



OPEN ACCESS

EDITED BY

Sergio J. Ochatt,
INRA UMR1347 Agroécologie, France

REVIEWED BY

Wei Wang,
Fujian Agriculture and Forestry University,
China
Saroj Kumar Sah,
Brookhaven National Laboratory (DOE),
United States

*CORRESPONDENCE

Jiasui Zhan

✉ Jiasui.zhan@slu.se

Maozhi Ren

✉ renmaozhi01@caas.cn

†These authors have contributed
equally to this work and share
first authorship

SPECIALTY SECTION

This article was submitted to
Plant Breeding,
a section of the journal
Frontiers in Plant Science

RECEIVED 14 December 2022

ACCEPTED 17 February 2023

PUBLISHED 01 March 2023

CITATION

Song Y, Wang Y, Yu Q, Sun Y, Zhang J,
Zhan J and Ren M (2023) Regulatory
network of GSK3-like kinases and their
role in plant stress response.
Front. Plant Sci. 14:1123436.
doi: 10.3389/fpls.2023.1123436

COPYRIGHT

© 2023 Song, Wang, Yu, Sun, Zhang, Zhan
and Ren. This is an open-access article
distributed under the terms of the [Creative
Commons Attribution License \(CC BY\)](#). The
use, distribution or reproduction in other
forums is permitted, provided the original
author(s) and the copyright owner(s) are
credited and that the original publication in
this journal is cited, in accordance with
accepted academic practice. No use,
distribution or reproduction is permitted
which does not comply with these terms.

Regulatory network of GSK3-like kinases and their role in plant stress response

Yun Song^{1†}, Ying Wang^{2,3,4†}, Qianqian Yu¹, Yueying Sun¹,
Jianling Zhang¹, Jiasui Zhan^{5*} and Maozhi Ren^{2,3,4*}

¹School of Life Sciences, Liaocheng University, Liaocheng, China, ²Institute of Urban Agriculture, Chinese Academy of Agricultural Sciences, Chengdu, China, ³Hainan Yazhou Bay Seed Laboratory, Sanya, China, ⁴National Nanfan Research Institute (Sanya), Chinese Academy of Agricultural Sciences, Sanya, China, ⁵Department of Forest Mycology and Plant Pathology, Swedish University of Agricultural Sciences, Uppsala, Sweden

Glycogen synthase kinase 3 (GSK3) family members are evolutionally conserved Ser/Thr protein kinases in mammals and plants. In plants, the GSK3s function as signaling hubs to integrate the perception and transduction of diverse signals required for plant development. Despite their role in the regulation of plant growth and development, emerging research has shed light on their multilayer function in plant stress responses. Here we review recent advances in the regulatory network of GSK3s and the involvement of GSK3s in plant adaptation to various abiotic and biotic stresses. We also discuss the molecular mechanisms underlying how plants cope with environmental stresses through GSK3s-hormones crosstalk, a pivotal biochemical pathway in plant stress responses. We believe that our overview of the versatile physiological functions of GSK3s and underlined molecular mechanism of GSK3s in plant stress response will not only opens further research on this important topic but also provide opportunities for developing stress-resilient crops through the use of genetic engineering technology.

KEYWORDS

glycogen synthase kinase 3 (GSK3), plant, hormone, abiotic stress, biotic stress

1 Introduction

As a major source of food, fuel, and fiber, plant supports human society and sustains the global ecosystem by photosynthesis (Waad et al., 2022; Zhang et al., 2022a). Plants are challenged throughout their life cycles by adverse environmental conditions including abiotic stresses such as drought, salinity, extreme temperatures, nutrient deficiency, and toxic metal levels in the soil as well as biotic stresses such as pathogen infection and herbivore attack (Peck and Mittler, 2020). These adverse environmental conditions limit the distribution of plants, threaten their growth, and reduce crop productivity, eventually resulting in devastating impacts on our economy. To reduce the impacts, it is necessary to

understand how plants adapt to these adverse environmental conditions. There is growing evidence that plants have evolved sophisticated mechanisms to respond to environmental stresses, with recent results from some model and crop species the involvement of glycogen synthase kinase 3 (GSK3) protein in such adaptation.

2 Identification of plant GSK3s

The glycogen synthase kinase GSK3, also known as shaggy-like kinase (SK), was first identified in humans and functions as a regulator of glycogen synthase (Woodgett, 1991; Li et al., 2021). Only two GSK3 isoforms (i.e., GSK3 α and GSK3 β) are present in human genomes. They regulate diverse biochemical and cellular processes (Beurel et al., 2015; Patel and Woodgett, 2017). In contrast to mammalian GSK3s, GSK3-like kinases in plants are encoded by multiple homologs of the genes and are grouped into four subfamilies (Table 1) (Li et al., 2021). For example, there are ten and nine GSK3-like kinases in the dicot *Arabidopsis thaliana* and the monocot rice (*Oryza sativa*), respectively (Qi et al., 2013; Youn and Kim, 2015). The GSK3-like genes have also been identified in several important crop species, such as barley (*Hordeum vulgare*), cotton (*Gossypium hirsutum*), maize (*Zea mays*), pepper (*Capsicum annuum*), potato (*Solanum tuberosum*), sorghum (*Sorghum bicolor*), soybean (*Glycine max*), wheat (*Triticum aestivum*) (Table 1) (Chen et al., 2003; Hirano et al., 2017; Qiu et al., 2018; Wang et al., 2018b; Cheng et al., 2020; Kloc et al., 2020; Wang et al., 2020; He et al., 2021; Huang et al., 2021; Hou et al., 2022; Wang et al., 2022; Zolkiewicz and Gruszka, 2022; Zhang et al., 2022b). Multiple copies of GSK3 in plant genomes indicate that this gene plays important and diverse roles in the evolutionary adaptation and life strategies of plants (Qi et al., 2013; Li et al., 2021). Indeed, despite evolutionary conservation, the specific function of GSK3 in plants can vary among species.

In plants, the best-known representative GSK3 is brassinosteroid insensitive 2 (BIN2/SK21). It is a key negative regulator of the plant steroid hormones brassinosteroid (BR) response in *Arabidopsis* (Li and Nam, 2002). The *BIN2* gene has two closest homologs i.e., *BIN2-like 1* (*BIL1*) and *BIN2-like 2* (*BIL2*) functioning redundantly with BIN2 to negatively regulate the BR signaling. The *bin2 bil1 bil2* triple mutants showed a constitutive BR-activation phenotype (Yan et al., 2009). The BR signaling has been well elucidated and proved to be an important regulator of plant physiological and biological processes including seed germination, cell division, elongation and differentiation, leaf senescence and response to biotic and abiotic stresses (Rozhon et al., 2010; Kondo et al., 2014; Dong et al., 2015; Anwar et al., 2018; Peres et al., 2019; Ackerman-Lavert and Savaldi-Goldstein, 2020; Tamaki et al., 2020; Zolkiewicz and Gruszka, 2022). BRs are recognized by the leucine-rich repeat receptor-like (LRR-RLK) protein brassinosteroid-insensitive 1 (BRI1) and its co-receptor BRI1 associated receptor kinase 1 (BAK1) at the membrane (Wang et al., 2008; Santiago et al., 2013). Moreover, BRI1 phosphorylates its inhibitor, BRI1 kinase inhibitor 1 (BKI1), guides the dissociation of BKI1 from the membrane, and enables the formation of the BRI1-

BAK1 receptor complex to fully initiate the signaling cascade (Wang and Chory, 2006). The active receptor complex phosphorylates downstream proteins, including the BR signaling kinases (BSKs), constitutive differential growth 1 (CDG1) protein, and finally *bri1* suppressor1 phosphatase (BSU1) (Tang et al., 2008; Kim et al., 2011). BSU1 and its homologs then dephosphorylate and inhibit the glycogen synthase kinase 3 kinase BIN2, which is a major repressor of the BR signaling (Kim et al., 2009). Without BR, BIN2 phosphorylates two key transcription factors *bri1*-EMS-suppressor 1 (BES1) and brassinazole-resistant 1 (BZR1), which eventually inhibits the BR downstream signaling (Li and Nam, 2002). Upon initiation of the BR signaling, as for the BIN2 inactivation, BZR1 and BES1 proteins bind to the promoters of the BR-responsive genes (Nolan et al., 2020).

In the monocot model rice, several numbers of OsSKs/OsGSK3s proteins are also found to function as negative regulators of BR signaling by phosphorylating and regulating the activity of several transcription factors involved in the BR-dependent gene expression (Tong et al., 2012; Zhang et al., 2012; Sun et al., 2015; Yang et al., 2016; Qiao et al., 2017; Xiao et al., 2017; Sun et al., 2018; Xia et al., 2018; Ying et al., 2018; Gao et al., 2019; Min et al., 2019; Lyu et al., 2020; Xiao et al., 2020). For example, OsSK22 can phosphorylate and stabilize OsPUB24 to promote the degradation of OsBZR1, which is similar to what was discovered in *Arabidopsis* (Min et al., 2019). Thus, OsSK22 was named as OsGSK2 and is widely considered as the rice ortholog of BIN2. In conclusion, the GSK3 proteins function as negative regulators of BR signaling, and their function is generally conserved among dicots and monocots.

3 Upstream regulators and downstream substrates of GSK3s

Emerging evidence has shown that GSK3s proteins can perceive upstream signals and be regulated at the post-translational level. Moreover, the downstream targets phosphorylated by the GSK3s proteins have also been extensively elucidated. In this section, we review how the GSK3s proteins are modulated by the known upstream regulators and how they regulate the downstream substrates through phosphorylation (Figure 1).

3.1 Upstream regulators of GSK3s

Numerous studies have revealed that the GSK3s proteins are mainly regulated at the post-translational level *via* modulation of protein stability, protein activity *via* various modifications (i.e., phosphorylation, acetylation and oxidation), and subcellular localization (Li et al., 2021). A series of GSK3s proteins, such as *AtBIN2*, *AtBIL1*, *AtBIL2*, *AtSK11*, *AtSK12*, *OsGSK2*, and *TaSG-D1*, is degraded through proteasome-mediated pathway (Li and Nam, 2002; Peng et al., 2008; Yan et al., 2009; Tong et al., 2012; Li et al., 2018; Cheng et al., 2020; Chen et al., 2020b). Moreover, the proteasome-mediated regulation of GSK3s is modulated *via* a conserved C-terminal TREE motif, and mutations in this motif

TABLE 1 GSK3s in various eukaryotes.

