

REVIEW ARTICLE

An Overview of Signaling Regulons During Cold Stress Tolerance in Plants

Amit Pareek¹, Ashima Khurana², Arun K. Sharma¹ and Rahul Kumar^{3,*}

¹Department of Plant Molecular Biology, University of Delhi, South Campus, Benito Juarez Road, Dhaula Kuan, New Delhi-110021, India; ²Ashima Khurana, Botany Department, Zakir Husain Delhi College, University of Delhi, New Delhi-110002, India; ³Repository of Tomato Genomics Resources, Department of Plant Sciences, University of Hyderabad, Hyderabad 500046, India

Abstract: Plants, being sessile organisms, constantly withstand environmental fluctuations, including low-temperature, also referred as cold stress. Whereas cold poses serious challenges at both physiological and developmental levels to plants growing in tropical or sub-tropical regions, plants from temperate climatic regions can withstand chilling or freezing temperatures. Several cold inducible genes have already been isolated and used in transgenic approach to generate cold tolerant plants. The conventional breeding methods and marker assisted selection have helped in developing plant with improved cold tolerance, however, the development of freezing tolerant plants through cold acclimation remains an unaccomplished task. Therefore, it is essential to have a clear understanding of how low temperature sensing strategies and corresponding signal transduction act during cold acclimation process. Herein, we synthesize the available information on the molecular mechanisms underlying cold sensing and signaling with an aim that the summarized literature will help develop efficient strategies to obtain cold tolerant plants.

ARTICLE HISTORY

Received: August 01, 2016
Revised: September 23, 2016
Accepted: October 05, 2016

DOI:
10.2174/1389202918666170228141345

Keywords: Cold, Calcium, Protein kinase, CBF, Signaling, Phosphorylation.

1. INTRODUCTION

In contrast to animals which preferentially opt for the 'avoid' response, plants being sessile usually adopt the 'overcome' strategy to counter any extreme environmental fluctuation. Temperature stress is one such factor which plants experience from their surrounding environment. Plant grow best at their optimum temperature range and any extreme fluctuation from this optima affects their growth and final yield [1]. Due to its wide-spread occurrence, low temperature or cold stress affects several facets of plant's life and causes extreme economic losses in agriculture. Plant endurance to low temperatures can be grouped into two types *i.e.* chilling tolerance (above 0°C) and freezing tolerance (below 0°C) [2]. Among various abiotic stresses, chilling stress influences the production and quality of economically important crops the most, especially in the tropical and subtropical climatic zones [3, 4]. In contrast, plants originating from temperate climatic regions are considered chilling tolerant because they can increase their freezing tolerance by cold acclimation process. Plants of tropical and sub-tropical origins lack this mechanism and are more prone to the adverse effect of chilling stress [5-8]. Depending on their

response to low temperature stress, plants have been categorized into chilling sensitive, chilling tolerant, and freezing tolerant. Chilling sensitive plants show metabolic complications on the exposure to the temperatures below their optima.

Important crops, such as rice, maize, soybean, cotton and tomato are chilling sensitive. On the contrary, chilling tolerant plants are able to survive the lower range of temperatures but not freezing temperature. The freezing tolerant plants can survive even in the freezing conditions [9].

2. PHYSIOLOGICAL CONSEQUENCES OF COLD STRESS ON PLANTS AND COLD TOLERANCE MECHANISM

Exposure of plants to chilling results in a number of transient biochemical perturbations, including thermodynamic slowdown of the kinetics of metabolic reactions. Further, it modulates the thermodynamic equilibrium of the cell which might cause the non-polar side chains of proteins to reorient towards the aqueous medium. Such reorientation impacts on the solubility and stability of globular proteins [10]. Low temperatures also cause rigidification of membrane, resulting in the disturbance of all membrane-related processes, and induction of cold-associated genes [11]. Chilling also leads to higher reactive oxygen species (ROS) accumulation as the ROS scavenging system does not function properly; due to reduced enzymes activity. In turn, ROS over accumulation has harmful effects on membranes and leads to ion leakage.

*Address correspondence to this author at the Repository of Tomato Genomics Resources, Department of Plant Sciences, University of Hyderabad, Hyderabad 500046, India; E-mail: rahulpmb@gmail.com

Altogether, low temperature directly affects DNA secondary structure, lowers enzymatic activities involved in fundamental processes such as transcription and translation, induces membrane rigidification, destabilizes protein complexes, stabilizes RNA secondary structure, impairs photosynthesis, and leads to ion leakage across membranes [7, 12-16].

Below sub-zero temperature, ice formation first takes place in the intercellular spaces of plant tissues and finally culminates in the intracellular symplastic freezing. The extracellular ice formation results in a drop in water potential and causes intracellular water to move out of the cell. It is followed by dehydration and shrinkage of cells causing freezing injuries [8, 17, 18]. The level of such dehydration is determined by the severity of temperature drop which increases with the decreasing temperatures. Finally, ice can penetrate the symplast and spoil the intracellular structures resulting in death of the tissue [19, 20]. Cold-induced dehydration results in various physiological effects, for example, precipitation of molecules, protein denaturation, membrane damaging effects and cell lysis [8, 21]. The signs and symptoms associated with chilling-induced stress injuries in chilling sensitive plants are varied and generally express within 48 to 72 h of exposure to the stress. The phenotypic signs of chilling stress consist of reduced leaf expansion, chlorosis, wilting, and necrosis [22]. Chilling also causes defect in plant reproductive development. For example, rice plants displayed sterility upon exposure to chilling temperatures during anthesis [23]. The severity of plant damage depends on multiple factors such as the developmental stage of plant, duration of the frost, rates of cooling and rewarming, and the extent of ice formation [24]. As a consequence, plants adopt two strategies to resist the frost-related injuries: first, prevention of ice formation in tissues; and second, tolerance to apoplastic extracellular ice. Further, an individual plant may utilize both types of mechanisms for frost resistance in different tissues [25].

3. COLD ACCLIMATION

Cold acclimation is a process where temperate plants acquire freezing tolerance upon previous exposure to low but non-freezing temperatures [26-28]. This ability is not found in plants from the tropical and sub-tropical regions. As a consequence, these plants cannot tolerate ice formation in their tissues. This process is considered as the first line of defence and has an important role in stabilizing plasma membranes against cold-induced injury [7, 29-31]. Several mechanisms, including processes like change in lipid composition [30] and accumulation of simple sugars [32] contribute to this stabilization. Additionally, LEA (late embryonic abundant) and hydrophilic proteins help stabilize membranes against cold-induced damage. Several chilling-related injuries can also be associated with ROS, especially in chilling sensitive plants [7, 33-35]. As the counteractive mechanisms, plants develop effective oxygen-scavenging systems which consist of several antioxidant enzymes such as ascorbate peroxidase, Superoxide Dismutase (SOD), Glutathione Reductase (GR) and catalase. Moreover, non-enzymatic antioxidants, such as ascorbic acid and reduced glutathione also help in minimizing the negative effects attributed by high ROS levels [36-38].

3.1. Perception of Cold

Stress perception determines the specificity of the signal transduction network and adaptation of plant's physiology in a particular environment [21]. Plants exhibit a variety of responses to the environmental temperature in a time based fashion. While a few of these responses are short term, other responses require long exposure to low temperature; sometimes for several days or weeks as in the case of vernalization process [39]. Evidence suggests that plant cell preferentially senses the rate of temperature change (dT/dt) over the absolute temperature as fast cooling of temperature between 22°C and 16°C have been found to generate strong depolarization of membrane than the slower cooling in cucumber [40]. Although the mechanism of sensing low temperature in plants remains unclear, the temperature dependent modifications of membrane fluidity were initially considered as the primary temperature sensor in cyanobacteria and yeast [11, 41].

Plasma membrane, being the interface between internal and external environment of the cell, is considered as a site for the perception of temperature change [7, 42-44]. In plants, the potential sensors of cold include Ca^{+2} influx channels, two-component histidine kinases and receptors associated with G-proteins [45]. The initial evidences established that plant response to low temperature involved an influx of Ca^{+2} from apoplast into the cytosol and a positive correlation exists between Ca^{+2} influx and the rate of temperature drop [7, 46-49]. Cellular Ca^{+2} dynamics are detected in response to cold within 40 s through a novel aquaporin-based Ca^{+2} signaling mechanism in *Arabidopsis* [50].

It has been suggested that the cold induced calcium transients may occur downstream to membrane rigidification and cytoskeletal reorganization in signal transduction pathway [7, 21, 51-53]. Further, stabilization and destabilization of cytoskeletal components such as actin microfilament at different temperatures, 4°C and 25°C respectively, can control cold stress responses by preventing both expression of *COR* genes and Ca^{2+} influx [51]. It is known that drugs that strengthen microfilaments decrease cold sensitivity. In contrast, the drugs that destabilize microfilaments can stimulate cold-dependent downstream processes even in the absence of cold, suggesting that cytoskeletal reorganization possibly participates in the sensor mechanisms [51]. Nonetheless, cytoskeletal reorganization was found not to be an absolute requirement for cold-induced responses and therefore it is not considered as the primary cold sensor [28].

Additionally, expression of the two-component response regulator-like proteins has been implicated in low temperature responses in *Arabidopsis* [54, 55] and *Synechocystis* [56-58]. Low temperature induced receptor-like protein kinases have also been suggested as possible cold sensors [7, 59, 60]. The extracellular domains of these proteins undergo a temperature-induced conformational modification and leads to induction of their kinase activity in cytoplasm. Analysis of cold-induced gene expression in transgenic or mutant plants with changes in membrane lipid saturation or sterol content revealed that membrane fluidity is a part of cold sensing mechanisms in higher plants. Besides, recent evidence also suggests an important role of chromatin remodelling in low temperature sensing [7, 61, 62]. The his-

tone remodelling proteins such as HOS15 (high expression of osmotically responsive genes), and AGC1 (aspartate/glutamate carrier) or histone subunits may play an equivalent role in cold sensing at lower temperatures. Taken together, it can be concluded that more than one thermo sensors are involved during cold sensing in plant cells [28].

3.2. Signal Transduction Mechanism

In general, the signal produced by physical factors such as cold converted to a genetic response which initiates changes in gene expression leading to physiological and metabolic changes in the cell and culminates in a response. Upon experiencing low temperature, plants identify the induced signal and transduce it to the nucleus.

3.2.1. Role of Calcium

Calcium (Ca^{+2}) is the most ubiquitous secondary messenger in eukaryotes [63, 64]. Within seconds of low temperature exposure, free cytosolic Ca^{+2} level is elevated by its influx from apoplast or vacuole [46, 49]. Such cytosolic Ca^{+2} oscillations can be recognized within a short time span, just few seconds or minutes after transferring the plant to low temperature. The extent of these Ca^{+2} oscillations also depends on the previous exposure of temperature stress to plants as recurring experience of low temperature leads to reduced Ca^{+2} oscillations, suggesting that plants have a Ca^{+2} signature memory associated with earlier temperature experiences [65]. The prompt Ca^{+2} influx is induced by activation of ionophores or Ca^{+2} channels agonists which in turn leads to activation of cold-acclimation-specific genes [7, 66, 67]. The cytosolic influx of Ca^{+2} during stress is needed for the expression of some cold-induced genes like *COR6* and *KINI* (Knotted1) in *Arabidopsis thaliana* [47-49]. The Ca^{+2} released from internal cellular reserves, mediated by inositol triphosphate, is upstream to the expression of C-repeat Binding Factors (CBFs) and Cold Responsive (COR) genes in the cold-signaling pathway [53, 68, 69].

3.2.1.1. Ca^{+2} Regulated Proteins (Decoders of the Calcium Signature)

The signal-specific Ca^{+2} signatures (cytosolic Ca^{+2} changes) are decoded by a large number of Ca^{+2} binding proteins in plants [70]. These proteins change their phosphorylation status on the elevation of intracellular Ca^{+2} level and function as Ca^{+2} sensors [7, 48, 71, 72]. The majority of Ca^{+2} sensors possess high affinity Ca^{+2} binding helix-turn-helix structures; also known as EF-hands [71, 73]. Ca^{+2} sensors have been broadly divided into two classes: sensor relays and sensor responders [74, 75]. Bonafide sensor relay proteins do not possess any known enzymatic or functional domains. Instead, upon binding to Ca^{+2} , these interact with another group of proteins and regulate their activities in downstream signaling. Some of the major sensors included in this group are calmodulin (CaM), CaM-like (CMLs) and calcineurin B-like proteins (CBLs) [76-79].

The sensor responders are protein kinases which consist of one or more EF-hand motif and whose activity is controlled by binding of Ca^{+2} to EF hand motifs. In this group, sensing *via* EF-motif and responses *via* protein kinase function are combined within a single protein. It includes Ca^{+2} -Dependent Protein Kinases (CDPKs), [80, 81], Ca^{+2} and

Ca^{+2} /CaM-dependent protein kinase (CCaMK) [82-84], cytosolic phospholipase A2 (cPLA2), phospholipase C (PLC) and some lipid (AtCLB, Calciosins, PLD, Annexins) or DNA binding proteins (SUB1, Calreticulin) [71, 85-88].

Calmodulin (CaM) is one of the most conserved and best characterized small acidic Ca^{+2} binding proteins found in eukaryotes [89]. Its binding to Ca^{+2} induces a structural change and relay the signal to downstream components. CaM activity is essential for the expression of cold inducible genes in many systems, including *Arabidopsis* and *Alfalfa* [90]. CaMs are constituted by a small gene family in plants [91-94]. Over-expression of *Arabidopsis CaM3* hinders cold induction of some of key cold responsive genes, including *RD29A*, *KINI* (Knotted1 Induced1) and *KIN2* (Knotted2 Induced2) [95]. In plants, CaM also presents an example of indirect regulation of gene expression by mediating through a CaM-binding protein kinase and a CaM-binding protein phosphatase [96].

