Sensing and regulation of C and N metabolism – novel features and mechanisms of the TOR and SnRK1 signaling pathways

Anthony Artins, Marina Martins, Christian Meyer, Alisdair Robert Fernie, Camila Caldana

the plant journal

SEB SOCIETY FOR EXPERIMENTAL BIOLOGY

The Plant Journal (2024) doi: 10.1111/tpj.16684

PERSPECTIVE

Sensing and regulation of C and N metabolism – novel features and mechanisms of the TOR and SnRK1 signaling pathways

Anthony Artins[1,†], Marina C. M. Martins[2,†], Christian Meyer[3], Alisdair R. Fernie[1,*] and Camila Caldana[1,*]

[1]*Max-Planck-Institute of Molecular Plant Physiology, Am Mühlenberg 1, 14476 Potsdam, Golm, Germany,*
[2]*in Press – Scientific Consulting and Communication Services, 05089-030 São Paulo, São Paulo, Brazil, and*
[3]*Institut Jean-Pierre Bourgin (IJPB), INRAE, AgroParisTech, Université Paris-Saclay, 78000 Versailles, France*

Received 16 December 2022; revised 25 January 2024; accepted 2 February 2024.
*For correspondence (e-mail caldana@mpimp-golm.mpg.de; fernie@mpimp-golm.mpg.de).
†These authors have contributed equally to this work.

SUMMARY

Carbon (C) and nitrogen (N) metabolisms are tightly integrated to allow proper plant growth and development. Photosynthesis is dependent on N invested in chlorophylls, enzymes, and structural components of the photosynthetic machinery, while N uptake and assimilation rely on ATP, reducing equivalents, and C-skeletons provided by photosynthesis. The direct connection between N availability and photosynthetic efficiency allows the synthesis of precursors for all metabolites and building blocks in plants. Thus, the capacity to sense and respond to sudden changes in C and N availability is crucial for plant survival and is mediated by complex yet efficient signaling pathways such as TARGET OF RAPAMYCIN (TOR) and SUCROSE-NON-FERMENTING-1-RELATED PROTEIN KINASE 1 (SnRK1). In this review, we present recent advances in mechanisms involved in sensing C and N status as well as identifying current gaps in our understanding. We finally attempt to provide new perspectives and hypotheses on the interconnection of diverse signaling pathways that will allow us to understand the integration and orchestration of the major players governing the regulation of the CN balance.

Keywords: CN balance, nutrient signaling, metabolism.

INTRODUCTION

Metabolism is at the heart of life as it ensures the conversion of nutrients into energy, synthesizes molecules necessary for growth and repair and recycles degradation products. The ability to rewire metabolic activity to maintain homeostasis is fundamental to drive organism adaptation in response to changes in environmental conditions (Judge & Dodd, 2020). Maintaining an optimal metabolic state is primordial for sessile and multicellular organisms such as plants, which must continuously adjust their physiology to adapt to changes in light intensity and duration, temperature, and the availability of water and nutrients. The stationary and photoautotrophic nature of plants requires the availability of sufficient surrounding nutrients, with carbon (C) and nitrogen (N) being the most limiting for plant metabolism, growth, development, and ultimately in the case of crops also productivity (Coruzz & Bush, 2001; Nunes-Nesi et al., 2010). In land plants, the sites where these two elements are absorbed are spatially separated. During the day, photosynthetic leaves fix atmospheric CO_2 by the Calvin-Benson cycle, using energy (ATP) and reducing power (NADPH) produced in the light reactions (Sharkey, 2019). The main end products of photosynthesis in higher plants are sucrose and starch. Sucrose is the C and energy source that fuels cellular activities and is, in most species, the preferential form of sugar exported to the heterotrophic sink organs. In contrast, starch is accumulated as a short-term storage pool in the chloroplast and is broken down when sucrose supply by photosynthesis is limited or not possible (.e.g., during the night) (Smith & Zeeman, 2020). Differently from C, inorganic N is absorbed from the soil by roots predominantly in the form of nitrate (NO_3^-) and ammonium (NH_4^+), but alternatively, organic N (e.g., amino acids, peptides, proteins, and other N-containing molecules) can be taken up (Enggrob et al., 2019; Guo et al., 2020). N is assimilated in root and/or

photosynthetic leaves by the action of several enzymes into Gln using 2-oxoglutarate (2-OG) derived from C assimilation and photorespiration as the N acceptor (Hodges, 2002). Therefore, sensing nutritional status coupled with the ability to convey these signals within the cells and between organs is crucial to coordinate metabolic pathways that adjust C/N partitioning and use in a temporally controlled manner. These functions are ensured by well-conserved eukaryotic signaling pathways including the TARGET OF RAPAMYCIN (TOR) and SUCROSE-NON-FERMENTING-1-RELATED PROTEIN KINASE 1 (SnRK1) (Figure 1).

In plants, the TOR kinase acts in a complex with the REGULATORY-ASSOCIATED PROTEIN OF TOR (RAPTOR), and LETHAL WITH SEC 13 PROTEIN 8 (LST8), which filter out signal transduction pathways converging to TOR and recruit substrates to target the regulation of specific biological processes (Aylett et al., 2016; Kim et al., 2002). TOR activity is regulated by a multitude of signals, with its activation being generally promoted by nutrient sufficiency and typically suppressed in situations of nutrient scarcity (Artins & Caldana, 2022; Caldana et al., 2019; Dobrenel et al., 2013; Shi et al., 2018). For instance, TOR promotes growth in response to C and N availability signals achieved through the phosphorylation of both, the E2Fa transcription factor and the RIBOSOMAL PROTEIN S6 KINASE 1 (S6K1), leading to the transcriptional reprogramming and activation of protein synthesis, respectively (Li et al., 2017; Liu et al., 2021; Schepetilnikov et al., 2013; Xiong et al., 2013). By contrast, nutrient/energy scarcity suppresses TOR activity leading to quiescent cells, and the activation of recycling pathways (Li et al., 2017; Pu, Soto-Burgos, & Bassham, 2017). A barrier hindering scientific progress in comprehending the impact of TOR inhibition and the identification of regulated metabolic processes is the lethality caused by TOR loss of function (Menand et al., 2002). Since this was discovered, innovative tools were developed that enable the reduction of TOR activity by genetic manipulation or chemical inhibition while avoiding lethality (Anderson et al., 2005; Caldana et al., 2013; Deprost et al., 2007; Montané & Menand, 2013, 2019; Moreau et al., 2012; Perdoux et al., 2023; Ren et al., 2012; Xiong et al., 2013). Downregulation of TOR signaling profoundly affects metabolic homeostasis with noticeable accumulation of C storage compounds (e.g., starch, raffinose, and lipids), reduction in sucrose levels, increased amino acid amounts, and perturbation of TCA metabolite levels. In addition, constitutive activation of the autophagy pathway occurs (Liu & Bassham, 2010; Mugume et al., 2020; Pu, Luo, & Bassham, 2017; Pu, Soto-Burgos, & Bassham, 2017). Indeed, autophagy is a key recycling process activated during energy-limiting conditions in an SnRK1-dependent fashion. SnRK1 assembles in heterotrimers composed of one catalytic α subunit that ensures the phosphorylation of substrates and two regulatory subunits β and γ (also occasionally referred to as βγ in plants) directing the composition and the localization of the complex in plant cells (Emanuelle et al., 2015). The function of this complex is crucial for plant survival, particularly in response to low energy levels brought about by different stresses that activate this signaling complex. Conversely, SnRK1 is shut down by energy abundance. Upon energy limitation, SnRK1 readjusts metabolism through the activation of energy conservation programs, such as the transcription of catabolic-related genes by phosphorylating bZIP transcription factors (Mair et al., 2015), autophagy by phosphorylating autophagy-related (ATG) proteins (Chen et al., 2017; Huang et al., 2019), and the regulation of metabolic enzymes (Cho et al., 2016; Nukarinen et al., 2016).

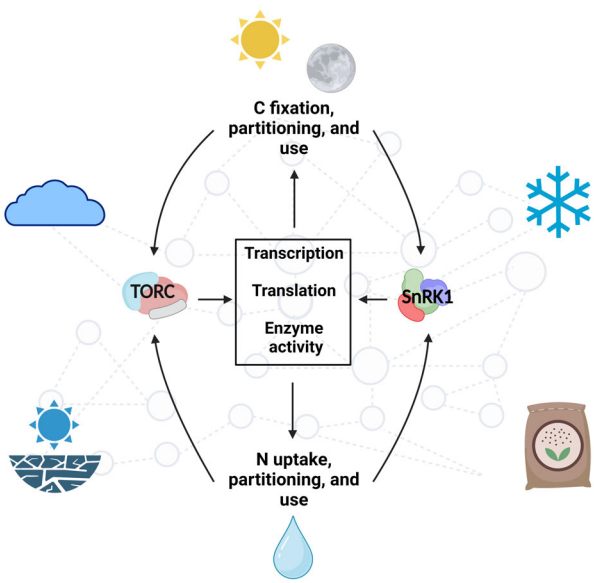

Figure 1. Schematic representation of the C and N sensing and metabolic regulation mediated by TORC and SnRK1 signaling pathways.
TORC and SnRK1 are central hubs that convey C- and N-related signals into the regulation of general metabolism (transcription, protein translation, and protein activity). At the periphery are represented the environmental conditions affecting C and N availability. Light–dark cycles are represented by the sun and the moon, cold is illustrated by a snowflake, fertilizer bag denotes nutrient availability, flooding/excess of water is represented by the water droplet, drought is illustrated by the sun/cracked soil and the cloud represented variation in light intensity. C, carbon; N, nitrogen; SnRK1, SUCROSE-NON-FERMENTING-1-RELATED PROTEIN KINASE 1; TORC, TARGET OF RAPAMYCIN COMPLEX. Image created with BioRender.com.

The regulation of C and N metabolisms by TOR and SnRK1 has been extensively discussed in previous reviews (Artins & Caldana, 2022; Dobrenel et al., 2016; Peixoto & Baena-González, 2022). However, our understanding of the sensing and regulation of N metabolism appears to lag behind that of C. In this review, the aim is to focus on the regulation of C/N metabolism and on the latest research findings that emphasize potential connections between essential N sensors and metabolic regulators such as PII and Nodule Inception-like proteins (NLPs) with TOR/SnRK1 signaling

pathways. Then, new perspectives will be proposed to highlight the intricate interplay between these key regulatory elements, providing a comprehensive understanding of C/N metabolism regulation.