Plant Species	Subgroup	Gene Name	Function	References
<i>Arabidopsis thaliana</i>	I	AtSK11, AtSK12, AtSK13	BR signal/Flower development/ Osmotic stress	Kondo et al., 2014; Tamaki et al., 2020; Li et al., 2018; Chen et al., 2020b; Stampfl et al., 2016; Dong et al., 2020; Dal Santo et al., 2012
	II	AtSK21, AtSK22, AtSK23	BR signal/Growth/Salt stress	Li and Nam, 2002; Yan et al., 2009; Song et al., 2021
	III	AtSK31, AtSK32	BR signal/Flower development/ Osmotic stress	Rozhon et al., 2010; Dong et al., 2015; Eremina et al., 2016
	IV	AtSK41, AtSK42	Osmotic stress	Youn and Kim, 2015
<i>Oryza sativa</i>	I	OsSK11, OsSK12, OsSK13	BR signal	Youn and Kim, 2015
	II	OsSK21, OsSK22, OsSK23, OsSK24	BR signal/Growth/Abiotic stress/ Biotic stress	Tong et al., 2012; Youn and Kim, 2015; Yang et al., 2016; Xiao et al., 2017; Gao et al., 2019; Min et al., 2019; Lyu et al., 2020; Xiao et al., 2020; Sun et al., 2015; Sun et al., 2018; Che et al., 2015; Liu et al., 2017; Koh et al., 2007; He et al., 2020
	III	OsSK31	BR signal	Youn and Kim, 2015
	IV	OsSK41	Growth	Xia et al., 2018; Ying et al., 2018; Hu et al., 2018
<i>Hordeum vulgare</i>	II	HvGSK1.1	Growth/Salt stress	Kloc et al., 2020
<i>Gossypium hirsutum</i>	I	GhSK11, GhSK12, GhSK13, GhSK14	BR signal/Fiber development/ Stress response	Wang et al., 2018b; Wang et al., 2020
	II	GhSK21, GhSK22, GhSK23, GhSK24, GhSK25, GhSK26	BR signal/Fiber development/ Stress response	Wang et al., 2018b; Song et al., 2021
	III	GhSK31, GhSK32, GhSK33, GhSK34, GhSK35, GhSK36	Fiber development/Stress response	Wang et al., 2018b
	IV	GhSK41, GhSK42, GhSK43, GhSK44	BR signal/Fiber development/ Stress response	Wang et al., 2018b; Wang et al., 2020
<i>Zea mays</i>	II	ZmSK1, ZmSK2	BR signal/Embryonic development	Wang et al., 2022
<i>Capsicum annuum</i>	II	CaSK23	Biotic stress	Qiu et al., 2018
<i>Solanum tuberosum</i>	I	StSK11, StSK12, StSK13	BR signal/Abiotic stress	Huang et al., 2021
	II	StSK21, StSK22, StSK23	BR signal/Salt stress	Huang et al., 2021
	III	StSK31, StSK32	BR signal/Abiotic stress	Huang et al., 2021
	IV	StSK41	Abiotic stress	Huang et al., 2021
<i>Sorghum bicolor</i>	II	SbBIN2	BR signal	Hirano et al., 2017
<i>Glycine max</i>	II	GmBIN2	Salt and drought stress	Wang et al., 2018a
	II	GmSK2-8	Legume-rhizobium symbiosis	He et al., 2021
<i>Triticum aestivum</i>	I	TaSK11-3A,3B,3D TaSK12-4A,5B,5D TaSK13-1A,1B,1D	Drought and salt stress	Zhang et al., 2022b

(Continued)

biological functions in plants. Plasma membrane recruitment of GSK3s modulates BR signaling in *Arabidopsis* and rice. In *Arabidopsis*, several proteins including octopus (OPS), tetratricopeptide thioredoxin-like 3 (TTL3), and brassinosteroid signaling kinase 3 (BSK3), interact with and recruit BIN2 to the plasma membrane, and prevent BIN2 inhibitory role in the nucleus in the BR signaling pathway. Among these proteins, TTL3 affects BIN2 subcellular localization and promotes the degradation of BIN2 (Anne et al., 2015; Amorim-Silva et al., 2019; Ren et al., 2019). As mentioned above, OsPPKL1 dephosphorylated and stabilized OsGSK3 in the cytoplasm to modulate BR signaling (Gao et al., 2019). We find that TTL3 not only influences BIN2 stability, but also affects the BIN2 subcellular localization. OsPPKL1 not only influences BIN2 through protein modifications, but also alters the BIN2 subcellular localization. These results together indicate that the upstream proteins can regulate GSK3s proteins in more ways than one. In rice, a calmodulin binding protein grain width 5 (GW5) can also physically interact with and recruit OsGSK32 to the plasma membrane, thus resulting in accumulation of unphosphorylated OsBZR1 and dwarf and low-tillering (DLT) to promote BR signaling (Liu et al., 2017). Moreover, GSK3s subcellular localization mediates plant transition from the salt stress response to growth recovery. BIN2 is mainly localized in the nucleus to regulate BR signaling and plant growth under salt stresses. In the recovery phase, BIN2 was recruited to the plasma membrane by the salt-triggered calcium sensors salt overly sensitive 3 (SOS3) and SOS3-like calcium binding protein 8 (SCaBP8) to regulate the salt stress response (Li et al., 2020b). Taking the above aspects into account, we can conclude that the altered subcellular localization of GSK3s proteins contributes to realize GSK3s proteins functions in the balance between plant growth and stress response. GSK3s subcellular localization also influences stomatal patterning. Stomatal cell lineage is an archetypal example of asymmetric cell division (ACD). The scaffold membrane protein polar localization during asymmetric division and redistribution (POLAR) can confine BIN2 and AtSK12 to the cytosol to drive ACD. After ACDs, BIN2 and AtSK12 phosphorylate and dissociate from POLAR (Houbaert et al., 2018).

3.2 Downstream targets of GSK3s

Like upstream regulation, GSK3s also intensively modulate downstream substrates through phosphorylation to accomplish their functions in regulating plant development and stress responses. GSK3s can phosphorylate a series of substrates including transcription factors, cofactors, kinases, scaffold proteins, cytoskeleton proteins, cyclins, metabolic enzymes, and components of the ubiquitin-proteasome system (UPS). The role of GSK3s in modulating proteins including kinases, scaffold proteins, cytoskeleton proteins, cyclins, metabolic enzymes, and components of the ubiquitin-proteasome system (UPS), has been extensively discussed in several excellent recent reviews (Youn and Kim, 2015; Li et al., 2021; Mao et al., 2021; Zolkiewicz and Gruszka, 2022). In this section, we mainly focus on the

discoveries about effects of GSK3s on the transcription factors and cofactors, which play essential roles in modulating stress responsive gene expression.

GSK3s-mediated phosphorylation of the transcription factors and cofactors, eventually affects the protein stability, localization, and activity of these substrates. Recent reports have revealed that GSK3-mediated phosphorylation not only promotes the degradation of the substrates but also stabilizes downstream targets. During stomatal patterning, BIN2 and MAPKs phosphorylate and promote the degradation of speechless (SPCH), which is a bHLH transcription factor in the nucleus required for stomatal initiation (Gudesblat et al., 2012). Phosphorylation and degradation of phytochrome interacting factor 3 (PIF3) and 4 (PIF4) are facilitated by BIN2 to control skotomorphogenesis and hypocotyl elongation, respectively (Bernardo-García et al., 2014; Ling et al., 2017). In plants, GSK3s also stabilize transcription factors through phosphorylation. A series of transcription factors, such as myeloblastosis family transcription factor-like (MYBL2; a MYB transcription factor), ATBS1-interacting factor 2 (AIF2; a bHLH transcription factor), abscisic acid insensitive 5 (ABI5; a bZIP transcription factor), upbeat 1 (UPB1; a bHLH transcription factor), TINY (AP2 family transcription factor) and RD26 (NAC family transcription factor), are phosphorylated and stabilized by BIN2 (Ye et al., 2012; Hu and Yu, 2014; Kim et al., 2017; Jiang et al., 2019; Xie et al., 2019; Li et al., 2020c). However, the underlying molecular mechanisms of substrates degradation or accumulation associated with BIN2-catalyzed phosphorylation have not been investigated. GSK3s-mediated regulation of subcellular localization in substrates is ubiquitous in plants. BIN2-catalyzed phosphorylation of BZR1/BZR2 promotes their binding to the 14-3-3 proteins, resulting in cytoplasmic retention and inhibition of BR-regulated gene expression (Gampala et al., 2007). In rice, phosphorylation of OsBZR1 and transcription factor ovate family protein 8 (OFP8) by OsGSK2 also results in their nuclear export (Yang et al., 2016). Furthermore, GSK3s-mediated phosphorylation can restrict the nuclear localization of their substrates. For example, the bHLH transcription factor enhancer of glabra 3 (EGL3) is phosphorylated by BIN2, thus remaining nuclear localization and participating in the BR-regulated root epidermal cell patterning (Cheng et al., 2014).

In addition, GSK3s have been early documented to affect the activity of transcription factors or cofactors. For example, phosphorylation of auxin response factors ARF7 and ARF19 by BIN2 suppresses their interaction with the AUX/IAAs repressors and enhances auxin signaling export in enhancing lateral root development (Cho et al., 2014). AtSK11 and AtSK12 phosphorylate the WD40 motif-containing transcriptional cofactor transparent testa glabra 1 (TTG1), influencing the interaction between TTG1 and a MYB domain transcription factor transparent testa 2 (TT2), which eventually influence the carbon partitioning between various parts of developing seed (Li et al., 2018). GSK3s also affect the DNA-binding ability or transcriptional activity of transcription factors, such as BES1, BZR1, ARF2, rice growth regulating factor GRF4 (reduced), golden 2-like 1 (GLK1) and cеста CES (enhanced) (Vert and Chory, 2006; Vert et al., 2008; Khan et al., 2014; Che et al., 2015;

Duan et al., 2015; Zhang et al., 2021). The transcription factors or cofactors targeted by GSK3s proteins regulate the expression of downstream plant stress responsive genes, and eventually allow GSK3s to participate in plant response to environmental stresses.

