Zorrilla JM, Solano R, Trevisan M, Pradervand S *et al.*: **Phytochrome interacting factors 4 and 5 control seedling growth in changing light conditions by directly controlling auxin signaling**. *Plant J* 2012, **71**:699-711.
A role for PIF genes in growth regulation under low light conditions was discovered. PIF4 and PIF5 bind to the promoter of auxin biosynthesis and signaling genes, controlling their expression, thereby regulating elongation growth.

34. Procko C, Crenshaw CM, Ljung K, Noel JP, Chory J: **Cotyledon-generated auxin is required for shade-induced hypocotyl growth in *Brassica rapa***. *Plant Physiol* 2014, **165**:1285-1301.

35. Sagar M, Chervin C, Roustant JP, Bouzayen M, Zouine M: **Under-expression of the auxin response factor Sl-ARF4 improves postharvest behavior of tomato fruits**. *Plant Signal Behav* 2013:8 http://dx.doi.org/10.4161/psb25647.

36. Albacete AA, Martinez-Andujar C, Perez-Alfocea F: **Hormonal and metabolic regulation of source-sink relations under salinity and drought: from plant survival to crop yield stability**. *Biotechnol Adv* 2014, **32**:12-30.

37. Reguera M, Peleg Z, Abdel-Tawab YM, Tumimbang EB, Delatorre CA, Blumwald E: **Stress-induced cytokinin synthesis increases drought tolerance through the coordinated regulation of carbon and nitrogen assimilation in rice**. *Plant Physiol* 2013, **163**:1609-1622.

38. Hachiya T, Sugiura D, Kojima M, Sato S, Yanagisawa S, Sakakibara H, Terashima I, Noguchi K: **High CO_2 triggers preferential root growth of *Arabidopsis thaliana* via two distinct systems under low pH and low N stresses**. *Plant Cell Physiol* 2014, **55**:269-280.

39. • Eviatar-Ribak T, Shalit-Kaneh A, Chappell-Maor L, Amsellem Z, Eshed Y, Lifschitz E: **A cytokinin-activating enzyme promotes tuber formation in tomato**. *Curr Biol* 2013, **23**:1057-1064.
A new role for cytokinins in tomato tuber formation was discovered. The cytokinin biosynthesis gene LOG1 induces de novo formation of tubers, interacting with miR156, a master regulator of juvenility.

40. Kushwah S, Laxmi A: **The interaction between glucose and cytokinin signal transduction pathway in *Arabidopsis thaliana***. *Plant Cell Environ* 2014, **37**:235-253.

41. Werner T, Holst K, Pors Y, Guivarc'h A, Mustroph A, Chriqui D, Grimm B, Schmulling T: **Cytokinin deficiency causes distinct changes of sink and source parameters in tobacco shoots and roots**. *J Exp Bot* 2008, **59**:2659-2672.

42. Arana MV, Marin-de la Rosa N, Maloof JN, Blazquez MA, Alabadi D: **Circadian oscillation of gibberellin signaling in Arabidopsis**. *Proc Natl Acad Sci U S A* 2011, **108**:9292-9297.

43. Hwang SJ, Hamayun M, Kim HY, Kim KU, Shin DH, Kim JE, Kim SY, Lee IJ: **Diurnal variation in endogenous gibberellin levels of rice shoots**. *J Crop Sci Biotech* 2007, **10**:129-132.

44. Li Y, Van den Ende W, Rolland F: **Sucrose induction of anthocyanin biosynthesis is mediated by DELLA**. *Mol Plant* 2014, **7**:570-572.

45. Loreti E, Povero G, Novi G, Solfanelli C, Alpi A, Perata P: **Gibberellins, jasmonate and abscisic acid modulate the sucrose-induced expression of anthocyanin biosynthetic genes in Arabidopsis**. *New Phytol* 2008, **179**:1004-1016.

46. Solfanelli C, Poggi A, Loreti E, Alpi A, Perata P: **Sucrose-specific induction of the anthocyanin biosynthetic pathway in Arabidopsis**. *Plant Physiol* 2006, **140**:637-646.