Similar to CaMs, Calcineurin B like (CBL) proteins (also called SOS3-like Ca^{+2} binding proteins, ScaBLs) form another group of Ca^{+2} sensors. These proteins (AtCBLs/SCaBPs) were first identified in *Arabidopsis* and lack any enzymatic activity [97-101]. Overexpression of *AtCBL1* has been found to confer increased stress tolerance in transgenic *Arabidopsis* plants. These plants showed decreased rate of water loss with upregulated CBF/DREB transcription factors and other related genes in non-stressed plants [102]. Whereas mutation of this gene affected the transcript levels of cold regulated genes, its overexpression induced the expression of early stress responsive transcription factors [102]. However, CBLs alone cannot function and require a group of serine/threonine protein kinases, named CBL-interacting protein kinases (CIPKs), to impart their roles under cold stress conditions [103]. In total, 10 *CBLs* and 26 *CIPKs* genes have been identified in *Arabidopsis* [104]. Likewise, 10 *CBLs* and 33 *CIPKs* are present in rice [101, 105]. Interactions CBLs and CIPKs have been found to be Ca^{+2} dependent in cold stress responses. [99, 106, 107]. For example, *CIPK3* has been suggested to act downstream of the Ca^{+2} signal [108]. Further, *CIPK7* is induced by cold and interacts with CBL1 both *in vitro* and *in vivo* conditions [103]. Moreover, overexpression of *OsCIPK3* in transgenic lines of rice, showed an improved cold tolerance and found better survival rate [109].

Calcium-dependent protein kinases (CDPKs) are other important sensors which are involved in response to abiotic stresses, including cold [81, 110-113]. These genes are also multigene family members. For example, it has been reported that this gene family is comprised of 34 *CDPK* members in *Arabidopsis* [81], 20 members in wheat [114], 29 members in tomato [115] and 31 members in rice [116]. CDPKs often have a conserved structure with an N-terminal variable domain, which mediate isoform specificity and localization [117, 118], a middle catalytic protein kinase domain, which is linked to a junction sequence, and C-terminally located CaM-like domain, which canonically harbours four EF-hands. A junction sequence acts like an auto-inhibitory region and keeps the kinase inactive using pseudo-substrate-binding mechanism [119-121]. Under low cytoplasmic calcium concentration, CDPK remains inactive due

to the blocking of catalytic site by auto-inhibitory region. Upon stress perception and calcium influx into the cell, calcium binding to the EF-hands triggers the intramolecular interaction between CaM-like domain and the auto-inhibitory domain causing the conformational change that leads to activation of the enzyme [120, 122, 123]. Subsequently, downstream responses such as phosphorylation and activation of many regulatory proteins including transcription factors, changes in ion fluxes across membranes, accumulation of stress-related metabolites and developmental growth processes are induced [124-127]. Transient transactivation assays of stress-responsive *CDPKs*-reporter gene constructs in transformed maize (*Zea mays*) protoplasts provided the first evidence of their involvement in specific signal/response pathways [128]. In rice, a membrane associated *CDPK* is activated after exposure to cold [129]. Similarly, *OsCPK7/OsCDPK13* or *OsCPK13/OsCDPK7* is activated by a 3 h cold treatment [7]. Further, overexpression of *OsCPK7/OsCDPK13* *OsCPK13/OsCDPK7* confers cold tolerance in transgenic rice [7, 130]. These studies suggested the possibility of involvement of *CDPKs* in Ca^{+2} mediated signaling during acquisition of cold tolerance. Genetic analysis also proved that *CDPKs* act as positive regulators [130] whereas CaM3 acts as a negative regulator of gene expression during cold tolerance [95]. Similar to *CIPKs*, *CDPKs* perform their functions by binding to their targets and a few potential targets of *CPK3* such as RARE COLD INDUCIBLE 1A (*RCI1A*) and ALCOHOL DEHYDROGENASE 1 (*ADH1*) have already been discovered in *Arabidopsis*. Further, cold inducible *CPK4* targets a b-ZIP transcription factor *ABF1*, encoded by an ABA- and cold-inducible gene, for phosphorylation. It shows that *ABF1* might participate in ABA-mediated cold acclimation in plants [131].

3.2.2. MAPK Cascade

MAPK family includes a large family of serine/threonine protein kinases in plants. A typical MAPK cascade is composed of three protein kinases. Inactive Mitogen Activated Protein Kinase Kinase Kinases (MAPKKKs) are activated by a stress signal messenger. Three kinds of MAPKKKs, including *CTR1*, *ANP1-3* and *MEKK* exist in *Arabidopsis thaliana*. Among these, *MEKK* is expressed in response to various abiotic stresses, including cold. Upon activation, they activate MAPKKs by phosphorylation at conserved serine/threonine residue. Activated MAPKKs in turn activate MAPKs by phosphorylating MAPK at both threonine and tyrosine residues in the TXY motif; which leads to phosphorylation of various effector proteins like enzymes or transcription factors [132]. MAPK cascade is conserved among eukaryotes and transduces extracellular stimuli for cellular responses [133]. MAPK pathways are also triggered by various abiotic stresses [134]. The role of MAPKs in cold acclimation was demonstrated in *Arabidopsis* by a MAPK pathway mediated by Ca^{2+} /CaM-CRLK1-MEKK1-MKK2-MPK4/6 under cold acclimation. A positive regulator of the cold tolerance, Ca^{2+} /Calmodulin-Regulated Receptor-Like Kinase (CRLK1) has been reported in plants [135]. CRLK1 has been found to interact and phosphorylate *MEKK1* [136, 137]. In turn, *MEKK1*, which is induced by cold, phosphorylates MKK2 during cold treatment [136]. It has been suggested that Ca^{2+} signaling occurs upstream of the MEKK1-MKK2 pathway [137]. Further, enzymatic activity of

MEKK1 is increased kinase in the presence of MKK2 after cold treatment. MKK2 also interacts with MPK4/MPK6 during cold signaling [138]. Such interaction was also validated genetically as *mkk2* mutant showed freezing sensitive phenotype, as no interaction of MKK2 with MPK4 nor MPK6, suggesting that MKK2 is present upstream to these two proteins during cold signaling [138]. Evidence suggests that MAP kinase pathways may also act independently of Ca^{+2} . More specifically, MPK4 and MPK6 were found to operate independently of *CPKs* [139, 140]. However, it is not clear how Ca^{+2} -dependent and Ca^{+2} -independent (MAP kinase) pathways leading from cold perception affect post-translational modifications of TFs responsible for the regulation of cold gene expression [69] and the interplay between calcium and MAPK signaling pathways warrants future investigation [141].

3.2.3. Transcription Factor CBF/DREB Regulon

Changes in gene expression profiles upon exposure to low temperatures are well established and many genes which are either up- or down-regulated have been identified [142, 143]. A multidisciplinary approach in tomato suggested the role of transcriptome reprogramming in cold acclimation. Early response (after a few hours of suboptimal growth temperature exposure), resulted in changes in the expression levels of stress-related proteins including those belonging to transcription factors, hormone biosynthesis and signaling. In contrast, a late response (after 24 h of exposure) induced stable changes in the gene expression resulted in extensive adjustment of metabolism, photosystems, transcription and translation machineries by stable changes in gene expression [144]. Homologs of DREB1/CBFs have been identified in many agronomic crops, such as rice, maize, soybean (*Glycine max*) and wheat (*Triticum aestivum*) [145]. DREB1/CBFs acts upstream to the cold-inducible genes, including cold-regulated genes (COR) and regulate their expression [142, 146]. Initially, promoter analysis of a cold inducible gene, *COR15A*, identified a region that conferred cold, abscisic acid (ABA) and drought responsive expression [147, 148]. Promoters of many other ABA-independent, cold- and drought-induced proteins contain one or more copies of Dehydration-Responsive/C-Repeat Element/Low Temperature Responsive Element (CRT or DRE or LTRE) *cis*-acting element. This element is attributed by the presence of CCGAC as its core sequence [147, 149, 150]. Additionally, many *COR* genes have ABA-responsive elements (ABREs) in their promoter, however, expression of *COR* genes is not strictly correlated by its presence as their transcript levels are regulated by both ABA-independent and ABA-dependent pathways [151, 152].

The *CRT/DRE/LTRE* element is recognized by a group of three similar cold induced transcription factors, known as either C-repeat binding factors, CBF1-3 or dehydration-responsive element binding factors DREB1A-C. These TFs control ABA-independent expression of *COR* genes in response to cold stress [150, 153-156]. The CBF pathway of *Arabidopsis* remains the best-understood regulatory pathway with its role in freezing tolerance [28, 157]. As reported, *CBF1(DREB1b)*, *CBF2(DREB1c)* and *CBF3(DREB1a)* are strongly and rapidly upregulated at the transcriptional level by low temperature and possess overlapping effects on *COR*

gene regulation [158]. The *CRT/DRE* is also recognized by a group of drought-inducible transcriptional activators such as DREB2A-B, which are structurally not related to the CBF/DREB1 group. Overexpression of the *CBF/DREB* genes has resulted in enhancement of cold tolerance in *Arabidopsis*, tobacco and other agricultural important species such as rice and wheat [153, 159]. Overexpression of *OsDREB1* in rice plants showed higher survival rate of transgenic plants in chilling (2°C) stress condition in comparison to the wild type [160]. Similarly, overexpression of a sweet pepper (*Capsicum annuum*) *CBF3* gene in tobacco plants showed enhanced chilling (4°C) tolerance through higher accumulations of proline, soluble sugars, unsaturated fatty acids, and lower accumulations of ROS [161]. *Arabidopsis* plant overexpressing *HbCBF1* gene of *Hevea brasiliensis* showed chilling resistance and activated expression of CBF pathway downstream target genes, such as *AtCOR15a* and *AtRD29a* [162]. *AtCBF3* overexpressing *Arabidopsis* transgenic plants also demonstrated enhanced tolerance to freezing stress [163, 164]. It was recently reported that freezing tolerance of *Muscadinia rotundifolia* *CBF2*-overexpressing transgenic *Arabidopsis* lines was enhanced along with an increased expression of the cold regulated genes *AtCOR47*, *AtCOR15A*, *AtRD29A*, *AtKIN1* and *AtSuSy* (*Arabidopsis* sucrose synthase 2) [165]. However, role of constitutive overexpression of either *AtCBF1* or *AtCBF3* genes in improving cold tolerance is not universal as their overexpression do not improve freezing tolerance in freezing-sensitive tomato plants. Further, studies in *CBF2*-deficient mutant have revealed that *CBF2*, which negatively regulate *CBF1* and *CBF3*, may have distinct function in freezing tolerance from the other CBFs [166]. However, it can also not be ruled out that coordinated action of CBFs are required for cold acclimation [167]. While *CBF1* and *CBF3* have a concerted additive effect in the induction of whole CBF regulon, they both are simultaneously required for the induction of CBF target genes [167, 168].

Transcription of *CBF* genes is subjected to both positive and negative regulation. Several regulators have already been identified as inducer of CBF expression 1 (ICE 1) proteins [169], inducer of CBF expression 2 (ICE2) proteins [170], MYB15 [171], calmodulin binding transcription activator 3 (CAMTA3) [172], ZAT12 [168] and Ethylene Insensitive 3 (EIN3) [173]. The promoter regions of the *CBF/DREB1* TFs lack *DRE* element, suggesting that they do not regulate their own expression. Further, mutational screens have determined the regulatory aspect of *CBFs* and identified additional components involved in the regulation of the cold-induced expression of *CBFs* [174]. ICE1 and ICE2 encode a MYC-like basic helix-loop-helix (bHLH) transcriptional activator and positively regulate *CBF1*, *CBF2* and *CBF3* by binding to the MYC recognition sequences present in their promoters. These TFs are known to act upstream to the most of other factors involved in cold stress responses. ICE1 and ICE2 are the master regulators of cold responses and control *COR* genes and *CBF/DREB1* [170, 175]. In response to low temperature, ICE1 is modified (stabilized and activated) by sumoylation involving the SIZ1 SUMO E3 ligase. This promotes ICE1 binding to the *CBF3* promoter and increases *CBF3* expression [176]. Further, over-expression of *ICE1* enhanced the expression of *CBF*

regulon under cold stress and improved the cold tolerance of transgenic *Arabidopsis* plants [169]. In contrast, *ice1* mutant showed inhibition of cold-induced transcription of a *CBF3* gene. Further, a dominant negative mutation of *ICE1* eliminates the cold-induced *CBF3* expression. These mutant plants also showed loss of freezing tolerance [169, 175]. However, the limited impact on the accumulation of *CBF2* transcripts in *ice1* indicated occurrence of diverse activation mechanisms within the *CBF/DREB1* family [169]. Similarly, over-expression of *SIICE1* led to improved chilling tolerance by inducing the expression of dehydrin Ci7 homolog (*SIDRCi7*), *SICBF1* and Δ 1-pyrroline-5-carboxylase synthase (*SIP5CS*) genes in tomato [177]. Recently, it has been reported that a central component of ABA signaling pathway, OPEN STOMATA 1 (OST1), plays a crucial role in cold response. *OST1* is induced by cold. *OST1* is known to contribute to the increased plant tolerance to freezing by phosphorylating ICE1; a biochemical event which enhances its stability [178]. Another important gene, SCRM, can function as an inducer of CBF expression1 (ICE 1). This gene along with its homolog SCRM2 is essential for the functions of SPEECHLESS (SPCH), MUTE, and FAMA during stomatal development. Both ICE1/SCRM and SCRM2 are redundant proteins and have overlapping functions. The evidences point towards a possible link between the transcriptional regulation of environmental adaptation and stomatal development in plants [179].

Feedback repression of transcription factors that regulates cold-responsive gene expression also seems to be an important mechanism for sustaining perfect cold-induced transcriptome (Fig. 1). For example, high expression of osmotically sensitive (*HOS1*) gene acts as a negative regulator of ICE1. *HOS1* encodes a RING E3 ligase and targets ICE1 and ICE2 for their proteasome-mediated degradation [170, 180]. One of the member of Zn finger transcription factor family, ZAT12, also acts as a negative regulator of *DREB1/CBFs*, though it is generally induced in this timeframe in *Arabidopsis* [168, 181]. *CBFs* are also negatively regulated by MYB15 transcription factor. Knockout mutants of *myb15* showed enhanced CBF expression and freezing tolerance after cold acclimation, whereas overexpression showed the opposite effect [171]. CAMTA3 (Calmodulin-binding transcription activator 3) was shown to be a positive regulator of *Arabidopsis DREB1C/CBF2*, through its binding to the CM2 *cis*-motif present in the promoter of that gene [172]. A quantitative trait locus COLD1 also contribute in the regulation of signaling pathway of cold tolerance. It encodes a regulator of G-protein signaling and localizes on plasma membrane and endoplasmic reticulum (ER). Its interaction with the α -subunit of G-protein activates Ca^{2+} channel for sensing decreased temperature and to accelerate G-protein GTPase activity [182].