4 Crosstalk between the GSK3s and phytohormones

Plant hormones are essential signaling compounds in regulating the interactions between plants and their complex biotic and abiotic environments. GSK3s have been found to mediate the crosstalk between BR and other hormones including auxin, abscisic acid (ABA), jasmonic acid (JA) and salicylic acid (SA). GSK3s coordinate actions of auxin through phosphorylating the auxin transcription factors (ARFs) including ARF2, ARF5, ARF7, ARF9, and OsARF4 (Vert et al., 2008; Cho et al., 2014; Han et al., 2018; Hu et al., 2018). The involvement of GSK3s proteins in the crosstalk with auxin mainly regulates plant developmental processes. ABA is a major stress related hormone that integrates a wide range of stress signals such as cold, salinity, osmolarity, and drought (Zhu, 2016; Chen et al., 2020a). Recent studies have uncovered that there are multifaceted interactions between GSK3s and ABA. Subgroup III snfl-related kinase 2s (SnRK2s) are key positive regulators in the ABA signaling pathway (Umezawa et al., 2009). SnRK2.2 and SnRK2.3 can interact with, be phosphorylated and thus be activated by BIN2, providing significant insight into the modulation of ABA signaling by GSK3s (Cai et al., 2014). BIN2 phosphorylates and stabilizes the bZIP-type transcription factor ABI5 of the ABA signaling pathway to mediate the antagonism of ABA by BR (Hu and Yu, 2014). But its activity on BES1 phosphorylation is affected by ABA insensitive 1 (ABI1) and 2 (ABI2), which are negative regulators of ABA signaling (Wang et al., 2018a). ABI1 and ABI2 interact with and dephosphorylate BIN2, thereby forming a PP2Cs-BIN2-SnRK2s module in the ABA signaling pathway. JA is another essential stress related hormone in plants, and the jasmonate ZIM domain (JAZ) proteins are key repressors of the JA pathway. GSK3s kinase proteins interact with and promote the degradation of JAZ proteins, and the interaction is ubiquitously present in plants including *Arabidopsis*, rice and cotton (He et al., 2020; Song et al., 2021). SA is a representative plant defense hormone that plays pivotal roles in immunity and systemic acquired resistance. The TGACG motif-binding transcription factors TGAs are known to mediate SA signaling. BIN2 phosphorylates and inhibits the activity of redox-sensitive clade I TGA4 during plant response to *Pst* DC3000. BR inactivates BIN2 and promotes SA responses by inactivating BIN2 (Kim et al., 2022). Moreover, recent results indicate that SA activates BIN2 which phosphorylates TGA3, enhancing TGA3 DNA binding ability, thereby activating *PR* gene expression and promoting disease resistance in *Arabidopsis* (Han et al., 2022). The advances displayed in this section indicates that GSK3s proteins function as hubs of phytohormones signaling pathways mainly through interacting with the transcription factors of these pathways, which eventually influence the expression of downstream responsive genes

of these phytohormones. The interaction between GSK3s and other key node genes of these phytohormones needs further investigation.

5 Involvement of the GSK3s in plant response to multiple stresses

Plants are challenged by various types of environmental stresses throughout their life cycles, which have profound effects on plant growth and survival. Accumulated evidence from recent findings has deciphered that GSK3s play a pivotal role in plant stress responses in model and crop species (Figure 2).

5.1 GSK3s in abiotic stresses

Soil salinization is a growing problem for agriculture worldwide. It is crucial to uncover the key components of the plant salt tolerance network. Recent studies have shown that GSK3s play important roles in regulating plant salinity stress responses. In *Arabidopsis*, overexpression of *AtGSK1* enhances plant resistance to sodium chloride (NaCl) stress, and induces the expression of some NaCl stress-responsive genes including the Ca²⁺-binding protein (*AtCPI*), the desiccation 29A (*RD29A*) and the chalcone synthase gene (*CHS1*), suggesting that *AtGSK1* is involved in the signal transduction pathway of NaCl stress responses (Piao et al., 2001). BIN2 is found to function as a molecular switch between plant salt stress response and growth through phosphorylating and affecting the activity of calcium sensors, such as SOS3, SCaBP8, and SOS2 (Li et al., 2020b). Heat shock proteins (HSPs), a group of highly conserved chaperone protein, are involved in the regulation of plant responses to salinity. HSP90 regulates the activity of the BIN2 kinase by modulating its subcellular localization (Samakovli et al., 2014). The co-chaperone heat shock protein (HSP)70-HSP90 organizing protein 1 (HOP1) and 2 (HOP2) affect HSP90-BIN2 interaction and are involved in plant salt tolerance by affecting BR signaling (Zhang et al., 2022). In rice, knockout mutants of *OsGSK1* showed enhanced tolerance to salt stress (Koh et al., 2007). Heterologous overexpression of a GSK3 gene from soybean *GmBIN2* enhanced plant tolerance to salt in *Arabidopsis*. GSK3-like kinase *GmSK2-8* is strongly induced in soybean under salt stress. *GmSK2-8* interacts with two nodulation signaling pathway 1 (*GmNSP1*) proteins *GmNSP1a* and *GmNSP1b*, which are key transcription factors involved in legume-rhizobium symbiosis. *GmSK2-8* phosphorylates the *GmNSP1a* protein, and thus suppresses nodule formation under salt stress (He et al., 2021). It is reported that the GSK3 family shows altered expression in response to salt stress treatments in *Solanum tuberosum* L. Overexpression of *StSK21* provides enhanced sensitivity to salt stress in *Arabidopsis* (Huang et al., 2021). In addition, the response of the GSK3 family to salt stress is also identified in cotton (Wang et al., 2018b). In barley (*Hordeum vulgare* L.), the RNAi-mediated silencing of the target *HvGSK1.1* gene enhances the BR-dependent signaling, and generates plants with improved agricultural traits under salt stress conditions (Kloc et al., 2020).

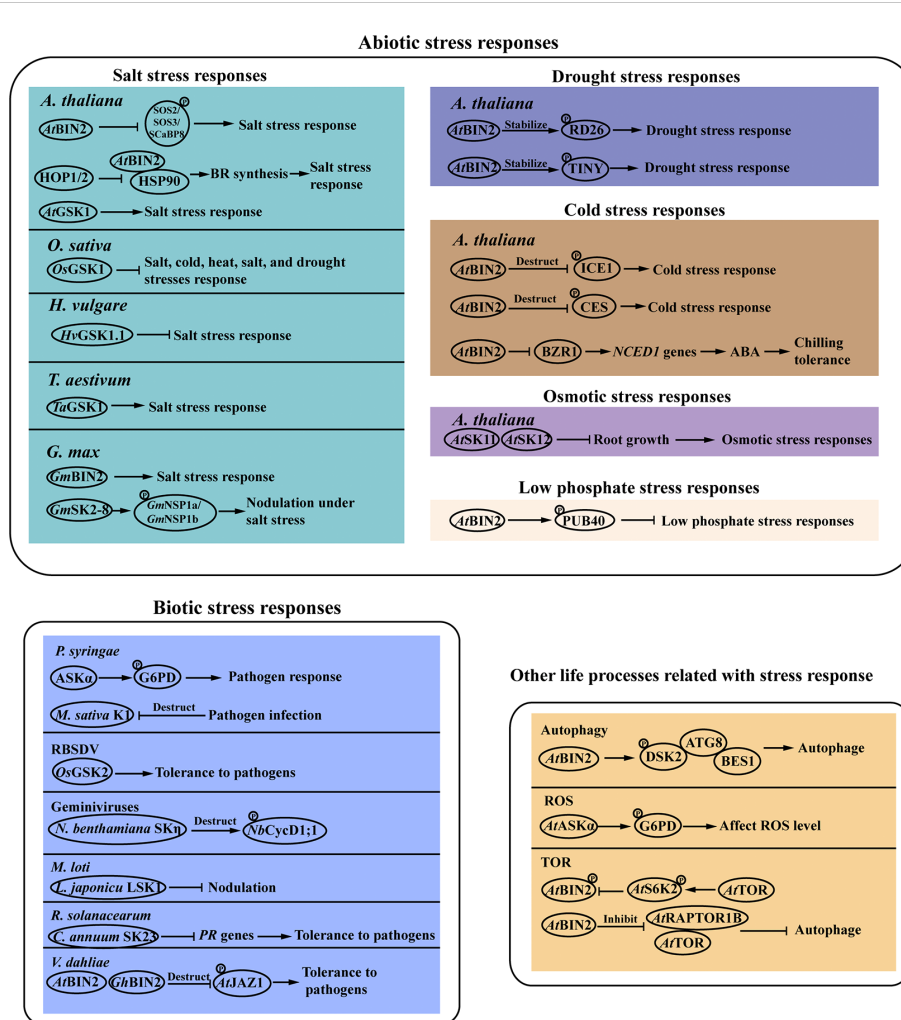


FIGURE 2
 Plant stress responses mediated by GSK3-like kinases. GSK3s participated in various stress response pathways. The detailed description is given in the text. Arrows and bar ends indicate stimulatory and inhibitory action, respectively. Abbreviations: GSK3, glycogen synthase kinase 3; BIN2, brassinosteroid insensitive 2; SOS, salt overly sensitive; SCaBP8, SOS3-like calcium binding protein 8; HOP 1/2: co-chaperone heat shock protein (HSP)70-HSP90 organizing protein 1/2; HSP90, heat shock protein 90; SK2, shaggy-like kinase 2; NSP1, nodulation signaling pathway 1; RD26, NAC family transcription factor; TINY, AP2 family transcription factor; PUB40, plant U-box 40 protein; ICE1, inducer of CBF expression 1; CES, cesa; CycD1;1, Cyclin D 1.1; LSK1, shaggy-like kinase 1; DSK2, dominant suppressor of KAR 2; ROS, reactive oxygen species; G6PD, glc-6-phosphate dehydrogenase; TOR, target of rapamycin; RAPTOR1B, regulatory-associated protein of TOR 1B; PR: pathogenesis-related; JAZ: jasmonate ZIM domain; ATG8: autophagy 8; BES1: *bri1*-EMS-suppressor 1; S6K2: ribosomal protein S6 kinase 2.