TOR-C signaling in mediating regulation of N metabolism

Common metabolic responses triggered by the downregulation of TOR signaling in photosynthetic organisms include a massive increase in the levels of amino acids, elevated hexoses and reduced sucrose contents, and starch and triacylglycerol accumulation (Moreau et al., 2012; Caldana et al., 2013; da Silva et al., 2021; Jüppner et al., 2018; Mubeen et al., 2018; Pancha et al., 2019; Ren et al., 2012; Salem et al., 2018). However, alterations in C/N metabolite abundance do not indicate whether a specific change is a direct or indirect consequence of TOR. That said they do suggest that TOR may have an impact on both C and N signaling and metabolic pathways, potentially serving as a means to modulate the reciprocal influence between them. Some evidence has come from work carried out using unicellular organisms. The first evidence that TOR is activated by C fixation comes from a recent work on the model unicellular organism *Chlamydomonas reinhardtii*, where feeding HCO_3^- as a C source for photosynthesis stimulated the phosphorylation of the RIBOSOMAL PROTEIN S6 (RPS6), a downstream target and known readout for TOR activity (Mallén-Ponce et al., 2022). Impairment of starch synthesis leads to a significant decrease in photosynthetic ability and a shift in the utilization of C fixed during photosynthesis, such as the ones observed in the *sta6* mutant that lacks functional ADP-glucose pyrophosphorylase crucial for starch synthesis (Saroussi et al., 2019). Despite the reduced C fixation in *sta6*, TOR kinase was hyperactivated. Metabolic profiling analysis revealed that the level of a set of amino acids was elevated, most notably for Gln (Mallén-Ponce et al., 2022), which is known to promote TOR signaling in other model organisms (González & Hall, 2017). The stimulation of Gln, among other amino acid levels in this mutant can be explained by a redirection of C toward amino acid synthesis, rather than starch, in order to maintain growth. Mallén-Ponce et al. (2022) elegantly identified that not only C fixation but also C assimilation contributed to the activation of TOR signaling (Mallén-Ponce et al., 2022). It has been shown that the rapid increase in amino acids under TOR repression results from stimulation of N uptake (increased ^{15}N uptake), assimilation (increased activity of GS and GOGAT), and draining of C and N to support upregulation of *de novo* amino acid synthesis (Mubeen et al., 2018). This would appear to represent an attempt to restore TOR activity to maintain metabolic homeostasis (Figure 2).

In Arabidopsis, nutrient limitation by extended darkness suppressed the increase in most amino acids triggered by TOR inhibition, reduced the ratio of C/N assessed by the 2-OG/Glu ratio, and abolished the fluctuations in this ratio

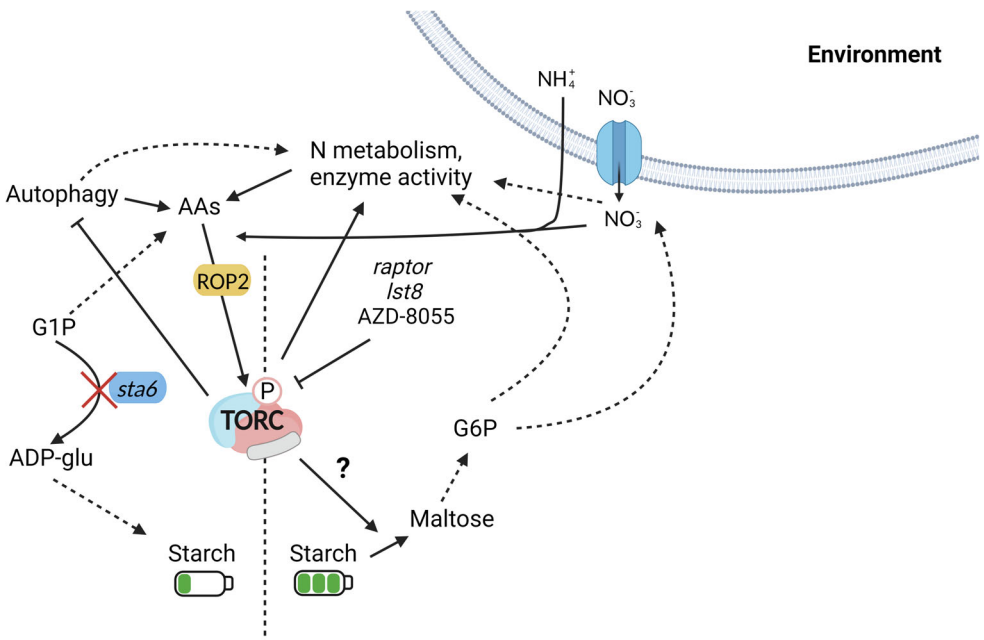

Figure 2. Novel and potential mechanism of the TORC signaling pathway leading to the regulation of C/N balance.
TORC plays a crucial role in the regulation of N metabolism by utilizing two pathways: C signaling and direct N sensing. An example of C signaling is observed in the Chlamydomonas mutant sta6, which redirects C toward amino acid synthesis and potentially influences N uptake and metabolism through the degradation products of starch, such as glucose-6-phosphate (G6P). On the other hand, direct N sensing requires the involvement of ROP2 to activate the TORC pathway. AAs, amino acids; ADP-glu, adenosine diphosphate glucose; G1P, glucose 1-phosphate; NO_3^-, nitrate; NO_4^+, ammonium; P, phosphate; ROP2, RHO-LIKE GTPASE FROM PLANTS 2; TORC, TARGET OF RAPAMYCIN COMPLEX. Dashed arrows and lines represent indirect and direct regulation, respectively. Image created with BioRender.com.

The Plant Journal published by Society for Experimental Biology and John Wiley & Sons Ltd.,
The Plant Journal, (2024), doi: 10.1111/tpj.16684

along the diel cycle, confirming that *de novo* amino acid synthesis depends on C availability (Mubeen et al., 2019). A recent study demonstrated that TOR activity is modulated by C fixation via the intracellular abundance of particular amino acids (Ala, Glu, Gln, Leu, and Val) in Chlamydomonas (Mallén-Ponce et al., 2022). These results nicely exemplify the link between C/N homeostasis and TOR, suggesting that TOR mediating sugar signaling and metabolism is tightly linked to N assimilation. In Arabidopsis, an illustration of the regulation of N metabolism mediated by the TOR-C signaling pathway can be proposed in the context of starch metabolism coupled with sugar signaling (Figure 2). For instance, TOR phosphorylates proteins involved in starch degradation (Han et al., 2022; Van Leene et al., 2019). Whether these phosphorylation events explain the modification of starch metabolism in TOR-inhibited plants remains to be characterized. Intermediate products of starch degradation, such as glucose 6-phosphate (G6P), are involved in at least three metabolic pathways namely the oxidative pentose phosphate pathway (OPPP), glycolysis, and trehalose metabolism, and can modulate the assimilation of inorganic N. First, the expression of the NO_3^- transporters NRT1.1 and 2.1 positively correlate with the abundance of G6P (Lejay et al., 2008). Second, G6P dehydrogenase, the first enzymatic step of the OPPP, converts G6P into P-gluconolactone simultaneously generating one molecule of NADPH. This NADPH is subsequently required for the reduction of NO_2^- into NH_4^+, and further incorporated into amino acids by the GOGAT (Jiang et al., 2022). This might represent a potential sugar-signaling action of TOR to regulate N metabolism in higher plants.

TOR: Novel aspects toward the regulation of N signaling and metabolism

Recent research has revealed that TOR responds to N-derived compounds to regulate N metabolism. Evidence that amino acids stimulate TOR activity in plants came from Arabidopsis mutants with impaired Leu synthesis that accumulate branched-chain amino acids (BCAAs) (Cao et al., 2019; Schaufelberger et al., 2019). The high levels of BCAAs were correlated with the increased phosphorylation status of the RIBOSOMAL PROTEIN S6 KINASE (S6K) (Cao et al., 2019), a conserved TOR target crucial for translation initiation (Henriques et al., 2013; Schepetilnikov et al., 2013). The exogenous supply of Gln and Ile to mature leaf discs of Arabidopsis also stimulated TOR activity and led to downstream effects on respiratory substrate use (O'Leary et al., 2020). Recently, 15 amino acids were assessed as to whether they could restore TOR activity in Arabidopsis seedlings starved for inorganic N (Liu et al., 2021). The highest effects were observed with Gln, Ala, Gly, and Cys. By contrast, Ser, Glu, Asp, and Leu exhibited only modest TOR activation, whereas Val, His, Ile, Thr, Met, Asn, and Lys displayed low levels of activation. A possible explanation for the observed responses to specific amino acids might be that they differentially modulate TOR activity according to tissue or cell type. In addition to the effects of the amino acids, these authors revealed that NO_3^- and NH_4^+ are primary N signals for TOR activation in the leaf primordium, stimulating cell proliferation and leaf development. Interestingly, under TORC repression either by chemical inhibition using AZD-8055 or genetic mutations in its components RAPTOR1B and LST8 the accumulation of Gln was effectively counteracted in the presence of the herbicide glufosinate-ammonium in the media, a potent inhibitor of GS (Ingargiola et al., 2023). Although impaired TORC function led to higher expression of genes encoding *GLUTAMATE SYNTHETASE 1* (*GS1*) isoforms and increased GS1 and GLUTAMATE SYNTHETASE 2 (GS2) protein levels, GS activity was lower. Since the decrease in GS activity was proportional to Gln levels, this could suggest a feedback mechanism. However, it remains to be elucidated if TOR also impacts GS activity via direct or indirect phosphorylation. Interestingly, short- (5 h) or long-term (24 h) stimulation of TOR activity by sucrose is suppressed when seedlings are co-treated with glufosinate-ammonium targeting GS, in a similar manner as AZD-8055 treatment (Ingargiola et al., 2023). This further illustrates that a functional N assimilation pathway is required for the sucrose-mediated TORC activity and that both, C and N signals are important to regulate the activity and function of this kinase. Although some TOR upstream and downstream targets were elucidated in photosynthetic organisms, the precise mechanisms involved in C/N sensing by this kinase complex are still enigmatic. Important components upstream of TOR described in animals and fungi such as the RAG and Rab GTPases (Wolfson & Sabatini, 2017) are missing in photosynthetic organisms. However, the RHO-LIKE GTPASE FROM PLANTS 2 (ROP2) has been identified as a key player in the activation of TOR signaling in plants, not only integrating glucose and auxin stimuli (Li et al., 2017; Schepetilnikov et al., 2017) but also N signals (Liu et al., 2021). This underscores the intricate signaling network, revealing plants ability to evolve sophisticated relay mechanisms that sense and trigger responses toward diverse signals. In this context, it is notable that plants can coordinate responses to signals associated with C, N, and hormonal cues, likely to interconnect the responses of their various tissues. Phosphoproteomics studies, performed on Arabidopsis cell cultures and whole seedlings, have revealed that key enzymes maintaining C/N balance are putatively phosphorylated by TOR such as GLUTAMATE DECARBOXYLASE 3 (AT2G02000), PHOSPHO*ENOL*PYRUVATE CARBOXYLASE 2 (AT2G42600), and PHOSPHO-*ENOL*PYRUVATE CARBOXYKINASE 1 and 2 (AT4G37870 and AT5G65690, respectively) (Scarpin et al., 2020; Van Leene et al., 2019). These findings suggest that the TOR pathway affects C and N metabolism at multiple levels in metabolic pathways.

To date, findings in the unicellular green algae *Chlamydomonas* and the multicellular photosynthetic organism Arabidopsis have started to shed light on the complexity of the regulatory mechanisms behind C/N interactions mediated by TOR (Figure 2). Nevertheless, further analyses in the multicellular environment are necessary to better understand these interactions and dissect their contribution to the C/N balance.

