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Histone Methylation - A Cornerstone for Plant Responses to Environmental Stresses?

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Abstract

Plants are sessile organisms and, as such, their survival relies on their ability to respond quickly all along their life cycle to any kind of environmental stimuli, including abiotic and biotic stresses. In this respect, plants have developed efficient mechanisms of protection and/or adaptation to minimize deleterious effects of stress on their growth and development. In a stress type-dependent manner, external signals are firstly sensed. This step is then followed by the activation of particular signalling pathways, resulting ultimately in the rapid and specific modulation of the plant transcriptome. Currently, transcriptional regulation is considered as a central process in the build-up of plant responses to both abiotic and biotic stresses. Among mechanisms involved in transcriptional regulation, the combined effect of different histone tail post-translational modifications (PTMs; e.g. acetylation and methylation) through the activity of particular histone-modifying enzymes can lead to changes in the local chromatin structure environment and hence the underlying DNA accessibility.

By focusing on histone lysine methylation, in this chapter we highlight our current understanding of the transcriptional roles played by chromatin-remodelling mechanisms in regulating plant response/adaptation to different biotic and abiotic stresses. Based on recent advances, we further discuss the stability and transmission of such methylation marks to subsequent generations, with the underlying idea of an epigenetically based transcriptional memory of stresses in plants.

Keywords: Histone methylation and demethylation, histone methyltransferases and demethylases, biotic and abiotic stresses

1. Introduction

Stress, as we currently think of it, is a highly subjective phenomenon defined as a state of threatened homeostasis. Depending on their nature, external stresses are usually divided into biotic (i.e. herbivorous insects and pathogens such as fungi, bacteria and viruses) or abiotic (i.e. including, among others, high or low temperature, submergence or drought and salinity). During their lifetime, all living organisms inevitably and constantly face all sorts of environmental stresses that often occur suddenly and/or simultaneously. Classically, different strategies can be applied to minimize deleterious effects of stresses, such as resistance, tolerance, avoidance or escape. Being sessile, plants cannot escape and are therefore more prone to the deleterious effect of unfavourable environmental growth conditions. Because responses are critical to ensure their survival, plants have developed specific and efficient strategies that allow them to precisely perceive different environmental stresses and respond and/or adapt to them [1, 2]. In addition to preformed defence traits, plants have evolved inducible defence strategies. Indeed, upon perception, each stress will raise a complex and more or less specific repertoire of cellular and molecular responses implemented by the plant to minimize or prevent damage. Particularly, the stimulation of a given stress-signalling pathway after pathogen detection will be integrated into the plant cell nucleus through a set of regulatory transcription factor cascades, which prioritizes defence over growth-related cellular functions, while conserving enough valuable resources for survival and reproduction [3, 4]. Supporting the idea that the capacity of a plant to rapidly reprogramme its gene expression at the transcriptional level is an essential and common component of all plant response strategies to stress and disturbance; more than 1,000 transcription factors were found to be involved in stress responses [5, 6]. Because eukaryotic genes function in the context of chromatin, modifications and remodelling of the chromatin configuration from permissive for transcription to restrictive, and vice versa, may be an integral part of mechanisms involved in this vital transcriptional reprogramming. In this chapter, we review and discuss the current knowledge about the functional impact of chromatin changes on the transcriptional regulation of genes under different stress conditions, with particular emphasis on histone methylation/demethylation.

2. Chromatin structure and histone methylation/demethylation

In eukaryotes, genomic DNA in the cell nucleus is packaged in a complex and evolutionarily conserved structure named chromatin, with nucleosome as the basic unit. The nucleosome complex contains about 160–241 base pairs (bp) of DNA, a nucleosome core particle and the H1 linker histone. The nucleosome core particle is composed of an octamer of core histones, consisting of two H3–H4 dimers associated with two H2A–H2B dimers. About 146 bp of DNA is wrapped in ~1.65 negatively supercoiled circles around the histone octamer, while the linker DNA associated with H1 varies in length from 8 to 114 bp [7]. At first sight, the chromatin as it is described appears as a barrier, restricting the access of all kinds of enzymes that process the DNA. However, nucleosomes are not merely static but highly dynamic entities. Indeed,

nucleosomes can be moved, stabilized/destabilized, disassembled/reassembled at particular genome locations in response to specific environmental signals or developmental cues [8]. This dynamic leads to a wide range of chromatin condensation states modulating the DNA accessibility, with euchromatin, being relaxed, and heterochromatin, being compacted. Therefore, in eukaryotic cells, an intimate connection exists between the structural organization of the genome and its functioning. For this reason, the level of chromatin condensation is directly related to all aspects of DNA metabolism, thus playing a major role in regulating transcription, DNA replication, DNA repair, recombination, transposition and chromosome segregation. In plants, changes in the chromatin structure were reported to affect various biological processes such as root growth, flowering, organogenesis, gametophyte or embryo formation [9–11].

In the nucleosome core particle, histones H2A, H2B, H3 and H4 possess two common regions, a histone-fold domain and a histone tail. The histone-fold domain is the most conserved region and the main element of histone dimerization [12]. The tail protrudes from the nucleosome core particle and is more variable and unstructured than the fold [13]. All four core histones have an N-terminal tail domain, but only histone H2A has an additional long C-terminal tail. Histone tails are extremely basic due to their particularly high content in basic amino acid residues, such as lysine and arginine [14]. Resulting positive charges allow them to closely associate with the negatively charged nucleosomal DNA through electrostatic interactions [15]. In addition, histone tails, especially N-terminal ones, may undergo diverse types of post-translational modifications such as acetylation or methylation. The great diversity of these modifications as well as the high number of amino acid residues that can be modified within histone tails, and the correlation between these modifications and various nuclear processes, lead to the hypothesis that the specific combination of histone modifications constitute a histone 'code' [16].

Technically, these histone marks can be localized by chromatin immunoprecipitation (ChIP) using specific antibodies against the modification [17]. Briefly, protein–DNA interactions are stabilized by cross-linking with formaldehyde; chromatin is sheared into small pieces to facilitate analysis and then immunoprecipitated using an antibody raised against a specific histone modification. Following enrichment, cross links are reversed to release DNA, which is then quantified by polymerase chain reaction (PCR) to measure the relative amount of the specific histone mark on selected plant genes. ChIP can also be combined with microarray hybridization (ChIP-chip) or high-throughput sequencing (ChIP-Seq), allowing the genome-wide discovery of DNA–histone modification interactions.