47. Teng S, Keurentjes J, Bentsink L, Koornneef M, Smeekens S: **Sucrose-specific induction of anthocyanin biosynthesis in Arabidopsis requires the MYB75/PAP1 gene**. *Plant Physiol* 2005, **139**:1840-1852.

48. Ribeiro DM, Araujo WL, Fernie AR, Schippers JH, Mueller-Roeber B: **Translatome and metabolome effects triggered by gibberellins during rosette growth in Arabidopsis**. *J Exp Bot* 2012, **63**:2769-2786.

49. Sun TP: **Gibberellin-GID1-DELLA: a pivotal regulatory module for plant growth and development**. *Plant Physiol* 2010, **154**:567-570.

50. Gallego-Bartolome J, Alabadi D, Blazquez MA: **DELLA-induced early transcriptional changes during etiolated development in *Arabidopsis thaliana***. *PLoS ONE* 2011, **6**:e23918.

51. Qi T, Song S, Ren Q, Wu D, Huang H, Chen Y, Fan M, Peng W, Ren C, Xie D: **The Jasmonate-ZIM-domain proteins interact with the WD-Repeat/bHLH/MYB complexes to regulate Jasmonate-mediated anthocyanin accumulation and trichome initiation in *Arabidopsis thaliana***. *Plant Cell* 2011, **23**:1795-1814.

52. Li QF, Wang C, Jiang L, Li S, Sun SS, He JX: **An interaction between BZR1 and DELLAs mediates direct signaling crosstalk between brassinosteroids and gibberellins in Arabidopsis**. *Sci Signal* 2012, **5**:ra72.

53. • Stewart Lilley JL, Gan Y, Graham IA, Nemhauser JL: **The effects of DELLAs on growth change with developmental stage and brassinosteroid levels**. *Plant J* 2013, **76**:165-173.
Members of the DELLA family were found to either repress or enhance brassinosteroid growth responses, depending on developmental stage. The effects of brassinosteroids, including synergistic interactions with gibberellins, were largely independent of PIFs, complicating current models of higher order transcriptional complexes driving growth.

54. Reinhold H, Soyk S, Simkova K, Hostettler C, Marafino J, Mainiero S, Vaughan CK, Monroe JD, Zeeman SC: **β-Amylase-like proteins function as transcription factors in Arabidopsis, controlling shoot growth and development**. *Plant Cell* 2011, **23**:1391-1403.

55. • Soyk S, Simkova K, Zurcher E, Luginbuhl L, Brand LH, Vaughan CK, Wanke D, Zeeman SC: **The enzyme-like domain of Arabidopsis nuclear beta-amylases is critical for DNA**

sequence recognition and transcriptional activation. *Plant Cell* 2014, **26**:1746-1763.
The authors show that transcriptional activation by BAM8 requires an intact substrate binding site. This supports the hypothesis that BZR1-BAMs act as metabolic sensors.

56. de Lucas M, Prat S: **PIFs get BRright: phytochrome interacting factors as integrators of light and hormonal signals**. *New Phytol* 2014, **202**:1126-1141.

57. Ni M, Tepperman JM, Quail PH: **PIF3 a phytochrome-interacting factor necessary for normal photoinduced signal transduction, is a novel basic helix-loop-helix protein**. *Cell* 1998, **95**:657-667.

58. Leivar P, Quail PH: **PIFs: pivotal components in a cellular signaling hub**. *Trends Plant Sci* 2011, **16**:19-28.

59. Ni W, Xu SL, Tepperman JM, Stanley DJ, Maltby DA, Gross JD, Burlingame AL, Wang ZY, Quail PH: **A mutually assured destruction mechanism attenuates light signaling in Arabidopsis**. *Science* 2014, **344**:1160-1164.

60. Nozue K, Covington MF, Duek PD, Lorrain S, Fankhauser C, Harmer SL, Maloof JN: **Rhythmic growth explained by coincidence between internal and external cues**. *Nature* 2007, **448**:358-361.