Researches show that the wheat (*Triticum aestivum* L.) *TaGSK1* gene is induced by NaCl stress, and expresses more strongly in salt-stress resistant lines than in salt-stress sensitive lines (Chen et al., 2003). From the above results we can see that some of the GSK3s proteins function as positive regulators of plant salt tolerance such as in soybean and wheat, while the GSK3s proteins reported in rice, potato, barley negatively regulate plant salt tolerance. In addition, different members in the *Arabidopsis* and cotton GSK3s family proteins show different response to the salt treatment. These results indicate that molecular mechanism of the GSK3s proteins in response to salt stress in different species or different members in the protein family is specific.

Drought stress causes a decline in the quantity of crop yields, and has become more accentuated recently due to climatic change. The GSK3 proteins are involved in drought stress tolerance. The stress-responsive NAC transcription factor RD26 participates in the

interaction between growth and drought stress signaling by the phosphorylation of BIN2. BIN2 directly interacted with and phosphorylated RD26, which is required for RD26 transcriptional activation on drought-responsive genes (Jiang et al., 2019). *Arabidopsis* stress-inducible AP2/ERF transcription factor TINY positively regulates drought responses by activating drought-responsive genes. The BR negative regulator BIN2 phosphorylates and stabilizes TINY, which provides a mechanism for BR-mediated down-regulation of TINY to prevent activation of stress responses (Xie et al., 2019).

GSK3s are also involved in osmotic, low temperature and low phosphate stresses. AtSK11 and AtSK12 are involved in the mild osmotic stress (-0.4 MPa) response in *Arabidopsis thaliana*. They negatively regulate the induction of root growth in response to mild osmotic stress (Dong et al., 2020). Plant U-box 40 protein (PUB40) is a ubiquitin E3 ligase and mediates the proteasomal degradation of

BZR1 in *Arabidopsis*. The interaction between PUB40 and BZR1 influences root tolerance to the low phosphate stress. BIN2 phosphorylates and stabilizes PUB40 to promote BZR1 degradation and enhances the interaction between PUB40 and BZR1, thus reducing plant tolerance to the low phosphate stress (Kim et al., 2019). Moreover, BIN2 is also regulated by the E3 ubiquitin ligase KIB1 as is mentioned above (Zhu et al., 2017). These results indicate that the E3 ubiquitin ligases play pivotal roles in the BIN2-mediated regulation of BR signaling pathway transduction. BR signaling and downstream transcriptional cascades are reported to be involved in regulating plant cold tolerance (Khan et al., 2014; Eremina et al., 2016; Li et al., 2017). As repressors of BR signaling, BIN2 and its homologs mediate the phosphorylation of BZR1 and inducer of CBF expression 1 (ICE1) to facilitate their degradation, and thus affect downstream transcriptional cascades related to cold stress response (Ye et al., 2019). BIN2 negatively regulates chilling tolerance in tomato. BIN2 also regulates the accumulation of BZR1, which controls the expression of ABA biosynthesis gene 9-cis-epoxycarotenoid dioxygenase 1 (*NCED1*) in tomato. These results demonstrate that BR signaling positively regulates chilling tolerance via ABA biosynthesis in tomato (An et al., 2023). Moreover, CESTA (CES) is a bHLH transcription factor of BR signaling and affects plant cold tolerance (Eremina et al., 2016). CES degradation is also promoted by BIN2-mediated phosphorylation, but whether and how this protein turnover is associated *in vivo* with cold stress response should be further explored.

5.2 GSK3s in biotic stresses

Biotic stresses including bacteria, fungi, oomycetes, viruses and insects, wreak havoc on agricultural products worldwide and increase the risk of starvation in many areas. Advancing researches have shown that GSK3s play multifaceted roles in plant responses to various kinds of biotic stresses and is tightly regulated during plant response to pathogen infection (Wrzaczek et al., 2007). It is reported that the GSK3-like kinase ASK α is identified as a positive regulator of plant immune signaling (Stampfl et al., 2016). Loss of ASK α attenuates, whereas its overexpression enhances, diverse pattern-triggered immunity (PTI) responses, which is the first layer of plant immunity against pathogenic microbes. The bacterial pathogen *Pseudomonas syringae* glucose-6-phosphate dehydrogenase (G6PD) is the key enzyme of the oxidative pentose phosphate pathway and is phosphorylated by ASK α . Rice black-streaked dwarf virus (RBSDV), a double-stranded RNA virus, causes acute growth abnormalities in plants and results in serious yield losses in cereal crops. Plants over-expressing OsGSK2 display milder symptoms than the control, suggesting a positive role of OsGSK2 in suppressing RBSDV infection in rice (He et al., 2020). Geminiviruses transmitted by whiteflies cause severe developmental abnormalities in plants. The C4 protein encoded by geminiviruses induces abnormal cell division that determines viral symptoms. The tomato leaf curl Yunnan virus (TLCYNV) C4 protein interacts with and affects the subcellular localization of

Nicotiana benthamiana GSK3 protein NbsK η , eventually impairing GSK3-mediated degradation of cell division associated protein NbCycD1;1 (Mei et al., 2018; Mei et al., 2020). In *Medicago sativa*, the GSK3-like kinase MsK1 is important for innate immunity and limits the severity of infection caused by virulent bacterial pathogen *P. syringae*. MsK1 activity is downregulated by the elicitor cellulase. Cellulase treatment also triggers the degradation of the MsK1 protein (Wrzaczek et al., 2007). In *Lotus japonicu*, nodulation is mainly formed through the symbiotic nitrogen-fixing bacterium *Mesorhizobium loti* infection. Studies show that lotus SHAGGY-like kinase 1 (LSK1) is required to suppress nodulation (Garagounis et al., 2019; Solovou et al., 2021). *Ralstonia solanacearum* is a devastating soil-borne bacterium that causes wilting disease in over 200 economically-important plant species. The GSK3/SHAGGY-like kinase CaSK23 negatively regulates plant response to *R. solanacearum* attack in *Capsicum annuum* (Qiu et al., 2018). We also find that BIN2 negatively regulates plant defence against *Verticillium dahliae* in *Arabidopsis* and cotton, consistent with others reports on the regulatory function of GSK3s proteins (Song et al., 2021).

5.3 GSK3s in other life processes related to stress response

Autophagy is a highly conserved quality control mechanism in which harmful or unwanted cellular components are delivered into lytic vacuoles for recycling, and can promote plant resistance to various stresses (Signorelli et al., 2019; Yang et al., 2020). The GSK3-like kinase is one of the key regulators of autophagy (Nolan et al., 2017). The dominant suppressor of KAR 2 (DSK2) is a ubiquitin receptor protein that targets BES1 to the autophagy pathway by interacting with ATG8, a ubiquitin-like protein that directs autophagosome formation and cargo recruitment. BIN2 can phosphorylate DSK2 and promote DSK2-ATG8 interaction, which ultimately targets BES1 for degradation (Nolan et al., 2017). Reactive oxygen species (ROS) play a key role in the acclimation process of plants to abiotic and biotic stresses (Choudhury et al., 2017). Researchers have found that the interaction of BIN2 and BES1 is dependent on oxygen, which can directly modify BIN2 (Song et al., 2019). In *Arabidopsis*, AtASK α regulates plant stress tolerance by activating glc-6-phosphate dehydrogenase (G6PD) responsible for maintaining cellular redox balance. Plants overexpressing ASK α have low levels of ROS in stress responses and are more tolerant to salt stress (Dal Santo et al., 2012; Stampfl et al., 2016). The target of rapamycin (TOR) is an atypical Ser/Thr protein kinase that is evolutionally conserved among yeasts, plants, and mammals. TOR signaling is involved in plant adaptation to nutrient deficiency and various abiotic stresses (Fu et al., 2020). The TOR downstream effector S6K2 can phosphorylate BIN2 protein, suggesting that BIN2 acts as a downstream effector of TOR signaling (Xiong et al., 2017). The regulatory-associated protein of TOR 1B (RAPTOR1B) is an important component of plant TOR complex. In the absence of BR, the BIN2 kinase directly phosphorylates and inhibits the

activity of RAPTOR1B. Furthermore, autophagy is negatively regulated by TOR. Phosphorylation of RAPTOR1B by BIN2 thus activates the autophagy pathway. In the presence of BR, the inhibition effect of BIN2 on RAPTOR1B is attenuated, and results in increased TOR activity and ATG13a phosphorylation, and decreased autophagy activity (Liao et al., 2022). These results suggest that BIN2 functions as a key hub in the crosstalk between TOR and BR signaling pathways. Further studies are required to fully elucidate whether and how BIN2 interacts with other components of TOR signaling pathway.

6 Conclusion

The glycogen synthase kinase 3 protein was first identified in animals, and functions as an ancestral kinase of the stress response in eukaryotes. With the identification of additional proteins and other novel substrates that regulate their functions, our knowledge of plant GSK3s has increased significantly over the last decades. It is now clear that the GSK3 proteins are involved in numerous stress-response pathways that influence animal health and plant reproduction. In animals, the GSK3s are activated under stress conditions, and determine cell fate based on its subcellular localization and specific partners (Racaud-Sultan and Vergnolle, 2021). GSK3s are found to be activated in pathologies such as inflammation and cancer, where adult stem cells are downregulated (Murata, 2018). Stem cells control tissue regeneration throughout the life of organisms, and should be protected from stressors. The microenvironment of adult stem cells is named “niche”. Numerous studies have shown that the GSK3s proteins are found to function as a sensor of the adult stem cell niche. Besides, the GSK3s are nodes of signaling pathways controlling survival, proliferation, adhesion and differentiation in adult stem cells (Racaud-Sultan and Vergnolle, 2021). Plant stem cells reside within the meristems and are also defined by their ability to self-renew and to generate new tissues (Heidstra and Sabatini, 2014). During plant growth, procambial and cambial cells in the vascular system self-proliferate and differentiate into xylem cells, and are mainly regulated by a peptide ligand and its receptor; tracheary element differentiation inhibitory factor (TDIF) and TDIF receptor (TDR) (Ito et al., 2006). Plant GSK3 proteins are crucial downstream components of TDIF–TDR signaling and regulate xylem cell differentiation (Kondo et al., 2014).