Methylation is the most abundant one compared with other histone PTMs. It can occur at both lysine (K) and arginine (R) residues of core histone tails. Further extending the indexing potential of this modification, mono-, di- and trimethylation of lysine and mono- and dimethylation (symmetric or asymmetric) of arginine are common at N-terminal tails of H2A, H2B, H3 and H4. Although histone acetylation is generally associated with active gene transcription, histone methylation can be associated with either active or silent gene expression, depending upon the histone, the methylated residue or the level (mono-, di- or tri-) of methylation. In *Arabidopsis*, genome-wide analyses revealed that trimethylations of H3K4 and H3K36

(H3K4me3 and H3K36me3) are generally enriched at actively transcribed genes, whereas H3K27me3 is associated with repressed genes and H3K9me2 and H4K20me1 are enriched at constitutive heterochromatin and silenced transposons [18]. For histone arginine methylation, a definitive role has not yet been clearly established. However, because the level of symmetric H3R2me2 and H4R3me2 was negatively correlated with the level of H3K4me3, a well-known mark reflecting active transcription, high levels of H3R2me2 and H4R3me2 are thought to cause transcriptional repression [19–21]. In contrast, asymmetric H4R3me2 was associated with gene activation [22, 23].

Histone methylation is relatively stable and can be established on lysine and arginine by two distinct families of enzymes, the histone lysine methyltransferases (HKMTs), all containing the evolutionary conserved catalytic SET domain in plants [24], and the protein arginine methyltransferases (PRMTs) [25], respectively. As a counterpart, methyl groups on histone can also be removed by at least two evolutionarily conserved classes of histone demethylases, the lysine-specific demethylase1 (LSD1) type and the Jumonji C (JmjC) domain-containing demethylases [26]. Histone methyltransferases and demethylases are well conserved in angiosperms and have been identified and classified on the basis of phylogenetic analyses and domain organization in several plants, including *Arabidopsis*, maize, tomato, rice, grapevine and *Brassica rapa*, [27–32]. However, cellular and molecular functions of many of these modifiers have not yet been addressed.

Although histone acetylation can directly modulate the chromatin structure, arginine and lysine methylation of histone tails can promote or prevent the docking of key transcriptional effector molecules, named readers, needed to ‘translate’ the code in order to determine the functional and structural outcome of the corresponding PTMs. Just as there are a large number of PTMs on histone tails, there are also numerous protein domains that recognize and bind to particular PTMs on these tails. For example, PTM-recognition domains such as plant homeo-domain (PHD) fingers, chromodomains and Tudor domains all recognize methylated lysine residues [33].

3. Histone methylation changes associated with biotic stress conditions

Biotic stress is the result of the damage done to plants by insects or pathogens, such as bacteria or fungi. Plant pathogens are generally divided into two distinct categories: biotrophs, which colonize living plant tissue and obtain nutrients from living host cells, and necrotrophs, which depend on dead host tissue for nutrients and reproduction. To fend off pathogens with different infection strategies, plants have evolved complex defence mechanisms. Classically, the pathogen-sensing machinery induces signalling cascades that promote the accumulation of hormones such as salicylic acid (SA) or jasmonic acid (JA)/ethylene (ET) [34]. These hormones then orchestrate the overall plant defence reaction locally and systemically by inducing the transcriptional activation of defence genes through an intricate signalling network. In this part, we highlight recent examples illustrating how histone methylations condition major steps leading to immunity, ranging from initial pathogen perception to hormonal homeostasis changes for antimicrobial effector expression.

3.1. Histone methylation/demethylation in the defence against biotrophic pathogens

The phytohormone SA plays an important role in plant defence, from the induction of pathogen resistance (*PR*) genes against biotrophic bacteria (e.g. *Pseudomonas syringae*) to the establishment of systemic acquired resistance (SAR) [35]. Several studies suggested that the SA signalling pathway is notably controlled by histone methylation. Under normal growth conditions, *Arabidopsis* mutants for *SNI1* (*Suppressor of NPR1, Inducible*), a negative regulator of SAR required to dampen the basal expression of *PR* genes, presented an increased H3K4me2 on *PR1* [36]. Rather than being a constitutive mark of transcription, H3K4me2 was proposed to be involved in the fine-tuning of tissue-specific expression [37]. Using the functional SA-analogue S-methyl benzo [1,2,3] thiadiazole-7-carbothioate (BTH), an increased level of H3K4me2 on *PR1* was observed in wild-type plants 48 h after treatment and was not detected in mutants. Interestingly, when expressed in yeast, *SNI1* also repressed transcription, suggesting a highly conserved mechanism of transcriptional repression. These results together with the structural similarity of *SNI1* with armadillo repeat (ARM) proteins (i.e. a motif known to mediate protein–protein interactions) imply that *SNI1* may form a scaffold for interaction with proteins that modulates the chromatin structure of *PR* genes, thus repressing their transcription. In addition, the presence of H3K4me2 detected on *PR1* before induction suggested that this mark is readily in place, providing the appropriate chromatin configuration for the efficient induction of *PR1* upon need. Using a similar approach, Alvarez-Venegas et al. [38] reported no significant changes in levels of H3K4me2 and H3K4me3 on *PR1* 24 h after the SA treatment [38]. This discrepancy may reflect differences in experimental conditions. Indeed, the action of the so-called ‘SA-analog’ BTH on gene transcription is significantly broader than the action of SA itself [39]. Moreover, samplings were performed 48 h versus 24 h after treatment. Together, because the H3K4 methylation increase does not occur immediately after the induction of *PR1*, this mark may not be directly related to the transcriptional induction itself, but later, for the maintenance/reinforcement of *PR1* expression.