61. Liu Z, Zhang Y, Liu R, Hao H, Wang Z, Bi Y: **Phytochrome interacting factors (PIFs) are essential regulators for sucrose-induced hypocotyl elongation in Arabidopsis**. *J Plant Physiol* 2011, **168**:1771-1779.

62. Toledo-Ortiz G, Johansson H, Lee KP, Bou-Torrent J, Stewart K, Steel G, Rodriguez-Concepcion M, Halliday KJ: **The HY5-PIF regulatory module coordinates light and temperature control of photosynthetic gene transcription**. *PLoS Genet* 2014, **10**:e1004416.

63. Sakuraba Y, Jeong J, Kang MY, Kim J, Paek NC, Choi G: **Phytochrome-interacting transcription factors PIF4 and PIF5 induce leaf senescence in Arabidopsis**. *Nat Commun* 2014, **5**:4636.

64. de Montaigu A, Giakountis A, Rubin M, Toth R, Cremer F, Sokolova V, Porri A, Reymond M, Weinig C, Coupland G: **Natural diversity in daily rhythms of gene expression contributes to phenotypic variation**. *Proc Natl Acad Sci U S A* 2015, **112**:905-910.

65. Sun J, Qi L, Li Y, Chu J, Li C: **PIF4-mediated activation of YUCCA8 expression integrates temperature into the auxin pathway in regulating arabidopsis hypocotyl growth**. *PLoS Genet* 2012, **8**:e1002594.

66. Franklin KA, Lee SH, Patel D, Kumar SV, Spartz AK, Gu C, Ye S, Yu P, Breen G, Cohen JD *et al.*: **Phytochrome-interacting factor 4 (PIF4) regulates auxin biosynthesis at high temperature**. *Proc Natl Acad Sci U S A* 2011, **108**:20231-20235.

67. Li L, Ljung K, Breton G, Schmitz RJ, Pruneda-Paz J, Cowing-Zitron C, Cole BJ, Ivans LJ, Pedmale UV, Jung HS *et al.*: **Linking photoreceptor excitation to changes in plant architecture**. *Genes Dev* 2012, **26**:785-790.

68. Nozue K, Harmer SL, Maloof JN: **Genomic analysis of circadian clock-, light-, and growth-correlated genes reveals phytochrome-interacting factor5 as a modulator of auxin signaling in Arabidopsis**. *Plant Physiol* 2011, **156**:357-372.

69. Stephenson PG, Fankhauser C, Terry MJ: **PIF3 is a repressor of chloroplast development**. *Proc Natl Acad Sci U S A* 2009, **106**:7654-7659.

70. Toledo-Ortiz G, Huq E, Rodriguez-Concepcion M: **Direct regulation of phytoene synthase gene expression and carotenoid biosynthesis by phytochrome-interacting factors**. *Proc Natl Acad Sci U S A* 2010, **107**:11626-11631.

71. Huq E, Al-Sady B, Hudson M, Kim C, Apel K, Quail PH: **Phytochrome-interacting factor 1 is a critical bHLH regulator of chlorophyll biosynthesis**. *Science* 2004, **305**:1937-1941.

72. Oh E, Zhu JY, Bai MY, Arenhart RA, Sun Y, Wang ZY: **Cell elongation is regulated through a central circuit of interacting transcription factors in the Arabidopsis hypocotyl**. *Elife* 2014:3.

73. • Chew YH, Wenden B, Flis A, Mengin V, Taylor J, Davey CL, Tindal C, Thomas H, Ougham HJ, de Reffye P *et al.*: **Multiscale digital Arabidopsis predicts individual organ and whole-organism growth**. *Proc Natl Acad Sci U S A* 2014, **111**:E4127-E4136.
A multiscale model successfully combined four existing models to connect genetic and biochemical events to Arabidopsis rosette growth. This approach sets the stage for incorporating a mechanistic view of how sugar and hormone regulatory pathways are integrated in growth control.