Although our understanding of GSK3s is advanced, many fundamental questions related to the gene family and its associated proteins remain unknown. For example, plants contain divergent GSK3-like kinases, but our current knowledge of the proteins comes mainly from subgroups I and II from a limited number of species. It requires understanding how GSK3s in other subgroups (e.g., III and IV) and species and what other regulatory substrates are involved in plant response to diverse environmental stimuli. The subgroups III and IV GSK3-like kinases and substrates

of GSK3-like kinases reviewed here potentially provide new alleles to improve stress resistance in crops through engineering, which is an effective strategy for crop breeding processes. As mentioned above, GSK3s primarily affect hormonal signaling. Whether and how GSK3s directly regulate hormone biosynthesis is unclear and needs to be addressed. Such knowledge gap can be effectively bridged by applying recently emerging technologies such as genome-editing systems, single cell transcriptomics and deep tissue proteomics for research. Deciphering these molecular mechanisms controlling GSK3s function in detail will contribute to a better understanding of how internal and external signals integrate and branch for plant adaptation to the environment, which can eventually be transferred to stress breeding to ensure food production and ecological sustainability.

Author contributions

MR, JsZ, YSo and YW conceived and planned this review paper. YSo and YW prepared and drafted the manuscript. JsZ, QY, YSu and JIZ revised the manuscript. All authors contributed to the article and approved the submitted version. All authors contributed to the article and approved the submitted version.

Funding

This research was funded by Shandong Provincial Natural Science Foundation, grant number ZR2021QC200, ZR2020QC037, ZR2020QB154, ZR2021MC079; the Local Financial Funds of Chengdu National Agricultural Science and Technology Center, grant number NASC2021ST08, NASC2021PC04, NASC2021KR03 and NASC2020AR08; Hainan Yazhou Bay Seed Laboratory (B21Y10210); Nanfan Special Project, CAAS (YBXM12).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

References

- Ackerman-Lavert, M., and Savaldi-Goldstein, S. (2020). Growth models from a brassinosteroid perspective. *Curr. Opin. Plant Biol.* 53, 90–97. doi: 10.1016/j.cpb.2019.10.008
- Amorim-Silva, V., García-Moreno, Á., Castillo, A. G., Lakhssassi, N., Esteban Del Valle, A., Pérez-Sancho, J., et al. (2019). TTL Proteins scaffold brassinosteroid signaling components at the plasma membrane to optimize signal transduction in *Arabidopsis*. *Plant Cell* 31 (8), 1807–1828. doi: 10.1105/tpc.19.00150
- An, S., Liu, Y., Sang, K., Wang, T., Yu, J., Zhou, Y., et al. (2023). Brassinosteroid signaling positively regulates abscisic acid biosynthesis in response to chilling stress in tomato. *J. Integr. Plant Biol.* 65 (1), 10–24. doi: 10.1111/jipb.13356
- Anne, P., Azzopardi, M., Gissot, L., Beaubiat, S., Hématy, K., and Palauqui, J. C. (2015). OCTOPUS negatively regulates BIN2 to control phloem differentiation in *Arabidopsis thaliana*. *Curr. Biol.* 25 (19), 2584–2590. doi: 10.1016/j.cub.2015.08.033
- Anwar, A., Liu, Y., Dong, R., Bai, L., Yu, X., and Li, Y. (2018). The physiological and molecular mechanism of brassinosteroid in response to stress: A review. *Biol. Res.* 51 (1), 46. doi: 10.1186/s40659-018-0195-2
- Bernardo-García, S., de Lucas, M., Martínez, C., Espinosa-Ruiz, A., Davière, J. M., and Prat, S. (2014). BR-Dependent phosphorylation modulates PIF4 transcriptional activity and shapes diurnal hypocotyl growth. *Genes Dev.* 28 (15), 1681–1694. doi: 10.1101/gad.243675.114
- Beurel, E., Grieco, S. F., and Jope, R. S. (2015). Glycogen synthase kinase-3 (GSK3): regulation, actions, and diseases. *Pharmacol. Ther.* 148, 114–131. doi: 10.1016/j.pharmthera.2014.11.016
- Cai, Z., Liu, J., Wang, H., Yang, C., Chen, Y., Li, Y., et al. (2014). GSK3-like kinases positively modulate abscisic acid signaling through phosphorylating subgroup III SnRK2s in *Arabidopsis*. *Proc. Natl. Acad. Sci. U S A.* 111 (26), 9651–9656. doi: 10.1073/pnas.1316717111
- Che, R., Tong, H., Shi, B., Liu, Y., Fang, S., Liu, D., et al. (2015). Control of grain size and rice yield by GL2-mediated brassinosteroid responses. *Nat. Plants.* 2, 15195. doi: 10.1038/nplants.2015.195
- Chen, K., Li, G. J., Bressan, R. A., Song, C. P., Zhu, J. K., and Zhao, Y. (2020a). Abscisic acid dynamics, signaling, and functions in plants. *J. Integr. Plant Biol.* 62 (1), 25–54. doi: 10.1111/jipb.12899
- Chen, G., Ma, W., Huang, Z., Xu, T., Xue, Y., and Shen, Y. (2003). Isolation and characterization of TaGSK1 involved in wheat salt tolerance. *Plant Science.* 165 (6), 1369–1375. doi: 10.1016/S0168-9452(03)00365-0
- Chen, Y., Song, S., Gan, Y., Jiang, L., Yu, H., and Shen, L. (2020b). SHAGGY-like kinase 12 regulates flowering through mediating CONSTANS stability in *Arabidopsis*. *Sci. Adv.* 6 (24), eaaw0413. doi: 10.1126/sciadv.aaw0413
- Cheng, X., Xin, M., Xu, R., Chen, Z., Cai, W., Chai, L., et al. (2020). A single amino acid substitution in STKc_GSK3 kinase conferring semispherical grains and its implications for the origin of *Triticum sphaerococcum*. *Plant Cell.* 32 (4), 923–934. doi: 10.1105/tpc.19.00580
- Cheng, Y., Zhu, W., Chen, Y., Ito, S., Asami, T., and Wang, X. (2014). Brassinosteroids control root epidermal cell fate via direct regulation of a MYB-bHLH-WD40 complex by GSK3-like kinases. *Elife.* 3, e02525. doi: 10.7554/eLife.02525
- Cho, H., Ryu, H., Rho, S., Hill, K., Smith, S., Audenaert, D., et al. (2014). A secreted peptide acts on BIN2-mediated phosphorylation of ARFs to potentiate auxin response during lateral root development. *Nat. Cell Biol.* 16 (1), 66–76. doi: 10.1038/ncb2893
- Choudhury, F., Rivero, R., Blumwald, E., and Mittler, R. (2017). Reactive oxygen species, abiotic stress and stress combination. *Plant J.* 90 (5), 856–867. doi: 10.1111/tpl.13299
- Dal Santo, S., Stampfl, H., Krasensky, J., Kempa, S., Gibon, Y., Petutschnig, E., et al. (2012). Stress-induced GSK3 regulates the redox stress response by phosphorylating glucose-6-phosphate dehydrogenase in *Arabidopsis*. *Plant Cell.* 24 (8), 3380–3392. doi: 10.1105/tpc.112.101279
- Dong, X., Nou, I. S., Yi, H., and Hur, Y. (2015). Suppression of ASK β (AtSK32), a clade III *Arabidopsis* GSK3, leads to the pollen defect during late pollen development. *Mol. Cells* 38 (6), 506–517. doi: 10.14348/molcells.2015.2323