The ARABIDOPSIS HOMOLOG OF TRITHORAX (*ATX1*) is a H3K4 trimethyltransferase providing basal resistance against *Pseudomonas syringae* *pv. tomato* (*Pst*); [40]. Despite being not induced by either *Pst* infection or SA, *ATX1* positively and directly regulates the expression of the transcription factor *WRKY70* through H3K4 trimethylation at the *WRKY70* promoter. In addition, *atx1* mutant shows induced expression of the JA-inducible *THI1.2* gene and the reduced *PR1* expression without detectable changes in their chromatin, resulting in impaired resistance to *Pst* infection. Since the transcriptional factor *WRKY70* was positioned at the convergence node of the SA and JA signalling pathways, activating the SA-responsive *PR1* gene and repressing the JA inducible genes [41], *ATX1* was proposed to indirectly regulate *PR1* and *THI1.2* through *WRKY70*. SET DOMAIN GROUP 8 (*SDG8*), another HKMT encoding the major *Arabidopsis* H3K36 di- and trimethyltransferase [42], was also involved in the plant-defence against *Pst*, but it was more upstream than *ATX1* [43]. Indeed, *SDG8* sustains the basal transcription of particular *R* genes (*RPM1* or *LAZ5*) by maintaining a basal level of H3K36me3, another histone mark tightly associated with active transcription. *SDG8* is also required for the transcriptional induction of these *R* genes upon BTH treatment or *Pst* inoculation. However, this induction occurs without any detectable increase of H3K36me3. Therefore, in resting

plants, SDG8 may establish a 'permissive' chromatin structure at some *R* genes by methylating H3K36, thus ensuring their basal expression and their transcriptional inducibility upon need. Similarly as *atx1* and *sdg8* mutants, loss-of-function mutants for the putative HKMT SDG7 were also found to be more sensitive to *Pst* infection than wild-type plants [44]. The expression of other *R* genes seems to be under the control of histone methylation. Indeed, enhanced downy mildew 2 (EDM2) impacts disease resistance by controlling levels of H3K9me2 at an alternative polyadenylation site in the immune receptor gene *RPP7*, thus regulating the balance between full-length *RPP7* transcripts and prematurely polyadenylated transcripts, which do not encode the *RPP7* immune receptor [45, 46]. EDM2, as an epigenetic 'reader', contains two stretches of atypical PHD-finger motifs known to dock specifically several forms of methylated or unmethylated lysine residues on histones [47]. Besides this, EDM2 was also proposed to cooperate within a large protein complex with EMSY-like (AtEML) members, harbouring an Agenet domain related to the Tudor domain family of epigenetic 'readers' [48].

Apart from *Arabidopsis*, little is known about the regulatory role of histone methylation in the defence against pathogen attack in other plant species. In rice, the JmjC protein gene *JMJ705* encoding a histone lysine demethylase that specifically reverses H3K27me2/3 was found induced during infection with the bacterial pathogen *Xanthomonas oryzae*. *JMJ705* was further involved in the dynamic removal of the basal H3K27me3 over defence-related genes, thereby increasing their basal expression and/or potentiating their higher expression upon biotic stress. Interestingly, the *JMJ705* overexpression resulted in an enhanced resistance to the bacterial pathogen, while its mutation reduces the plant resistance [49].

3.2. Histone methylation/demethylation in the defence against necrotrophic pathogens

While to combat biotrophic pathogens the plant activates mainly the SA signalling pathway, the activation of the JA/ET signalling pathway is prominent to mediate defences against necrotrophic pathogens and herbivorous insect attacks [50]. The involvement of histone methylation in the defence against necrotrophic pathogens is far less documented as compared with the defence against biotrophic pathogens. Besides being more susceptible to *Pst* [43], *sdg8* mutants were also reported to be more sensitive to necrotrophic fungal pathogens such as *Alternaria brassicicola* (*Alt*) and *Botrytis cinerea* [51]. This increased susceptibility was the consequence of the inefficient transcriptional induction of different genes along the JA/ET signalling pathway that was correlated with a stably weak level of H3K36me3 at these genes. Inversely, in wild-type plants, H3K36me3 together with gene expression were increased upon *Alt* infection or stimulation with exogenous MeJA. Under resting conditions, a similarly weak level of H3K36me3 was correlated with a reduced basal expression in *sdg8*. On that account, H3K36 methylation was proposed to act as a 'permissive' mark correlated with gene activity and readily in place at a subset of JA/ET signalling-related genes to raise their rapid and efficient transcriptional induction when required [52]. Interestingly, a stable and very low level of H3K27me3 was detected in defence effector genes. Because H3K27me3 is often associated with epigenetic silencing [53], this low H3K27me3 level may provide these genes with a reduced probability for undesired silencing, thus participating in the reactivity of plants to pathogen infections.

4. Histone methylation changes associated with abiotic stress conditions

Abiotic stresses such as heat, cold, drought, salinity and nutrient deficiency are inherent to every ecosystem and essentially unavoidable. Abiotic stresses are considered the most harmful factors in terms of growth and productivity of crops worldwide [54, 55], especially when they occur in combinations [56]. Here, we summarize and discuss various studies in order to clarify the functional involvement of different histone methylation marks in setting up plant responses to adverse environmental growth conditions.

4.1. Histone methylation/demethylation and the plant stress hormone ABA

The phytohormone abscisic acid (ABA) is a crucial signalling molecule playing versatile functions in regulating many developmental processes, including seed dormancy and germination [57, 58]. ABA also plays a pivotal role in adaptive stress processes, integrating both biotic and abiotic environmental constraints in a complex network of interacting pathways with crosstalks at different levels [59–61]. Currently, ABA is considered as a global regulator of stress responses that can dominantly control the switch in priority between the responses to biotic or abiotic stress, allowing plants to respond to the most severe threat [62].

The transition from heterotrophic to autotrophic development at the post-germinative stage (i.e. embryonic state) is highly vulnerable to osmotic stress [63]. During a period of osmotic stress, ABA promotes the expression of transcription factors such as *ABI3* and *ABI5*, which in turn delay germination and lead to osmotolerance and survival [64]. In *Arabidopsis*, mutation in *PICKLE* (*PKL*), encoding a putative chromatin modifier, results in increased and abnormally sustained expression of *ABI3* and *ABI5* in response to exogenous ABA treatment. This sustained expression was correlated with reduced levels of H3K9me2 and H3K27me2, two methylation marks found in the chromatin of silent genes [65]. Based on these results, it was suggested that *PKL* might act on *ABI3* and *ABI5* to promote directly or indirectly the formation of a repressed chromatin state through a so-far-unknown mechanism.

In adult plants, the establishment of a response and tolerance to drought stress by ABA has been extensively studied and is well discussed in several outstanding reviews [58, 66]. Briefly, under drought conditions, water stress perception triggers ABA biosynthesis and increased tissue ABA accumulation, resulting in stomatal closure and reduced transpiration. Among major enzymes involved in the ABA biosynthesis pathway, NINE-CIS-EPOXYCAROTENOID DIOXYGENASE 3 (*NCED3*) is thought to be the rate-limiting enzyme [67]. In *Arabidopsis*, the increased transcription of *NCED3* upon dehydration was correlated with the binding of the HKMT *ATX1* and the increased level of H3K4me3 at *NCED3* [68]. Therefore, the loss-of-function *atx1* mutant showed less tolerance to dehydration, notably because of the lower enrichment of RNA Polymerase II (RNAPII) and H3K4me3 at *NCED3* under stress. *ATX1*-modified H3K4me3 may thus have an important function in the transcriptional regulation of *NCED3*. However, it is still unclear whether this function is directly linked with the transcriptional induction or is more related to the reinforcement of the increased transcription upon stress perception.