SnRK1 mediates major signaling pathways intersecting C/N metabolism

SnRK1 activity depends on the phosphorylation of the kinase domain T-loop of the α-subunit (Martínez-Barajas & Coello, 2020). This subunit is translocated to the nucleus, where it interacts with chromatin and activates the transcription of more than a thousand genes, repressing energy-consuming processes (Baena-González et al., 2007; Henninger et al., 2022; Ramon et al., 2019). Part of this transcription regulation is mediated by S1- and C class *BASIC LEUCINE ZIPPER* (*bZIP*) transcription factors, which form heterodimers and control metabolic reprogramming. Although these bZIPs were identified as targets of SnRK1 (Baena-González et al., 2007; Ma et al., 2011; Pedrotti et al., 2018), only bZIP63 was demonstrated to be directly phosphorylated by this kinase *in vivo* (Mair et al., 2015). *bZIP63* mutants display faster starch degradation mediated by the upregulation of transcripts involved in this process (*α-GLUCAN, WATER DIKINASE1/STARCH EXCESS1*; *PHOSPHOGLUCAN, WATER DIKINASE*; and *DISPROPORTIONATING ENZYME 2*) and impaired growth (Viana et al., 2021). The *bzip63-2* mutant also has lower 2-OG, but unaltered Glu and Gln levels, further corroborating the limiting C availability. Given that bZIP63 regulates and is regulated by the circadian clock, this transcription factor was proposed as a link between the efficient use of C reserves and growth under diel cycles (Frank et al., 2018; Viana et al., 2021). The interaction of bZIP63 and SnRK1 is stronger in the presence of bZIP2, and these three components form a complex on the promoter region of *ELECTRON-TRANSFER FLAVOPROTEIN: UBIQUINONE OXIDOREDUCTASE* (*ETFQO*) to trigger its transcription (Pedrotti et al., 2018). ETFQO is involved in BCAA catabolism, and its activation would ensure an alternative respiratory pathway to support respiration under conditions of carbohydrate limitation. These studies show that bZIP63 has a more far-reaching effect on plant metabolism, connecting gene regulation, cellular adaptation, and C and N pools. Another SnRK1 target, bZIP53, is involved in the regulation of Pro and BCAA catabolism via the transcriptional modulation of *PROLINE DEHYDROGENASE 1* and *BRANCHED-CHAIN AMINO ACID TRANSFERASE 2*, respectively. Such a modulation occurs not only under energy starvation (Dietrich et al., 2011) but also during the diurnal cycle (Garg et al., 2019). The interaction of bZIP63 and SnRK1 is also necessary for bZIP63 to activate the promoter region of the cytosolic PYRUVATE, ORTHOPHOSPHATE DIKINASE, allowing sugars to be made from pyruvate (a major product of protein breakdown) and fuelling gluconeogenesis during seedling establishment (Henninger et al., 2022) (Figure 3).

Another mechanism by which SnRK1 regulates transcription is by the retention of transcription factors in the cytosol. Limitation in N is widely recognized to accelerate the floral transition, but only recently the underlying mechanism started to be uncovered. (Sanagi et al., 2021) identified that the FLOWERING BHLH 4 (FBH4) transcription factor acts as a crucial regulator of N-responsive flowering in Arabidopsis. FBH4 is a highly phosphorylated protein under optimal N conditions, but exhibits decreased phosphorylation levels in low N conditions which facilitates its nuclear localization. This promotes the transcriptional activation of the core photoperiodic flowering pathway genes *CONSTANS* (*CO*) and *FLOWERING LOCUS T* (*FT*). In this context, SnRK1 was found to directly phosphorylate FBH4, leading to its retention in the cytoplasm under normal N conditions. However, decreasing N levels reduce the activity of SnRK1 and therefore the phosphorylation of FBH4, resulting in its nuclear localization and the transcriptional activation of target genes.

More recently, the interconnection between C and N signaling by SnRK1 started to be better explored in the context of seed storage. SnRK1 integrates C signals to regulate seed N storage. Zeins are the main N storage compound of maize seeds; their levels are partly adjusted through the transcriptional regulation of zein-encoding genes by *Opaque2* (*O2*) transcription factor. Increase in sucrose levels reduces the activity of ZmSnRK1, precluding the phosphorylation and degradation of the E3 ubiquitin ligase ZmRFWD3 (Li, Qi, et al., 2020). Enhanced sucrose and ZmRFWD3 levels promote *O2* nuclear translocation, increasing the transcription of genes involved in zein synthesis and storage, corroborating the negative effect of the SnRK1 signaling pathway over N metabolism, probably to maintain C/N homeostasis in the seeds. Interestingly, SnRK1 regulates sheath-to-panicle remobilization of nonstructural carbohydrates (NSC) during rice grain filling. This study revealed that OsSnRK1 activates proteins related to NSC transport via phosphorylation leading to the modification of starch degradation, sucrose metabolism, phloem transport, sugar transport across the tonoplast, and glycolysis in rice sheaths (Hu et al., 2022). Following this study, the feedback loop regulation between T6P and SnRK1 mediated by the NAC23 transcription factor in response to sugar availability was identified in rice. High sugar content downregulates *TPS1* levels via *OsNAC23*, stimulating sucrose export from source to sink organs. Meanwhile, high T6P represses *OsSnRK1a* preventing the degradation of *OsNAC23*, usually occurring in low sugar

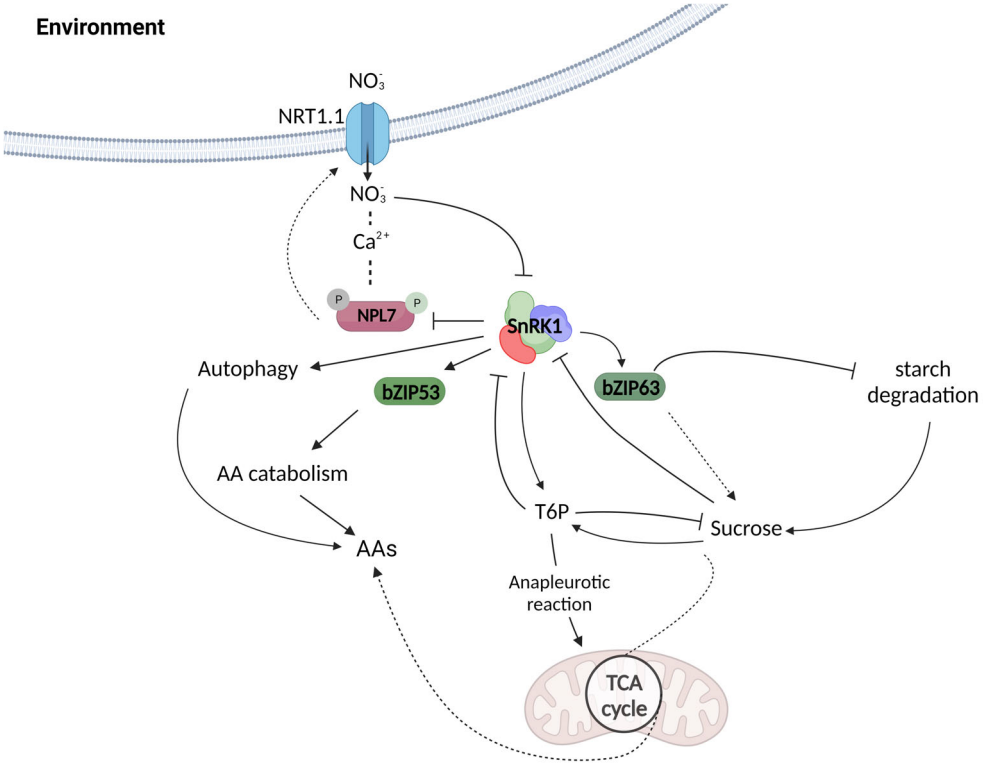

Figure 3. Novel SnRK1-dependent mechanisms to maintain C/N balance.
SnRK1 governs the regulation of C/N balance at various levels including metabolic, transcriptomic, and protein. This intricate process involves the participation of additional C/N players such as T6P, bZIPs, and NPLs, among others. For instance, SnRK1 plays a role in regulating the C status by inhibiting starch degradation or facilitating the catabolism of amino acids through bZIP. Additionally, T6P regulates enzymes involved in C assimilation and central metabolism, while NPLs are responsible for regulating the uptake of NO_3^-. SnRK1 activates autophagy to recycle cellular compounds. AA, amino acid; bZIP, BASIC LEUCINE ZIPPER; Ca_2^+, calcium; NO_3^-, nitrate; NPL7, NIN-LIKE PROTEIN 7; NRT1.1 NITRATE TRANSPORTER1.1; T6P, trehalose 6-phosphate; TCA, tricarboxylic acid. Solid arrows represent a single enzymatic reaction. Dashed arrows and lines represent indirect and direct regulation or enzymatic reactions. Image created with BioRender.com.

availability conditions to lower the remobilization of C to sink organs (mostly grain) and maintain C homeostasis in leaves. In addition, overexpression of *OsNAC23* leads to a rice yield increase of over 13%, denoting that manipulation of this gene is of great interest to improve agronomic traits (Li et al., 2022). Thus, in seeds, C/N metabolism appears to be under tight regulatory control.

SnRK1α1 (also known as KIN10) regulates the phosphorylation status of about 500 proteins (Cho et al., 2016; Li, Sanagi, et al., 2020; Nukarinen et al., 2016; Van Leene et al., 2022), including RAPTOR1B and some crucial enzymes in C (e.g., SUCROSE PHOSPHATE SYNTHASE – SPS, TREHALOSE PHOSPHATE SYNTHASE – TPS, FRUCTOSE-2,6 PHOSPHATE BIPHOSPHATASE) and N (e.g., nitrate reductase) metabolism. This shows that besides massively reprogramming gene expression (Baena-González et al., 2007; Wang et al., 2020), SnRK1 interacts with other C/N signaling pathways and controls the synthesis of important metabolites that play regulatory roles. Trehalose-6-phosphate (T6P), the intermediate of trehalose synthesis, is considered a signal of sucrose availability in plants and also regulates sucrose homeostasis in growing sink organs (Fichtner et al., 2021; Yadav et al., 2014). The negative feedback loop by which high T6P levels reduce sucrose content involves decreasing the supply of hexose phosphates for sucrose synthesis via SUCROSE PHOSPHATE SYNTHASE (SPS) and diverting the flux of C into respiratory pathways (Figueroa & Lunn, 2016). Although the molecular mechanism has not yet been fully elucidated, T6P activates the phosphorylation of the enzymes NR and PEPC, the latter important for the anaplerotic synthesis of organic acids (Figueroa et al., 2016). Thus, T6P also connects C and N metabolisms. The activity of SnRK1 is allosterically inhibited by T6P and other sugar phosphates, such as glucose-6-phosphate and glucose-1-phosphate (Baena-González & Lunn, 2020; Nunes et al., 2013; Zhang et al., 2009). In addition, T6P was shown to reduce the T-loop phosphorylation of KIN10, lowering KIN10 association with the upstream GEMINIVIRUS REP-INTERACTING KINASE 1 necessary for SnRK1 activation (Zhai et al., 2018). Genetic manipulation of SnRK1 catalytic subunits affects sucrose and T6P levels

in mature rosettes (Peixoto et al., 2021). Furthermore, the expression of SnRK1-induced genes matches the opposite behavior of T6P levels along the diel cycle, peaking at the end of the night and reaching a minimum at the end of the day. These results led to the conclusion that SnRK1 plays a role in sucrose homeostasis and transcriptome remodeling during the diel cycle and SnRK1 activity is influenced by diel fluctuations in T6P. Phosphoproteomics and interactome analyses revealed that class II TPS isoforms, which instead of having a catalytic activity to form T6P are regulatory proteins, repress SnRK1 kinase activity, nuclear SnRK1 signaling, and the subcellular localization of the α subunits (Van Leene et al., 2022). Thus, we are beginning to understand the complex relationship between SnRK1 and T6P, which occurs at many levels (Figure 3).

