Review
Genetic Mechanisms of Cold Signaling in Wheat (Triticum aestivum L.)

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Abstract: Cold stress is a major environmental factor affecting the growth, development, and productivity of various crop species. With the current trajectory of global climate change, low temperatures are becoming more frequent and can significantly decrease crop yield. Wheat (Triticum aestivum L.) is the first domesticated crop and is the most popular cereal crop in the world. Because of a lack of systematic research on cold signaling pathways and gene regulatory networks, the underlying molecular mechanisms of cold signal transduction in wheat are poorly understood. This study reviews recent progress in wheat, including the ICE-CBF-COR signaling pathway under cold stress and the effects of cold stress on hormonal pathways, reactive oxygen species (ROS), and epigenetic processes and elements. This review also highlights possible strategies for improving cold tolerance in wheat.

Keywords: cold stress; wheat; hormonal; reactive oxygen species; epigenetic regulation

1. Introduction

Higher plants are sessile organisms that suffer from various environmental stresses throughout their life cycle, such as cold, heat, drought, and salinity. Cold stress is vital for limiting plant geographical distribution and influencing plant growth and development, and ultimately determines yield and quality [1,2]. After a long interaction with their environment, plants have evolved complex and sophisticated mechanisms to adapt to cold stress. Cold signals are transduced from the plasma membrane to the nucleus, leading to a series of cold-induced cellular responses and the induction of cold-responsive genes. The main cold-responsive genes in plants are C-REPEAT BINDING FACTORs (CBFs), INDUCER of CBF EXPRESSION (ICE), and COLD-REGULATED (COR) genes [3,4]. It has been established that the ICE-CBF-COR signaling pathway is a universal pathway associated with cold tolerance in plants [2,5,6]. In this pathway, CBFs/DEHYDRATION-RESPONSIVE ELEMENT BINDING FACTOR 1s (DREB1s) is rapidly induced by cold conditions. Additionally, CBFs/DREB1s proteins can bind to the promoter regions of COR genes to activate their transcription in Arabidopsis [7,8].

Low-temperature conditions seriously affect the growth and development of wheat grown in temperate regions [9]. Exposure to low temperatures changes various biochemical processes and induces membrane damage in wheat [9,10]. The effects of cold stress on wheat growth, development, and yield are determined not only by the degree and duration of low-temperature conditions but also by the growth stage in which the cold stress events occur [11]. Cold stress can significantly reduce the viable leaf area and the soluble carbohydrate accumulation, ultimately negatively affecting the final yield [12,13]. During the reproductive phase, wheat is susceptible to cold stress. The grain number will be decreased by low temperatures if stress occurs before anthesis [14]. Moreover, pollen tube elongation and gametophyte tissue development will be disrupted under cold stress, particularly in pollen tapetal cells, which can lead to pollen sterility [15,16]. Cold
stress can alter sink-source distribution by increasing the accumulation of soluble carbohydrates to regulate grain filling in wheat [9]. In addition, low-temperature events could also happen during vegetative stages in wheat and are detrimental to wheat growth and development since they cause leaves to wilt [17]. The leaf mass ratio and relative growth rate are significantly increased under low-temperature conditions. Furthermore, the flag leaf size and wheat biomass both decrease under cold stress [18,19]. Biomass allocation is essential for grain yield formation under cold stress, and the appropriate allocation is responsible for reproductive growth proportion and yield formation [20]. Diploid and tetraploid wheat have large leaf areas and produce no or low yield under cold stress. In contrast, hexaploid wheats have relatively low leaf areas and higher rates of grain yield among these species [13].

Cold stress has been categorized into two primary groups: chilling stress (0–15 °C) and freezing stress (<0 °C), which depends on how the plants are affected [1,21]. The cellular and molecular responses of plants to cold stress have been intensively studied. At present, plants have acquired highly sophisticated systems to cope with cold stress. For instance, plants activate a series of biochemical and physiological changes in their cells, such as altering the transcription of cold-responsive genes, regulating hormone levels and responses, producing ROS to stimulate the accumulation of compatible osmolytes and antioxidants, and remodeling genome-wide epigenetic modifications [8,22]. Significant progress has been made over the past few decades in understanding how signaling pathways control cold stress responses in plants. However, current knowledge of the cold signal transduction pathway in wheat is limited. In this review, we summarize the most recent studies assessing cold stress response in wheat and highlight possible strategies for improving cold tolerance in wheat.