- Dong, L., Wang, Z., Liu, J., and Wang, X. (2020). AtSK11 and AtSK12 mediate the mild osmotic stress-induced root growth response in *Arabidopsis*. *Int. J. Mol. Sci.* 21 (11), 3991. doi: 10.3390/ijms21113991
- Duan, P., Ni, S., Wang, J., Zhang, B., Xu, R., Wang, Y., et al. (2015). Regulation of OsGRF4 by OsmiR396 controls grain size and yield in rice. *Nat. Plants.* 2, 15203. doi: 10.1038/nplants.2015.203
- Eremina, M., Unterholzner, S. J., Rathnayake, A. I., Castellanos, M., Khan, M., Kugler, K. G., et al. (2016). Brassinosteroids participate in the control of basal and acquired freezing tolerance of plants. *Proc. Natl. Acad. Sci. U S A.* 113 (40), E5982–e5991. doi: 10.1073/pnas.1611477113
- Fu, L., Wang, P., and Xiong, Y. (2020). Target of rapamycin signaling in plant stress responses. *Plant Physiol.* 182 (4), 1613–1623. doi: 10.1104/pp.19.01214
- Gampala, S., Kim, T., He, J., Tang, W., Deng, Z., Bai, M., et al. (2007). An essential role for 14-3-3 proteins in brassinosteroid signal transduction in *Arabidopsis*. *Dev. Cell.* 13 (2), 177–189. doi: 10.1016/j.devcel.2007.06.009
- Gao, X., Zhang, J., Zhang, X., Zhou, J., Jiang, Z., Huang, P., et al. (2019). Rice qGL3/OsPPLK1 functions with the GSK3/SHAGGY-like kinase OsGSK3 to modulate brassinosteroid signaling. *Plant Cell.* 31 (5), 1077–1093. doi: 10.1105/tpc.18.00836
- Garagounis, C., Tsikou, D., Plitsi, P. K., Psarrakou, I. S., Avramidou, M., Stedel, C., et al. (2019). Lotus SHAGGY-like kinase 1 is required to suppress nodulation in *Lotus japonicus*. *Plant J.* 98 (2), 228–242. doi: 10.1111/tpl.14207
- Gudesblat, G., Schneider-Pizoń, J., Betti, C., Mayerhofer, J., Vanhoutte, I., van Dongen, W., et al. (2012). SPEECHLESS integrates brassinosteroid and stomata signalling pathways. *Nat. Cell Biol.* 14 (5), 548–554. doi: 10.1038/ncb2471
- Han, S., Cho, H., Noh, J., Qi, J., Jung, H. J., Nam, H., et al. (2018). BIL1-mediated MP phosphorylation integrates PXY and cytokinin signalling in secondary growth. *Nat. Plants.* 4 (8), 605–614. doi: 10.1038/s41477-018-0180-3
- Han, Q., Tan, W., Zhao, Y., Yang, F., Yao, X., Lin, H., et al. (2022). Salicylic acid-activated BIN2 phosphorylation of TGA3 promotes *Arabidopsis* PR gene expression and disease resistance. *EMBO J.* 41 (19), e110682. doi: 10.15252/embj.2022110682
- Hao, Y., Wang, H., Qiao, S., Leng, L., and Wang, X. (2016). Histone deacetylase HDA6 enhances brassinosteroid signaling by inhibiting the BIN2 kinase. *Proc. Natl. Acad. Sci. U S A.* 113 (37), 10418–10423. doi: 10.1073/pnas.1521363113
- He, C., Gao, H., Wang, H., Guo, Y., He, M., Peng, Y., et al. (2021). GSK3-mediated stress signaling inhibits legume-rhizobium symbiosis by phosphorylating GmNSP1 in soybean. *Mol. Plant* 14 (3), 488–502. doi: 10.1016/j.molp.2020.12.015
- He, Y., Hong, G., Zhang, H., Tan, X., Li, L., Kong, Y., et al. (2020). The OsGSK2 kinase integrates brassinosteroid and jasmonic acid signaling by interacting with OsJAZ4. *Plant Cell.* 32 (9), 2806–2822. doi: 10.1105/tpc.19.00499
- Heidstra, R., and Sabatini, S. (2014). Plant and animal stem cells: similar yet different. *Nat. Rev. Mol. Cell Biol.* 15 (5), 301–312. doi: 10.1038/nrm3790
- Hirano, K., Kawamura, M., Araki-Nakamura, S., Fujimoto, H., Ohmae-Shinohara, K., Yamaguchi, M., et al. (2017). Sorghum DW1 positively regulates brassinosteroid signaling by inhibiting the nuclear localization of BRASSINOSTEROID INSENSITIVE 2. *Sci. Rep.* 7 (1), 126. doi: 10.1038/s41598-017-00096-w
- Hou, L., Li, Z., Shaheen, A., Zhang, K., Wang, J., Gao, X., et al. (2022). Zea mays GSK2 gene is involved in brassinosteroid signaling. *Plant Growth Regulation.* 97 (1), 117–125. doi: 10.1007/s10725-022-00806-z
- Hou, J., Zheng, X., Ren, R., Shi, Q., Xiao, H., Chen, Z., et al. (2022). The histone deacetylase 1/GSK3/SHAGGY-like kinase 2/BRASSINAZOLE-RESISTANT 1 module controls lateral root formation in rice. *Plant Physiol.* 189 (2), 858–873. doi: 10.1093/plphys/kiac015
- Houbaert, A., Zhang, C., Tiwari, M., Wang, K., de Marcos Serrano, A., Savatin, D. V., et al. (2018). POLAR-guided signalling complex assembly and localization drive asymmetric cell division. *Nature.* 563 (7732), 574–578. doi: 10.1038/s41586-018-0714-x
- Hu, Z., Lu, S. J., Wang, M. J., He, H., Sun, L., Wang, H., et al. (2018). A novel QTL qTGW3 encodes the GSK3/SHAGGY-like kinase OsGSK3/OsSK41 that interacts with OsARF4 to negatively regulate grain size and weight in rice. *Mol. Plant* 11 (5), 736–749. doi: 10.1016/j.molp.2018.03.005
- Hu, Y., and Yu, D. (2014). BRASSINOSTEROID INSENSITIVE2 interacts with ABSICISIC ACID INSENSITIVE5 to mediate the antagonism of brassinosteroids to abscisic acid during seed germination in *Arabidopsis*. *Plant Cell.* 26 (11), 4394–4408. doi: 10.1105/tpc.114.130849
- Huang, S., Liu, Y., Deng, R., Lei, T., Tian, A., Ren, H., et al. (2021). Genome-wide identification and expression analysis of the GSK gene family in *Solanum tuberosum* l. under abiotic stress and phytohormone treatments and functional characterization of StSK21 involvement in salt stress. *Gene.* 766, 145156. doi: 10.1016/j.gene.2020.145156
- Ito, Y., Nakanomyo, I., Motose, H., Iwamoto, K., Sawa, S., Dohmae, N., et al. (2006). Dodeca-CLE peptides as suppressors of plant stem cell differentiation. *Science.* 313 (5788), 842–845. doi: 10.1126/science.1128436
- Jiang, H., Tang, B., Xie, Z., Nolan, T., Ye, H., Song, G. Y., et al. (2019). GSK3-like kinase BIN2 phosphorylates RD26 to potentiate drought signaling in *Arabidopsis*. *Plant J.* 100 (5), 923–937. doi: 10.1111/tpl.14484
- Khan, M., Rozhon, W., Unterholzner, S. J., Chen, T., Eremina, M., Wurzing, B., et al. (2014). Interplay between phosphorylation and SUMOylation events determines CESTA protein fate in brassinosteroid signalling. *Nat. Commun.* 5, 4687. doi: 10.1038/ncomms5687
- Kim, T., Guan, S., Burlingame, A., and Wang, Z. (2011). The CDG1 kinase mediates brassinosteroid signal transduction from BRI1 receptor kinase to BSU1 phosphatase and GSK3-like kinase BIN2. *Mol. Cell.* 43 (4), 561–571. doi: 10.1016/j.molcel.2011.05.037
- Kim, T., Guan, S., Sun, Y., Deng, Z., Tang, W., Shang, J., et al. (2009). Brassinosteroid signal transduction from cell-surface receptor kinases to nuclear transcription factors. *Nat. Cell Biol.* 11 (10), 1254–1260. doi: 10.1038/ncb1970
- Kim, E., Lee, S., Park, C., Kim, S., Hsu, C., Xu, S., et al. (2019). Plant U-Box40 mediates degradation of the brassinosteroid-responsive transcription factor BZR1 in *Arabidopsis* roots. *Plant Cell.* 31 (4), 791–808. doi: 10.1105/tpc.18.00941