The emerging role of SnRK1-NIN-LIKE PROTEINs in N signaling

Besides phosphorylating NR involved in nitrate assimilation (Jossier et al., 2009), SnRK1 has been linked also to nitrate-signaling. NIN-LIKE PROTEINs (NLPs) have emerged as master regulators in NO_3^- signaling by initiating transcriptional reprogramming (Mu & Luo, 2019; Yan & Nambara, 2023). NITRATE TRANSPORTER 1.1 detects NO_3^- levels at the plasma membrane, generating a calcium influx that leads to the phosphorylation of NPL7 and its nuclear retention (Alvarez et al., 2020) (Figure 3). Recently, KIN10 was demonstrated to phosphorylate NPL7 under C starvation, promoting its cytoplasmic localization and degradation via the proteasome pathway (Wang et al., 2022). Conversely, NO_3^- resupply induced KIN10 degradation. NO_3^- was demonstrated to directly bind to NLP7, triggering a conformational change that allows NPL7 to be retained in the nucleus and thereby perform its transcription activator function (Liu et al., 2022). In this pioneering study, it was found that mutation of all seven Arabidopsis NLP transcription factors abolished plants primary nitrate responses and the developmental programs which they orchestrate. The activation of the synthetic nitrate-responsive reporter *4xNRE-min-LUC* (where NRE denotes a nitrate-responsive *cis*-element widely found in the nitrite reductase gene promoter) was found to be compromised in the *npl7* leaf cell mutant in response to 0.5 mM NO_3^-. Further examination revealed that the nitrate reporter was constitutively activated in cells expressing solely the C-terminal domain of NLP7 (C-NLP7), whereas remained inactive in cells expressing its N-terminal domain (N-NPL7). This observation suggests that N-NPL7 functions as a nitrate repressor domain within the full-length NLP7. To substantiate the repressive role of N-NLP7, the authors engineered a chimeric construct comprising NLP7 and the *Lotus japonicus* NIN (*Lj*NIN), known for constitutively activating the *4xNRE-min-LUC* reporter. Remarkably, only the chimeric version N-NLP7-C-*Lj*NIN abolished the constitutive activation of the reporter and conferred activation solely in the presence of NO_3^-. Further biochemical analysis unveiled that NLP7 directly and selectively binds NO_3^-, as exemplified by microscale thermophoresis and surface plasmon resonance, with a dissociation constant of ~52 μM. The comprehensive exploration of nitrate binding dynamics, coupled with the observation of nucleocytoplasmic reshuttling through a meticulously designed mCitrine-NLP7 biosensor, has unveiled striking similarities to the bacterial nitrate sensor NreA in terms of both biochemistry properties and sequences. This insightful analysis enabled the authors to predict the nuclear localization signal (NLS) within NPL7. Further, through site-directed mutation of the NLS, the study uncovered NPL7 potential impact on various cellular processes, including transcription, transport, metabolism, development, and biomass accumulation (Liu et al., 2022). Thus, NPL7 was also proposed as a new plant NO_3^- sensor and a range of evidence supports further roles in integrating N and P signals (Maeda et al., 2018), growth, and development (Wang et al., 2018; Yu et al., 2016), nodule formation (Marsh et al., 2007), as well as root cap cell release (Kumar et al., 2023). A recent study has additionally focussed on the NPL7 homolog NLP6 (Cheng et al., 2023). Intriguingly NLP6, like NLP7, has a nitrate-dependent nuclear retention mechanism but the nucleo-cytosolic shuttling of both NLP6 and NLP7 are independent of one another. The transcriptomic analysis of the respective mutants revealed that NLP6 and NLP7 might play non-redundant roles as NPL6 activated fewer and different target genes than NLP7. In addition, genetic mutation of *nlp7*, but not *nlp6* leads to overt shoot growth defects (Liu et al., 2022), depicting their potential functional dissimilarities. Recent studies suggest that NLP2 and NLP7 are not only regulators of the primary nitrate responses unlike NLP4, -5, and -8 but are also involved in the regulation of genes in response to ammonium (Cheng et al., 2023; Durand et al., 2023). So far, NLP7 is the best-studied member of the family with considerable insight into its role in the above-mentioned processes. An additional study that is of particular note with respect to C-N interactions is that of (Ariga et al., 2022) which elucidated the NLP7-HOMEOBOX PROTEIN52/54 (HB52/54)-VAR2 module and its response to diverse light and nitrogen conditions. The players HB52/54 regulate the light-dependent expression of *VAR2* which encodes chloroplast proteases involved in the quality control of photodamaged proteins. Intriguingly, this module was found to underpin photosynthetic light energy utilization under high light, as exemplified by genetic enhancements of NPL7 and HB52/54. This was translated by the ability of these plants to maintain adequate photosynthetic activity and fitness when facing photooxidative stress and fluctuating N availability. This study, alongside that of Durand et al. (2023) on NLP2, thus provides strong support for the major role of

NLPs in regulating not only nitrate assimilation but also energy and carbon skeleton supply. This fact notwithstanding, our understanding of the mechanisms by which this is achieved remains fragmentary and in need of further experimentation.

TOR-SnRK1-autophagy signaling is a major player in the regulation of the C/N balance

One biological process maintaining C/N homeostasis during nutrient deprivation is autophagy, in which cellular components can be degraded and recycled in lytic vacuoles. Briefly, cytosolic constituents (proteins, protein complexes, lipid droplets, and organelles) are sequestered into a double-membrane structure named the autophagosome, which is trafficked and delivered to the vacuole for degradation by hydrolases and proteases (Marshall & Vierstra, 2018; Tang & Bassham, 2018). Signaling pathways controlling nutrient status such as TOR and SnRK1 contribute to the regulation of autophagy. Downregulation of *TOR* expression leads to plants having constitutive autophagy accessed by the levels of ATG transcripts and the presence of autophagosomes (Deprost et al., 2007; Liu & Bassham, 2010; Menand et al., 2002), while *TOR* overexpression inhibits autophagy activation (Pu, Luo, & Bassham, 2017). So far, TOR has been shown to negatively regulate autophagy by dissociating the ATG1/ATG13 kinase complex (Mugume et al., 2020). This mechanism seems to occur through the recruitment of one ATG13 isoform by RAPTOR (Son et al., 2018), enabling its phosphorylation alongside that of ATG1 (Van Leene et al., 2019). Moreover, C availability leads to the stabilization of BRASSINAZOLE-RESISTANT 1 (BZR1) mediated by the TOR-brassinosteroid signaling axis, preventing BZR1 degradation by autophagy during hypocotyl elongation (Zhang et al., 2016). BRASSINOSTEROID-INSENSITIVE 2 (BIN2) directly phosphorylates RAPTOR1B, inhibiting TOR-dependent ATG13 phosphorylation and thereby activating autophagy (Liao et al., 2022). This crosstalk between nutrient availability and hormones ensures a supply and demand trade-off for plant growth. In contrast, BZR1 has also been demonstrated to upregulate the transcription of *ATG* genes and autophagosome formation under N starvation in tomato, to degrade unfolded and denatured proteins re-establishing N levels (Wang et al., 2019). The SnRK1 complex was found to be a positive regulator of autophagy. Incubation of transgenic lines overexpressing *ATG8E*, important for autophagosome formation, with T6P inhibited but did not completely block autophagy activation in response to different abiotic stresses, including C and N starvation (Soto-Burgos & Bassham, 2017). These authors also showed through a series of experiments that autophagy is both under the combined control of SnRK1/TOR as well as being controlled by each of them independently. In addition, KIN10 also interacts with ATG1 and ATG13 isoforms *in vitro*, while phosphorylation of ATG1 increases under *KIN10* overexpression (Chen et al., 2017). ATG6 is involved in phagophore decoration with phosphatidylinositol-3-phosphate and *in vitro* ATG6 phosphorylation by SnRK1 promoted autophagy.

PII protein

The prokaryotic trimeric PII protein (*GlnB* and *GlnK* genes) are important C/N integrators regulating the expression of transporters and enzymes involved in N assimilation, including GS (Forchhammer, 2008; Forchhammer et al., 2022; Uhrig et al., 2009). PII is a sensor of energy (ATP) and C-skeletons (2-OG) availability thus bringing about allosteric and covalent modifications such as uridylylation in response to the N status (Uhrig et al., 2009). Plants and algae also contain a highly homologous chloroplastic PII protein, first identified in Arabidopsis (Chen et al., 2006; Hsieh et al., 1998; Uhrig et al., 2009). Previous studies have shown that inhibition of 2-oxoglutarate dehydrogenase by phosphonate analogs of 2-OG resulted in alterations of gene expression in Arabidopsis, that cannot be explained by a direct effect of the phosphonate inhibitors on PII (Araújo et al., 2012). Whatever the metabolic signals, it is clear that they are perceived and bound by a flexible loop domain protruding from each PII monomer in the trimeric complex (the T-loop) (Forchhammer, 2008). Although the cyanobacterial phosphorylation site is conserved in plant sequences, no phosphorylation of this residue was reported (Smith et al., 2004).

PII regulates the first committed step of Arg biosynthesis by interacting with the chloroplastic N-ACETYL GLUTAMATE KINASE (NAGK), both in plants and cyanobacteria (Chen et al., 2006; Ferrario-Méry et al., 2006). The formation of a NAGK-PII protein complex reduces the feedback inhibition by Arg, presumably under conditions in which C-skeletons are available in the form of 2-OG. Interestingly, PII mutants accumulate fewer amino acids, including Arg and Gln, in NH_4^+ grown Arabidopsis plants whereas sugar and starch levels were found to be higher (Ferrario-Méry et al., 2005, 2008). The Arabidopsis PII mutants also displayed a higher nitrite uptake in the chloroplast, in which nitrite is further reduced into NH_4^+ and then Gln, but only in the light (Ferrario-Méry et al., 2008). This could indicate that the PII protein is needed to adjust N assimilation to photosynthesis and the availability of C-skeletons.