Interactions between low temperature and other abiotic stresses are also known to have an effect on cold-regulated gene expression. For example, pre-exposure of plants to NaCl has been found to delay the low-temperature induced expression of cold-inductive genes [183]. Some of these interactions may be mediated by the cold-inducible and drought-inducible transcription factors *via* interacting with DRE elements. However, the role of other nodes within the signal transduction network has also been suggested and

their validation warrants further investigations [65]. In such a similar study, transcriptome profiling of the model legume, *Lotus japonicus*, under cold stress condition identified different types of cold-inducible transcription factors such as AP2/ERF, NAC, MYB, and WRKY families and other putative novel transcription factors. The findings of this study can serve as a template for future research [184]. Likewise, comparative transcriptome profiling of three maize inbred lines indicated that cold acclimation process in plants involves modifications in the photosynthetic apparatus, cell wall properties and developmental processes [185]. Comparative transcriptomic and proteomic analyses have identified specific regulatory targets during CA (cold acclimation) and DA (de acclimation) processes in *Arabidopsis*. Based on the accumulated evidences, it is expected that identification of several putative targets of translational regulation under cold stress will help understand the mechanism of RNA regulation during CA and DA in other plants [186]. High-throughput transcriptome analysis of rice germinating seeds of two *indica* genotypes further identified novel genes related to cold tolerance [187]. Altogether, understanding the cold signaling regulon will help in the transcriptome engineering of crop plants for enhanced tolerance to multiple abiotic stresses.

3.2.4. ABA

ABA plays a central role in abiotic stress tolerance as it is involved in the integration of various stress signals [22, 188, 189]. Cold stress is known to mildly enhance endogenous ABA levels in plants. Further evidence suggests that exogenous application of ABA induces cold tolerance in herbaceous plants [16, 188, 190]. Global transcriptional response to cold stress in chilling tolerant Japonica rice suggested a role of ABA signaling in chilling tolerance [191]. Gene expression analyses have further identified a common set of stress-responsive genes induced under both cold and ABA [45, 192]. These observations suggested that ABA accumulates in response to low temperature and it is important for providing improved freezing tolerance. Further, promoter analysis of cold-inducible genes of *Arabidopsis* plants revealed the abundance of ABRE in the promoters [149, 193]. Reduced cold acclimation was also reported in ABA-deficient *aba1* and ABA-insensitive *abi1-1* mutants of *Arabidopsis* and stress was found to induce lethality in these mutants [152].

Similarly, ABA application was found to induce expression of temperature responsive genes (*ZmCOI6.1*, *ZmACA1*, *ZmDREB2A* and *ZmERF3*) in *Zea mays* [194]. Two major *cis*-acting elements, ABRE and CRT/DRE (C-repeat/DREs), which function in ABA-dependent and ABA-independent manner, respectively, contribute independently or in concert with the ABA-induced gene expression [195]. ABA-dependent gene expression is usually controlled by transcription factors that are part of bZIP (ABRE-binding factors or AREB's), MYC and MYB families [69]. A global promoter analysis indicated that both ABRE and CRT/DRE are conserved in cold-inducible promoters of soybean and *Arabidopsis*. Though, ABRE is also conserved in rice, CRT/DREs show variation in cold inducible promoters [196]. ABA can also enhance the expression level of *CBF1*, *CBF2*, *CBF3*, and *ICE1* genes, but such induction is considerably lower

than that caused by cold [197]. ICE1 also participate in ABA-dependent pathways (glucose and ABA signaling), suggesting that ICE1 might play a new role in cross-talk between ABA-independent and ABA-dependent pathways [198]. Many experts have reported that both ABA-independent and ABA-dependent pathways regulate cold-responsive genes [69, 199].

3.2.5. Cytokinins

Cytokinin signal transduction pathway plays a significant role in cold signaling [200, 201]. The multistep phosphorelay cytokinin signaling pathway is composed of sensor histidine kinases (AHK2, AHK3, AHK4), histidine phosphotransfer proteins (AHPs), and downstream response regulators (ARRs). Transcription of Cytokinin Response Factors (CRFs), the downstream component of this pathway, is induced after exposure to cold (4 °C). Likewise, in comparison to the CRF4 overexpressing plants, the *crf4* mutant (lacking the expression of *CRF4*) plants showed more sensitivity to freezing temperatures [202]. A number of temperature responsive proteins such as LL-diaminopimelate aminotransferase and peroxisomal malate dehydrogenase are involved in early response to cytokinin. Role of calcium has been implicated in the cytokinin-mediated responses under cold stress and a molecular link between cytokinin and calcium signaling has been established. It was observed that inhibition of calcium signaling affected the cytokinin-mediated regulation of several phosphoproteins [203]. Another hint that cytokinin is involved in the regulation of cold tolerance is provided by the fact that both cytokinin- and temperature shocks-altered proteomes share a high proportion of co-regulated proteins [204]. Numerous studies have also established the role of cytokinins in cold mediated adaptive mechanisms in response to the increased concentration of cytokinin [200, 201, 205, 206].

3.2.6. H₂O₂

Over the years, H₂O₂ has become an established signaling molecule. Its small size mobile, long half-life (1 ms) and high permeability across membrane allow H₂O₂ to traverse through cellular membranes and migrate to different compartments to mediate different biological outcomes, including the one that leads to its own synthesis [207-213]. H₂O₂ performs a vital role in induction of physiological, biochemical and molecular responses under stress conditions in plants [214].

At low concentration, it functions generally as a mediator of signaling pathways and results in stress acclimation; however, at higher concentration it causes cellular damage and cell death. The multi-functionality of H₂O₂ actions such as stress alleviation on one side and the risks at higher concentrations requires a very strict control of H₂O₂ concentration in plant cells. H₂O₂ has been found to accumulate in response to various biotic and abiotic stresses, including cold [33, 215]. Likewise, exogenous application of H₂O₂ induces low temperature stress tolerance in maize. During cold acclimation H₂O₂ act as a signal to induce synthesis of ROS-scavenging enzymes [216, 217]. H₂O₂ enhance the antioxidant capacity of cells by alleviating the activities of antioxidant enzymes, such as Ascorbate Peroxidase (APX), Catalase (CAT), and Superoxide Dismutase (SOD) [218]. It has been

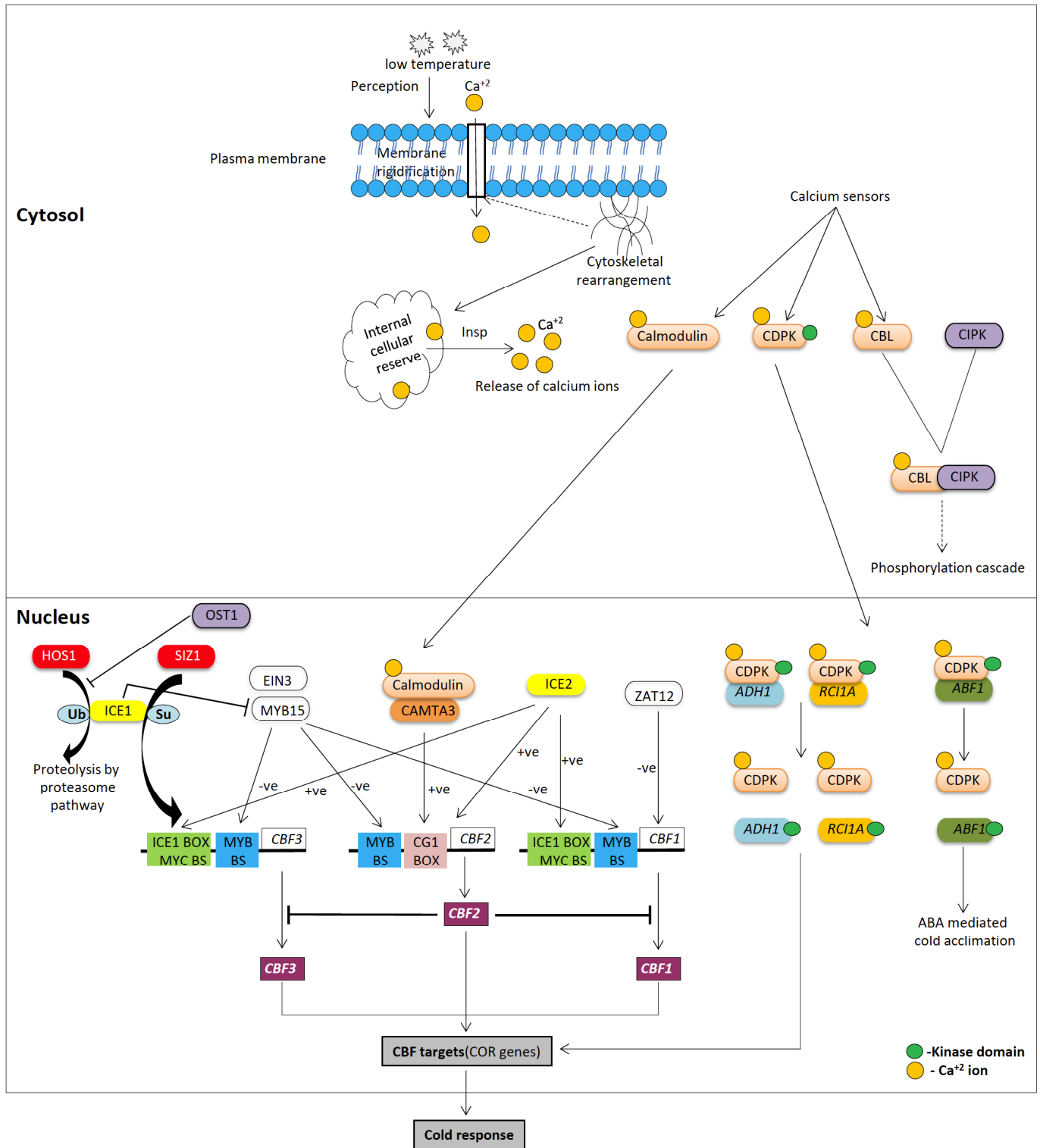


Fig. (1). Schematic representation of signaling network in response to low temperature stress. It shows the early events of cold perception, leading expression of COR genes regulated by CBF transcription factors. Characterized Ca²⁺ sensor proteins and their target proteins are also shown. Refer to text for detailed descriptions. CBF/DREB, C-repeat binding factors/DRE-binding proteins; CBL/CIPK, calcineurin B-like protein/CBL-interacting protein kinase; CAMTA, Calmodulin-binding transcription activator; COR, cold-regulated; HOS, high expression of osmotically responsive gene; ICE1, inducer of CBF expression 1; RC11A, Rare cold inducible 1A and ADH1, Alcohol dehydrogenase 1; ABF1, ABRE binding factor 1; EIN3, Ethylene Insensitive; HOS1, high expression of osmotically responsive genes; SIZ1, E3 SUMO ligase.

observed that exogenous application of H₂O₂ resulted in increased activities of APX, CAT, GPX, and GST in manila grass and APX, POD and GR activities in mascarene which

protect plants against damage by chilling [219]. Additional studies revealed that H₂O₂ functions as a mediator in stress responses, *via* interacting with many other important signal

molecules (Ca^{+2} , SA, ABA, JA, ethylene, NO) [220-224]. Functional characterization of a cold induced *MfSAMS1* (*Medicago sativa* subsp. *falcata* S-adenosyl methionine synthetase 1) in tobacco showed that H_2O_2 , ABA and NO interactions mediated its cold-induced expression and cold acclimation in falcate. Overexpression of *MfSAMS1* favoured polyamine synthesis and oxidation. As a consequence, it improved H_2O_2 -induced antioxidant protection and led to enhanced cold tolerance in transgenic plants [225]. H_2O_2 has also been observed to communicate with ethylene in response to cold stress [226]. Notably, H_2O_2 regulates the activities of many signaling components such as protein kinases, protein phosphatases and various transcription factors (TFs) [69, 227].

3.2.7. Cytoskeleton Rearrangement

Plant cytoskeleton maintains proximity with the plasma membrane that provides an important platform for signal perception and transduction [228, 229]. The bond between plasma membrane and cytoskeleton arises through a hydrophobic domain, which is present either on the tubulin molecule or it is facilitated indirectly through interaction with an integral membrane protein [230]. For example, Phospholipase D (PLD) has been confirmed for having the ability to make structural and signaling connections between cortical microtubules and the plasma membrane [231-234]. Role of cytoskeletal reorganization and PLD activation in cold acclimation has also been reported [235, 236]. In this mechanism, activation of PLD leads to cytoskeletal reorganization by releasing the cortical array of microtubules from plasma membrane [232]. Further, the enhanced production of PLD has been found to confer improved frost tolerance after cold acclimation [237].

The cytoskeleton plays a key role as low temperature sensor in plants during cold stress signaling and acclimation process [238, 239]. The activities of various ion channels in plant cells have been analysed to show the importance of cytoskeleton reorganization [239-242]. Based on the Ca^{+2} channel activity under cold, it was found that specific type of cytoskeletal components (microtubules and actin filaments) are involved in cold sensing by regulating the activity of these ion channels. The subsequent membrane rigidification further assists this hypothesis [51, 243, 244]. A synergistic increase in Ca^{+2} influx in the cold shocked tobacco plants treated with oryzalin and cytochalasin (destabilizers of microtubules and microfilaments, respectively) further established the link between cytoskeleton and Ca^{+2} ions [245]. Exposure of plants to low temperatures has been found to result in destabilization and depolymerisation of microtubules. Upon continuous exposure to low temperature, cold labile microtubules are swapped with cold stable microtubules. In cold stress-treated root tip cells of cucumber (*Cucumis sativus* L.), stable cortical microtubules were found to be located both under the plasma membrane as well as in the cytoplasm. It was suggested that these additional microtubules might be associated with organelles [246]. In wheat (*T. aestivum* L.), three members of α -tubulin gene family were induced during cold acclimation. A fourth member showed increased mRNA level for up to 14 days during cold acclimation and had decreased levels after 36 days of cold treatment [247]. In tobacco, a mutational screen identified both

aryl carbamate (a blocker of microtubule assembly) and chilling tolerant mutants. The carbamate tolerant mutants were also resistant to chilling stress. It was observed that the stability of microtubules in cold treatment can be improved by Microtubule Associated Proteins (MAPs). In case of *Arabidopsis thaliana*, nine such genes constitute the evolutionarily conserved *MAP65* family and the presence of *At-MAP65-1* provides more resistance to microtubules in cold stress [248]. An Actin Depolymerizing Factor (ADF) has also been characterized for its role in cold acclimation in wheat. The accumulation of ADF was higher in freezing tolerant wheat cultivars compared to less tolerant cultivar. Thus, cytoskeletal rearrangements and again remodelling of the actin cytoskeleton was proposed to be very important for the improvement of frost tolerance in plants [249].