2. ICE-CBF-COR Signaling Pathway in Cold Stress

Plants in temperate regions, such as winter wheat, have evolved adaptive responses known as cold acclimation, where plants acquire freezing tolerance after prior exposure to low non-freezing temperatures [8]. It is well known that the ICE-CBF-COR signaling pathway is essential for cold acclimation [3]. In addition to Arabidopsis, the ICE-CBF-COR cascade has been identified in rice [23] and wheat [6,24].

ICE genes encode a class of MYC-like bHLH transcriptional factors upstream of the cold signaling pathway [25]. The C-terminal regions of ICE have highly conserved regions for specific interactions with downstream cold regulatory genes [5,24–27]. The homologs of ICE have been identified as TaICE41 and TaICE87 in wheat (Figure 1). Overexpression of TaICE41 or TaICE87 in Arabidopsis enhanced cold tolerance, suggesting the significance of ICE homologs in cold stress response [24]. HOS1 (HIGH EXPRESSION OF OSMOTICALLY RESPONSIVE GENE 1), an E3 ubiquitin ligase, reduces the stability of ICE1 protein by ubiquitination under cold stress [28]. In addition, the stability of ICE1 protein is enhanced by SUMO E3 ligase SIZ1 (SAP and Miz) through sumoylation in response to cold stress [29]. ICE1 is phosphorylated by the cold-activated protein kinase OPEN STOMATA 1 (OST1), resulting in weakened interaction between ICE1 and HOS1 to increase the stability of ICE1 under cold stress [30]. Furthermore, the stability of OsICE1 is up-regulated by OsMPK3 (MAP KINASE 3) through phosphorylation in rice in response to cold stress [31]. These results indicate that the posttranslational modification of ICE1 is crucial for its role in response to cold stress. However, whether TaICEs have similar regulatory mechanisms in wheat responses to cold stress needs further study.

CBFs (CBF1, CBF2, and CBF3), which belong to the AP2/ERF multi-gene family, can be activated by ICE in the cold signaling pathway of plants [3,25]. CBFs are key components for increasing the cold tolerance of plants [32–34]. The overexpression of CBFs in rice, maize, barley, wheat, and other plant species significantly enhances the cold tolerance of transgenic plants [35–39]. However, the cdfs triple mutant in Arabidopsis show reduced cold tolerance and larger biomass than wild type [40]. These results indicate CBFs may act to balance cold tolerance and plant growth. However, whether CBFs are important regulators
of growth and cold tolerance to enhance the biomass of wheat requires further study. Several CBF genes have been characterized in Triticeae species, including 37 genes from hexaploid wheat [41], 20 genes from barley [36], 13 genes from Triticum monococcum [42], 11 genes from rye [43], ten genes from durum wheat [44], ten genes from Aegilops biuncialis [5], four genes from Brachypodium distachyon [45,46], and one gene from Aegilops tauschii [41]. TaCBF14 and TaCBF15, two wheat CBF transcription factors, play significant roles in cold stress response (Figure 1) [38]. Overexpression of TaCBF14 or TaCBF15 in barley enhances the expression of HeCOR14b, a cold-regulated gene in barley, increasing cold tolerance [38]. Additionally, T. aestivum ABIOTIC STRESS-INDUCED DNA BINDING FACTOR a (TaAIDFa) is markedly activated by cold stress [47]. Overexpression of TaAIDFa in Arabidopsis increases the transcription of the cold-regulated genes like RD29A and COR15A to enhance the cold tolerance of transgenic lines [47].

CORs generally refer to the protective substances encoded by cold-regulated genes. The protective substances such as osmolytes and cryoprotective proteins accumulate to facilitate cold acclimation and freezing tolerance [1,6]. CBFs are known to bind to the C-REPEAT/DEHYDRATION RESPONSIVE ELEMENT (CRT/DRE) sequence (TACCGCAT) in the promoters of COR genes for their transcription activation in response to cold stress.

