



HISTONE MODIFICATIONS IN RESPONSE TO ABIOTIC STRESS

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ABSTRACT Plants, being sessile, are subjected to multitudinous untoward environmental conditions perpetuated by a complex concurrence of abiotic factors that possess the ability to negatively impact their growth, development or productivity. Stress conditions induce a plethora of plant responses, ranging from changes in growth rates and growth yields to altered gene expression and cellular metabolism. Under adverse conditions, plants perceive stimuli from the surrounding environment and in due course of time have developed extensive regulatory mechanisms that generate variations in gene, in response. Histone modifications such as H3K9ac, H4ac, H3K4me3, H3K9me2, H3K27me3, H3K23ac, H3K27ac, along with DNA methylation have been found to be associated with altered gene expression in response to abiotic stresses which includes drought, extreme temperatures, and high salinity conditions. This review provides a comprehensive overview of histone modifications that occur as part of chromatin changes, in response to drought, salinity, heat, cold and nutrient stress.

KEYWORDS : histone modifications, abiotic stress, plants, epigenetics

Introduction

Histones are the protein components of nucleosomes. Their main functions are to compact DNA and regulate chromatin, in turn, influencing gene regulation. The basic core histone octamer consists of H2A, H2B, H3 and H4. Each histone has both a C-terminal and an N-terminal end. The N-terminal end (enriched with basic amino acids) is subject to a variety of post-translational modifications, such as acetylation, phosphorylation, methylation etc. and these modifications alter the activity of the genes wrapped around the core histone producing various effects depending on the type of modification and the residue that is modified at the histone tail. As this influences the chromatin structure, it plays a major role in regulation of processes such as transcription, DNA repair, and replication. Histone modification sites have been identified by mass-spectrometry and biochemical assays (Earley et al., 2007; Zhang et al., 2007) in *Arabidopsis*. Histone modifying enzymes such as histone acetyltransferases (HATs), histone deacetylases (HDACs), histone methyltransferases (HMTs), and histone demethylases (HDMs) maintain such modifications.

Histone Modifications In Salt Stress Response

It has been identified that salinity stress responses in plants are influenced by phosphorylation, acetylation, and methylation. Transcriptionally active genes are usually associated with histone acetylation, and the gene activation is moderated by antipathetic actions between the *HAT* and *HDAC* proteins. In *Arabidopsis*, hypersensitivity to salt was observed in a mutant for the transcriptional adaptor ADA2b, which attunes HAT activity, intimating towards the impression that HATs play a pivotal role in salinity tolerance (Kaldis et al., 2011). Likewise in maize roots, an increase in the expression level of genes responsible for cell wall expansion and extension such as *ZmEXPB2* and *ZmXET1* was discovered under high salinity and has been ascribed to the upregulated H3K9 acetylation in the promoter and coding regions of the said genes (Li et al., 2014).

Histone Modifications In Drought Stress Response

Drought-responsive genes have been identified and studied in order to understand the networking associated with drought response in plants. It has been established that expression of drought stress responsive genes is proportional with the intensity of drought stress. A correlation was found between expression levels of the drought responsive genes and changes in histone modifications (Kim et al., 2008, 2012; To and Kim, 2014). Certain drought stress upregulated genes, such as *RD20* and *RD29A* (*Arabidopsis*) were found to be more enhanced with certain histone modifications such as H3K4me3 and H3K9ac, under strong drought conditions with a predominant enrichment of histone

acetylation (Kim et al., 2008, 2012). A gene in *Arabidopsis* encoding a major enzyme in the ABA biosynthesis pathway, NCED3, was determined to be activated by the binding of HMT Arabidopsistrithorax-like 1 (ATX1) via a H3K4me3 modification and subsequently an increment in binding was observed under drought conditions (Ding et al., 2011). Plants that were ATX1 mutants displayed lower transcript levels of drought stress responsive genes such as *RD29A* and *RD29B* which goes to show that ATX1 mediated modifications might play an important role in the stress response which could be used as an advantage in the process of stress priming. Interestingly, the chromatin resetting mechanism that works after the advent of non-stressful conditions entails massive amounts of histone deacetylation on the drought stress upregulated genes and nucleosome replacement. During recovery from drought stress, drought stress-response genes, *RD29A*, *RD20*, and *AtGOLS2* exhibited a speedy decrement in the histone modification H3K9ac and also the RNA Pol II that carries out transcription was also removed from these regions. Demethylation is carried out at a significantly slower rate than deacetylation (Kim et al., 2012). Histone acetylation status has also been correlated with drought stress and ABA responses in plants. The histone acetylation levels increase on the drought-responsive genes such as *RD20*, *RD29A*, and *RD29B* and H3K9ac is enriched rapidly in these gene regions (Kim et al., 2008). In rice, drought stress substantially induced four HAT genes (*OsHAC703*, *OsHAG703*, *OsHAF701*, and *OsHAM701*) and enhanced acetylation of H3K9, H3K18, H3K27, and H4K5 under drought stress conditions was observed. Expression and overexpression of certain plant-specific HDAC (histone deacetylases) genes was shown to elicit responses to stress-related plant hormones such as ABA, jasmonic acid, salicylic acid and also result in enhanced drought stress tolerance and ABA insensitivity (Sridha & Wu, 2006; Demetriou et al., 2009).