It is plausible that the signaling pathway of the PII protein was rewired after the integration of cyanobacteria in early eukaryotes to suit the specific needs of photosynthetic organisms. For example, it was shown that PII regulates the plastidic fatty acid synthesis in Arabidopsis (Feria Bourrellier et al., 2010). Indeed, the biotin carboxyl carrier protein subunits of the plastidial ACETYL-CoA CARBOXYLASE (ACCase) were purified by affinity PII affinity chromatography. ACCase is an initiating step enzyme for the synthesis of fatty acids in plastids. PII inhibited ACCase

activity, which was completely reversed in the presence of 2-OG, thus connecting lipid synthesis to the availability of C. PII expression was, furthermore, strongly enhanced during early embryo maturation in a WRINKLED-1 dependent manner (Baud et al., 2010). This suggests that PII activity is needed for the regulation of C/N interactions during seed development and the coordination of the synthesis of storage proteins, that require N, and storage lipids. Recently, it was found that PII and NAGK interact together in dot-like aggregates within the chloroplast and that these aggregates co-localize with plastidial vesicles involved in protein degradation such as RUBISCO-containing bodies (Krieger et al., 2021). This could suggest that PII controls not only enzyme activities but also enzyme stability in large complexes which could be involved in substrate channeling during lipid or amino acids synthesis within the plastids while integrating both C and N information by sensing Gln and 2-OG levels.

Finally, the fact that PII mutants or overexpressors exhibit small, and often subtle, physiological and metabolic changes could indicate that the PII protein was conserved during evolution in photosynthetic organisms to fine-tune various C and N biosynthetic activities within the plastids in response to developmental (e.g., in developing seeds) or C/N balance signals. Our deeper understanding of the cyanobacterial PII allows a more prominent embedding in the PII signal and its links to other signaling pathways (Barske et al., 2023; Forchhammer et al., 2022; Mantovani et al., 2022; Scholl et al., 2020). However, the integration of plant PII signaling with the overall metabolic state of the cell could require connections to other signaling pathways such as those involving TOR and SnRK1 kinases. Considerable further research is required in this direction (Figure 4). That said the recent finding that CO_2 can interact with lysine residues in the PII protein provides an intriguing further possible link between C and N metabolism that could be bridged by this protein (King et al., 2022).

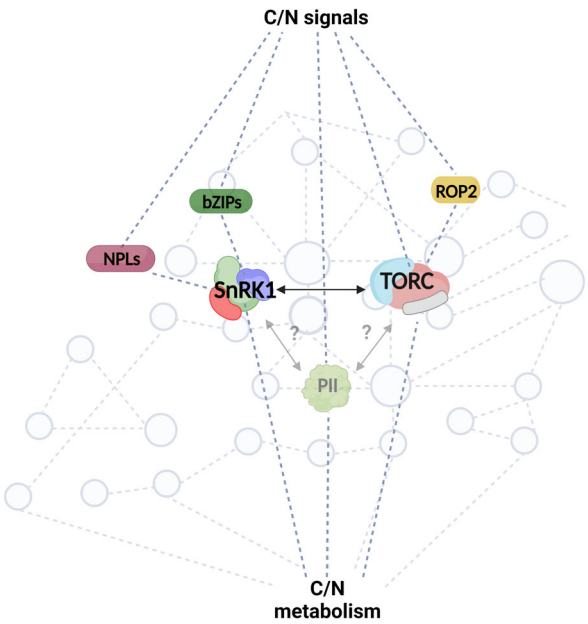

Figure 4. Overview of the interconnections between C/N signaling pathways and hypothetical connection between TOR/SnRK1 and PII.
The sensing and metabolic network involved in C/N signaling incorporates novel components like bZIPs, NPLs, and ROPs, as well as potential new ones such as PII being interconnected with TORC and SnRK1. bZIPs, BASIC LEUCINE ZIPPERS; NINs, NIN-LIKE PROTEINS; ROPs, RHO-LIKE GTPASES; SnRK1, SUCROSE-NON-FERMENTING-1-RELATED PROTEIN KINASE 1, TORC, TARGET OF RAPAMYCIN COMPLEX. Image created with BioRender.com.

FUTURE CHALLENGES

The signaling network involving nutrient acquisition, partition, use, and allocation during plant growth and development is highly complex. Significant advances have been made in the last decades to unravel how C and N homeostasis is achieved, such as the identification of new upstream and downstream targets in major signaling pathways. This involved genetic screening of mutants and generation of transgenic lines combined with omics technologies and other fine approaches (e.g., affinity purification and cell biology) to capture responses to perturbations in C and N status. These findings have enabled a broader understanding of how these pathways operate and interact with each other to adjust metabolism according to C and N signals and demands aiming at homeostasis, especially in unicellular algae *Chlamydomonas*. Nevertheless, there is far more to be investigated as several mechanisms related to signal sensing and transduction remain unknown. In addition, the complexity of plant physiology is often overlooked, such as the function of these signaling pathways in the communication between source and sink tissues and cells which is of fundamental importance for plant productivity. We summarize major future challenges:

- The identification of additional enzymes, transporters, and receptors that facilitate the C and N sensing and relay information to TOR and SnRK1: the function of many components annotated as part of this signaling network are still not fully elucidated. A deeper knowledge might provide additional information on how these components operate not only within the cell but also between organs along the plant life cycle. This can be unraveled by performing genome-wide association studies using ecotypes subjected to various C and N conditions coupled with treatments that directly affect the activity of TOR and SnRK1.
- The mechanism by which TOR influences N sensing and metabolism remains poorly understood, despite recent and interesting findings. The role of TOR in the regulation of mRNA translation suggests a tight connection

with N status. Exploring possible connections between TOR and other signaling modules, such as NINs, could enhance our understanding of the intricate relationship between TOR and N metabolism.

- Unravel how these signaling pathways (TOR, SnRK1, and PII) coordinate multiple signals into metabolic and physiological responses according to tissue-specific requirements: this kind of information will provide hints on how these pathways decode and transduce signal-specificity locally and systemically to orchestrate growth and development.
- Establish the molecular and metabolic hierarchy of TOR and SnRK1 signaling pathways under a range of developmental and environmental conditions, which can be untangled by performing isotope labeling.

ACKNOWLEDGEMENTS

This work was supported by the Max Planck Society. CM is partly supported by a French State grant (Saclay Plant Sciences, ANR-17-EUR-0007, EUR SPS-GSR). We apologize in advance to colleagues whose work we were not able to cover in this review.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

Alvarez, J.M., **Schinke, A.-L.**, **Brooks, M.D.**, **Pasquino, A.**, **Leonelli, L.**, **Varala, K.** ***et al.*** (2020) Transient genome-wide interactions of the master transcription factor NLP7 initiate a rapid nitrogen-response cascade. *Nature Communications*, **11**, 1157. Available from: https://doi.org/10.1038/s41467-020-14979-6

Anderson, G.H., **Veit, B.** & **Hanson, M.R.** (2005) The Arabidopsis AtRaptor genes are essential for post-embryonic plant growth. *BMC Biology*, **3**, 1–11.

Araújo, W.L., **Tohge, T.L.**, **Nunes-Nesi, A.**, **Daloso, D.M.**, **Nimick, M.**, **Krahnert, I.** ***et al.*** (2012) Phosphonate analogs of 2-oxoglutarate perturb metabolism and gene expression in illuminated Arabidopsis leaves. *Frontiers in Plant Science*, **3**, 114.

Ariga, T., **Sakuraba, Y.**, **Zhuo, M.**, **Yang, M.** & **Yanagisawa, S.** (2022) The Arabidopsis NLP7-HB52/54-VAR2 pathway modulates energy utilization in diverse light and nitrogen conditions. *Current Biology*, **32**, 5344–5353.e6.

Artins, A. & **Caldana, C.** (2022) The metabolic homeostaTOR: the balance of holding on or letting grow. *Current Opinion in Plant Biology*, **66**, 102196.

Aylett, C.H.S., **Sauer, E.**, **Imseng, S.**, **Boehringer, D.**, **Hall, M.N.**, **Ban, N.** ***et al.*** (2016) Architecture of human mTOR complex 1. *Science*, **351**, 48–52. Available from: https://doi.org/10.1126/science.aaa3870

Baena-González, E. & **Lunn, J.E.** (2020) SnRK1 and trehalose 6-phosphate – two ancient pathways converge to regulate plant metabolism and growth. *Current Opinion in Plant Biology*, **55**, 52–59.

Baena-González, E., **Rolland, F.**, **Thevelein, J.M.** & **Sheen, J.** (2007) A central integrator of transcription networks in plant stress and energy signalling. *Nature*, **448**, 938–942.

Barske, T., **Spät, P.**, **Schubert, H.**, **Walke, P.**, **Maček, B.** & **Hagemann, M.** (2023) The role of serine/threonine-specific protein kinases in cyanobacteria – SpkB is involved in acclimation to fluctuating conditions in *Synechocystis* sp. PCC 6803. *Molecular & Cellular Proteomics*, **22**, 100656.

Baud, S., **Feria Bourrellier, A.B.**, **Azzopardi, M.**, **Berger, A.**, **Dechorgnat, J.**, **Daniel-Vedele, F.** ***et al.*** (2010) PII is induced by WRINKLED1 and fine-tunes fatty acid composition in seeds of *Arabidopsis thaliana*. *The Plant Journal*, **64**, 291–303.

Caldana, C., **Li, Y.**, **Leisse, A.**, **Zhang, Y.**, **Bartholomaeus, L.**, **Fernie, A.R.** ***et al.*** (2013) Systemic analysis of inducible target of rapamycin mutants reveal a general metabolic switch controlling growth in *Arabidopsis thaliana*. *The Plant Journal*, **73**, 897–909. Available from: https://doi.org/10.1111/tpj.12080

Caldana, C., **Martins, M.C.M.**, **Mubeen, U.** & **Urrea-Castellanos, R.** (2019) The magic 'hammer' of TOR: the multiple faces of a single pathway in the metabolic regulation of plant growth and development. *Journal of Experimental Botany*, **70**, 2217–2225.

Cao, P., **Kim, S.-J.**, **Xing, A.**, **Schenck, C.A.**, **Liu, L.**, **Jiang, N.** ***et al.*** (2019) Homeostasis of branched-chain amino acids is critical for the activity of TOR signaling in Arabidopsis. *eLife*, **8**, e50747.

Chen, L., **Su, Z.Z.**, **Huang, L.**, **Xia, F.N.**, **Qi, H.**, **Xie, L.J.** ***et al.*** (2017) The AMP-activated protein kinase kin10 is involved in the regulation of autophagy in Arabidopsis. *Frontiers in Plant Science*, **8**, 1201.

Chen, Y.M., **Ferrar, T.S.**, **Lohmeier-Vogel, E.M.**, **Morrice, N.**, **Mizuno, Y.**, **Berenger, B.** ***et al.*** (2006) The PII signal transduction protein of *Arabidopsis thaliana* forms an arginine-regulated complex with plastid N-acetyl glutamate kinase. *The Journal of Biological Chemistry*, **281**, 5726–5733.