Figure 1. ICE-CBF-COR signaling pathway plays a vital role in wheat. Cold stress alters the fluidity of plasma membrane and activates protein kinases. Furthermore, kinases positively regulate cold tolerance in wheat by phosphorylating TaICE proteins, including TaICE41, TaICE87. TaICE directly binds to the promoters of TaCBFs to regulate its expression. Additionally, TaCBFs bind to the CRT/DRE sequence in the promoters of TaCOR genes, such as Wrab15, Wrab17, Wrab18, Wrab19, WCS19, WCS120, Wcor14, and Wcor15, for their transcription activation in response to cold stress.
stress [48,49]. The expression of ABA-dependent COR genes (Wrab15/17/18/19) and ABA-independent COR genes (WCS19, WCS120, Wcor14, and Wcor15) are significantly increased by cold stress in wheat (Figure 1) [50]. The expression of DRE-BINDING PROTEIN 1 (TaDREB1), a wheat homolog of Arabidopsis DREB2, is elevated under cold stress [51]. The transcription of the WHEAT COLD SPECIFIC 120 (WCS120) gene is activated by TaDREB1 and increases cold tolerance in winter wheat [52]. The expression of wheat DREB2 (WDREB2), also a wheat homolog of Arabidopsis DREB2, is activated by cold [53]. The WDREB2 transcription factor directly affects the expression of wheat COR genes such as Wrab19 in response to cold stress [53].

3. Cold Stress Influences Hormonal Responses

Plant hormones (Phytohormones), which function as small molecules to regulate various cellular processes and work as chemical messengers to communicate cellular activities, are produced in very low concentrations in higher plants [54]. Phytohormones are needed for plants to deal with abiotic stresses, including salinity, drought, and low temperature, by mediating a wide range of adaptive responses [55]. These phytohormones include auxin, abscisic acid (ABA), ethylene, cytokinins (CKs), gibberellins (GAs), jasmonic acid (JA), brassinosteroids (BRs), salicylic acid (SA), and strigolactones (SLs). In recent years, the phytohormone signaling pathway has been investigated by genetic and biochemical approaches, and a growing body of evidence indicates that the elements in hormonal signaling pathways contribute to regulating plant cold tolerance [33].

Auxin, a tryptophan derivative most commonly present in the form of indole-3-acetic acid (IAA), plays an essential role in plant development and cold stress response. The YUCCA genes encode the key rate-limiting enzymes in the auxin biosynthetic pathway and are involved in the regulation of plant growth and development. The transcript levels of OsYUCCAs are strongly induced by low temperatures; however, the expression of IAA catabolism-related genes, Oryza sativa GRETCHEN HAGENs (OsGHs), is down-regulated, resulting in significantly increased IAA content in rice under cold stress (Table 1) [56]. In colder/ambient temperatures, CLAVATA (CLV) peptide signaling promotes flower development by stimulating auxin-dependent growth. In contrast, at higher temperatures, YUCCA genes are activated to maintain flower development bypass CLV signaling [57–59]. There are 15 genes among 63 TaYUCCAs that are induced by drought and heat stress in wheat, though it is unclear whether the expression of these genes is regulated by cold stress. Arabidopsis AUXIN RESPONSE FACTOR (ARF) genes, which regulate the expression of auxin-responsive genes by binding to the auxin response element in their promoters, are up-regulated during cold acclimation (Table 1) [60]. In wheat, 46 genes from 69 TaARFs are also up-regulated in response to cold stress (Table 1) [61].