CONCLUSION AND FUTURE PROSPECTS

Research on cold tolerance mechanism has made our understanding better on adaptation of plants under cold stress but there is more to be discovered in this field. The current review covers the involvement and acting mechanisms of different players in cold signal transduction by which plants develop cold tolerance. Briefly, sensing of low temperature is initiated by plasma membrane rigidification or by histidine two component system or calcium channels which lead to influx of calcium ions into cytosol. The signal is then transferred to the nucleus by decoders of calcium for transcriptional regulation through CBF-dependent or CBF-independent mechanisms. Though, the role of master regulator ICE1 in cold signaling is largely known, more research about the mechanism of modification and regulation of ICE1 is necessary. Moreover, better understanding of the molecular mechanisms underlying the cross talk among different signaling pathways at various points is necessary and remains an area of intense research in the near future.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Research in the author's laboratory is supported by the grants from Department of Biotechnology, Govt. of India and Department of Science and Technology, Govt. of India (IFA-LSPA-15). RK thanks Prof. R. P. Sharma, Department of Plant Sciences, University of Hyderabad, for his support in carrying out the research work.

REFERENCES

- [1] Rathore, A.C.; Raizada, A.; Prakash, J.J.; Sharda, V.N. Impact of chilling injury on common fruit plants in the Doon Valley. *Curr. Sci.*, **2012**, *102*(8), 1107-1111.
- [2] Miura, K.; Furumoto, T. Cold signaling and cold response in plants. *Int. J. Mol. Sci.*, **2013**, *14*(3), 5312-5337.
- [3] Solanke, A.U.; Sharma, A.K. Signal transduction during cold stress in plants. *Physiol. Mol. Biol. Plants*, **2008**, *14*(1-2), 69-79.
- [4] Xu, Z.; Zhang, R.; Wang, D.; Qiu, M.; Feng, H.; Zhang, N.; Shen, Q. Enhanced control of cucumber wilt disease by *Bacillus amyloliquefaciens* SQR9 by altering the regulation of its DegU phosphorylation. *Appl. Environ. Microbiol.*, **2014**, *80*(9), 2941-2950.
- [5] Prasad, T.K.; Anderson, M.D.; Martin, B.A.; Stewart, C.R. Evidence for chilling-induced oxidative stress in maize seedlings

- and a regulatory role for hydrogen-peroxide. *Plant Cell*, **1994**, *6*(1), 65-74.
- [6] Foyer, C.H.; Lopez-Delgado, H.; Dat, J.F.; Scott, I.M. Hydrogen peroxide- and glutathione-associated mechanisms of acclimatory stress tolerance and signalling. *Physiol. Plant.*, **1997**, *100*(2), 241-254.
- [7] Abbasi, F.; Onodera, H.; Toki, S.; Tanaka, H.; Komatsu, S. *OsCDPK3*, a calcium-dependent protein kinase gene from rice, is induced by cold and gibberellin in rice leaf sheath. *Plant Mol. Biol.*, **2004**, *55*(4), 541-552.
- [8] Thomashow, M.F. Plant cold acclimation: Freezing tolerance genes and regulatory mechanisms. *Annu. Rev. Plant Physiol. Plant Mol. Biol.*, **1999**, *50*, 571-599.
- [9] Sanghera, G.S.; Wani, S.H.; Hussain, W.; Singh, N.B. Engineering cold stress tolerance in crop plants. *Curr. Genom.*, **2011**, *12*(1), 30-43.
- [10] Siddiqui, K.S.; Cavicchioli, R. Cold-adapted enzymes. *Annu. Rev. Biochem.*, **2006**, *75*, 403-433.
- [11] Murata, N.; Los, D.A. Membrane fluidity and temperature perception. *Plant Physiol.*, **1997**, *115*(3), 875-879.
- [12] Nayyar, H.; Chander, K.; Kumar, S.; Bains, T. Glycine betaine mitigates cold stress damage in Chickpea. *Agron. Sustain. Dev.*, **2005**, *25*(3), 381-388.
- [13] Nayyar, H.; Bains, T.; Kumar, S. Low temperature induced floral abortion in chickpea: relationship to abscisic acid and cryoprotectants in reproductive organs. *Environ. Exp. Bot.*, **2005**, *53*(1), 39-47.
- [14] Nayyar, H.; Bains, T.S.; Kumar, S. Chilling stressed chickpea seedlings: effect of cold acclimation, calcium and abscisic acid on cryoprotective solutes and oxidative damage. *Environ. Exp. Bot.*, **2005**, *54*(3), 275-285.
- [15] Nayyar, H.; Bains, T.S.; Kumar, S.; Kaur, G. Chilling effects during seed filling on accumulation of seed reserves and yield of chickpea. *J. Sci. Food Agri.*, **2005**, *85*(11), 1925-1930.
- [16] Nayyar, H.; Chander, S. Protective effects of polyamines against oxidative stress induced by water and cold stress in chickpea. *J. Agro. Crop Sci.*, **2004**, *190*(5), 355-365.
- [17] Dowgert, M.F.; Steponkus, P.L. Behavior of the plasma membrane of isolated protoplasts during a freeze-thaw cycle. *Plant Physiol.*, **1984**, *75*(4), 1139-1151.
- [18] Olien, C.R.; Smith, M.N. Ice adhesions in relation to freeze stress. *Plant Physiol.*, **1977**, *60*(4), 499-503.
- [19] Gusta, L.V.; Wisniewski, M.; Nesbitt, N.T.; Gusta, M.L. The effect of water, sugars, and proteins on the pattern of ice nucleation and propagation in acclimated and nonacclimated canola leaves. *Plant Physiol.*, **2004**, *135*(3), 1642-1653.
- [20] Ruelland, E.; Vaultier, M.N.; Zachowski, A.; Hurry, V. Cold signalling and cold acclimation in plants. *Adv. Bot. Res.*, **2009**, *49*, 35-150.
- [21] Smallwood, M.; Bowles, D.J. Plants in a cold climate. *Philosophical Transactions of the Royal Society of London Series B-Biol. Sci.*, **2002**, *357*(1423), 831-846.
- [22] Mahajan, S.; Tuteja, N. Cold, salinity and drought stresses: An overview. *Arch. Biochem. Biophys.*, **2005**, *444*(2), 139-158.
- [23] Wen, J.Q.; Oono, K.; Imai, R. Two novel mitogen-activated protein signaling components, OsMEK1 and OsMAP1, are involved in a moderate low-temperature signaling pathway in rice. *Plant Physiol.*, **2002**, *129*(4), 1880-1891.
- [24] Beck, E.H.; Heim, R.; Hansen, J. Plant resistance to cold stress: Mechanisms and environmental signals triggering frost hardening and dehardening. *J. Biosci.*, **2004**, *29*(4), 449-459.
- [25] Sarkar, A.K. Ice formation and propagation in plants of cold climate region. *Int. J. Rec. Sci. Res.*, **2015**, *6*(10), 7098-7102.
- [26] Hughes, M.A.; Dunn, M.A. The molecular biology of plant acclimation to low temperature. *J. Exp. Bot.*, **1996**, *47*(296), 291-305.
- [27] Mohapatra, S.S.; Poole, R.J.; Dhindsa, R.S. Abscisic Acid-regulated gene expression in relation to freezing tolerance in alfalfa. *Plant Physiol.*, **1988**, *87*(2), 468-473.
- [28] Knight, M.R.; Knight, H. Low-temperature perception leading to gene expression and cold tolerance in higher plants. *New Phytol.*, **2012**, *195*(4), 737-751.
- [29] Webb, M.S.; Uemura, M.; Steponkus, P.L. A comparison of freezing-injury in oat and rye: two cereals at the extremes of freezing tolerance. *Plant Physiol.*, **1994**, *104*(2), 467-478.
- [30] Uemura, M.; Steponkus, P.L. Effect of cold acclimation on the lipid composition of the inner and outer membrane of the chloroplast envelope isolated from rye leaves. *Plant Physiol.*, **1997**, *114*(4), 1493-1500.
- [31] Zhao, C.; Zhang, Z.; Xie, S.; Si, T.; Li, Y.; Zhu, J.K. Mutational evidence for the critical role of CBF genes in cold acclimation in *Arabidopsis*. *Plant Physiol.*, **2016**, *171*, 2744-2759.
- [32] Strauss, G.; Hauser, H. Stabilization of lipid bilayer vesicles by sucrose during freezing. *Proc. Natl. Acad. Sci. USA*, **1986**, *83*(8), 2422-2426.
- [33] OKane, D.; Gill, V.; Boyd, P.; Burdon, B. Chilling, oxidative stress and antioxidant responses in *Arabidopsis thaliana* callus. *Planta*, **1996**, *198*(3), 371-377.
- [34] Guo, Z.; Ou, W.; Lu, S.; Zhong, Q. Differential responses of antioxidative system to chilling and drought in four rice cultivars differing in sensitivity. *Plant Physiol. Biochem.*, **2006**, *44*(11-12), 828-836.
- [35] Guo, Z.; Ou, W.; Lu, S.; Zhong, Q. Differential responses of antioxidative system to chilling and drought in four rice cultivars differing in sensitivity. *Plant Physiol. Biochem.*, **2006**, *44*(11-12), 828-836.
- [36] Anderson, M.D.; Prasad, T.K.; Martin, B.A.; Stewart, C.R. Differential gene-expression in chilling-acclimated maize seedlings and evidence for the involvement of abscisic-acid in chilling tolerance. *Plant Physiol.*, **1994**, *105*(1), 331-339.
- [37] Guo, Z.F.; Tan, H.Q.; Zhu, Z.H.; Lu, S.Y.; Zhou, B.Y. Effect of intermediates on ascorbic acid and oxalate biosynthesis of rice and in relation to its stress resistance. *Plant Physiol. Biochem.*, **2005**, *43*(10-11), 955-962.
- [38] Suzuki, N.; Koussevitzky, S.; Mittler, R.; Miller, G. ROS and redox signalling in the response of plants to abiotic stress. *Plant Cell Environ.*, **2012**, *35*(2), 259-270.
- [39] Medina, J.; Catala, R.; Salinas, J. The CBFs: Three *Arabidopsis* transcription factors to cold acclimate. *Plant Sci.*, **2011**, *180*(1), 3-11.
- [40] Minorsky, P.V. Temperature sensing by plants - a review and hypothesis. *Plant Cell Environ.*, **1989**, *12*(2), 119-135.
- [41] Vigh, L.; Los, D.A.; Horvath, I.; Murata, N. The primary signal in the biological perception of temperature: Pd-catalyzed hydrogenation of membrane lipids stimulated the expression of the *desA* gene in *Synechocystis* PCC6803. *Proc. Natl. Acad. Sci. USA*, **1993**, *90*(19), 9090-9094.
- [42] Uemura, M.; Tominaga, Y.; Nakagawara, C.; Shigematsu, S.; Minami, A.; Kawamura, Y. Responses of the plasma membrane to low temperatures. *Physiol. Plant.*, **2006**, *126*(1), 81-89.
- [43] Vaultier, M.N.; Cantrel, C.; Vergnolle, C.; Justin, A.M.; Demandre, C.; Benhassaine-Kesri, G.; Cicek, D.; Zachowski, A.; Ruelland, E. Desaturase mutants reveal that membrane rigidification acts as a cold perception mechanism upstream of the diacylglycerol kinase pathway in *Arabidopsis* cells. *FEBS Lett.*, **2006**, *580*(17), 4218-4223.
- [44] Wang, X.M.; Li, W. Q.; Li, M.Y.; Welti, R. Profiling lipid changes in plant response to low temperatures. *Physiol. Plant.*, **2006**, *126*(1), 90-96.
- [45] Xiong, L.M.; Schumaker, K.S.; Zhu, J.K. Cell signaling during cold, drought, and salt stress. *Plant Cell*, **2002**, *14*, S165-S183.
- [46] Knight, M.R.; Campbell, A.K.; Smith, S.M.; Trewavas, A.J. Transgenic plant aequorin reports the effects of touch and cold-shock and elicitors on cytoplasmic calcium. *Nature*, **1991**, *352*(6335), 524-526.
- [47] Knight, H.; Trewavas, A.J.; Knight, M.R. Cold calcium signaling in *Arabidopsis* involves two cellular pools and a change in calcium signature after acclimation. *Plant Cell*, **1996**, *8*(3), 489-503.
- [48] Monroy, A.F.; Sarhan, F.; Dhindsa, R.S. Cold-induced changes in freezing tolerance, protein-phosphorylation, and gene-expression - evidence for a role of calcium. *Plant Physiol.*, **1993**, *102*(4), 1227-1235.
- [49] Monroy, A.F.; Dhindsa, R.S. Low-temperature signal-transduction - induction of cold acclimation-specific genes of alfalfa by calcium at 25-degrees-C. *Plant Cell*, **1995**, *7*(3), 321-331.
- [50] Zhu, X.H.; Feng, Y.; Liang, G.M.; Liu, N.; Zhu, J.K. Aequorin-based luminescence imaging reveals stimulus- and tissue-specific Ca^{2+} dynamics in *Arabidopsis* plants. *Mol. Plant*, **2013**, *6*(2), 444-455.
- [51] Orvar, B. L.; Sangwan, V.; Omann, F.; Dhindsa, R.S. Early steps in cold sensing by plant cells: the role of actin cytoskeleton and membrane fluidity. *Plant J.*, **2000**, *23*(6), 785-794.
- [52] Sangwan, V.; Foulds, I.; Singh, J.; Dhindsa, R.S. Cold-activation of *Brassica napus* BN115 promoter is mediated by structural changes