Cheng, Y.H., **Durand, M.**, **Brehaut, V.**, **Hsu, F.C.**, **Kelemen, Z.**, **Texier, Y.** ***et al.*** (2023) Interplay between NIN-LIKE PROTEINs 6 and 7 in nitrate signaling. *Plant Physiology*, **192**, 3049–3068. Available from: https://doi.org/10.1093/plphys/kiad242

Cho, H.-Y., **Wen, T.-N.**, **Wang, Y.-T.** & **Shih, M.-C.** (2016) Quantitative phosphoproteomics of protein kinase SnRK1 regulated protein phosphorylation in Arabidopsis under submergence. *Journal of Experimental Botany*, **67**, 2745–2760. Available from: https://doi.org/10.1093/jxb/erw107

Coruzz, G. & **Bush, D.R.** (2001) Nitrogen and carbon nutrient and metabolite signaling in plants. *Plant Physiology*, **125**, 61–64.

da Silva, V.C.H., **Martins, M.C.M.**, **Calderan-Rodrigues, M.J.**, **Artins, A.**, **Monte Bello, C.C.**, **Gupta, S.** ***et al.*** (2021) Shedding light on the dynamic role of the "target of rapamycin" kinase in the fast-growing C4 species *Setaria viridis*, a suitable model for biomass crops. *Frontiers in Plant Science*, **12**, 637508.

Deprost, D., **Yao, L.**, **Sormani, R.**, **Moreau, M.**, **Leterreux, G.**, **Bedu, M.** ***et al.*** (2007) The Arabidopsis TOR kinase links plant growth, yield, stress resistance and mRNA translation. *EMBO Reports*, **8**, 864–870.

Dietrich, K., **Weltmeier, F.**, **Ehlert, A.**, **Weiste, C.**, **Stahl, M.**, **Harter, K.** ***et al.*** (2011) Heterodimers of the Arabidopsis transcription factors bZIP1 and bZIP53 reprogram amino acid metabolism during low energy stress. *Plant Cell*, **23**, 381–395. Available from: https://doi.org/10.1105/tpc.110.075390

Dobrenel, T., **Caldana, C.**, **Hanson, J.**, **Robaglia, C.**, **Vincentz, M.**, **Veit, B.** ***et al.*** (2016) TOR signaling and nutrient sensing. *Annual Review of Plant Biology*, **67**, 261–285.

Dobrenel, T., **Marchive, C.**, **Azzopardi, M.**, **Clément, G.**, **Moreau, M.**, **Sormani, R.** ***et al.*** (2013) Sugar metabolism and the plant target of rapamycin kinase: a sweet operaTOR? *Frontiers in Plant Science*, **4**, 93.

Durand, M., **Brehaut, V.**, **Clement, G.**, **Kelemen, Z.**, **Macé, J.**, **Feil, R.** ***et al.*** (2023) The Arabidopsis transcription factor NLP2 regulates early nitrate responses and integrates nitrate assimilation with energy and carbon skeleton supply. *Plant Cell*, **35**, 1429–1454. Available from: https://doi.org/10.1093/plcell/koad025

Emanuelle, S., **Hossain, M.I.**, **Moller, I.E.**, **Pedersen, H.L.**, **van de Meene, A.M.L.**, **Doblin, M.S.** ***et al.*** (2015) SnRK1 from *Arabidopsis thaliana* is an atypical AMPK. *The Plant Journal*, **82**, 183–192. Available from: https://doi.org/10.1111/tpj.12813

Enggrob, K.L., **Jakobsen, C.M.**, **Pedersen, I.F.** & **Rasmussen, J.** (2019) Newly depolymerized large organic N contributes directly to amino acid uptake in young maize plants. *The New Phytologist*, **224**, 689–699. Available from: https://doi.org/10.1111/nph.16070

Feria Bourrellier, A.B., **Valot, B.**, **Guillot, A.**, **Ambard-Bretteville, F.**, **Vidal, J.** & **Hodges, M.** (2010) Chloroplast acetyl-CoA carboxylase activity is 2-oxoglutarate-regulated by interaction of PII with the biotin carboxyl carrier subunit. *Proceedings of the National Academy of Sciences of the United States of America*, **107**, 502–507.

Ferrario-Méry, S., **Besin, E.**, **Pichon, O.**, **Meyer, C.** & **Hodges, M.** (2006) The regulatory PII protein controls arginine biosynthesis in Arabidopsis. *FEBS Letters*, **580**, 2015–2020. Available from: https://doi.org/10.1016/j.febslet.2006.02.075

Ferrario-Méry, S., **Bouvet, M.**, **Leleu, O.**, **Savino, G.**, **Hodges, M.** & **Meyer, C.** (2005) Physiological characterisation of Arabidopsis mutants affected in the expression of the putative regulatory protein PII. *Planta*, **223**, 28–39.

Ferrario-Méry, S., **Meyer, C.** & **Hodges, M.** (2008) Chloroplast nitrite uptake is enhanced in Arabidopsis PII mutants. *FEBS Letters*, **582**, 1061–1066.

Fichtner, F., **Barbier, F.F.**, **Annunziata, M.G.**, **Feil, R.**, **Olas, J.J.**, **Mueller-Roeber, B.** ***et al.*** (2021) Regulation of shoot branching in Arabidopsis by trehalose 6-phosphate. *The New Phytologist*, **229**, 2135–2151.

Figueroa, C.M., **Feil, R.**, **Ishihara, H.**, **Watanabe, M.**, **Kölling, K.**, **Krause, U.** ***et al.*** (2016) Trehalose 6–phosphate coordinates organic and amino acid metabolism with carbon availability. *The Plant Journal*, **85**, 410–423. Available from: https://doi.org/10.1111/tpj.13114

Figueroa, C.M. & **Lunn, J.E.** (2016) A tale of two sugars: trehalose 6-phosphate and sucrose. *Plant Physiology*, **172**, 7–27.

Forchhammer, K. (2008) PII signal transducers: novel functional and structural insights. *Trends in Microbiology*, **16**, 65–72.

Forchhammer, K., **Selim, K.A.** & **Huergo, L.F.** (2022) New views on PII signaling: from nitrogen sensing to global metabolic control. *Trends in Microbiology*, **30**, 722–735.

Frank, A., **Matiolli, C.C.**, **Viana, A.J.C.**, **Hearn, T.J.**, **Kusakina, J.**, **Belbin, F.E.** ***et al.*** (2018) Circadian entrainment in Arabidopsis by the sugar-responsive transcription factor bZIP63. *Current Biology*, **28**, 2597–2606.e6.

Garg, A., **Kirchler, T.**, **Fillinger, S.**, **Wanke, F.**, **Stadelhofer, B.**, **Stahl, M.** ***et al.*** (2019) Targeted manipulation of bZIP53 DNA-binding properties influences Arabidopsis metabolism and growth. *Journal of Experimental Botany*, **70**, 5659–5671. Available from: https://doi.org/10.1093/jxb/erz309

González, A. & **Hall, M.N.** (2017) Nutrient sensing and TOR signaling in yeast and mammals. *The EMBO Journal*, **36**, 397–408. Available from: https://doi.org/10.15252/embj.201696010

Guo, N., **Hu, J.**, **Yan, M.**, **Qu, H.**, **Luo, L.**, **Tegeder, M.** ***et al.*** (2020) *Oryza sativa* lysine-histidine-type transporter 1 functions in root uptake and root-to-shoot allocation of amino acids in rice. *The Plant Journal*, **103**, 395–411. Available from: https://doi.org/10.1111/tpj.14742

Han, C., **Hua, W.**, **Li, J.**, **Qiao, Y.**, **Yao, L.**, **Hao, W.** ***et al.*** (2022) TOR promotes guard cell starch degradation by regulating the activity of β-AMYLASE1 in Arabidopsis. *Plant Cell*, **34**, 1038–1053.

Henninger, M., **Pedrotti, L.**, **Krischke, M.**, **Draken, J.**, **Wildenhain, T.**, **Fekete, A.** ***et al.*** (2022) The evolutionarily conserved kinase SnRK1 orchestrates resource mobilization during Arabidopsis seedling establishment. *Plant Cell*, **34**, 616–632. Available from: https://doi.org/10.1093/plcell/koab270

Henriques, R., **Magyar, Z.** & **Bögre, L.** (2013) S6K1 and E2FB are in mutually antagonistic regulatory links controlling cell growth and proliferation in Arabidopsis. *Plant Signaling & Behavior*, **8**, e24367. Available from: https://doi.org/10.4161/psb.24367

Hodges, M. (2002) Enzyme redundancy and the importance of 2-oxoglutarate in plant ammonium assimilation. *Journal of Experimental Botany*, **53**, 905–916.

Hsieh, M.-H., **Lam, H.-M.**, **van de Loo, F.J.** & **Coruzzi, G.** (1998) A PII-like protein in Arabidopsis: putative role in nitrogen sensing. *Proceedings of the National Academy of Sciences of the United States of America*, **95**, 13965–13970.

Hu, Y., **Liu, J.**, **Lin, Y.**, **Xu, X.**, **Xia, Y.**, **Bai, J.** ***et al.*** (2022) Sucrose nonfermenting-1-related protein kinase 1 regulates sheath-to-panicle transport of nonstructural carbohydrates during rice grain filling. *Plant Physiology*, **189**, 1694–1714.

Huang, X., **Zheng, C.**, **Liu, F.**, **Yang, C.**, **Zheng, P.**, **Lu, X.** ***et al.*** (2019) Genetic analyses of the Arabidopsis ATG1 kinase complex reveal both kinase-dependent and independent autophagic routes during fixed-carbon starvation. *Plant Cell*, **31**, 2973–2995. Available from: https://doi.org/10.1105/tpc.19.00066

Ingargiola, C., **Jéhanno, I.**, **Forzani, C.**, **Marmagne, A.**, **Broutin, J.**, **Clément, G.** ***et al.*** (2023) The Arabidopsis target of rapamycin kinase regulates ammonium assimilation and glutamine metabolism. *Plant Physiology*, **192**, 2943–2957. Available from: https://doi.org/10.1093/plphys/kiad216

Jiang, Z., **Wang, M.**, **Nicolas, M.**, **Ogé, L.**, **Pérez-Garcia, M.D.**, **Crespel, L.** ***et al.*** (2022) Glucose-6-phosphate dehydrogenases: the hidden players of plant physiology. *International Journal of Molecular Sciences*, **23**, 16128.

Jossier, M., **Bouly, J.P.**, **Meimoun, P.**, **Arjmand, A.**, **Lessard, P.**, **Hawley, S.** ***et al.*** (2009) SnRK1 (SNF1-related kinase 1) has a central role in sugar and ABA signalling in *Arabidopsis thaliana*. *The Plant Journal*, **59**, 316–328. Available from: https://doi.org/10.1111/j.1365-313X.2009.03871.x

Judge, A. & **Dodd, M.S.** (2020) Metabolism. *Essays in Biochemistry*, **64**, 607–647.

Jüppner, J., **Mubeen, U.**, **Leisse, A.**, **Caldana, C.**, **Wiszniewski, A.**, **Steinhauser, D.** ***et al.*** (2018) The target of rapamycin kinase affects biomass accumulation and cell cycle progression by altering carbon/nitrogen balance in synchronized *Chlamydomonas reinhardtii* cells. *The Plant Journal*, **93**, 355–376. Available from: https://doi.org/10.1111/tpj.13787

Kim, D.H., **Sarbassov, D.D.**, **Ali, S.M.**, **King, J.E.**, **Latek, R.R.**, **Erdjument-Bromage, H.** ***et al.*** (2002) mTOR interacts with Raptor to form a nutrient-sensitive complex that signals to the cell growth machinery. *Cell*, **110**, 163–175.