Abscisic acid (ABA) is the most important phytohormone due to its role in plant adaptation to biotic and abiotic stresses [62]. ABA-deficient mutants in Arabidopsis show defects in freezing tolerance, with the induced expression of COR genes, suggesting that ABA is involved in cold signaling [63,64]. Additionally, ABA contents are moderately decreased after cold treatment [30]. SUCROSE NON-FERMENTING 1-RELATED PROTEIN KINASE 2s (SnRK2s) are important protein kinases in ABA signaling, and their role in abiotic and biotic stress signaling has been extensively characterized in Arabidopsis. The SnRK2 homologs in wheat appear to play a critical role in cold signaling. PKABA1, the first SnRK2 protein identified in wheat, is rapidly induced in seedlings when ABA levels increase in response to cold stress [65]. Furthermore, the expression of TaSnRK2.3, TaSnRK2.4, and TaSnRK2.8 can be induced by cold stress, suggesting that they are essential in cold signal transduction (Table 1) [66–68]. Overexpression of TaSnRK2.3 or TaSnRK2.8 in Arabidopsis increases cold tolerance, which is due to the increased expression of cold-responsive genes, and the enhanced accumulation of stress-associated metabolites such as proline [67]. Recent studies have identified 10 SnRK2 homologs in wheat, and the expression of these genes is induced by cold stress [69]. Although ABA and cold signaling are closely related, it is unclear what
the exact role of ABA in regulating plant cold stress responses is. Further work is needed to elucidate the molecular mechanisms of ABA when regulating cold signaling pathways.

Ethylene, a gaseous plant hormone, is important in various cellular and developmental processes, as well as during abiotic and biotic stress responses [70–75]. It is reported that cold stress can alter endogenous ethylene levels in many plant species. Cold stress inhibits ethylene production in Arabidopsis [76]; however, the ethylene levels are increased in winter rye under cold stress [77]. T. aestivum ethylene-responsive factor 1 (TaERF1), the first member of the ERF gene family identified in wheat, is induced by cold stress (Table 1). Additionally, TaERF1 overexpression can activate COR genes and improve freezing tolerance in transgenic Arabidopsis [78]. Pathogen-induced ethylene response factor 1 (TaPIE1) in wheat positively regulates freezing stresses by activating cold-regulated genes downstream of the ethylene signaling pathway and by modulating related physiological traits (Table 1) [79].

Gibberellins (GAs) play vital roles in abiotic stress response and adaptation. DELLA proteins are master regulators of GA-responsive growth and development [80]. Cold stress activates the expression of GA 2-oxidase genes to reduce the content of GA, resulting in the enhanced accumulation of DELLA proteins [81]. It is reported that overexpression of CBFs reduces the bioactive GA levels to suppress plant growth and flowering. CBF1-overexpression plants exhibit dwarfism and late-flowering phenotypes due to limited accumulation of bioactive GA [81]. Additionally, the cbfs mutants display impaired cold tolerance and larger architecture than the wild type after acclimation [40,82]. These results indicate that both the content and signal components of GA are related to cold signaling and CBFs may be associated with GA signaling to balance low-temperature adaption and growth. DELLAs act early in the cold signaling pathway as regulators of GROWTH REGULATORY FACTORS (GRFs). Cold-induced CBF genes are decreased in GRF5-overexpression lines, indicating that GRFs can repress CBF expression under cold stress (Table 1) [83]. Overexpression of SLENDER RICE 1 (SLR1), a gene that encodes the rice DELLA protein, enhances chilling tolerance. When rice seedlings are subjected to chilling stress, the cold-induced SLR1 (Table 1) releases the repressive effect of OsGRF6 on OsGA2ox1. The increased OsGA2ox1 expression then decreases the active GA levels to enhance rice chilling tolerance [84]. Rht-B1b and Rht-D1b, the most important and common semi-dwarfing genes, encode GA-insensitive forms of DELLA proteins that likely have a reduced affinity for the GA receptor in wheat [85]. It has been reported that the Rht-B1b and Rht-D1b mutant alleles are not responsive to GA at warmer temperatures but are responsive at colder temperatures (Table 1) [86]. This suggests that Rht-B1b and Rht-D1b play vital roles in response to cold stress.