4.2. Histone methylation/demethylation in response to water stresses

Water stresses including drought or submergence are major environmental factors limiting plant growth and crop productivity worldwide [69, 70]. Consequently, plants have evolved a variety of biochemical and physiological mechanisms to respond/adapt to these stresses [71, 72]. In the following section, we distinctly address the involvement of histone methylation in responses to drought and submergence.

4.2.1. Drought stress

Using *Arabidopsis*, the molecular response to water deficit was found to rely notably on the transcriptional regulation of stress-inducible genes with products thought to function in drought tolerance and response [73]. Using ChIP analyses in 15-day-old *Arabidopsis* seedlings, the level of the active mark H3K4me3 was found gradually enriched in response to dehydration stress, preferentially on the coding region of four drought-inducible genes (*RD29A*, *RD29B*, *RD20* and *RAP2.4*), and was correlated with their upregulation [74]. Consistent with this result, *ATX1* was reported to be required for the efficient transcriptional induction of *RD29A* and *RD29B* during a dehydration stress response in an ABA-independent manner [68]. Also, for unknown reasons, it is worth noting that upon exogenous ABA treatment the transcriptional induction of *RD29A* and *RD29B* was stronger in *atx1* mutants than in wild-type plants (their basal transcript levels were lower in *atx1* than in wild-type, while their transcript levels upon ABA treatment were identical [68]). Next, for the ABA-dependent *RD29A* and ABA-independent *RAP2.4* genes, a time lag was observed between their transcriptional induction and the increase in H3K4me3 [74]. Based on these findings and the rapid saturation in RNAPII enrichment compared with H3K4me3 (i.e. already saturated 1 h after stress exposure for RNAPII, while H3K4me3 was still increasing up to 5 h), Kim et al. [74] concluded that the H3K4me3 enrichment may be established, gradually, in response to drought stress after full transcriptional activation of *RD29A* and *RAP2.4*. Because the timing of H3K4me3 enrichment followed subsequent to the RNAPII enrichment, H3K4me3 might be dispensable for the initiation of transcription. Finally, the gradual increase of H3K4me3 further indicates that the longer the stress lasts, the more H3K4me3 will be enriched, suggesting that the epigenetic responsiveness must depend on the intensity of a stress [75].

In a similar approach but using ChIP-Seq, van Dijk et al. [76] established the whole-genome distribution patterns of H3K4me1, H3K4me2 and H3K4me3 in 4-week-old rosette *Arabidopsis* leaves under dehydration stress conditions. They also observed a strong correlation between H3K4me3 abundance and transcripts levels from responding genes. Indeed, among the most strongly downregulated genes, an increase in H3K4me1 and a decrease in H3K4me3 were detected, suggesting the involvement of a histone demethylase in modulating the expression of a subset of stress-responsive genes. Supporting this finding, a putative PKDM7 subfamily-like H3K4 demethylase homologue and two putative demethylase enzymes containing a JmjC domain were found to be drought-inducible in two barley cultivars and in young peanut plants, respectively [77, 78]. Surprisingly, in contrast to the classical genome-wide H3K4me3 enrichment around the transcriptional start site observed in all other eukaryotes [79], H3K4me3 displayed a broader distribution on dehydration and ABA-inducible

genes. Such an unusual profile may reflect a function not strictly related to transcription initiation, as will be discussed later in the stress memory section.

Through a genome-wide approach in rice seedling, Zong et al. [80] also uncovered a weak but positive correlation between H3K4me3 enrichment and the transcript level of some drought-responsive genes under drought stress. This correlation was extended to many genes involved in stress-related metabolite and hormone signalling pathways, further supporting the role played by H3K4me3 in the stress response [80]. However, because H3K4me3 is not the only histone mark for gene activation, this weak correlation may reflect that other active histone marks may also play important roles in regulating gene expression in response to stress in rice. Although these large data sets have provided much information on drought responses in rice, more detailed analyses will be required to elucidate whether the observed variations in H3K4 methylation are a cause or a consequence of the transcriptional changes triggered by water stress. Moreover, identifying key histone modification enzymes is indispensable to better understand the transcriptional regulatory network of the abiotic stress response.

4.2.2. Submergence

Submergence is a complex stress that encompasses many changes in environmental factors, including light intensity, pH and dissolved oxygen concentration. Alcoholic fermentation is important for the survival of plants especially under anaerobic environments [81]. In rice, *alcohol dehydrogenase 1 (ADH1)* and *pyruvate decarboxylase 1 (PDC1)* genes are involved in this anaerobic metabolism and their expression is reversibly induced (i.e. activated upon submergence and repressed upon re-aeration) [82]. Using these two genes as a model, Tsuji et al. [83] observed that the level of H3K4 methylation, specifically at both the 5'- and 3'-coding regions of *ADH1* and *PDC1*, was changed from a dimethylated state to a trimethylated state upon their transcriptional upregulation in response to submergence. This change was reverted back to its initial level following re-aeration, indicating that in this particular case, H3K4me3 does not serve as a memory mark of a prior transcriptional activity. Similarly to drought, these results highlight the dynamic and reversible change of histone H3K4 methylation at stress-related genes in response to the occurrence and disappearance of a stress.

4.3. Histone methylation/demethylation in response to salt stress

Salinity is also a serious factor affecting plants in several ways (i.e. water stress, ion toxicity, nutritional disorders, oxidative stress, alteration of metabolic processes, membrane disorganization, genotoxicity, reduction of cell division and expansion), thus limiting plant growth, development and survival [84]. In *Arabidopsis*, a NaCl or ABA treatment has been shown to induce the transcription of a range of abiotic stress-responsive genes (*ABI1*, *ABI2*, *KAT1*, *KAT2*, *DREB2A*, *RD29A* and *RD29B*). Using ChIP, this induction was found significantly correlated with an increase in the active mark H3K4me3 and a decrease in the repressive mark H3K9me2 [85]. Also, suggesting a link between different histone PTMs, mutations in the histone deacetylase HDA6 partially suppressed the H3K4me3 increase observed in response to stress, while the H3K9me2 decrease was not affected. Since histone acetylation and H3K4 trimethylation are often associated with gene activation [86], the repressive function of HDA6 may

suggest that acetylation on histone H3 is required for K4 methylation to occur [87]. Unfortunately, because ChIP experiments were not normalised against the total H3 density, it is difficult to attribute the decrease in H3K9me₂ to either the active removal of methyl groups by a histone demethylases or the active removal of nucleosome in response to a stress. Supporting the second possibility, the nucleosome density of two other drought stress-inducible genes (*RD20* and *RAP2.4*) was found to gradually decrease in response to drought stress [74].