- in membranes and cytoskeleton, and requires Ca^{2+} influx. *Plant J.*, **2001**, 27(1), 1-12.
- [53] Chinnusamy, V.; Zhu, J.K.; Sunkar, R. Gene regulation during cold stress acclimation in plants. *Methods Mol. Biol.*, **2010**, 639, 39-55.
- [54] Urao, T.; Yakubov, B.; Yamaguchi-Shinozaki, K.; Shinozaki, K., Stress-responsive expression of genes for two-component response regulator-like proteins in *Arabidopsis thaliana*. *FEBS Lett.*, **1998**, 427(2), 175-178.
- [55] Wulfetange, K.; Lomin, S.N.; Romanov, G.A.; Stolz, A.; Heyl, A.; Schmulling, T. The cytokinin receptors of *Arabidopsis* are located mainly to the endoplasmic reticulum. *Plant Physiol.*, **2011**, 156(4), 1808-1818.
- [56] Suzuki, I.; Los, D.A.; Kanesaki, Y.; Mikami, K.; Murata, N. The pathway for perception and transduction of low-temperature signals in *Synechocystis*. *EMBO J.*, **2000**, 19(6), 1327-1334.
- [57] Suzuki, I.; Kanesaki, Y.; Mikami, K.; Kanehisa, M.; Murata, N. Cold-regulated genes under control of the cold sensor Hik33 in *Synechocystis*. *Mol. Microbio.*, **2001**, 40(1), 235-244.
- [58] Cybulski, L.E.; de Mendoza, D. Bilayer hydrophobic thickness and integral membrane protein function. *Curr. Protein Pept. Sci.*, **2011**, 12(8), 760-766.
- [59] Hong, S.W.; Jon, J.H.; Kwak, J.M.; Nam, H.G. Identification of a receptor-like protein kinase gene rapidly induced by abscisic acid, dehydration, high salt, and cold treatments in *Arabidopsis thaliana*. *Plant Physiol.*, **1997**, 113(4), 1203-1212.
- [60] Kreps, J.A.; Wu, Y.J.; Chang, H.S.; Zhu, T.; Wang, X.; Harper, J. F. Transcriptome changes for *Arabidopsis* in response to salt, osmotic, and cold stress. *Plant Physiol.*, **2002**, 130(4), 2129-2141.
- [61] Kumar, S.V.; Wigge, P.A. H2A.Z-containing nucleosomes mediate the thermosensory response in *Arabidopsis*. *Cell*, **2010**, 140(1), 136-147.
- [62] Kumar, S.V.; Lucyshyn, D.; Jaeger, K.E.; Alos, E.; Alvey, E.; Harberd, N.P.; Wigge, P.A. Transcription factor PIF4 controls the thermosensory activation of flowering. *Nature*, **2012**, 484(7393), 242-U127.
- [63] Galon, Y.; Finkler, A.; Fromm, H. Calcium-regulated transcription in plants. *Mol. Plant.*, **2010**, 3(4), 653-69.
- [64] Ranty, B.; Aldon, D.; Cotelle, V.; Galaud, J.P.; Thuleau, P.; Mazars, C. Calcium sensors as key hubs in plant responses to biotic and abiotic stresses. *Front. Plant Sci.*, **2016**, 7, 327.
- [65] Knight, H.; Knight, M.R. Abiotic stress signalling pathways: specificity and cross-talk. *Trends Plant Sci.*, **2001**, 6(6), 262-267.
- [66] Jenkins, G.I. Signal transduction networks and the integration of responses to environmental stimuli. *Adv. Bot. Res. Adv. Plant Pathol.*, **1999**, 29, 53-73.
- [67] Malho, R.; Moutinho, A.; van der Luit, A.; Trewavas, A.J. Spatial characteristics of calcium signalling: the calcium wave as a basic unit in plant cell calcium signalling. *Philosophical Transactions of the Royal Society of London Series B-Biological Sciences*, **1998**, 353(1374), 1463-1473.
- [68] Chinnusamy, V.; Zhu, J.; Zhu, J.K. Cold stress regulation of gene expression in plants. *Trends Plant Sci.*, **2007**, 12(10), 444-451.
- [69] Thakur, P.; Nayyar, H. Facing the Cold Stress by Plants in the Changing Environment: Sensing, Signaling, and Defending Mechanisms. In *Plant Acclimation to Environmental Stress*, Tuteja, N.; Singh Gill, S. Eds. Springer New York: New York, NY, **2013**; pp 29-69.
- [70] Poovaiah, B.W.; Du, L.; Wang, H.; Yang, T. Recent advances in calcium/calmodulin-mediated signaling with an emphasis on plant-microbe interactions. *Plant Physiol.*, **2013**, 163(2), 531-542.
- [71] Day, I.S.; Reddy, V.S.; Ali, G.S.; Reddy, A.S.N. Analysis of EF-hand-containing proteins in *Arabidopsis*. *Genome Biol.*, **2002**, 3(10), RESEARCH0056.
- [72] Boonburapong, B.; Buaboocha, T. Genome-wide identification and analyses of the rice calmodulin and related potential calcium sensor proteins. *BMC Plant Biol.*, **2007**, 7, 4.
- [73] Reddy, A.S.; Ali, G.S.; Celesnik, H.; Day, I.S. Coping with stresses: Roles of calcium- and calcium/calmodulin-regulated gene expression. *Plant Cell*, **2011**, 23(6), 2010-2032.
- [74] Sanders, D.; Pelloux, J.; Brownlee, C.; Harper, J. F. Calcium at the crossroads of signaling. *Plant Cell*, **2002**, 14, S401-S417.
- [75] Kudla, J.; Batistic, O.; Hashimoto, K. Calcium signals: The lead currency of plant information processing. *Plant Cell*, **2010**, 22(3), 541-563.
- [76] Reddy, V.S.; Day, I.S.; Thomas, T.; Reddy, A.S.N. KIC, a novel Ca^{2+} binding protein with one EF-hand motif, interacts with a microtubule motor protein and regulates trichome morphogenesis. *Plant Cell*, **2004**, 16(1), 185-200.
- [77] McCormack, E.; Tsai, Y.C.; Braam, J. Handling calcium signaling: *Arabidopsis* CaMs and CMLs. *Trends Plant Sci.*, **2005**, 10(8), 383-389.
- [78] Luan, S. The CBL-CIPK network in plant calcium signaling. *Trends Plant Sci.*, **2009**, 14(1), 37-42.
- [79] DeFalco, T.A.; Bender, K.W.; Snedden, W.A. Breaking the code: Ca^{2+} sensors in plant signalling. *Biochem. J.*, **2010**, 425, 27-40.
- [80] Roberts, D.M.; Harmon, A.C. Calcium-modulated proteins - targets of intracellular calcium signals in higher-plants. *Annu. Rev. Plant Physiol. Plant Mol. Biol.*, **1992**, 43, 375-414.
- [81] Cheng, S.H.; Willmann, M.R.; Chen, H.C.; Sheen, J. Calcium signaling through protein kinases. The *Arabidopsis* calcium-dependent protein kinase gene family. *Plant Physiol.*, **2002**, 129(2), 469-485.
- [82] Shimazaki, K.; Kinoshita, T.; Nishimura, M. Involvement of calmodulin and calmodulin-dependent myosin light chain kinase in blue light-dependent H^{+} pumping by guard-cell protoplasts from vicia-faba L. *Plant Physiol.*, **1992**, 99(4), 1416-1421.
- [83] Pandey, S.; Tiwari, S.B.; Tyagi, W.; Reddy, M.K.; Upadhyaya, K. C.; Sopory, S.K. A Ca^{2+} /CaM-dependent kinase from pea is stress regulated and *in vitro* phosphorylates a protein that binds to AtCaM5 promoter. *Euro. J. Biochem.*, **2002**, 269(13), 3193-3204.
- [84] Wang, J.P.; Munyampundu, J.P.; Xu, Y.P.; Cai, X.Z. Phylogeny of plant calcium and calmodulin-dependent protein kinases (CCaMKs) and functional analyses of tomato CCaMK in disease resistance. *Front. Plant Sci.*, **2015**, 6, 1075.
- [85] Yang, T.B.; Poovaiah, B.W. Calcium/calmodulin-mediated signal network in plants. *Trends Plant Sci.*, **2003**, 8(10), 505-512.
- [86] Harper, J.F.; Harmon, A. Plants, symbiosis and parasites: A calcium signalling connection. *Nat. Rev. Mol. Cell Biol.*, **2005**, 6(7), 555-566.
- [87] de Silva, K.; Laska, B.; Brown, C.; Sederoff, H.W.; Khodakovskaya, M. *Arabidopsis thaliana* calcium-dependent lipid-binding protein (AtCLB): a novel repressor of abiotic stress response. *J. Exp. Bot.*, **2011**, 62(8), 2679-2689.
- [88] Tuteja, N. Integrated Calcium Signaling in Plants. *Signaling in Plants*, Mancuso, S.; Baluka, F.E. Eds. Springer Berlin Heidelberg: Berlin, Heidelberg, **2009**; pp. 29-49.
- [89] Kim, M.C.; Chung, W.S.; Yun, D.J.; Cho, M.J. Calcium and calmodulin-mediated regulation of gene expression in plants. *Mol. Plant*, **2009**, 2(1), 13-21.
- [90] Tahtiharju, S.; Sangwan, V.; Monroy, A.F.; Dhindsa, R.S.; Borg, M. The induction of kin genes in cold-acclimating *Arabidopsis thaliana*. Evidence of a role for calcium. *Planta*, **1997**, 203(4), 442-447.
- [91] Bender, K.W.; Snedden, W.A. Calmodulin-related proteins step out from the shadow of their namesake. *Plant Physiol.*, **2013**, 163(2), 486-495.
- [92] Zhu, X.; Dunand, C.; Snedden, W.; Galaud, J.P. CaM and CML emergence in the green lineage. *Trends Plant Sci.*, **2015**, 20(8), 483-489.
- [93] Boonburapong, B.; Buaboocha, T. Genome-wide identification and analyses of the rice calmodulin and related potential calcium sensor proteins. *BMC Plant Biol.*, **2007**, 7, 4.
- [94] Zhao, Y.; Liu, W.; Xu, Y.P.; Cao, J.Y.; Braam, J.; Cai, X.Z. Genome-wide identification and functional analyses of calmodulin genes in Solanaceous species. *BMC Plant Biol.*, **2013**, 13, 70.
- [95] Townley, H.E.; Knight, M.R. Calmodulin as a potential negative regulator of *Arabidopsis* COR gene expression. *Plant Physiol.*, **2002**, 128(4), 1169-1172.
- [96] Liu, H.T.; Li, G.L.; Chang, H.; Sun, D.Y.; Zhou, R.G.; Li, B. Calmodulin-binding protein phosphatase PP7 is involved in thermotolerance in *Arabidopsis*. *Plant Cell Environ.*, **2007**, 30(2), 156-164.
- [97] Liu, J.P.; Zhu, J.K. A calcium sensor homolog required for plant salt tolerance. *Science*, **1998**, 280(5371), 1943-1945.
- [98] Kudla, J.; Xu, Q.; Harter, K.; Grisseum, W.; Luan, S. Genes for calcineurin B-like proteins in *Arabidopsis* are differentially regulated by stress signals. *Pro. Nat. Acad. Sci. USA*, **1999**, 96(8), 4718-4723.
- [99] Gong, D.M.; Guo, Y.; Schumaker, K.S.; Zhu, J.K. The SOS3 family of calcium sensors and SOS2 family of protein kinases in *Arabidopsis*. *Plant Physiol.*, **2004**, 134(3), 919-926.
- [100] Luan, S.; Kudla, J.; Rodriguez-Concepcion, M.; Yalovsky, S.; Grisseum, W. Calmodulins and calcineurin B-like proteins:

- Calcium sensors for specific signal response coupling in plants. *Plant Cell*, **2002**, *14*, S389-S400.
- [101] Kolukisaoglu, U.; Weinl, S.; Blazevic, D.; Batistic, O.; Kudla, J. Calcium sensors and their interacting protein kinases: Genomics of the *Arabidopsis* and rice CBL-CIPK signaling networks. *Plant Physiol.*, **2004**, *134*(1), 43-58.
- [102] Albrecht, V.; Weinl, S.; Blazevic, D.; D'Angelo, C.; Batistic, O.; Kolukisaoglu, U.; Bock, R.; Schulz, B.; Harter, K.; Kudla, J. The calcium sensor CBL1 integrates plant responses to abiotic stresses. *Plant J.*, **2003**, *36*(4), 457-470.
- [103] Huang, C.L.; Ding, S.; Zhang, H.; Du, H.; An, L.Z. CIPK7 is involved in cold response by interacting with CBL1 in *Arabidopsis thaliana*. *Plant Sci.*, **2011**, *181*(1), 57-64.
- [104] Lyzenga, W.J.; Liu, H.; Schofield, A.; Muise-Hennessey, A.; Stone, S.L. *Arabidopsis* CIPK26 interacts with KEG, components of the ABA signalling network and is degraded by the ubiquitin-proteasome system. *J. Exp. Bot.*, **2013**, *64*(10), 2779-2791.
- [105] Meena, M.K.; Ghawana, S.; Dwivedi, V.; Roy, A.; Chattopadhyay, D. Expression of chickpea CIPK25 enhances root growth and tolerance to dehydration and salt stress in transgenic tobacco. *Front. Plant Sci.*, **2015**, *6*, 683.
- [106] Shin, H.S.; Brown, R.M. GTPase activity and biochemical characterization of a recombinant cotton fiber annexin. *Plant Physiol.*, **1999**, *119*(3), 925-934.
- [107] Kim, M.C.; Panstruga, R.; Elliott, C.; Muller, J.; Devoto, A.; Yoon, H.W.; Park, H.C.; Cho, M.J.; Schulze-Lefert, P. Calmodulin interacts with MLO protein to regulate defence against mildew in barley. *Nature*, **2002**, *416*(6879), 447-450.
- [108] Kim, K.N.; Cheong, Y.H.; Grant, J.J.; Pandey, G.K.; Luan, S. CIPK3, a calcium sensor-associated protein kinase that regulates abscisic acid and cold signal transduction in *Arabidopsis*. *Plant Cell*, **2003**, *15*(2), 411-423.
- [109] Xiang, Y.; Huang, Y.; Xiong, L. Characterization of stress-responsive CIPK genes in rice for stress tolerance improvement. *Plant Physiol.*, **2007**, *144*(3), 1416-1428.
- [110] Harmon, A.C.; Gribskov, M.; Harper, J.F. CDPKs - a kinase for every Ca²⁺ signal? *Trends Plant Sci.*, **2000**, *5*(4), 154-159.
- [111] Ludwig, A.A.; Romeis, T.; Jones, J. D.G. CDPK-mediated signalling pathways: Specificity and cross-talk. *J. Exp. Bot.*, **2004**, *55*(395), 181-188.
- [112] Chinnusamy, V.; Schumaker, K.; Zhu, J.K. Molecular genetic perspectives on cross-talk and specificity in abiotic stress signalling in plants. *J. Exp. Bot.*, **2004**, *55*(395), 225-236.
- [113] Klimecka, M.; Muszynska, G. Structure and functions of plant calcium-dependent protein kinases. *Acta Biochim. Pol.*, **2007**, *54*(2), 219-233.
- [114] Li, A.L.; Zhu, Y.F.; Tan, X.M.; Wang, X.; Wei, B.; Guo, H.Z.; Zhang, Z.L.; Chen, X.B.; Zhao, G.Y.; Kong, X.Y.; Jia, J.Z.; Mao, L. Evolutionary and functional study of the CDPK gene family in wheat (*Triticum aestivum* L.). *Plant Mol. Biol.*, **2008**, *66*(4), 429-443.
- [115] Hu, Z.; Lv, X.; Xia, X.; Zhou, J.; Shi, K.; Yu, J.; Zhou, Y. Genome-wide identification and expression analysis of calcium-dependent protein kinase in tomato. *Front Plant Sci.*, **2016**, *7*, 469.
- [116] Ray, S.; Agarwal, P.; Arora, R.; Kapoor, S.; Tyagi, A.K. Expression analysis of calcium-dependent protein kinase gene family during reproductive development and abiotic stress conditions in rice (*Oryza sativa* L. ssp indica). *Mol. Genet. Genomics*, **2007**, *278*(5), 493-505.
- [117] Harmon, A.C.; Gribskov, M.; Harper, J.F. CDPKs - a kinase for every Ca²⁺ signal? *Trends Plant Sci.*, **2000**, *5*(4), 154-159.
- [118] Ito, T.; Nakata, M.; Fukazawa, J.; Ishida, S.; Takahashi, Y. Alteration of substrate specificity: the variable N-terminal domain of tobacco Ca²⁺-dependent protein kinase is important for substrate recognition. *Plant Cell*, **2010**, *22*(5), 1592-604.
- [119] Christodoulou, J.; Malmendal, A.; Harper, J.F.; Chazin, W.J. Evidence for differing roles for each lobe of the calmodulin-like domain in a calcium-dependent protein kinase. *J. Biol. Chem.*, **2004**, *279*(28), 29092-29100.
- [120] Wernimont, A.K.; Amani, M.; Qiu, W.; Pizarro, J.C.; Artz, J.D.; Lin, Y. H.; Lew, J.; Hutchinson, A.; Hui, R. Structures of parasitic CDPK domains point to a common mechanism of activation. *Proteins-Struct. Funct. Bioinfo.*, **2011**, *79*(3), 803-820.
- [121] Liese, A.; Romeis, T. Biochemical regulation of *in vivo* function of plant calcium-dependent protein kinases(CDPK). *B. B. A. Mol. Cell Res.*, **2013**, *1833*(7), 1582-1589.
- [122] Harper, J.E.; Breton, G.; Harmon, A. Decoding Ca²⁺ signals through plant protein kinases. *Annu. Rev. Plant Biol.*, **2004**, *55*, 263-288.
- [123] Gao, X.; Cox, K.L.Jr.; He, P. Functions of calcium-dependent protein kinases in plant innate immunity. *Plants(Basel)*, **2014**, *3*(1), 160-76.
- [124] Weckwerth, P.; Ehlert, B.; Romeis, T. ZmCPK1, a calcium-independent kinase member of the *Zea mays* CDPK gene family, functions as a negative regulator in cold stress signalling. *Plant Cell Environ.*, **2015**, *38*(3), 544-558.
- [125] Tuteja, N.; Mahajan, S. Calcium signaling network in plants: an overview. *Plant Signal Behav.*, **2007**, *2*(2), 79-85.
- [126] Mori, I.C.; Murata, Y.; Yang, Y.Z.; Munemasa, S.; Wang, Y.F.; Andreoli, S.; Tiriace, H.; Alonso, J.M.; Harper, J.F.; Ecker, J.R.; Kwak, J.M.; Schroeder, J.I. CDPKs CPK6 and CPK3 function in ABA regulation of guard cell S-type anion- and Ca²⁺-permeable channels and stomatal closure. *PLoS Biol.*, **2006**, *4*(10), 1749-1762.
- [127] Dodd, A.N.; Kudla, J.; Sanders, D. The language of calcium signaling. *Annu. Rev. Plant Biol.*, **2010**, *61*, 593-620.
- [128] Sheen, J. Ca²⁺-dependent protein kinases and stress signal transduction in plants. *Science*, **1996**, *274*(5294), 1900-1902.
- [129] Martin, M.L.; Busconi, L. A rice membrane-bound calcium-dependent protein kinase is activated in response to low temperature. *Plant Physiol.*, **2001**, *125*(3), 1442-1449.
- [130] Saijo, Y.; Hata, S.; Kyoizuka, J.; Shimamoto, K.; Izui, K. Over-expression of a single Ca²⁺-dependent protein kinase confers both cold and salt/drought tolerance on rice plants. *Plant J.*, **2000**, *23*(3), 319-327.
- [131] Barrero-Gil, J.; Salinas, J. Post-translational regulation of cold acclimation response. *Plant Sci.*, **2013**, *205-206*, 48-54.
- [132] Rodriguez, M.C.S.; Petersen, M.; Mundy, J. Mitogen-activated protein kinase signaling in plants. *Annu. Rev. Plant Biol.*, **2010**, *61*, 621-649.
- [133] Nakagami, H.; Pitzschke, A.; Hirt, H. Emerging MAP kinase pathways in plant stress signalling. *Trends Plant Sci.*, **2005**, *10*(7), 339-346.
- [134] Ligerink, W.; Hirt, H. Mitogen-activated protein(MAP) kinase pathways in plants: Versatile signaling tools. *Int. Rev. Cytol.*, **2001**, *201*, 209-275.
- [135] Yang, T.B.; Chaudhuri, S.; Yang, L.H.; Du, L.Q.; Poovaiyah, B.W. A calcium/calmodulin-regulated member of the receptor-like kinase family confers cold tolerance in plants. *J. Biol. Chem.*, **2010**, *285*(10), 7119-7126.
- [136] Furuya, T.; Matsuoka, D.; Nanmori, T. Phosphorylation of *Arabidopsis thaliana* MEKK1 via Ca²⁺ signaling as a part of the cold stress response. *J. Plant Res.*, **2013**, *126*(6), 833-840.
- [137] Furuya, T.; Matsuoka, D.; Nanmori, T. Membrane rigidification functions upstream of the MEKK1-MKK2-MPK4 cascade during cold acclimation in *Arabidopsis thaliana*. *FEBS Lett.*, **2014**, *588*(11), 2025-2030.
- [138] Teige, M.; Scheikl, E.; Eulgem, T.; Doczi, F.; Ichimura, K.; Shinozaki, K.; Dangl, J.L.; Hirt, H. The MKK2 pathway mediates cold and salt stress signaling in *Arabidopsis*. *Mol. Cell.*, **2004**, *15*(1), 141-152.
- [139] Mehlmer, N.; Wurzinger, B.; Stael, S.; Hofmann-Rodrigues, D.; Csaszar, E.; Pfister, B.; Bayer, R.; Teige, M. The Ca²⁺-dependent protein kinase CPK3 is required for MAPK-independent salt-stress acclimation in *Arabidopsis*. *Plant J.*, **2010**, *63*(3), 484-498.
- [140] Wurzinger, B.; Mair, A.; Pfister, B.; Teige, M. Cross-talk of calcium-dependent protein kinase and MAP kinase signaling. *Plant Signal Behav.*, **2011**, *6*(1), 8-12.
- [141] Saidi, Y.; Finka, A.; Goloubinoff, P. Heat perception and signalling in plants: a tortuous path to thermotolerance. *New Phytol.*, **2011**, *190*(3), 556-565.
- [142] Fowler, S.; Thomashow, M.F. *Arabidopsis* transcriptome profiling indicates that multiple regulatory pathways are activated during cold acclimation in addition to the CBF cold response pathway. *Plant Cell*, **2002**, *14*(8), 1675-1690.
- [143] Seki, M.; Narusaka, M.; Abe, H.; Kasuga, M.; Yamaguchi-Shinozaki, K.; Carninci, P.; Hayashizaki, Y.; Shinozaki, K., Monitoring the expression pattern of 1300 *Arabidopsis* genes under drought and cold stresses by using a full-length cDNA microarray. *Plant Cell*, **2001**, *13*(1), 61-72.
- [144] Barrero-Gil, J.; Huertas, R.; Rambla, J.L.; Granell, A.; Salinas, J. Tomato plants increase their tolerance to low temperature in a chilling acclimation process entailing comprehensive transcriptional