The phytohormone jasmonic acid (JA) and its methyl ester, methyl jasmonate (MJ), act as signaling molecules in response to environmental stimuli. Cold stress rapidly increases endogenous JA levels by up-regulating the expression of JA biosynthesis genes, such as LIPOXYGENASE 1 (LOX1), ALLENE OXIDE SYNTHASE 1 (AOS1), ALLENE OXIDE CYCLASE 1 (AOC1), JASMONATE RESISTANT 1 (JAR1) in Arabidopsis and OsLOX2, OsAOS, OsAOC, Oryza sativa 12-OXOPHYTODIENOATE REDUCTASE 1 (OsOPR1) in rice (Table 1) [56,87]. The accumulation of JA induced by cold stress is due to the repression of ICE1 by JASMONATE ZIM-DOMAIN 1/4 (JAZ1/4), repressors of jasmonate signaling, resulting in the induction of CBFs expression in Arabidopsis [87]. Wheat TaJAZ genes are up-regulated in response to low temperatures (Table 1) [88]. Additionally, endogenous JA levels increase under cold stress in wheat [89]. Exogenous MJ treatment tends to up-regulate the transcription of COR genes, such as WCS19 and WCS120, and increase the activity of superoxide dismutase (SOD) and peroxidase (PO) to promote wheat cold tolerance [90,91]. Rice HAN1 (“han” means “chilling” in Chinese), which functions as an oxidase to reduce the accumulation of the active to inactive, decreases the expression of CBF/DREB1s in rice under cold stress [92]. Arabidopsis OPR3 is one of the major players in the JA biosynthesis pathway. Transgenic wheat plants with AtOPR3-overexpression have increased the accumulation of JA and improved cold tolerance [93].
Brassinosteroids (BRs) play a vital role in plant development and stress tolerance. COR gene expression and cold tolerance in *Arabidopsis* are increased by exogenous BR treatment [94]. Exogenous BR treatment promotes growth recovery of maize seedlings following chilling treatment [95] and increases cold tolerance in winter rye and winter wheat [96,97]. BRASSINOSTEROID INSENSITIVE 2 (BIN2) negatively regulates the freezing tolerance in *Arabidopsis* [98]. Knockout mutants of *Oryza sativa* GLYCINE SYNTHASE 3-LIKE GENE 1 (OsGSK1), an ortholog of *Arabidopsis* BIN2, show enhanced cold tolerance (Table 1) [99]. The expression of *T. aestivum* SHAGGY KINASE 5 (TaSK5), an abiotic stress-inducible GSK3/SHAGGY-like kinase in wheat, is induced at the early stages of cold acclimation (Table 1) [100]. The BRASSINOSTEROID-INSENSITIVE 1 (BRI1) encodes a transmembrane receptor kinase as a BR receptor. Its mutation results in defective BR signaling and increases cold stress tolerance in *Arabidopsis* (Table 1) [101]. The enhanced expression of its wheat homologous *TaBRI1* in *Arabidopsis* leads to better cold tolerance than the wild-type plants by maintaining membrane integrity [102]. Furthermore, overexpression of *TaBRI1* in *Arabidopsis* and the ortholog of BRII in rice or barley increases the silique size and seed yield [103,104]. Therefore, *TaBRI1* is involved in cold tolerance and is a suitable gene for improving crop yields under conditions of extreme environmental stress.

**Table 1.** List of phytohormones in response to cold stress.

| Item          | Gene                  | Function of Gene                                           | Regulated by Cold Stress | Reference   |
|---------------|-----------------------|------------------------------------------------------------|--------------------------|-------------|
| Auxin         | *OsYUCCA2/3/6/7*      | Important gene in Auxin/IPA (indole-3-pyruvic acid) biosynthesis | Up-regulated             | [56]        |
|               | *OsGH3-1/2/5/6/11*    | Auxin/IAA (indole-3-acetic acid) catabolism-related genes  | Down-regulated           | [56]        |
|               | *ARFs*                | Regulate the expression of auxin-responsive genes          | Up-regulated             | [60]        |
|               | *TaARFs*              | Regulate the expression of auxin-responsive genes          | Up-regulated             | [61]        |
| ABA           | *TaSnRK2.3/4/2.8*     | Important serine/threonine protein kinase in ABA signaling network | Up-regulated             | [66–68]     |
| Ethylene      | *TaERF1*              | A member of the ethylene response factor subfamily of ERF/AP2 transcription factor family | Up-regulated             | [78]        |
|               | *TaPIE1*              | Pathogen-induced ethylene response factor to active stress-related genes | Up-regulated             | [79]        |
| Gibberellin   | *GRF5*                | Growth regulating factor encoding transcription activator. | Up-regulated             | [83]        |
|               | *SLR1*                | A gene that encodes the rice DELLA protein to active OsGA2ox1 expression | Up-regulated             | [84]        |
|               | *Rht-B1b, Rht-D1b*    | The most important and widely used semi-dwarfing genes      | Up-regulated             | [86]        |
| Jasmonic acid | *LOX1, AOS1, AOC1, JAR1* | JA biosynthesis genes in *Arabidopsis*                     | Up-regulated             | [56]        |
|               | *OsLOX2, OsAOS, OsAOC, OsOPR1* | JA biosynthesis genes in rice                              | Up-regulated             | [87]        |
|               | *TaJAZs*              | The repressors of jasmonate signaling                       | Up-regulated             | [88]        |
| Brassinosteroids | *OsGSK1*            | BR negative regulator                                       | Up-regulated             | [99]        |
|               | *TaSK5*               | An abiotic stress-inducible GSK3 in wheat                   | Up-regulated             | [100]       |
|               | *TaBRI1*              | BR receptor                                                 | Up-regulated             | [101]       |
4. ROS and Cold Stress