- Kim, Y., Song, J., Park, S., Jeong, Y., and Kim, S. (2017). Brassinosteroid-induced transcriptional repression and dephosphorylation-dependent protein degradation negatively regulate BIN2-interacting AIF2 (a BR signaling-negative regulator) bHLH transcription factor. *Plant Cell Physiol.* 58 (2), 227–239. doi: 10.1093/pcp/pcw223
- Kim, Y., Youn, J., Roh, J., Kim, J., Kim, S., and Kim, T. (2022). Brassinosteroids enhance salicylic acid-mediated immune responses by inhibiting BIN2 phosphorylation of clade I TGA transcription factors in *Arabidopsis*. *Mol. Plant* 15 (6), 991–1007. doi: 10.1016/j.molp.2022.05.002
- Kloc, Y., Dmochowska-Boguta, M., Zielezinski, A., Nadolska-Orczyk, A., Karlowski, W. M., and Orczyk, W. (2020). Silencing of HvGSK1.1-a GSK3/SHAGGY-like kinase enhances barley (*Hordeum vulgare* L.) growth in normal and in salt stress conditions. *Int. J. Mol. Sci.* 21 (18), 6616. doi: 10.3390/ijms21186616
- Koh, S., Lee, S., Kim, M., Koh, J., Lee, S., An, G., et al. (2007). T-DNA Tagged knockout mutation of rice OsGSK1, an orthologue of *Arabidopsis* BIN2, with enhanced tolerance to various abiotic stresses. *Plant Mol. Biol.* 65 (4), 453–466. doi: 10.1007/s11103-007-9213-4
- Kondo, Y., Ito, T., Nakagami, H., Hirakawa, Y., Saito, M., Tamaki, T., et al. (2014). Plant GSK3 proteins regulate xylem cell differentiation downstream of TDIF-TDR signalling. *Nat. Commun.* 5, 3504. doi: 10.1038/ncomms4504
- Li, T., Lei, W., He, R., Tang, X., Han, J., Zou, L., et al. (2020c). Brassinosteroids regulate root meristem development by mediating BIN2-UPB1 module in *Arabidopsis*. *PLoS Genet.* 16 (7), e1008883. doi: 10.1371/journal.pgen.1008883
- Li, J., and Nam, K. H. (2002). Regulation of brassinosteroid signaling by a GSK3/SHAGGY-like kinase. *Science*. 295 (5558), 1299–1301. doi: 10.1126/science.1065769
- Li, J., Terzaghi, W., Gong, Y., Li, C., Ling, J., Fan, Y., et al. (2020a). Modulation of BIN2 kinase activity by HY5 controls hypocotyl elongation in the light. *Nat. Commun.* 11 (1), 1592. doi: 10.1038/s41467-020-15394-7
- Li, H., Ye, K., Shi, Y., Cheng, J., Zhang, X., and Yang, S. (2017). BZR1 positively regulates freezing tolerance via CBF-dependent and CBF-independent pathways in *Arabidopsis*. *Mol. Plant* 10 (4), 545–559. doi: 10.1016/j.molp.2017.01.004
- Li, C., Zhang, B., Chen, B., Ji, L., and Yu, H. (2018). Site-specific phosphorylation of TRANSPARENT TESTA GLABRA1 mediates carbon partitioning in *Arabidopsis* seeds. *Nat. Commun.* 9 (1), 571. doi: 10.1038/s41467-018-03013-5
- Li, C., Zhang, B., and Yu, H. (2021). GSK3s: nodes of multilayer regulation of plant development and stress responses. *Trends Plant Sci.* 26 (12), 1286–1300. doi: 10.1016/j.tplants.2021.07.017
- Li, J., Zhou, H., Zhang, Y., Li, Z., Yang, Y., and Guo, Y. (2020b). The GSK3-like kinase BIN2 is a molecular switch between the salt stress response and growth recovery in *Arabidopsis thaliana*. *Dev. Cell.* 55 (3), 367–380.e366. doi: 10.1016/j.devcel.2020.08.005
- Liao, C., Pu, Y., Nolan, T., Montes, C., Guo, H., Walley, J., et al. (2022). Brassinosteroids modulate autophagy through phosphorylation of RAPTOR1B by the GSK3-like kinase BIN2 in *Arabidopsis*. *Autophagy*. 24, 1–18. doi: 10.1080/15548627.2022.2124501
- Ling, J., Li, J., Zhu, D., and Deng, X. (2017). Noncanonical role of *Arabidopsis* COP1/SPA complex in repressing BIN2-mediated PIF3 phosphorylation and degradation in darkness. *Proc. Natl. Acad. Sci. U S A.* 114 (13), 3539–3544. doi: 10.1073/pnas.1700850114
- Liu, J., Chen, J., Zheng, X., Wu, F., Lin, Q., Heng, Y., et al. (2017). GW5 acts in the brassinosteroid signalling pathway to regulate grain width and weight in rice. *Nat. Plants*. 3, 17043. doi: 10.1038/nplants.2017.43
- Lyu, J., Wang, D., Duan, P., Liu, Y., Huang, K., Zeng, D., et al. (2020). Control of grain size and weight by the GSK2-LARGE1/OML4 pathway in rice. *Plant Cell*. 32 (6), 1905–1918. doi: 10.1105/tpc.19.00468
- Mao, J., Li, W., Liu, J., and Li, J. (2021). Versatile physiological functions of plant GSK3-like kinases. *Genes (Basel)*. 12 (5), 697. doi: 10.3390/genes12050697
- Mei, Y., Yang, X., Huang, C., Zhang, X., and Zhou, X. (2018). Tomato leaf curl yunnan virus-encoded C4 induces cell division through enhancing stability of cyclin D1.1 via impairing NbSKn1-mediated phosphorylation in *Nicotiana benthamiana*. *PLoS Pathog.* 14 (1), e1006789. doi: 10.1371/journal.ppat.1006789
- Mei, Y., Zhang, F., Wang, M., Li, F., Wang, Y., and Zhou, X. (2020). Divergent symptoms caused by geminivirus-encoded C4 proteins correlate with their ability to bind NbSKn1. *J. Virol.* 94 (20), e1307-20. doi: 10.1128/jvi.01307-20
- Min, H., Cui, L., Oh, T., Kim, J., Kim, T., and Kim, W. T. (2019). OsBZR1 turnover mediated by OsSK22-regulated U-box E3 ligase OsPUB24 in rice BR response. *Plant J.* 99 (3), 426–438. doi: 10.1111/tpj.14332
- Murata, M. (2018). Inflammation and cancer. *Environ. Health Prev. Med.* 23 (1), 50. doi: 10.1186/s12199-018-0740-1
- Nolan, T., Brennan, B., Yang, M., Chen, J., Zhang, M., Li, Z., et al. (2017). Selective autophagy of BES1 mediated by DSK2 balances plant growth and survival. *Dev. Cell*. 41 (1), 33–46. doi: 10.1016/j.devcel.2017.03.013
- Nolan, T., Vukašinović, N., Liu, D., Russinova, E., and Yin, Y. (2020). Brassinosteroids: multidimensional regulators of plant growth, development, and stress responses. *Plant Cell*. 32 (2), 295–318. doi: 10.1105/tpc.19.00335
- Patel, P., and Woodgett, J. R. (2017). Glycogen synthase kinase 3: a kinase for all pathways? *Curr. Top. Dev. Biol.* 123, 277–302. doi: 10.1016/bs.ctdb.2016.11.011
- Peck, S., and Mittler, R. (2020). Plant signaling in biotic and abiotic stress. *J. Exp. Bot.* 71 (5), 1649–1651. doi: 10.1093/jxb/eraa051
- Peng, P., Yan, Z., Zhu, Y., and Li, J. (2008). Regulation of the *Arabidopsis* GSK3-like kinase BRASSINOSTEROID-INSENSITIVE 2 through proteasome-mediated protein degradation. *Mol. Plant* 1 (2), 338–346. doi: 10.1093/mp/ssn001
- Peres, A., Soares, J. S., Tavares, R. G., Righetto, G., Zullo, M. A. T., Mandava, N. B., et al. (2019). Brassinosteroids, the sixth class of phytohormones: a molecular view from the discovery to hormonal interactions in plant development and stress adaptation. *Int. J. Mol. Sci.* 20 (2), 331. doi: 10.3390/ijms20020331
- Piao, H., Lim, J., Kim, S., Cheong, G., and Hwang, I. (2001). Constitutive over-expression of AtGSK1 induces NaCl stress responses in the absence of NaCl stress and results in enhanced NaCl tolerance in *Arabidopsis*. *Plant J.* 27 (4), 305–314. doi: 10.1046/j.1365-313x.2001.01099.x
- Qi, X., Chanderbali, A. S., Wong, G. K., Soltis, D. E., and Soltis, P. S. (2013). Phylogeny and evolutionary history of glycogen synthase kinase 3/SHAGGY-like kinase genes in land plants. *BMC Evol. Biol.* 13, 143. doi: 10.1186/1471-2148-13-143
- Qiao, S., Sun, S., Wang, L., Wu, Z., Li, C., Li, X., et al. (2017). The RLA1/SMO51 transcription factor functions with OsBZR1 to regulate brassinosteroid signaling and rice architecture. *Plant Cell*. 29 (2), 292–309. doi: 10.1105/tpc.16.00611
- Qiu, A., Wu, J., Lei, Y., Cai, Y., Wang, S., Liu, Z., et al. (2018). CaSK23, a putative GSK3/SHAGGY-like kinase of *Capsicum annuum*, acts as a negative regulator of pepper's response to *Ralstonia solanacearum* attack. *Int. J. Mol. Sci.* 19 (9), 2698. doi: 10.3390/ijms19092698
- Racaud-Sultan, C., and Vergnolle, N. (2021). GSK3 β , a master kinase in the regulation of adult stem cell behavior. *Cells*. 10 (2), 225. doi: 10.3390/cells10020225
- Ren, H., Willige, B. C., Jaillais, Y., Geng, S., Park, M. Y., Gray, W. M., et al. (2019). BRASSINOSTEROID-SIGNALING KINASE 3, a plasma membrane-associated scaffold protein involved in early brassinosteroid signaling. *PLoS Genet.* 15 (1), e1007904. doi: 10.1371/journal.pgen.1007904
- Rozhon, W., Mayerhofer, J., Petutschnig, E., Fujioka, S., and Jonak, C. (2010). ASKtheta, a group-III *Arabidopsis* GSK3, functions in the brassinosteroid signalling pathway. *Plant J.* 62 (2), 215–223. doi: 10.1111/j.1365-313X.2010.04145.x
- Samakovi, D., Margaritopoulou, T., Prassinou, C., Milioni, D., and Hatzopoulos, P. (2014). Brassinosteroid nuclear signaling recruits HSP90 activity. *New Phytol.* 203, 743–757. doi: 10.1111/nph.12843
- Santiago, J., Henzler, C., and Hothorn, M. (2013). Molecular mechanism for plant steroid receptor activation by somatic embryogenesis co-receptor kinases. *Science*. 341 (6148), 889–892. doi: 10.1126/science.1242468
- Signorelli, S., Tarkowski, L. P., Van den Ende, W., and Bassham, D. C. (2019). Linking autophagy to abiotic and biotic stress responses. *Trends Plant Sci.* 24 (5), 413–430. doi: 10.1016/j.tplants.2019.02.001
- Solovou, T., Garagounis, C., Kyriakis, E., Bobas, C., Papadopoulos, G. E., Skamnaki, V. T., et al. (2021). Mutagenesis of a lotus japonicus GSK3 β /Shaggy-like kinase reveals functionally conserved regulatory residues. *Phytochemistry*. 186, 112707. doi: 10.1016/j.phytochem.2021.112707
- Song, S., Wang, H., Sun, M., Tang, J., Zheng, B., Wang, X., et al. (2019). Reactive oxygen species-mediated BIN2 activity revealed by single-molecule analysis. *New Phytol.* 223 (2), 692–704. doi: 10.1111/nph.15669
- Song, Y., Zhai, Y., Li, L., Yang, Z., Ge, X., Yang, Z., et al. (2021). BIN2 negatively regulates plant defence against *Verticillium dahliae* in *Arabidopsis* and cotton. *Plant Biotechnol. J.* 19 (10), 2097–2112. doi: 10.1111/pbi.13640
- Stampfl, H., Fritz, M., Dal Santo, S., and Jonak, C. (2016). The GSK3/Shaggy-like kinase ASK α contributes to pattern-triggered immunity. *Plant Physiol.* 171 (2), 1366–1377. doi: 10.1104/pp.15.01741
- Sun, S., Chen, D., Li, X., Qiao, S., Shi, C., Li, C., et al. (2015). Brassinosteroid signaling regulates leaf erectness in *Oryza sativa* via the control of a specific U-type cyclin and cell proliferation. *Dev. Cell*. 34 (2), 220–228. doi: 10.1016/j.devcel.2015.05.019
- Sun, S., Wang, T., Wang, L., Li, X., Jia, Y., Liu, C., et al. (2018). Natural selection of a GSK3 determines rice mesocotyl domestication by coordinating strigolactone and brassinosteroid signaling. *Nat. Commun.* 9 (1), 2523. doi: 10.1038/s41467-018-04952-9
- Tamaki, T., Oya, S., Naito, M., Ozawa, Y., Furuya, T., Saito, M., et al. (2020). VISUAL-CC system uncovers the role of GSK3 as an orchestrator of vascular cell type ratio in plants. *Commun. Biol.* 3 (1), 184. doi: 10.1038/s42003-020-0907-3
- Tang, W., Kim, T., Osés-Prieto, J., Sun, Y., Deng, Z., Zhu, S., et al. (2008). BSKs mediate signal transduction from the receptor kinase BRI1 in *Arabidopsis*. *Science*. 321 (5888), 557–560. doi: 10.1126/science.1156973
- Tong, H., Liu, L., Jin, Y., Du, L., Yin, Y., Qian, Q., et al. (2012). DWARF AND LOW-TILLERING acts as a direct downstream target of a GSK3/SHAGGY-like kinase to mediate brassinosteroid responses in rice. *Plant Cell*. 24 (6), 2562–2577. doi: 10.1105/tpc.112.097394
- Umezawa, T., Sugiyama, N., Mizoguchi, M., Hayashi, S., Myouga, F., Yamaguchi-Shinozaki, K., et al. (2009). Type 2C protein phosphatases directly regulate abscisic acid-activated protein kinases in *Arabidopsis*. *Proc. Natl. Acad. Sci. U S A.* 106 (41), 17588–17593. doi: 10.1073/pnas.0907095106
- Vert, G., and Chory, J. (2006). Downstream nuclear events in brassinosteroid signalling. *Nature*. 441 (7089), 96–100. doi: 10.1038/nature04681
- Vert, G., Walcher, C. L., Chory, J., and Nemhauser, J. L. (2008). Integration of auxin and brassinosteroid pathways by auxin response factor 2. *Proc. Natl. Acad. Sci. U S A.* 105 (28), 9829–9834. doi: 10.1073/pnas.0803996105