Histone Modifications In Nutrient Stress Response

Histone modifications play an important role in attaining homeostasis for a majority of nutrients. Mutations in these lead to imbalance in acquisition, accumulation and retention of the nutrients. With respect to this, a lot of studies carried out in accordance with histone modifications in response to nutrient stress have focused on histone methylation, since it seems to be a driving factor in many nutrient-related mechanisms and is important in modulating transcription factor binding (Huang XY et al., 2016). A study showed that to achieve iron homeostasis in plants, a symmetric dimethylation of histone H4R3 (H4R3me2) was required (Fan H et al., 2013). Consequently, a mutation in the *Arabidopsis* Protein MethylTransferase 5 (PRMT 5), which catalyzes the symmetric dimethylation reaction of H4R3, lead to mutant plants with higher iron accumulation in shoots and affected

expression of several bHLH genes that regulate iron intake in *Arabidopsis* (Wang N et al., 2013). Another research study reported a case of histone acetylation - regulated nutrient homeostasis with the observation that mutation of the histone acetyltransferase General Control Non-repressed 5 (GCN5) gene results in altered and damaged iron translocation from the root to the shoot in *Arabidopsis*. GCN5 was shown to directly bind to the promoters of five iron- related genes, including Ferric Reductase Defective 3 (FRD3) - which is a key factor involved in iron nutrition - modulate their acetylation levels of histone 3 lysine 9 (H3K9ac) and histone 3 lysine (H3K14ac) levels, and consecutively regulate their transcript expression (Xing J et al., 2015). Alfin-like 6 (AL6) is a gene involved in root hair elongation in *Arabidopsis*. AL6 mutants exhibit a pleiotropic phenotype including reduced anthocyanin accumulation and very short root hairs, in response to low levels of Pi (Chandrika et al., 2013). A study on the involvement of trimethylated lysine 4 of histone H3 (H3K4me3) under phosphate starvation, revealed that AL6 contains a Plant HomeoDomain (PHD) finger that can bind to H3K4me3 (Lee et al., 2009). The authors suggest that since H3K4me3 is a binding site for transcription factors and activators for mRNA elongation and maturation; and AL6 gene is able to bind to it, AL6 might affect the transcript maturation and constancy of crucial genes involved in root hair elongation (Chandrika et al., 2013). Another recent study in *Arabidopsis* revealed that histone acetylation was involved in Pi homeostasis through observation of histone deacetylase 19 gene. It was found that HD 19 played a vital role in controlling root cell elongation in conditions where Pi was inadequate and also regulated a certain essential phosphate starvation genes, including some involved in Pi sensing and signaling (Chen et al., 2015).

Histone Modifications In Cold Stress Response

Induction of flowering can be brought about in plants using the process of vernalization which involves exposure of the plant to cold temperatures. In *Arabidopsis*, vernalization is involved in epigenetic regulation induced by environmental stresses and has been shown to be achieved by long-term exposure to cold temperatures (Song et al., 2012). On the other hand, short term exposure to non- freezing low temperatures has been found to enhance freezing tolerance, and this process is known as cold acclimation. Several genes and epigenetic regulators have been found to be upregulated under low-temperature induced stress conditions, suggesting that the epigenetic and transcriptional changes of the target genes may be attributed to their up-regulation. In maize, an increase in histone acetylation on cold-responsive genes, *ZmdREB1* and *ZmCOR413* was observed. In addition to this, the HDAC expression was upregulated in maize during cold acclimation and an inclusive deacetylation of H3 and H4 was also ascertained (Hu et al., 2011). OsDREB1b gene in rice was differentially regulated at the transcriptional level and the histone acetylation levels were found to be enriched in this gene under cold stress (Roy et al., 2014). Histone Deacetylase 6 (HDA6) plays an essential role in regulating cold acclimation that confers freezing tolerance in *Arabidopsis*. Its expression was shown to be induced by long-term low temperature treatments, and a mutation in this gene resulted in sensitivity to freezing stress (To et al., 2011). Furthermore, in *Arabidopsis*, cold-responsive genes COR15A and AtGolS3 experienced an intermittent decrease in H3K27me3 enrichment during cold stress treatment (Kwon et al., 2009). In consequence, it can be concluded that the acquisition of stress tolerance through changes in the expression of cold-responsive genes as a result of epigenetic changes induced by cold stress is feasible. Histone acetyltransferases (HATs) are associated with transcriptionally active genes (Berger, 2002; Kuo et al., 2000) and GCN5 is one such HAT in *Arabidopsis*. ADA2b, a transcriptional activator of HATs, was reported to interact with GCN5, and enhance the HAT activity of GCN5 (Stockinger et al., 2001). Additionally, it was observed that the induction of COR (cold-regulated) genes by low temperature was delayed, and the final mRNA expression levels were also reduced in ada2b and gcn5 mutants of *Arabidopsis*. An increase in freezing tolerance exhibited by the ada2b mutants hint that ADA2b works toward freezing tolerance repression via histone acetylation (Vlachonassios et al., 2003).

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