Abiotic stresses typically increase ROS levels, including hydrogen peroxide (H$_2$O$_2$), superoxide radical (O$_2^{•−}$), hydroxyl radical (OH•), and singlet oxygen (¹O$_2$), all of which are toxic to plant cells [105–107]. Several pieces of evidence suggest that plant responses to cold stress are directly linked to ROS signaling [108–111]. It has been proven that low-temperature conditions depress the activities of ROS-scavenging enzymes, such as ascorbate peroxidase (APX), catalase (CAT), superoxide dismutase (SOD), dehydroascorbate reductase (DHAR), monodehydroascorbate reductase (MDHAR), glutathione S-transferase (GST), glutathione reductase (GR), and peroxiredoxin (PRX). These cold-regulated antioxidant enzymes play a key role in enhancing cold tolerance [107,112,113]. The H$_2$O$_2$ contents of 'dongnongdongmai1' ('dn1'), a winter wheat variety, are significantly increased under cold stress. Additionally, ABA treatment enhances cold tolerance in wheat by increasing the activities of TaSOD, TaAPX, TaCAT, TaGR, TaDHAR, and TaMDHAR [107]. The ABA-stress-ripening (ASR), which functions as a transcription factor, can be induced by low temperatures [114]. The levels of ROS and the activities of antioxidant enzymes under abiotic stress are regulated by ASRs, suggesting that ASR plays an important role in regulating ROS homeostasis [87,115].

5. Cold-Induced Epigenetic Processes and Elements

Epigenetic mechanisms play an important role in response to cold stress. The plant epigenome is highly dynamic, and cold stress can quickly reshape genome-wide epigenetic modifications [120]. Changes in DNA methylation and histone modification and the regulation of epigenetic elements, such as small RNA (sRNA) and long noncoding RNA (lncRNA), are the key modulators of plant stress responses [121,122].

The proteins containing methyl-CpG-binding domain (MBD) can recognize DNA methylation. TaMBD6, including a typical MBD domain at the N-terminal, is induced by prolonged chilling in wheat, indicating that the protein is potentially involved in recognizing DNA methylation during vernalization [123]. Wheat requires various vernalization genes in response to cold stress to adjust floral initiation, such as T. aestivum VERNALIZATION 1 (TaVRN1), TaVRN2, TaVRN3/FLOWERING LOCUS T1 (TaFT1), TaVRN-D4, and VERNALIZATION-RELATED 2 (VER2) [124,125]. In wheat and barley (Hordeum vulgare), the TaVRN1, HvVRN1, TaVRN2, and TaVRN3/TaFT1 gene are regulated by epigenetic modification (Figure 2). Two histone modification markers include histone 3 lysine 4 trimethylation (H3K4me3), which is a modification associated with active gene transcription, and H3K27me3, which is a modification associated with gene repression. Vernalization enriches H3K4me3 levels at the TaVRN1 and TaVRN3/TaFT1 promoters (Figure 2), while no significant changes are observed in H3K27me3 levels at the same regions of the TaVRN1 and TaVRN3/TaFT1 promoters in winter wheat. Furthermore, TaVRN1 and TaVRN3/TaFT1 are up-regulated by vernalization to accelerate floral transition in winter wheat [126]. TaVRN2, a dominant repressor of flowering, is down-regulated by vernalization [127]. Increased levels of H3K27me3 at the TaVRN1 promoter explain the repression of TaVRN2 gene expression in winter wheat (Figure 2) [126]. Before cold (vernalization), the increased levels of H3K27me3 at the HvVRN1 chromatin reduce the transcription of HvVRN1 in barley. Vernalization increases levels of H3K4me3, the active histone modification marks, and decreases levels of H3K27me3 at HvVRN1 (Figure 2) [128]. The novel transcript TaVRN1 ALTERNATIVE SPlicing (VAS), induced by vernalization, functions as a lncRNA derivative from the sense strand of the TaVRN1 gene to regulate TaVRN1 transcription during...
the flowering of winter wheat [129]. Additionally, TaVRN1 is the earliest target of TaVRN-D4 among the TaVRN1, TaVRN2, and TaVRN3 genes [130]. VER2 encodes a jacalin-like lectin and promotes TaVRN1 upregulation by physically interacting with the RNA-binding protein GLYCINE-RICH RNA-BINDING PROTEIN 2 (TaGRP2) after prolonged cold exposure [131]. However, whether the expression of TaVRN-D4 and VER2 is associated with DNA methylation requires further study.