In soya bean and in response to a high NaCl concentration, these histone methylation marks were also found altered at some salinity-induced transcription factors (i.e. MYB, b-ZIP and AP2/DREB family members) that were primarily identified by microarray analysis [88]. For some genes, their transcriptional induction was correlated with an increased level of histone acetylation and H3K4me₃, accompanied or not with a reduced level of DNA methylation and H3K9me₂ in various parts of the promoter or coding regions. For other genes, DNA methylation had no influence on histone methylation. This work perfectly reflects the heterogeneity of the effect of salinity on histone methylation and DNA methylation, and supports the role(s) of histone methylation changes in the expression of some transcription factors important for salinity tolerance.

As mentioned above, H3K4me₃ was found to be involved in the transcriptional induction of stress-responsive gene upon salt stress exposure. In plants, the JmjC-domain-containing histone demethylases JMJ14, JMJ15 and JMJ18 have been reported to display an H3K4me_{2/3} demethylase activity as well as to regulate diverse aspects of chromatin function and development [89–95]. Recently, the overexpression of *JMJ15* was reported to preferentially down-regulate many stress-related genes preferentially marked by H3K4me_{2/3} and to enhance salt stress tolerance [96]. In contrast, the loss-of-function mutant was more sensitive to salt. Despite the fact that an increased JMJ15 level may regulate stress-responsive gene transcription programmes in *Arabidopsis*, the role of H3K4me₃ resetting in these processes is still very elusive.

Besides histone lysine methylation, arginine methylation was also involved in establishing the transcriptional response to salt stress. The protein arginine methyltransferase 5 (PRMT5), also named Shk1 kinase-binding protein1 (SKB1), is a type II methyltransferase that catalyses symmetric H4R3 dimethylation, a repressive mark known to promote flowering through the repression of the floral repressor *FLOWERING LOCUS C (FLC)* in *Arabidopsis* [20, 97]. Interestingly, gain-of-function *SKB1* mutants showed an enhanced salt stress tolerance and sensitivity to ABA [98]. As a consequence of PRMT5 disassociating from chromatin, the H4R3me₂ level at stress-responsive genes was reduced during salt stress, resulting in their induced expression. Suggesting an additional function of PRMT5 on non-histone proteins, the methylation level of the U6 small nuclear ribonucleoprotein Sm-like4 (LSM4, a core protein of the spliceosome) was increased in response to salt stress and ABA. Since splicing defects were observed in the *prmt5/skb1* and *lsm4* mutants, with both of them being hypersensitive to salt stress, authors proposed that PRMT5 might mediate plant development and salt response by altering the methylation status of H4R3me₂ and LSM4, linking transcriptional regulation to pre-mRNA splicing [98].

4.4. Histone methylation/demethylation in response to temperature

In plants, temperature stresses are classically classified into different types according to temperature exposure, which may be warm, high, chilling or freezing temperature. Due to global warming and because temperature stress greatly affects plant growth and development, immunity and circadian rhythm, and poses a serious threat to the global food supply, the genetic mechanisms of plant responses to heat have been well studied. Plants exposed to temperature stresses modulate the transcription of a large number of genes involved in distinct biochemical and physiological response pathways and networks of phytohormones or secondary metabolites, ultimately leading to increased tolerance to hazardous temperature stresses [99–102]. The role played by histone methylation during the plant response to a heat or a cold stress is discussed separately hereafter.

4.4.1. Heat stress

Heat stress during seed development decreases the seed size in many cereals, resulting in severe yield losses [103, 104]. In rice, a molecular mechanism involving the putative rice polycomb repressive complex 2 (PRC2) gene *Fertilization-Independent Endosperm1* (*OsFIE1*) was suggested as being a potential key component involved in regulating the thermal sensitivity of seed enlargement during endosperm development [105]. When developing seeds were exposed to a heat stress, both DNA methylation and H3K9 methylation were reduced on *OsFIE1* resulting in its derepression. Under heat stress, syncytial stage-specific MADS-box genes involved in seed size regulation were precociously repressed, due to the increased deposition of H3K27me3 silencing marks by the PRC2 complex [105]. In the unicellular green alga *Chlamydomonas reinhardtii*, histone modification was also affected by heat stress [106]. Indeed, after heat stress, the level of H3K4me1 was found decreased and the level of histone acetylation increased at promoter regions of active genes compared with inactive regions. As a hypothesis, authors proposed that upon heat stress, the heat shock transcription factor HSF1 might promote chromatin remodelling and RNAPII recruitment for transcription initiation/elongation [106]. Finally, while addressing molecular mechanisms of the response of cotton anthers to high temperature, two jmjC domain-containing genes, putatively involved in histone demethylation, were found significantly repressed during anther development under heat stress [107].

Because euchromatin is gene rich and usually transcriptionally active, investigation about the role of histone methylation in temperature stress acclimation was largely centred on euchromatin-associated coding regions. Focusing on the transcriptionally silent heterochromatin, mainly constituted of repetitive DNA sequences, some works demonstrated the transcriptional activation of normally silent transposable element embedded within heterochromatic regions under stress conditions [108]. Intriguingly, such activation under heat stress can occur without alteration of DNA methylation and with only minor changes in both H3K9me2 and H3K4me3 [109, 110]. In summary, these works suggest that temperature stress-mediated transcription of tandem-repeat elements might play a vital role in the adaptation of plants to temperature stimuli, offering an efficient mechanism by which heat or cold could promote the expression of some stress-responsive genes. Upon activation and when inserted into or very close to a

gene, such transposable elements could interfere with the expression of this gene, giving rise to deleterious mutations, genetic instability or positive contribution to gene regulation and adaptation [111].