- Waadt, R., Seller, C. A., Hsu, P. K., Takahashi, Y., Munemasa, S., and Schroeder, J. I. (2022). Plant hormone regulation of abiotic stress responses. *Nat. Rev. Mol. Cell Biol.* 23 (10), 680–694. doi: 10.1038/s41580-022-00479-6
- Wang, L., Cheng, H., Xiong, F., Ma, S., Zheng, L., Song, Y., et al. (2020). Comparative phosphoproteomic analysis of BR-defective mutant reveals a key role of GhSK13 in regulating cotton fiber development. *Sci. China Life Sci.* 63 (12), 1905–1917. doi: 10.1007/s11427-020-1728-9
- Wang, X., and Chory, J. (2006). Brassinosteroids regulate dissociation of BKI1, a negative regulator of BRI1 signaling, from the plasma membrane. *Science*. 313 (5790), 1118–1122. doi: 10.1126/science.1127593
- Wang, X., Kota, U., He, K., Blackburn, K., Li, J., Goshe, M. B., et al. (2008). Sequential transphosphorylation of the BRI1/BAK1 receptor kinase complex impacts early events in brassinosteroid signaling. *Dev. Cell*. 15 (2), 220–235. doi: 10.1016/j.devcel.2008.06.011
- Wang, L., Su, A., Wu, X., Chen, Q., Xin, D., Qi, Z., et al. (2018). Overexpression of GmBIN2, a soybean glycogen synthase kinase 3 gene, enhances tolerance to salt and drought in transgenic *Arabidopsis* and soybean hairy roots. *J. Integr. Agric.* 17 (9), 13. doi: 10.1016/S2095-3119(17)61863-X
- Wang, H., Tang, J., Liu, J., Hu, J., Liu, J., Chen, Y., et al. (2018a). Abscisic acid signaling inhibits brassinosteroid signaling through dampening the dephosphorylation of BIN2 by AB11 and AB12. *Mol. Plant* 11 (2), 315–325. doi: 10.1016/j.molp.2017.12.013
- Wang, Y., Xu, J., Yu, J., Zhu, D., and Zhao, Q. (2022). Maize GSK3-like kinase ZmSK2 is involved in embryonic development. *Plant Sci.* 318, 111221. doi: 10.1016/j.plantsci.2022.111221
- Wang, L., Yang, Z., Zhang, B., Yu, D., Liu, J., Gong, Q., et al. (2018b). Genome-wide characterization and phylogenetic analysis of GSK gene family in three species of cotton: evidence for a role of some GSKs in fiber development and responses to stress. *BMC Plant Biol.* 18 (1), 330. doi: 10.1186/s12870-018-1526-8
- Woodgett, J. R. (1991). A common denominator linking glycogen metabolism, nuclear oncogenes and development. *Trends Biochem. Sci.* 16 (5), 177–181. doi: 10.1016/0968-0004(91)90071-3
- Wrzaczek, M., Rozhon, W., and Jonak, C. (2007). A proteasome-regulated glycogen synthase kinase-3 modulates disease response in plants. *J. Biol. Chem.* 282 (8), 5249–5255. doi: 10.1074/jbc.M610135200
- Xia, D., Zhou, H., Liu, R., Dan, W., Li, P., Wu, B., et al. (2018). GL3.3, a novel QTL encoding a GSK3/SHAGGY-like kinase, epistatically interacts with GS3 to produce extra-long grains in rice. *Mol. Plant* 11 (5), 754–756. doi: 10.1016/j.molp.2018.03.006
- Xiao, Y., Liu, D., Zhang, G., Tong, H., and Chu, C. (2017). Brassinosteroids regulate OFP1, a DLT interacting protein, to modulate plant architecture and grain morphology in rice. *Front. Plant Sci.* 8. doi: 10.3389/fpls.2017.01698
- Xiao, Y., Zhang, G., Liu, D., Niu, M., Tong, H., and Chu, C. (2020). GSK2 stabilizes OFP3 to suppress brassinosteroid responses in rice. *Plant J.* 102 (6), 1187–1201. doi: 10.1111/tpj.14692
- Xie, Z., Nolan, T., Jiang, H., Tang, B., Zhang, M., Li, Z., et al. (2019). The AP2/ERF transcription factor TINY modulates brassinosteroid-regulated plant growth and drought responses in *Arabidopsis*. *Plant Cell*. 31 (8), 1788–1806. doi: 10.1105/tpc.18.00918
- Xiong, F., Zhang, R., Meng, Z., Deng, K., Que, Y., Zhuo, F., et al. (2017). Brassinosteroid insensitive 2 (BIN2) acts as a downstream effector of the target of rapamycin (TOR) signaling pathway to regulate photoautotrophic growth in *Arabidopsis*. *New Phytol.* 213 (1), 233–249. doi: 10.1111/nph.14118
- Yan, Z., Zhao, J., Peng, P., Chihara, R. K., and Li, J. (2009). BIN2 functions redundantly with other *Arabidopsis* GSK3-like kinases to regulate brassinosteroid signaling. *Plant Physiol.* 150 (2), 710–721. doi: 10.1104/pp.109.138099
- Yang, C., Luo, M., Zhuang, X., Li, F., and Gao, C. (2020). Transcriptional and epigenetic regulation of autophagy in plants. *Trends Genet.* 36 (9), 676–688. doi: 10.1016/j.tig.2020.06.013
- Yang, C., Shen, W., He, Y., Tian, Z., and Li, J. (2016). OVATE family protein 8 positively mediates brassinosteroid signaling through interacting with the GSK3-like kinase in rice. *PLoS Genet.* 12 (6), e1006118. doi: 10.1371/journal.pgen.1006118
- Ye, K., Li, H., Ding, Y., Shi, Y., Song, C., Gong, Z., et al. (2019). BRASSINOSTEROID-INSENSITIVE2 negatively regulates the stability of transcription factor ICE1 in response to cold stress in *Arabidopsis*. *Plant Cell*. 31 (11), 2682–2696. doi: 10.1105/tpc.19.00058
- Ye, H., Li, L., Guo, H., and Yin, Y. (2012). MYBL2 is a substrate of GSK3-like kinase BIN2 and acts as a corepressor of BES1 in brassinosteroid signaling pathway in *Arabidopsis*. *Proc. Natl. Acad. Sci. U S A.* 109 (49), 20142–20147. doi: 10.1073/pnas.1205232109
- Ying, J., Ma, M., Bai, C., Huang, X., Liu, J., Fan, Y., et al. (2018). TGW3, a major QTL that negatively modulates grain length and weight in rice. *Mol. Plant* 11 (5), 750–753. doi: 10.1016/j.molp.2018.03.007
- Youn, J., and Kim, T. (2015). Functional insights of plant GSK3-like kinases: multi-taskers in diverse cellular signal transduction pathways. *Mol. Plant* 8 (4), 552–565. doi: 10.1016/j.molp.2014.12.006
- Zhang, K., Duan, M., Zhang, L., Li, J., Shan, L., Zheng, L., et al. (2022). HOP1 and HOP2 are involved in salt tolerance by facilitating the brassinosteroid-related nucleocytoplasmic partitioning of the HSP90-BIN2 complex. *Plant Cell Environ.* 45 (12), 3551–3565. doi: 10.1111/pce.14441
- Zhang, D., Tan, W., Yang, F., Han, Q., Deng, X., Guo, H., et al. (2021). A BIN2-GLK1 signaling module integrates brassinosteroid and light signaling to repress chloroplast development in the dark. *Dev. Cell*. 56 (3), 310–324.e317. doi: 10.1016/j.devcel.2020.12.001
- Zhang, C., Xu, Y., Guo, S., Zhu, J., Huan, Q., Liu, H., et al. (2012). Dynamics of brassinosteroid response modulated by negative regulator LIC in rice. *PLoS Genet.* 8 (4), e1002686. doi: 10.1371/journal.pgen.1002686
- Zhang, P., Zhang, L., Chen, T., Jing, F., Liu, Y., Ma, J., et al. (2022b). Genome-wide identification and expression analysis of the GSK gene family in wheat (*Triticum aestivum* L.). *Mol. Biol. Rep.* 49 (4), 2899–2913. doi: 10.1007/s11033-021-07105-2
- Zhang, H., Zhu, J., Gong, Z., and Zhu, J. K. (2022a). Abiotic stress responses in plants. *Nat. Rev. Genet.* 23 (2), 104–119. doi: 10.1038/s41576-021-00413-0
- Zhu, J. (2016). Abiotic stress signaling and responses in plants. *Cell*. 167 (2), 313–324. doi: 10.1016/j.cell.2016.08.029
- Zhu, J., Li, Y., Cao, D., Yang, H., Oh, E., Bi, Y., et al. (2017). The f-box protein KIB1 mediates brassinosteroid-induced inactivation and degradation of GSK3-like kinases in *Arabidopsis*. *Mol. Cell*. 66 (5), 648–657.e644. doi: 10.1016/j.molcel.2017.05.012
- Zolkiewicz, K., and Gruszka, D. (2022). Glycogen synthase kinases in model and crop plants - from negative regulators of brassinosteroid signaling to multifaceted hubs of various signaling pathways and modulators of plant reproduction and yield. *Front. Plant Sci.* 13. doi: 10.3389/fpls.2022.939487