Histone acetylation is up-regulated in cold-responsive genes like ZmDREB1 in maize under cold stress [132]. Additionally, cold stress induces higher levels of histone acetylation in the OsDREB1b promoter [133]. The level of acetylation is decreased by the up-regulated expression of HISTONE DEACETYLASEs (HDACs) in maize during cold acclimation [132]. MicroRNA (miRNA) is a class of sRNA that plays a critical role in plant growth and development. miRNA398 (miR398) participates in regulating plant responses to low temperatures in winter turnip rape (Brassica rapa L.) [134]. Additionally, the expression of wheat miR398 (tae-miR398) decreases in response to low temperature [135]. It is reported that tae-miR398 regulates cold tolerance by downregulating its target, COPPER-ZINC SUPEROXIDE DISMUTASE 1 (CSD1). Furthermore, the expression of CSD1 is indirectly regulated by IncRNAs (IncrR9A, IncrR117, and IncrR616). The regulation of miR398 induces a regulatory loop that is critical for cold tolerance in wheat [135]. Genome-wide association studies and annotations should be performed to outline the intricately epigenomic landscape, particularly in cereal crops subject to cold stress.

6. Conclusions and Perspectives: Improving Cold Tolerance in Wheat

Global food security is a problem of worldwide importance. The rapid increased population and unpredictable climatic events highlight the need to increase crop productivity. Understanding the perception and signaling cascades activated by cold stress response can help develop new technologies that can alleviate yield losses triggered by cold stress. Advances in molecular technologies and a rapidly expanding knowledge of the mechanisms regulating wheat response to cold stress will contribute to improvements in the efficiency of cereal crops.

Phytohormones are dominating regulatory factors of plant growth, development, and signaling networks involved in various abiotic stress responses. This indicates that...
phytohormones are associated with the cross-talk between environmental stress signals and plant growth. In addition, a growing body of evidence suggests the vital role of the ROS signaling pathway in plant development and stress response in wheat. However, the regulatory mechanisms of plant hormones and ROS in response to cold stress at the biochemical level are still poorly understood. Building comprehensive regulation networks in phytohormones, ROS signaling, and cold tolerance in wheat requires a combination of transcriptomes, proteomics, and metabolomics methods while analyzing mutants and protein–protein interactions.

Systematic research into epigenetic mechanisms in response to abiotic stress, including cold stress, heat stress, drought stress, and salt stress, must be performed under field conditions where multiple stress factors frequently coexist. Inheritable epigenetic processes and elements such as sRNA and lncRNA regulatory mechanisms, histone modification, and DNA methylation could provide within-generation and trans-generational stress memory. More powerful and versatile tools are needed to study epigenetic mechanisms in cereals like wheat in a trans-generational memory context since these epigenetic variations could improve stress tolerance in the offspring.

To successfully develop varieties equipped for cold stress, it is necessary to identify the extent of genetic variation for these traits in wheat. Therefore, future work must identify core components involved in the wheat cold signaling pathway that improve cold tolerance in wheat and increase its production in cold temperatures.

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