King, D.T., **Zhu, S.**, **Hardie, D.B.**, **Serrano-Negrón, J.E.**, **Madden, Z.**, **Kolappan, S.** ***et al.*** (2022) Chemoproteomic identification of CO_2-dependent lysine carboxylation in proteins. *Nature Chemical Biology*, **18**, 782–791.

Krieger, N., **Pastryk, K.-F.**, **Forchhammer, K.** & **Kolukisaoglu, Ü.** (2021) Arabidopsis PII proteins form characteristic foci in chloroplasts indicating novel properties in protein interaction and degradation. *International Journal of Molecular Sciences*, **22**, 12666.

Kumar, N., **Caldwell, C.** & **Iyer-Pascuzzi, A.S.** (2023) The NIN-LIKE PROTEIN 7 transcription factor modulates auxin pathways to regulate root cap development in Arabidopsis. *Journal of Experimental Botany*, **74**, 3047–3059. Available from: https://doi.org/10.1093/jxb/erad058

Lejay, L., **Wirth, J.**, **Pervent, M.**, **Cross, J.M.F.**, **Tillard, P.** & **Gojon, A.** (2008) Oxidative pentose phosphate pathway-dependent sugar sensing as a mechanism for regulation of root ion transporters by photosynthesis. *Plant Physiology*, **146**, 2036–2053.

Li, C., **Qi, W.**, **Liang, Z.**, **Yang, X.**, **Ma, Z.** & **Song, R.** (2020) A SnRK1-ZmRFWD3-opaque2 signaling axis regulates diurnal nitrogen accumulation in maize seeds. *Plant Cell*, **32**, 2823–2841.

Li, X., **Cai, W.**, **Liu, Y.**, **Li, H.**, **Fu, L.**, **Liu, Z.** ***et al.*** (2017) Differential TOR activation and cell proliferation in Arabidopsis root and shoot apexes. *Proceedings of the National Academy of Sciences of the United States of America*, **114**, 2765–2770.

Li, X., **Sanagi, M.**, **Lu, Y.**, **Nomura, Y.**, **Stolze, S.C.**, **Yasuda, S.** ***et al.*** (2020) Protein phosphorylation dynamics under carbon/nitrogen-nutrient stress and identification of a cell death-related receptor-like kinase in Arabidopsis. *Frontiers in Plant Science*, **11**, 377.

Li, Z., **Wei, X.**, **Tong, X.**, **Zhao, J.**, **Liu, X.**, **Wang, H.** ***et al.*** (2022) The OsNAC23-Tre6P-SnRK1a feed-forward loop regulates sugar homeostasis and grain yield in rice. *Molecular Plant*, **15**, 706–722.

Liao, C.-Y., **Pu, Y.**, **Nolan, T.M.**, **Montes, C.**, **Guo, H.**, **Walley, J.W.** ***et al.*** (2022) Brassinosteroids modulate autophagy through phosphorylation of RAPTOR1B by the GSK3-like kinase BIN2 in Arabidopsis. *Autophagy*, **24**, 1293–1310.

Liu, K.-H., **Liu, M.**, **Lin, Z.**, **Wang, Z.F.**, **Chen, B.**, **Liu, C.** ***et al.*** (2022) NIN-like protein 7 transcription factor is a plant nitrate sensor. *Science*, **377**, 1419–1425. Available from: https://doi.org/10.1126/science.add1104

Liu, Y. & **Bassham, D.C.** (2010) TOR is a negative regulator of autophagy in *Arabidopsis thaliana*. *PLoS One*, **5**, e11883. Available from: https://doi.org/10.1371/journal.pone.0011883

Liu, Y., **Duan, X.**, **Zhao, X.**, **Ding, W.**, **Wang, Y.** & **Xiong, Y.** (2021) Diverse nitrogen signals activate convergent ROP2-TOR signaling in Arabidopsis. *Developmental Cell*, **56**, 1283–1295.e5.

Ma, J., **Hanssen, M.**, **Lundgren, K.**, **Hernández, L.**, **Delatte, T.**, **Ehlert, A.** ***et al.*** (2011) The sucrose-regulated Arabidopsis transcription factor bZIP11 reprograms metabolism and regulates trehalose metabolism. *The New Phytologist*, **191**, 733–745.

Maeda, Y., **Konishi, M.**, **Kiba, T.**, **Sakuraba, Y.**, **Sawaki, N.**, **Kurai, T.** ***et al.*** (2018) A NIGT1-centred transcriptional cascade regulates nitrate signalling and incorporates phosphorus starvation signals in Arabidopsis. *Nature Communications*, **9**, 1376.

Mair, A., **Pedrotti, L.**, **Wurzinger, B.**, **Anrather, D.**, **Simeunovic, A.**, **Weiste, C.** ***et al.*** (2015) SnRK1-triggered switch of bZIP63 dimerization mediates the low-energy response in plants. *eLife*, **4**, e05828.

Mallén-Ponce, M.J., **Pérez-Pérez, M.E.** & **Crespo, J.L.** (2022) Photosynthetic assimilation of CO_2 regulates TOR activity. *Proceedings of the National Academy of Sciences of the United States of America*, **119**, e2115261119. Available from: https://doi.org/10.1073/pnas.2115261119

Mantovani, O., **Reimann, V.**, **Haffner, M.**, **Herrmann, F.P.**, **Selim, K.A.**, **Forchhammer, K.** ***et al.*** (2022) The impact of the cyanobacterial carbon-regulator protein SbtB and of the second messengers cAMP and c-di-AMP on CO_2-dependent gene expression. *The New Phytologist*, **234**, 1801–1816. Available from: https://doi.org/10.1111/nph.18094

Marsh, J.F., **Rakocevic, A.**, **Mitra, R.M.**, **Brocard, L.**, **Sun, J.**, **Eschstruth, A.** ***et al.*** (2007) *Medicago truncatula* NIN is essential for Rhizobial-

independent nodule organogenesis induced by autoactive calcium/calmodulin-dependent protein kinase. *Plant Physiology*, **144**, 324–335. Available from: https://doi.org/10.1104/pp.106.093021

Marshall, R.S. & **Vierstra, R.D.** (2018) Autophagy: the master of bulk and selective recycling. *Annual Review of Plant Biology*, **69**, 173–208. Available from: https://doi.org/10.1146/annurev-arplant-042817-040606

Martínez-Barajas, E. & **Coello, P.** (2020) Review: how do SnRK1 protein kinases truly work? *Plant Science*, **291**, 110330.

Menand, B., **Desnos, T.**, **Nussaume, L.**, **Berger, F.**, **Bouchez, D.**, **Meyer, C.** ***et al.*** (2002) Expression and disruption of the Arabidopsis TOR (target of rapamycin) gene. *Proceedings of the National Academy of Sciences of the United States of America*, **99**, 6422–6427.

Montané, M.-H. & **Menand, B.** (2013) ATP-competitive mTOR kinase inhibitors delay plant growth by triggering early differentiation of meristematic cells but no developmental patterning change. *Journal of Experimental Botany*, **64**, 4361–4374.

Montané, M.-H. & **Menand, B.** (2019) TOR inhibitors: from mammalian outcomes to pharmacogenetics in plants and algae. *Journal of Experimental Botany*, **70**, 2297–2312.

Moreau, M., **Azzopardi, M.**, **Clément, G.**, **Dobrenel, T.**, **Marchive, C.**, **Renne, C.** ***et al.*** (2012) Mutations in the Arabidopsis homolog of LST8/GβL, a partner of the target of rapamycin kinase, impair plant growth, flowering, and metabolic adaptation to long days. *Plant Cell*, **24**, 463–481.

Mu, X. & **Luo, J.** (2019) Evolutionary analyses of NIN-like proteins in plants and their roles in nitrate signaling. *Cellular and Molecular Life Sciences*, **76**, 3753–3764. Available from: https://doi.org/10.1007/s00018-019-03164-8

Mubeen, U., **Giavalisco, P.** & **Caldana, C.** (2019) TOR inhibition interrupts the metabolic homeostasis by shifting the carbon-nitrogen balance in *Chlamydomonas reinhardtii*. *Plant Signaling & Behavior*, **14**, 1670595.

Mubeen, U., **Jüppner, J.**, **Alpers, J.**, **Hincha, D.K.** & **Giavalisco, P.** (2018) Target of rapamycin inhibition in *Chlamydomonas reinhardtii* triggers de novo amino acid synthesis by enhancing nitrogen assimilation. *Plant Cell*, **30**, 2240–2254.

Mugume, Y., **Kazibwe, Z.** & **Bassham, D.C.** (2020) Target of rapamycin in control of autophagy: puppet master and signal integrator. *International Journal of Molecular Sciences*, **21**, 8259.

Nukarinen, E., **Nägele, T.**, **Pedrotti, L.**, **Wurzinger, B.**, **Mair, A.**, **Landgraf, R.** ***et al.*** (2016) Quantitative phosphoproteomics reveals the role of the AMPK plant ortholog SnRK1 as a metabolic master regulator under energy deprivation. *Scientific Reports*, **6**, 31697.

Nunes, C., **Primavesi, L.F.**, **Patel, M.K.**, **Martinez-Barajas, E.**, **Powers, S.J.**, **Sagar, R.** ***et al.*** (2013) Inhibition of SnRK1 by metabolites: tissue-dependent effects and cooperative inhibition by glucose 1-phosphate in combination with trehalose 6-phosphate. *Plant Physiology and Biochemistry*, **63**, 89–98.

Nunes-Nesi, A., **Fernie, A.R.** & **Stitt, M.** (2010) Metabolic and signaling aspects underpinning the regulation of plant carbon nitrogen interactions. *Molecular Plant*, **3**, 973–996.

O'Leary, B.M., **Oh, G.G.K.**, **Lee, C.P.** & **Millar, A.H.** (2020) Metabolite regulatory interactions control plant respiratory metabolism via target of rapamycin (TOR) kinase activation. *Plant Cell*, **32**, 666–682.

Pancha, I., **Shima, H.**, **Higashitani, N.**, **Igarashi, K.**, **Higashitani, A.**, **Tanaka, K.** ***et al.*** (2019) Target of rapamycin-signaling modulates starch accumulation via glycogenin phosphorylation status in the unicellular red alga *Cyanidioschyzon merolae*. *The Plant Journal*, **97**, 485–499. Available from: https://doi.org/10.1111/tpj.14136

Pedrotti, L., **Weiste, C.**, **Nägele, T.**, **Wolf, E.**, **Lorenzin, F.**, **Dietrich, K.** ***et al.*** (2018) Snf1-RELATED KINASE1-controlled C/S1-bZIP signaling activates alternative mitochondrial metabolic pathways to ensure plant survival in extended darkness. *Plant Cell*, **30**, 495–509.