4.4.2. Cold stress

The increased tolerance of plants to cold is referred as 'cold acclimation'. Cold acclimation differs from vernalization, as the last one requires a long-term exposure to cold temperatures, while cold acclimation can be achieved in a couple of days under non-freezing low temperatures [112]. Locally, histone methylation changes in cold-responsive genes were addressed in *Arabidopsis*. Upon cold stress, the repressive mark H3K27me3 decreased, in both a histone occupancy-dependent (i.e. arising from the lowering nucleosome density) and -independent (i.e. as the result of the activity of a not yet identified histone demethylase) manner, on the cold-responsive genes, cold-regulated 15A (*COR15A*) and galactinol synthase 3 (*ATGOLS3*; [113]). Interestingly, the decrease in H3K27me3 upon stimulation occurred more gradually than their rapid transcriptional induction, so that their activation may not be inhibited by H3K27me3 itself but rather lead to the removal of H3K27me3. Also, while the transcription of *COR15A* and *ATGOLS3* was completely repressed to the initial level upon returning plants to normal growth conditions, the H3K27me3 decrease was maintained. Given that this decrease does not affect the transcriptional induction of *COR15A* and *ATGOLS3* upon re-exposure to cold temperatures, such chromatin change can so far only be view as a 'reminiscence' of a recent transcriptional activity and not as a stress memory implicated in a gene priming process.

In maize during cold stress, changes in histone modifications, including the heterochromatic marks H3K9me2 and DNA methylation, were assessed through a genome-wide approach [114]. The more detailed analysis of the two knob-associated tandem-repetitive sequences, the 180-bp repeat and the 350-bp repeat termed TR-1, demonstrated that their selectively and transiently cold-activated transcription was correlated with a decreased H3K9me2 and DNA methylation, together with an increased H3K9 acetylation. Such cold-induced transcriptional activation of tandem repeats is selective and transient, and the silencing state is recovered as the treatment continues.

5. Histone methylation as a memory mark of stress

In animals, the formation of memory immune cells after primary antigen recognition confers long-lasting resistance, resulting in an accelerated and a more effective immune response in case of second exposure. Despite the absence of such memory immune cells, plants often acquire a systemic immunity to further infections after a primary localized infection [115]. This requires the accumulation of the plant hormone SA in systemic tissues and is called systemic acquired resistance (reviewed in [116]. The SAR is also associated with gene priming in systemic tissues, in which defence genes will be expressed more rapidly and robustly in case of a second attack [117]. At the transcriptional level, gene expression is primarily influenced by the chromatin structure, which in turn is controlled partly by processes, often referred to

as 'epigenetic' processes, which can be transmitted through mitosis and/or inherited through meiosis [118]. Therefore, chromatin remodelling through histone methylation offers a potential mechanism for short-/long-term stress memory within the lifespan of an individual, referred to as somatic memory, and/or across generations, referred to as transgenerational memory.

5.1. Somatic stress memory

In *Arabidopsis*, a priming event, either treatment with BTH or infection with *Pseudomonas syringae* *pv.* *maculicola*, systematically resulted in an increase in the level of H3K4me2/me3 at defence gene promoters (namely the WRKY transcription factors *WRKY6*, *WRKY29* and *WRKY52*) that are normally found on active genes, while the genes remain inactive [119]. More interestingly, this increase also occurs in leaves distal to localized foliar infection. Hence, even if the histone-modifying enzyme involved in this process remains unidentified, results from Jaskiewicz et al. [119] clearly suggest that histone methylation might create a 'memory' of the primary infection that is associated with an amplified reaction to a second stress stimulus. Further, Luna et al. [120] observed that promoters of SA-inducible *PR1*, *WRKY6* and *WRKY53* in the progeny of *Pst*-inoculated *Arabidopsis* plants were enriched with acetylated histone, while the promoter of the JA-inducible gene *PLANT DEFENSIN1.2* (*PDF1.2*) showed an increased level of H3K27me3. For decades, the signalling protein *NON EXPRESSOR OF PR1* (*NPR1*) has been implicated in mediating SAR induction [115] and also the crosstalk between SA- and JA/ET-dependent defence pathways, enabling plants to mount an appropriate defence reaction, depending on the nature of the attacker and the stage of infection [121, 122]. More recently, *NPR1* has been proposed to play a critical role in the expression of the transgenerational SAR as progeny from *npr1* failed to develop transgenerational defence phenotypes and failed to present enrichment for H3K27me3 at the *PDF1.2* promoter [120]. Together, these findings suggested that one or more systemic signals are stored as an immune memory on defence-related gene promoters in the form of histone modifications, thus providing the plant with a life-long protection, which can be transmitted to subsequent generations.

Besides being involved in defence priming related to biotic stress, histone methylation was also proposed as a priming strategy against drought. To further explore the functional impact of histone methylation on biotic stress responses in *Arabidopsis*, Kim et al. [123] followed chromatin dynamics of several drought genes (*RD20*, *RD29A* and *AtGOLS2*) and a rehydration-inducible gene (*ProDH*) during drought and rehydration. As previously discussed, a strong correlation was observed between H3K4me3 enrichment (i.e. especially in gene bodies) and transcription for drought genes upon drought [74, 123]. Such a correlation was also detected for the rehydration gene upon rehydration [123]. Suggesting a memory role for H3K4me3, RNAPII rapidly disappeared after rehydration at drought genes, while H3K4me3 was gradually decreased. Concomitantly, by training plants with up to four successive drought treatments, Ding et al. [124] uncovered the existence of two distinct subsets of genes within the dehydration stress-response gene fraction. The 'non-trainable' genes (e.g. the ABA-independent *RD29A* and *COR15A*) have repetitively similar transcription rates during each stress treatment, while 'trainable' ones (e.g. the ABA-dependent *RD29B* and *RAB18*) increased

the magnitude of their subsequent transcriptional response, relative to their initial stress response. Using ChIP, Ding et al. [124] observed that the H3K4me3 enrichment at 'trainable' genes, especially in gene bodies, was atypically retained from the preceding transcription after rehydration. Even more interestingly, the RNAPII phosphorylated at C-terminal domain (CTD) repeat serine 5 (Ser5P; associated with transcription initiation) was found stalled on these genes as a memory mark from a previously transcribed state. In contrast to 'trainable' genes, the stress-induced H3K4me3 and Ser5P enrichment at 'non-trainable' genes was decreased to its basal level during recovery [124]. Moreover, this transcriptional memory can persist in the absence of inducing signals at least for 5 days, but is lost after 7 days. Supporting a specific role for H3K4me3 in stress memory, other active chromatin marks such as acetylation of histones H3 and H4 were found rapidly increased at drought genes upon stress and decreased at comparable levels as before induction quickly after recovery [123, 124]. Consistent with an activating role of ATX1 at dehydration stress-response genes [68, 125, 126], dehydration-induced transcript levels were diminished in *atx1* plants [127]. However, ATX1 does not seem to have a critical impact on drought stress memory in *Arabidopsis*. Indeed, while being less increased than in wild-type plants, trainable genes still produced increased transcripts in trained, relative to untrained, *atx1* plants and retained high H3K4me3 levels during the watered recovery states. ATX1, ATX2, SDG25 and SET DOMAIN GROUP2/ATX-RELATED3 (SDG2/ATXR3) belong to the same class III of H3K4me3 methyltransferases and are thought to act, partially redundantly, as H3K4 methyltransferase [128–134]. More recently, SDG2 has been found to be essential for the full transcriptional activation of various hormone-responsive genes upon hormone treatment (i.e. including the ABA-dependant *RD29A*) via its H3K4 trimethyltransferase activity [135]. It is, therefore, likely that the other class III HKMT might also contribute to the drought stress memory. In summary, these results suggest that in addition to be a good marker of gene activation when found around promoter and 5' regions of genes, H3K4me3 might also play a role in establishing a transcriptional short-term somatic memory of drought stress when found in gene bodies.