- and metabolic adjustments. *Plant Cell Environ.*, **2016**, *39*(10), 2303-2318.
- [145] Zhuang, L.; Yuan, X.; Chen, Y.; Xu, B.; Yang, Z.; Huang, B. PpCBF3 from cold-tolerant kentucky bluegrass involved in freezing tolerance associated with up-regulation of cold-related genes in transgenic *Arabidopsis thaliana*. *PLoS One*, **2015**, *10*(7), e0132928.
- [146] Maruyama, K.; Sakuma, Y.; Kasuga, M.; Ito, Y.; Seki, M.; Goda, H.; Shimada, Y.; Yoshida, S.; Shinozaki, K.; Yamaguchi-Shinozaki, K. Identification of cold-inducible downstream genes of the *Arabidopsis* DREB1A/CBF3 transcriptional factor using two microarray systems. *Plant J.*, **2004**, *38*(6), 982-993.
- [147] Baker, S.S.; Wilhelm, K.S.; Thomashow, M.F. The 5'-Region of *Arabidopsis-Thaliana* Cor15a has Cis-Acting elements that confer cold-regulated, drought-regulated and ABA-regulated gene-expression. *Plant Mol. Biol.*, **1994**, *24*(5), 701-713.
- [148] Novillo, F.; Alonso, J.M.; Ecker, J.R.; Salinas, J. CBF2/DREB1C is a negative regulator of CBF1/DREB1B and CBF3/DREB1A expression and plays a central role in stress tolerance in *Arabidopsis*. *Proc. Natl. Acad. Sci. USA*, **2004**, *101*(11), 3985-90.
- [149] Yamaguchishinozaki, K.; Shinozaki, K. A novel cis-acting element in an *Arabidopsis* gene is involved in responsiveness to drought, low-temperature, or high-salt stress. *Plant Cell*, **1994**, *6*(2), 251-264.
- [150] Maruyama, K.; Todaka, D.; Mizoi, J.; Yoshida, T.; Kidokoro, S.; Matsukura, S.; Takasaki, H.; Sakurai, T.; Yamamoto, Y. Y.; Yoshiwara, K.; Kojima, M.; Sakakibara, H.; Shinozaki, K.; Yamaguchi-Shinozaki, K. Identification of cis-acting promoter elements in cold- and dehydration-induced transcriptional pathways in *Arabidopsis*, rice, and soybean. *DNA Res.*, **2012**, *19*(1), 37-49.
- [151] Ishitani, M.; Liu, J.P.; Halfter, U.; Kim, C.S.; Shi, W.M.; Zhu, J.K. SOS3 function in plant salt tolerance requires N-myristoylation and calcium binding. *Plant Cell*, **2000**, *12*(9), 1667-1677.
- [152] Shinozaki, K.; Yamaguchi-Shinozaki, K. Molecular responses to dehydration and low temperature: differences and cross-talk between two stress signaling pathways. *Curr. Opin. Plant Biol.*, **2000**, *3*(3), 217-223.
- [153] Liu, Q.; Kasuga, M.; Sakuma, Y.; Abe, H.; Miura, S.; Yamaguchi-Shinozaki, K.; Shinozaki, K. Two transcription factors, DREB1 and DREB2, with an EREBP/AP2 DNA binding domain separate two cellular signal transduction pathways in drought- and low-temperature-responsive gene expression, respectively, in *Arabidopsis*. *Plant Cell*, **1998**, *10*(8), 1391-1406.
- [154] Shinwari, Z.K.; Nakashima, K.; Miura, S.; Kasuga, M.; Seki, M.; Yamaguchi-Shinozaki, K.; Shinozaki, K. An *Arabidopsis* gene family encoding DRE/CRT binding proteins involved in low-temperature-responsive gene expression. *Biochem. Biophys. Res. Commun.*, **1998**, *250*(1), 161-170.
- [155] Gilmour, S.J.; Zarka, D.G.; Stockinger, E.J.; Salazar, M.P.; Houghton, J.M.; Thomashow, M.F. Low temperature regulation of the *Arabidopsis* CBF family of AP2 transcriptional activators as an early step in cold-induced COR gene expression. *Plant J.*, **1998**, *16*(4), 433-442.
- [156] Stockinger, E.J.; Gilmour, S.J.; Thomashow, M.F. *Arabidopsis thaliana* CBF1 encodes an AP2 domain-containing transcriptional activator that binds to the C-repeat/DRE, a cis-acting DNA regulatory element that stimulates transcription in response to low temperature and water deficit. *Proc. Natl. Acad. Sci. USA*, **1997**, *94*(3), 1035-1040.
- [157] Thomashow, M.F. Molecular basis of plant cold acclimation: insights gained from studying the CBF cold response pathway. *Plant Physiol.*, **2010**, *154*(2), 571-577.
- [158] Gilmour, S.J.; Fowler, S.G.; Thomashow, M.F. *Arabidopsis* transcriptional activators CBF1, CBF2, and CBF3 have matching functional activities. *Plant Mol. Biol.*, **2004**, *54*(5), 767-781.
- [159] Jaglo-Ottosen, K.R.; Gilmour, S.J.; Zarka, D.G.; Schabenberger, O.; Thomashow, M.F. *Arabidopsis* CBF1 overexpression induces COR genes and enhances freezing tolerance. *Science*, **1998**, *280*(5360), 104-106.
- [160] Ito, Y.; Katsura, K.; Maruyama, K.; Taji, T.; Kobayashi, M.; Seki, M.; Shinozaki, K.; Yamaguchi-Shinozaki, K. Functional analysis of rice DREB1/CBF-type transcription factors involved in cold-responsive gene expression in transgenic rice. *Plant Cell Physiol.* **2006**, *47*(1), 141-153.
- [161] Yang, S.; Tang, X.F.; Ma, N.N.; Wang, L.Y.; Meng, Q.W. Heterology expression of the sweet pepper CBF3 gene confers elevated tolerance to chilling stress in transgenic tobacco. *J. Plant Physiol.*, **2011**, *168*(15), 1804-1812.
- [162] Cheng, H.; Cai, H.; Fu, H.; An, Z.; Fang, J.; Hu, Y.; Guo, D.; Huang, H. Functional characterization of hevea brasiliensis CRT/DRE binding factor 1 gene revealed regulation potential in the CBF pathway of tropical perennial tree. *PLoS One*, **2015**, *10*(9), e0137634.
- [163] Jaglo-Ottosen, K.R.; Gilmour, S.J.; Zarka, D.G.; Schabenberger, O.; Thomashow, M.F. *Arabidopsis* CBF1 overexpression induces COR genes and enhances freezing tolerance. *Science*, **1998**, *280*(5360), 104-106.
- [164] Kasuga, M.; Liu, Q.; Miura, S.; Yamaguchi-Shinozaki, K.; Shinozaki, K. Improving plant drought, salt, and freezing tolerance by gene transfer of a single stress-inducible transcription factor. *Nat. Biotechnol.*, **1999**, *17*(3), 287-291.
- [165] Wu, J.; Folta, K. M.; Xie, Y.; Jiang, W.; Lu, J.; Zhang, Y. Overexpression of *Muscadinia rotundifolia* CBF2 gene enhances biotic and abiotic stress tolerance in *Arabidopsis*. *Protoplasma*, **2016**, *254*(1), 239-251.
- [166] Novillo, F.; Alonso, J.M.; Ecker, J.R.; Salinas, J. CBF2/DREB1C is a negative regulator of CBF1/DREB1B and CBF3/DREB1A expression and plays a central role in, stress tolerance in *Arabidopsis*. *Proc. Natl. Acad. Sc. USA*, **2004**, *101*(11), 3985-3990.
- [167] Novillo, F.; Medina, J.; Salinas, J. *Arabidopsis* CBF1 and CBF3 have a different function than CBF2 in cold acclimation and define different gene classes in the CBF regulon. *Proc. Natl. Acad. Sci. USA*, **2007**, *104*(52), 21002-21007.
- [168] Maruyama, K.; Takeda, M.; Kidokoro, S.; Yamada, K.; Sakuma, Y.; Urano, K.; Fujita, M.; Yoshiwara, K.; Matsukura, S.; Morishita, Y.; Sasaki, R.; Suzuki, H.; Saito, K.; Shibata, D.; Shinozaki, K.; Yamaguchi-Shinozaki, K. Metabolic pathways involved in cold acclimation identified by integrated analysis of metabolites and transcripts regulated by DREB1A and DREB2A. *Plant Physiol.*, **2009**, *150*(4), 1972-1980.
- [169] Chinnusamy, V.; Ohta, M.; Kanrar, S.; Lee, B.H.; Hong, X.H.; Agarwal, M.; Zhu, J.K. ICE1: a regulator of cold-induced transcriptome and freezing tolerance in *Arabidopsis*. *Genes Dev.*, **2003**, *17*(8), 1043-1054.
- [170] Kim, Y.S.; Lee, M.; Lee, J.H.; Park, C.M. The unified ICE-CBF pathway provides a transcriptional feedback control of freezing tolerance during cold acclimation in *Arabidopsis*. *Plant Mol. Biol.*, **2015**, *89*(1-2), 187-201.
- [171] Agarwal, M.; Hao, Y.; Kapoor, A.; Dong, C.H.; Fujii, H.; Zheng, X.; Zhu, J. K. A R2R3 type MYB transcription factor is involved in the cold regulation of CBF genes and in acquired freezing tolerance. *J. Biol. Chem.*, **2006**, *281*(49), 37636-37645.
- [172] Doherty, C.J.; Van Buskirk, H.A.; Myers, S.J.; Thomashow, M.F. Roles for *Arabidopsis* CAMTA transcription factors in cold-regulated gene expression and freezing tolerance. *Plant Cell*, **2009**, *21*(3), 972-984.
- [173] Shi, Y.; Tian, S.; Hou, L.; Huang, X.; Zhang, X.; Guo, H.; Yang, S. Ethylene signaling negatively regulates freezing tolerance by repressing expression of CBF and type-A ARR genes in *Arabidopsis*. *Plant Cell*, **2012**, *24*(6), 2578-2595.
- [174] Ishitani, M.; Xiong, L.; Stevenson, B.; Zhu, J.K. Genetic analysis of osmotic and cold stress signal transduction in *Arabidopsis*: interactions and convergence of abscisic acid-dependent and abscisic acid-independent pathways. *Plant Cell*, **1997**, *9*(11), 1935-1949.
- [175] Lee, B.H.; Henderson, D.A.; Zhu, J.K. The *Arabidopsis* cold-responsive transcriptome and its regulation by ICE1. *Plant Cell*, **2005**, *17*(11), 3155-3175.
- [176] Miura, K.; Jin, J.B.; Lee, J.; Yoo, C.Y.; Stirm, V.; Miura, T.; Ashworth, E.N.; Bressan, R.A.; Yun, D.J.; Hasegawa, P.M. SIZ1-mediated sumoylation of ICE1 controls CBF3/DREB1A expression and freezing tolerance in *Arabidopsis*. *Plant Cell*, **2007**, *19*(4), 1403-1414.
- [177] Miura, K.; Shiba, H.; Ohta, M.; Kang, S. W.; Sato, A.; Yuasa, T.; Iwaya-Inoue, M.; Kamada, H.; Ezura, H. SIICE1 encoding a MYC-type transcription factor controls cold tolerance in tomato. *Plant Biotechnol. J.*, **2012**, *29*(3), 253-260.
- [178] Ding, Y.; Li, H.; Zhang, X.; Xie, Q.; Gong, Z.; Yang, S. OST1 kinase modulates freezing tolerance by enhancing ICE1 stability in *Arabidopsis*. *Dev. Cell*, **2015**, *32*(3), 278-289.
- [179] Kanaoka, M.M.; Pillitteri, L.J.; Fujii, H.; Yoshida, Y.; Bogenschutz, N.L.; Takabayashi, J.; Zhu, J.K.; Torii, K.U. SCREAM/ICE1 and SCREAM2 specify three cell-state transitional

- steps leading to *Arabidopsis* stomatal differentiation. *Plant Cell*, **2008**, *20*(7), 1775-1785.
- [180] Dong, C.H.; Agarwal, M.; Zhang, Y.Y.; Xie, Q.; Zhu, J.K. The negative regulator of plant cold responses, HOS1, is a RING E3 ligase that mediates the ubiquitination and degradation of ICE1. *Proc. Natl. Acad. Sci. USA*, **2006**, *103*(21), 8281-8286.
- [181] Figueiredo, D.D.; Barros, P.M.; Cordeiro, A.M.; Serra, T.S.; Lourenco, T.; Chander, S.; Oliveira, M.M.; Saibo, N.J. Seven zinc-finger transcription factors are novel regulators of the stress responsive gene OsDREB1B. *J. Exp. Bot.*, **2012**, *63*(10), 3643-3656.
- [182] Ma, Y.; Dai, X.Y.; Xu, Y.Y.; Luo, W.; Zheng, X.M.; Zeng, D.L.; Pan, Y.J.; Lin, X.L.; Liu, H.H.; Zhang, D.J.; Xiao, J.; Guo, X.Y.; Xu, S.J.; Niu, Y.D.; Jin, J.B.; Zhang, H.; Xu, X.; Li, L.G.; Wang, W.; Qian, Q.; Ge, S.; Chong, K. COLD1 confers chilling tolerance in rice. *Cell*, **2015**, *162*(1), 222-222.
- [183] Xiong, L.M.; Ishitani, M.; Zhu, J.K. Interaction of osmotic stress, temperature, and abscisic acid in the regulation of gene expression in *Arabidopsis*. *Plant Physiol.*, **1999**, *119*(1), 205-211.
- [184] Calzadilla, P.I.; Maiale, S.J.; Ruiz, O.A.; Escaray, F.J. Transcriptome response mediated by cold stress in *Lotus japonicus*. *Front. Plant Sci.*, **2016**, *7*, 374.
- [185] Sobkowiak, A.; Jonczyk, M.; Adamczyk, J.; Szczepanik, J.; Solecka, D.; Kuciara, I.; Hetmanczyk, K.; Trzcinska-Danielewicz, J.; Grzybowski, M.; Skoneczny, M.; Fronk, J.; Sowinski, P. Molecular foundations of chilling-tolerance of modern maize. *BMC Genomics*, **2016**, *17*, 125.
- [186] Nakaminami, K.; Matsui, A.; Nakagami, H.; Minami, A.; Nomura, Y.; Tanaka, M.; Morosawa, T.; Ishida, J.; Takahashi, S.; Uemura, M.; Shirasu, K.; Seki, M. Analysis of differential expression patterns of mRNA and protein during cold-acclimation and de-acclimation in *Arabidopsis*. *Mol. Cell Proteomics*, **2014**, *13*(12), 3602-3611.
- [187] Dametto, A.; Sperotto, R.A.; Adamski, J.M.; Blasi, E.A.; Cargnelutti, D.; de Oliveira, L.F.; Ricachenevsky, F.K.; Fregonezi, J.N.; Mariath, J.E.; da Cruz, R.P.; Margis, R.; Fett, J. P. Cold tolerance in rice germinating seeds revealed by deep RNAseq analysis of contrasting indica genotypes. *Plant Sci.*, **2015**, *238*, 1-12.
- [188] Swamy, P.M.; Smith, B.N. Role of abscisic acid in plant stress tolerance. *Curr. Sci.*, **1999**, *76*(9), 1220-1227.
- [189] Sah, S. K.; Reddy, K. R.; Li, J., Abscisic acid and abiotic stress tolerance in crop plants. *Front. Plant Sci.*, **2016**, *7*, 571.
- [190] Xing, W.B.; Rajashekar, C.B. Glycine betaine involvement in freezing tolerance and water stress in *Arabidopsis thaliana*. *Environ. Exp. Bot.*, **2001**, *46*(1), 21-28.
- [191] Chawade, A.; Lindlof, A.; Olsson, B.; Olsson, O. Global expression profiling of low temperature induced genes in the chilling tolerant japonica rice *Jumli Marshi*. *PLoS One*, **2013**, *8*(12), e81729.
- [192] Nakamura, T.; Yazaki, J.; Kishimoto, N.; Kikuchi, S.; Robertson, A. J.; Gusta, L. V.; Ishikawa, M. Comparison of long-term up-regulated genes during induction of freezing tolerance by cold and ABA in bromegrass cell cultures revealed by microarray analyses. *J. Plant Growth Regul.*, **2013**, *71*(2), 113-136.
- [193] Seki, M.; Narusaka, M.; Ishida, J.; Kamiya, A.; Nakajima, M.; Enju, A.; Oono, Y.; Satou, M.; Akiyama, K.; Sakurai, T.; Fujita, M.; Nanjo, T.; Yamaguchi-Shinozaki, K.; Carninci, P.; Kawai, J.; Hayashizaki, Y.; Shinozaki, K., Monitoring the expression pattern of *Arabidopsis* genes using full-length CDNA microarray. *Plant Cell Physiol.*, **2002**, *43*, S1-S1.
- [194] Nguyen, H.T.; Leipner, J.; Stamp, P.; Guerra-Peraza, O. Low temperature stress in maize (*Zea mays* L.) induces genes involved in photosynthesis and signal transduction as studied by suppression subtractive hybridization. *Plant Physiol. Biochem.*, **2009**, *47*(2), 116-122.
- [195] Narusaka, Y.; Nakashima, K.; Shinwari, Z.K.; Sakuma, Y.; Furihata, T.; Abe, H.; Narusaka, M.; Shinozaki, K.; Yamaguchi-Shinozaki, K. Interaction between two cis-acting elements, ABRE and DRE, in ABA-dependent expression of *Arabidopsis* rd29A gene in response to dehydration and high-salinity stresses. *Plant J.*, **2003**, *34*(2), 137-148.
- [196] Maruyama, K.; Todaka, D.; Mizoi, J.; Yoshida, T.; Kidokoro, S.; Matsukura, S.; Takasaki, H.; Sakurai, T.; Yamamoto, Y. Y.; Yoshiwara, K.; Kojima, M.; Sakakibara, H.; Shinozaki, K.; Yamaguchi-Shinozaki, K. Identification of cis-acting promoter elements in cold and dehydration-induced transcriptional pathways in *Arabidopsis*, rice, and soybean. *DNA Res.*, **2012**, *19*(1), 37-49.
- [197] Theocharis, A.; Clement, C.; Barka, E.A. Physiological and molecular changes in plants grown at low temperatures. *Planta*, **2012**, *235*(6), 1091-105.
- [198] Liang, C.H.; Yang, C.C. Identification of ICE1 as a negative regulator of ABA-dependent pathways in seeds and seedlings of *Arabidopsis*. *Plant Mol. Biol.*, **2015**, *88*(4-5), 459-70.
- [199] Xiong, L.; Ishitani, M.; Zhu, J.K. Interaction of osmotic stress, temperature, and abscisic acid in the regulation of gene expression in *Arabidopsis*. *Plant Physiol.*, **1999**, *119*(1), 205-12.
- [200] Jeon, J.; Kim, N.Y.; Kim, S.; Kang, N.Y.; Novak, O.; Ku, S.J.; Cho, C.; Lee, D.J.; Lee, E.J.; Strnad, M.; Kim, J. A subset of cytokinin two-component signaling system plays a role in cold temperature stress response in *Arabidopsis*. *J. Biol. Chem.*, **2010**, *285*(30), 23371-23386.
- [201] Jeon, J.; Kim, J. *Arabidopsis* response Regulator1 and *Arabidopsis* histidine phosphotransfer Protein2(AHP2), AHP3, and AHP5 function in cold signaling. *Plant Physiol.*, **2013**, *161*(1), 408-424.
- [202] Zwack, P.J.; Compton, M.A.; Adams, C.I.; Rashotte, A.M. Cytokinin response factor 4(CRF4) is induced by cold and involved in freezing tolerance. *Plant Cell Rep.*, **2016**, *35*(3), 573-584.
- [203] Cerny, M.; Dycka, F.; Bobal'ova, J.; Brzobohaty, B. Early cytokinin response proteins and phosphoproteins of *Arabidopsis thaliana* identified by proteome and phosphoproteome profiling. *J. Exp. Bot.*, **2011**, *62*(3), 921-937.
- [204] Cerny, M.; Jedelsky, P.L.; Novak, J.; Schlosser, A.; Brzobohaty, B. Cytokinin modulates proteomic, transcriptomic and growth responses to temperature shocks in *Arabidopsis*. *Plant Cell Environ.*, **2014**, *37*(7), 1641-1655.
- [205] Kosova, K.; Prasil, I.T.; Vitamvas, P.; Dobrev, P.; Motyka, V.; Flokova, K.; Novak, O.; Tureckova, V.; Rolcik, J.; Pesek, B.; Travnickova, A.; Gaudinova, A.; Galiba, G.; Janda, T.; Vlasakova, E.; Prasilova, P.; Vankova, R. Complex phytohormone responses during the cold acclimation of two wheat cultivars differing in cold tolerance, winter Samanta and spring Sandra. *J. Plant Physiol.*, **2012**, *169*(6), 567-576.
- [206] Belintani, N.G.; Guerezoni, J.T.S.; Moreira, R.M.P.; Vieira, L.G.E. Improving low-temperature tolerance in sugarcane by expressing the ipt gene under a cold inducible promoter. *Biol. Plant.*, **2012**, *56*(1), 71-77.
- [207] Bienert, G.P.; Schjoerring, J.K.; Jahn, T.P. Membrane transport of hydrogen peroxide. *Biochim. Biophys. Acta Biomembr.*, **2006**, *1758*(8), 994-1003.
- [208] Neill, S.; Desikan, R.; Hancock, J. Hydrogen peroxide signalling. *Curr. Opin. Plant Biol.*, **2002**, *5*(5), 388-395.
- [209] Huang, C.S.; Li, J.X.; Ke, Q.D.; Leonard, S.S.; Jiang, B.H.; Zhong, X.S.; Costa, M.; Castranova, V.; Shi, X.L. Ultraviolet-induced phosphorylation of p70(S6K) at Thr(389) and Thr(421)/Ser(424) involves hydrogen peroxide and mammalian target of rapamycin but not Akt and atypical protein kinase C. *Cancer Res.*, **2002**, *62*(20), 5689-5697.
- [210] Yang, T.; Poovaiah, B.W. Hydrogen peroxide homeostasis: Activation of plant catalase by calcium/calmodulin. *Proc. Natl. Acad. Sci. USA*, **2002**, *99*(6), 4097-4102.
- [211] Mittler, R. Oxidative stress, antioxidants and stress tolerance. *Trends Plant Sci.*, **2002**, *7*(9), 405-410.
- [212] de Pinto, M.C.; Paradiso, A.; Leonetti, P.; De Gara, L. Hydrogen peroxide, nitric oxide and cytosolic ascorbate peroxidase at the crossroad between defence and cell death. *Plant J.*, **2006**, *48*(5), 784-795.
- [213] Van Breusegem, F.; Dat, J.F. Reactive oxygen species in plant cell death. *Plant Physiol.*, **2006**, *141*(2), 384-390.
- [214] Dat, J.; Vandenebeele, S.; Vranova, E.; Van Montagu, M.; Inze, D.; Van Breusegem, F. Dual action of the active oxygen species during plant stress responses. *Cell. Mol. Life Sci.*, **2000**, *57*(5), 779-795.
- [215] Laloi, C.; Apel, K.; Danon, A. Reactive oxygen signalling: the latest news. *Curr. Opin. Plant Biol.*, **2004**, *7*(3), 323-328.
- [216] Hossain, M.A.; Bhattacharjee, S.; Armin, S.M.; Qian, P.; Xin, W.; Li, H.Y.; Burritt, D.J.; Fujita, M.; Tran, L.S. Hydrogen peroxide priming modulates abiotic oxidative stress tolerance: insights from ROS detoxification and scavenging. *Front. Plant Sci.*, **2015**, *6*, 420.
- [217] Prasad, T.K.; Anderson, M.D.; Martin, B.A.; Stewart, A.R. Evidence for chilling-induced oxidative stress in maize seedlings and a regulatory role for hydrogen peroxide. *Plant Cell*, **1994**, *6*(1), 65-74.