Peixoto, B. & **Baena-González, E.** (2022) Management of plant central metabolism by SnRK1 protein kinases. *Journal of Experimental Botany*, **73**, 7068–7082. Available from: https://doi.org/10.1093/jxb/erac261

Peixoto, B., **Moraes, T.A.**, **Mengin, V.**, **Margalha, L.**, **Vicente, R.**, **Feil, R.** ***et al.*** (2021) Impact of the SnRK1 protein kinase on sucrose homeostasis and the transcriptome during the diel cycle. *Plant Physiology*, **187**, 1357–1373. Available from: https://doi.org/10.1093/plphys/kiab350/6329648

Perdoux, R., **Barrada, A.**, **Boulaiz, M.**, **Garau, C.**, **Belbachir, C.**, **Lecampion, C.** ***et al.*** (2023) A drug-resistant mutation in plant target of rapamycin validates the specificity of ATP-competitive TOR inhibitors in vivo. *The Plant Journal*. Available from: https://doi.org/10.1111/tpj.16564

Pu, Y., **Luo, X.** & **Bassham, D.C.** (2017) TOR-dependent and -independent pathways regulate autophagy in *Arabidopsis thaliana*. *Frontiers in Plant Science*, **8**, e11883.

Pu, Y., **Soto-Burgos, J.** & **Bassham, D.C.** (2017) Regulation of autophagy through SnRK1 and TOR signaling pathways. *Plant Signaling & Behavior*, **12**, e1395128. Available from: https://doi.org/10.1080/15592324.2017.1395128

Ramon, M., **Dang, T.V.T.**, **Broeckx, T.**, **Hulsmans, S.**, **Crepin, N.**, **Sheen, J.** ***et al.*** (2019) Default activation and nuclear translocation of the plant cellular energy sensor SnRK1 regulate metabolic stress responses and development. *Plant Cell*, **31**, 1614–1632. Available from: https://doi.org/10.1105/tpc.18.00500

Ren, M., **Venglat, P.**, **Qiu, S.**, **Feng, L.**, **Cao, Y.**, **Wang, E.** ***et al.*** (2012) Target of rapamycin signaling regulates metabolism, growth, and life span in Arabidopsis. *Plant Cell*, **24**, 4850–4874.

Salem, M.A., **Li, Y.**, **Bajdzienko, K.**, **Fisahn, J.**, **Watanabe, M.**, **Hoefgen, R.** ***et al.*** (2018) RAPTOR controls developmental growth transitions by altering the hormonal and metabolic balance. *Plant Physiology*, **177**, 565–593.

Sanagi, M., **Aoyama, S.**, **Kubo, A.**, **Lu, Y.**, **Sato, Y.**, **Ito, S.** ***et al.*** (2021) Low nitrogen conditions accelerate flowering by modulating the phosphorylation state of FLOWERING BHLH 4 in Arabidopsis. *Proceedings of the National Academy of Sciences of the United States of America*, **118**, e2022942118. Available from: https://doi.org/10.1073/pnas.2022942118

Saroussi, S., **Karns, D.A.J.**, **Thomas, D.C.**, **Bloszies, C.**, **Fiehn, O.**, **Posewitz, M.C.** ***et al.*** (2019) Alternative outlets for sustaining photosynthetic electron transport during dark-to-light transitions. *Proceedings of the National Academy of Sciences of the United States of America*, **166**, 11518–11527. Available from: https://doi.org/10.1073/pnas.1903185116

Scarpin, M.R., **Leiboff, S.** & **Brunkard, J.O.** (2020) Parallel global profiling of plant tor dynamics reveals a conserved role for larp1 in translation. *eLife*, **9**, 58795.

Schaufelberger, M., **Galbier, F.**, **Herger, A.**, **de Brito Francisco, R.**, **Roffler, S.**, **Clement, G.** ***et al.*** (2019) Mutations in the Arabidopsis ROL17/isopropylmalate synthase 1 locus alter amino acid content, modify the TOR network, and suppress the root hair cell development mutant lrx1. *Journal of Experimental Botany*, **70**, 2313–2323.

Schepetilnikov, M., **Dimitrova, M.**, **Mancera-Martínez, E.**, **Geldreich, A.**, **Keller, M.**, **Ryabova, L.A.** ***et al.*** (2013) TOR and S6K1 promote translation reinitiation of uORF-containing mRNAs via phosphorylation of eIF3h. *The EMBO Journal*, **32**, 1087–1102.

Schepetilnikov, M., **Makarian, J.**, **Srour, O.**, **Geldreich, A.**, **Yang, Z.**, **Chicher, J.** ***et al.*** (2017) GTPase ROP2 binds and promotes activation of target of rapamycin, TOR, in response to auxin. *The EMBO Journal*, **36**, 886–903. Available from: https://doi.org/10.15252/embj.201694816

Scholl, J., **Dengler, L.**, **Bader, L.** & **Forchhammer, K.** (2020) Phosphoenolpyruvate carboxylase from the cyanobacterium *Synechocystis* sp. PCC 6803 is under global metabolic control by PII signaling. *Molecular Microbiology*, **114**, 292–307. Available from: https://doi.org/10.1111/mmi.14512

Sharkey, T.D. (2019) Discovery of the canonical Calvin–Benson cycle. *Photosynthesis Research*, **140**, 235–252. Available from: https://doi.org/10.1007/s11120-018-0600-2

Shi, L., **Wu, Y.** & **Sheen, J.** (2018) TOR signaling in plants: conservation and innovation. *Development*, **145**, dev160887.

Smith, A.M. & **Zeeman, S.C.** (2020) Starch: a flexible, adaptable carbon store coupled to plant. *Growth*, **71**, 217–245. Available from: https://doi.org/10.1146/annurev-arplant-050718-100241

Smith, C.S., **Morrice, N.A.** & **Moorhead, G.B.G.** (2004) Lack of evidence for phosphorylation of *Arabidopsis thaliana* PII: implications for plastid carbon and nitrogen signaling. *Biochimica et Biophysica Acta, Proteins and Proteomics*, **1699**, 145–154.

Son, O., **Kim, S.**, **Kim, D.**, **Hur, Y.S.**, **Kim, J.** & **Cheon, C.I.** (2018) Involvement of TOR signaling motif in the regulation of plant autophagy. *Biochemical and Biophysical Research Communications*, **501**, 643–647.

Soto-Burgos, J. & **Bassham, D.C.** (2017) SnRK1 activates autophagy via the TOR signaling pathway in *Arabidopsis thaliana*. *PLoS One*, **12**, e0182591. Available from: https://doi.org/10.1371/journal.pone.0182591

Tang, J. & **Bassham, D.C.** (2018) Autophagy in crop plants: what's new beyond Arabidopsis? *Open Biology*, **8**, 180162.

Uhrig, R.G., **Ng, K.K.S.** & **Moorhead, G.B.G.** (2009) PII in higher plants: a modern role for an ancient protein. *Trends in Plant Science*, **14**, 505–511.

Van Leene, J., **Eeckhout, D.**, **Gadeyne, A.**, **Matthijs, C.**, **Han, C.**, **De Winne, N.** ***et al.*** (2022) Mapping of the plant SnRK1 kinase signalling network

reveals a key regulatory role for the class II T6P synthase-like proteins. *Nature Plants*, **8**, 1245–1261.

Van Leene, J., **Han, C.**, **Gadeyne, A.**, **Eeckhout, D.**, **Matthijs, C.**, **Cannoot, B.** ***et al.*** (2019) Capturing the phosphorylation and protein interaction landscape of the plant TOR kinase. *Nature Plants*, **5**, 316–327.

Viana, A.J.C., **Matiolli, C.C.**, **Newman, D.W.**, **Vieira, J.G.P.**, **Duarte, G.T.**, **Martins, M.C.M.** ***et al.*** (2021) The sugar-responsive circadian clock regulator bZIP63 modulates plant growth. *The New Phytologist*, **231**, 1875–1889. Available from: https://doi.org/10.1111/nph.17518

Wang, H., **Han, C.**, **Wang, J.-G.**, **Chu, X.**, **Shi, W.**, **Yao, L.** ***et al.*** (2022) Regulatory functions of cellular energy sensor SnRK1 for nitrate signalling through NLP7 repression. *Nature Plants*, **8**, 1094–1107. Available from: https://doi.org/10.1038/s41477-022-01236-5

Wang, W., **Hu, B.**, **Yuan, D.**, **Liu, Y.**, **Che, R.**, **Hu, Y.** ***et al.*** (2018) Expression of the nitrate transporter gene OsNRT1.1A/OsNPF6.3 confers high yield and early maturation in rice. *Plant Cell*, **30**, 638–651. Available from: https://doi.org/10.1105/tpc.17.00809

Wang, Y., **Cao, J.-J.**, **Wang, K.-X.**, **Xia, X.-J.**, **Shi, K.**, **Zhou, Y.-H.** ***et al.*** (2019) BZR1 mediates brassinosteroid-induced autophagy and nitrogen starvation in tomato. *Plant Physiology*, **179**, 671–685.

Wang, Y., **Wang, L.**, **Micallef, B.J.**, **Tetlow, I.J.**, **Mullen, R.T.**, **Feil, R.** ***et al.*** (2020) AKINβ1, a subunit of SnRK1, regulates organic acid metabolism and acts as a global modulator of genes involved in carbon, lipid, and nitrogen metabolism. *Journal of Experimental Botany*, **71**, 1010–1028.

Wolfson, R.L. & **Sabatini, D.M.** (2017) The Dawn of the age of amino acid sensors for the mTORC1 pathway. *Cell Metabolism*, **26**, 301–309.

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

Yadav, U.P., **Ivakov, A.**, **Feil, R.**, **Duan, G.Y.**, **Walther, D.**, **Giavalisco, P.** ***et al.*** (2014) The sucrose–trehalose 6-phosphate (Tre6P) nexus: specificity and mechanisms of sucrose signalling by Tre6P. *Journal of Experimental Botany*, **65**, 1051–1068.

Yan, D. & **Nambara, E.** (2023) Conserved and unique functions of NIN-like proteins in nitrate sensing and signaling. *Plant Science*, **336**, 111842.

Yu, L.H., **Wu, J.**, **Tang, H.**, **Yuan, Y.**, **Wang, S.M.**, **Wang, Y.P.** ***et al.*** (2016) Overexpression of Arabidopsis NLP7 improves plant growth under both nitrogen-limiting and -sufficient conditions by enhancing nitrogen and carbon assimilation. *Scientific Reports*, **6**, 27795.

Zhai, Z., **Keereetaweep, J.**, **Liu, H.**, **Feil, R.**, **Lunn, J.E.** & **Shanklin, J.** (2018) Trehalose 6-phosphate positively regulates fatty acid synthesis by stabilizing WRINKLED1. *Plant Cell*, **30**, 2616–2627.

Zhang, Y., **Primavesi, L.F.**, **Jhurreea, D.**, **Andralojc, P.J.**, **Mitchell, R.A.C.**, **Powers, S.J.** ***et al.*** (2009) Inhibition of SNF1-related protein Kinase1 activity and regulation of metabolic pathways by Trehalose-6-phosphate. *Plant Physiology*, **149**, 1860–1871.

Zhang, Z., **Zhu, J.Y.**, **Roh, J.**, **Marchive, C.**, **Kim, S.K.**, **Meyer, C.** ***et al.*** (2016) TOR signaling promotes accumulation of BZR1 to balance growth with carbon availability in Arabidopsis. *Current Biology*, **26**, 1854–1860.