Using a large-scale approach, the distribution of H3K4me2, H3K4me3, H3K9me2 and H3K27me3 was analysed in *Arabidopsis* seedlings, which have been treated with mild salt stress in the seedling stage, resulting in an increased tolerance upon an additional salt stress application [136]. At low resolution in primed seedlings, H3K4me2 and H3K4me3 most commonly consisted of higher peaks of pre-existing enriched histone modification domains, named islands, whereas H3K9me2 produced the least differences. By contrast, majority of differences in H3K27me3 resulted from a higher number of islands with lower genome coverage. At high resolution, changes in H3K27me3 were already detectable a few hours after salt addition, suggesting that demethylation of H3K27me3 operates at a speed that is comparable to that of transcriptional regulation. Interestingly, this effect fades over time; however, it is still clearly visible after a 10-day-growth period in control conditions. In response to a second stress treatment, genes with high responsiveness, such as *HKT1* (i.e. encoding a root-specific Na transporter) and *PIP2E* (i.e. encoding a plasma membrane aquaporin), experienced a decrease of H3K27me3, whereas genes with lower responsiveness, such as *GH3.1* and *GH3.3* (i.e. encoding auxin and JA-amino acid-conjugating enzymes, respectively), experienced an

increase of H3K27me₃. Conversely, another group reported that in plants that have experienced several exposures to dehydration stress no significant change in the level of H3K27me₃ could be detected on trainable and non-trainable genes, or during transcriptionally active/inactive gene states [137]. However, the high H3K27me₃ level present at inactive dehydration stress memory genes did not interfere with the transition to an active transcription and with the accumulation of H3K4me₃ [138]. Together, the function of H3K27me₃ in genes that dynamically change transcription seems to depend on the type of environmental stimuli.

In contrast to H3K27me₃, the higher level of H3K4me₃ retained at the trainable gene *RD29B*, when its transcription is low, further supports the idea that H3K4me₃ works as a 'memory' histone mark of a previously active state [138]. Generally, H3K4me₃ and H3K27me₃ play antagonistic roles in gene transcription and are therefore mutually repulsive at developmental genes [37, 139]. Seemingly, the presence of both marks, referred as 'bivalent domains', was first described in mammalian stem cells and was proposed to represent a pluripotent chromatin state that poises genes for activation upon appropriate developmental cues [140, 141]. Further work is required to determine whether H3K4me₃ and H3K27me₃ co-exist at certain genes whose expression is rapidly altered in response to environmental stimuli.

Because plant stress research has traditionally focused on single stresses, we separately described priming in response to abiotic or biotic environmental cues. However, in nature, plants are constantly exposed to mild environmental stresses during their lifetime. While testing how different environmental histories can affect the response of the plant to a subsequent biotic stress, Singh et al. [142] reported that *Arabidopsis* plants exposed to a recurrent abiotic stress (i.e. heat, cold or salt) were more resistant to *Pst* than plants grown in a more stable environment. This enhanced resistance was due to the priming of commonly used marker genes of pattern-triggered immunity (PTI; *WRKY53*, *FLG22-INDUCED RECEPTOR KINASE1 (FRK1)* and *NDR1/HIN1-LIKE10 (NHL10)*). Indeed, enrichment for epigenetic marks associated with transcriptional activation, such as H3K4me₂ and H3K4me₃, at PTI-responsive genes was observed after the exposure to recurrent stress, resulting in an enrichment of RNA polymerase II and a primed transcription in response to a subsequent bacterial infection. Collectively, these works on somatic stress memory promote the idea that, in plant, the environmental history can shape/modulate the response to stress, providing a mechanistic link between histone methylation and gene priming.

5.2. Transgenerational stress memory

The transgenerational stress memory refers to the transmittance of certain environmental responses from one generation to the next, thus providing the offspring of environmentally challenged plants with an adaptive advantage for better fitness (i.e. improve plant stress tolerance and impart developmental flexibility; [143]). Compared with DNA methylation and RNA interference (RNAi), very few studies suggest the involvement of histone methyltransferases and histone methylation changes in this process [144]. In *Arabidopsis*, changes in DNA methylation, histone modifications and gene expression were followed in the progeny of plants exposed to salt stress over one generation [145]. Although the DNA from the progeny of plants exposed to salt stress was globally hypomethylated, the majority of genes and promoters

causing methylation changes were hypermethylated and lowly expressed. In addition, DNA hypermethylation was correlated with an increased level of the repressive mark H3K9me2. Among these hypermethylated genes, a large number was encoding different histone methyltransferases, such as the *Arabidopsis* *SU(VAR)3-9* homologues *SUVH2*, *SUVH5*, *SUVH8*, involved in H3K9 methylation, or the PRC2 subunit *CURLY LEAF (CLF)*, involved in H3K27 methylation. Following this work, the progeny of heat-stressed plants was used to explore epigenetic variations under both normal and stressed conditions, in comparison to the progeny of control plants [146]. Similarly to salt stress, the progeny of plants exposed to heat stress had a global decrease of genomic DNA methylation and a reduced expression of several *SUVH* genes, which correlated with their enrichment in H3K9me2. Together, the hypermethylation of *SUVH* genes in the progeny of stressed plants may represent a protective mechanism against hypermethylation of the entire genome. Interestingly, in both works [145, 146], the transposon expression was elevated in the progeny of stressed plants. Because main targets of the *SUVH* pathway are transposable elements [24], the authors proposed that a decrease in the expression of *SUVH* genes might contribute to transposon activation, which at opportune times can create intragenomic potential upon transposition to facilitate adaptation in response to environmental changes [147]. In summary, these works suggested a role for histone methylation in the inheritance of stress memory; however, whether histone methylation changes are heritable through multiple generations and whether they sustain the acquisition of adaptive traits is still a matter of debate [148]. However, the evidence to date favours the view that stress-induced transgenerational changes in chromatin might increase the survival chances of the plant species, rather than each individual, by broadening the phenotypic plasticity and the genetic variation within the population [149, 150].