- [218] Xia, X.J.; Wang, Y.J.; Zhou, Y.H.; Tao, Y.; Mao, W.H.; Shi, K.; Asami, T.; Chen, Z.X.; Yu, J.Q. Reactive oxygen species are involved in brassinosteroid- induced stress tolerance in cucumber. *Plant Physiol.*, **2009**, *150*(2), 801-814.
- [219] Wang, Y.; Li, J.; Wang, J.; Li, Z. Exogenous H₂O₂ improves the chilling tolerance of manilagrass and mascarene grass by activating the antioxidative system. *J. Plant Growth Reg.*, **2010**, *61*(2), 195-204.
- [220] Gundlach, H.; Müller, M.J.; Kutchan, T.M.; Zenk, M.H. Jasmonic acid is a signal transducer in elicitor-induced plant-cell cultures. *Proc. Natl. Acad. Sci. USA*, **1992**, *89*(6), 2389-2393.
- [221] Dempsey, D.A.; Klessig, D.F. Signals in Plant-Disease Resistance. *Bulletin De L Institut Pasteur*, **1995**, *93*(3), 167-186.
- [222] Desikan, R.; Cheung, M.K.; Clarke, A.; Golding, S.; Sagi, M.; Fluhr, R.; Rock, C.; Hancock, J.; Neill, S. Hydrogen peroxide is a common signal for darkness- and ABA-induced stomatal closure in *Pisum sativum*. *Funct. Plant Biol.*, **2004**, *31*(9), 913-920.
- [223] Wendehenne, D.; Durner, J.; Klessig, D.F. Nitric oxide: a new player in plant signalling and defence responses. *Curr. Opin. Plant Biol.*, **2004**, *7*(4), 449-455.
- [224] Liu, Q.; Zhou, G.Y.; Wen, C.K. Ethylene signal transduction in *Arabidopsis*. *Zhi Wu Sheng Li Yu Fen Zi Sheng Wu Xue Xue Bao*, **2004**, *30*(3), 241-250.
- [225] Guo, Z.F.; Tan, J.L.; Zhuo, C.L.; Wang, C.Y.; Xiang, X.; Wang, Z. Y., Abscisic acid, H₂O₂ and nitric oxide interactions mediated cold-induced S-adenosylmethionine synthetase in *Medicago sativa* subsp *falcata* that confers cold tolerance through up-regulating polyamine oxidation. *Plant Biotechnol. J.*, **2014**, *12*(5), 601-612.
- [226] Neill, S.J.; Desikan, R.; Clarke, A.; Hancock, J.T. Nitric oxide is a novel component of abscisic acid signaling in stomatal guard cells. *Plant Physiol.*, **2002**, *128*(1), 13-16.
- [227] Cheng, Y.L.; Song, C.P. Hydrogen peroxide homeostasis and signaling in plant cells. *Science in China Series C-Life Sciences*, **2006**, *49*(1), 1-11.
- [228] Gilroy, S.; Trewavas, A. Signal processing and transduction in plant cells: the end of the beginning? *Nat. Rev. Mol. Cell Biol.*, **2001**, *2*(4), 307-314.
- [229] Wasteneys, G.O.; Galway, M.E. Remodelling the cytoskeleton for growth and form: An overview with some new views. *Annu. Rev. Plant Biol.*, **2003**, *54*, 691-722.
- [230] Sonesson, A.; Berglund, M.; Staxen, I.; Widell, S. The characterization of plasma membrane-bound tubulin of cauliflower using triton X-114 fractionation. *Plant Physiol.*, **1997**, *115*(3), 1001-1007.
- [231] Gardiner, J.C.; Harper, J.D.I.; Weerakoon, N.D.; Collings, D.A.; Ritchie, S.; Gilroy, S.; Cyr, R.J.; Marc, J. A 90-kD phospholipase D from tobacco binds to microtubules and the plasma membrane. *Plant Cell*, **2001**, *13*(9), 2143-2158.
- [232] Dhonukshe, P.; Laxalt, A.M.; Goedhart, J.; Gadella, T.W.J.; Munnik, T. Phospholipase D activation correlates with microtubule reorganization in living plant cells. *Plant Cell*, **2003**, *15*(11), 2666-2679.
- [233] Drobak, B.K.; Franklin-Tong, V.E.; Staiger, C.J. The role of the actin cytoskeleton in plant cell signaling. *New Phytol.*, **2004**, *163*(1), 13-30.
- [234] Hong, Y.Y.; Zheng, S.Q.; Wang, X.M. Dual functions of phospholipase D alpha 1 in plant response to drought. *Mol. Plant*, **2008**, *1*(2), 262-269.
- [235] Ruelland, E.; Cantrel, C.; Gawer, M.; Kader, J.C.; Zachowski, A., Activation of phospholipases C and D is an early response to a cold exposure in *Arabidopsis* suspension cells. *Plant Physiol.*, **2002**, *130*(2), 999-1007.
- [236] Welti, R.; Li, W.Q.; Li, M.Y.; Sang, Y.M.; Biesiada, H.; Zhou, H.E.; Rajashekar, C.B.; Williams, T.D.; Wang, X.M. Profiling membrane lipids in plant stress responses - Role of phospholipase D alpha in freezing-induced lipid changes in *Arabidopsis*. *J. Biol. Chem.*, **2002**, *277*(35), 31994-32002.
- [237] Li, W.Q.; Li, M.Y.; Zhang, W.H.; Welti, R.; Wang, X.M. The plasma membrane-bound phospholipase D delta enhances freezing tolerance in *Arabidopsis thaliana*. *Nat. Biotech.*, **2004**, *22*(4), 427-433.
- [238] Dodd, A.N.; Jakobsen, M.K.; Baker, A.J.; Telzerow, A.; Hou, S. W.; Laplaze, L.; Barrot, L.; Poethig, R.S.; Haseloff, J.; Webb, A. A.R. Time of day modulates low-temperature Ca²⁺ signals in *Arabidopsis*. *Plant J.*, **2006**, *48*(6), 962-973.
- [239] Thion, L.; Mazars, C.; Thuleau, P.; Graziana, A.; Rossignol, M.; Moreau, M.; Ranjeva, R. Activation of plasma membrane voltage-dependent calcium-permeable channels by disruption of microtubules in carrot cells. *FEBS Lett.*, **1996**, *393*(1), 13-18.
- [240] Thion, L.; Mazars, C.; Nacry, P.; Bouchez, D.; Moreau, M.; Ranjeva, R.; Thuleau, P. Plasma membrane depolarization-activated calcium channels, stimulated by microtubule-depolymerizing drugs in wild-type *Arabidopsis thaliana* protoplasts, display constitutively large activities and a longer half-life in ton 2 mutant cells affected in the organization of cortical microtubules. *Plant J.*, **1998**, *13*(5), 603-610.
- [241] Thuleau, P.; Schroeder, J.I.; Ranjeva, R. Recent advances in the regulation of plant calcium channels: evidence for regulation by G-proteins, the cytoskeleton and second messengers. *Curr. Opin. Plant Biol.*, **1998**, *1*(5), 424-427.
- [242] Zimmermann, S.; Ehrhardt, T.; Plesch, G.; Müller-Rober, B. Ion channels in plant signaling. *Cell. Mol. Life Sci.*, **1999**, *55*(2), 183-203.
- [243] Abdrakhamanova, A.; Wang, Q.Y.; Khokhlova, L.; Nick, P. Is microtubule disassembly a trigger for cold acclimation? *Plant Cell Physiol.*, **2003**, *44*(7), 676-686.
- [244] Nick, P.; Heuing, A.; Ehmann, B. Plant chaperonins: a role in microtubule-dependent wall formation? *Protoplasma*, **2000**, *211*(3-4), 234-244.
- [245] Mazars, C.; Thion, L.; Thuleau, P.; Graziana, A.; Knight, M.R.; Moreau, M.; Ranjeva, R. Organization of cytoskeleton controls the changes in cytosolic calcium of cold-shocked *Nicotiana plumbaginifolia* protoplasts. *Cell Calcium*, **1997**, *22*(5), 413-420.
- [246] Zhao, Y.D.; Dai, X.H.; Blackwell, H.E.; Schreiber, S.L.; Chory, J. SIR1, an upstream component in auxin signaling identified by chemical genetics. *Science*, **2003**, *301*(5636), 1107-1110.
- [247] Farajalla, M.R.; Gulick, P.J. The alpha-tubulin gene family in wheat (*Triticum aestivum* L.) and differential gene expression during cold acclimation. *Genome*, **2007**, *50*(5), 502-510.
- [248] Mao, G.J.; Chan, J.; Calder, G.; Doonan, J.H.; Lloyd, C.W. Modulated targeting of GFP-AtMAP65-1 to central spindle microtubules during division. *Plant J.*, **2005**, *43*(4), 469-478.
- [249] Ouellet, F.; Carpentier, E.; Cope, M.J.T.V.; Monroy, A.F.; Sarhan, F. Regulation of a wheat actin-depolymerizing factor during cold acclimation. *Plant Physiol.*, **2001**, *125*(1), 360-368.