6. Discussion and perspectives

Recent advances, especially in *Arabidopsis*, have uncovered that chromatin remodelling through histone methylation changes are not only restricted to developmental needs but also an integral part of the very complex cascade of events that lead to abiotic/biotic stress tolerance, resistance and short-/long-term memory. Currently, a preliminary view is emerging, indicating that histone methylation changes, providing specific chromatin configurations, can be classified into several interrelated categories when involved in stress responses (Fig. 1): (i) histone methylation changes that are basally present on stress-related genes to establish a 'permissive' chromatin state that may either limit the spreading of repressive chromatin marks and/or potentiate a rapid transcriptional induction upon need; (ii) histone methylation changes that are transiently induced from an inactive or a permissive chromatin state by stress, to either facilitate the transcriptional initiation and/or reinforce transcription of stress-responding genes, and finally, histone methylation changes that are established in response to a stress; (iii) maintained for a certain time during the lifespan of an individual (i.e. somatic memory) or (iv) transmitted to one or more subsequent generations (i.e. transgenerational memory).

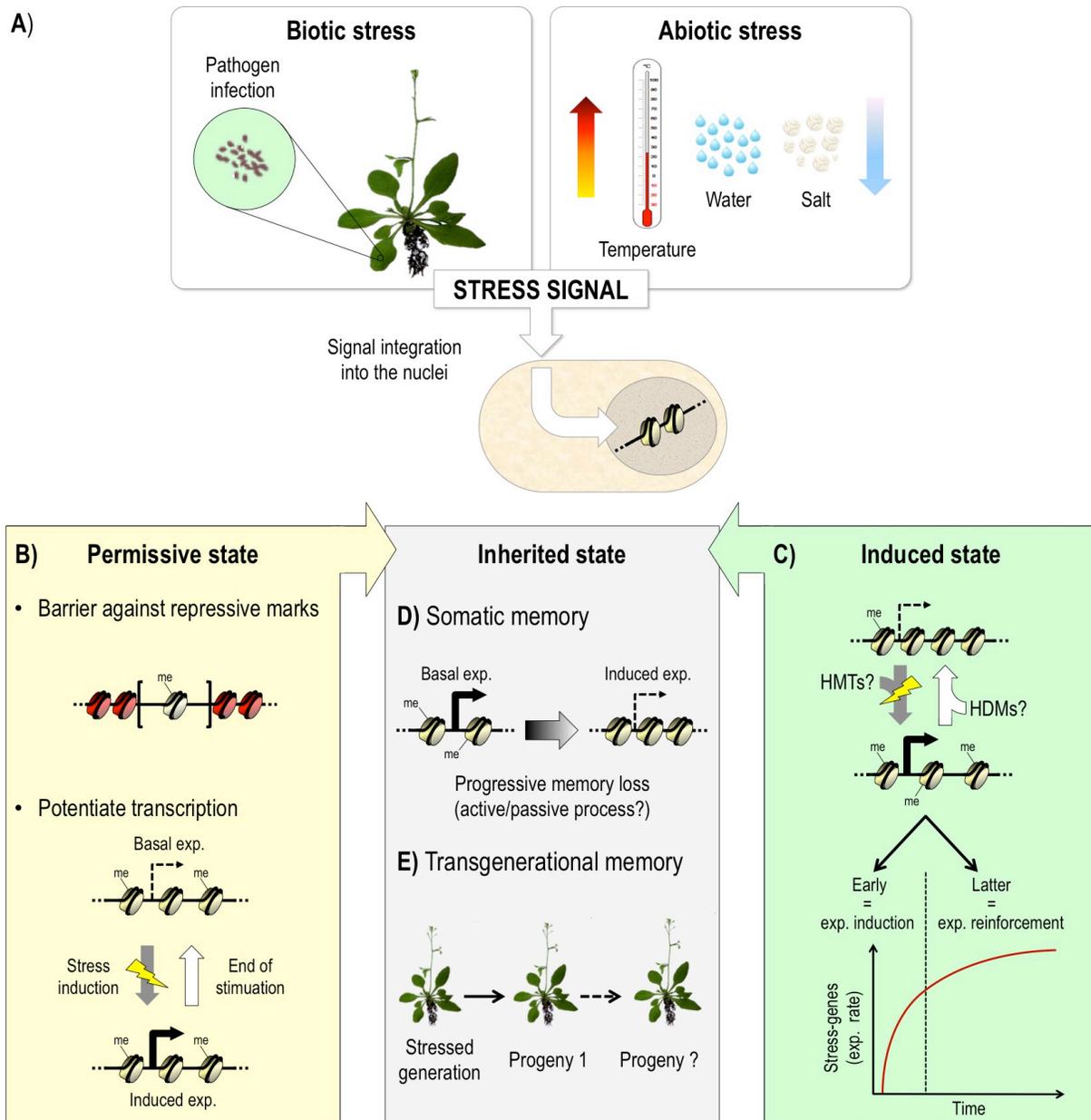


Figure 1. Hypothetical model depicting the role of histone methylation/demethylation in regulating plant stress responses. (A) Plants exposed either to biotic or abiotic stresses integrate the signal stress into the cell nuclei, where it affects the chromatin structure through histone methylation changes. According to our knowledge, these histone methylation changes can be classified into several interrelated categories. (B) The permissive state represents a more loosened chromatin state that will either offer a protection against repressive marks (represented with nucleosomes in red) and/or potentiates a rapid transcriptional induction upon stress induction. (C) The induced state represents histone methylation changes that are transiently induced by a stress signal. If methylation changes occur early during the stress-response process, they might participate to the transcriptional induction of stress-responding genes, while if they occur later, they might reinforce the transcription of stress-responding genes. Both permissive and the induced states can be maintained allowing a faster and/or stronger transcriptional induction of stress-responding genes upon a subsequent challenge. The memorized chromatin state can be maintained (D) for a certain time during the lifespan of an individual and referred as the somatic memory, or (E) transmitted to one or more subsequent generations and referred as the transgenerational memory.

Nonetheless, this emerging view is facing many gaps, inaccuracies and divergences, mainly related to numerous difficulties inherent to the study of such a dynamic and acute process. In this respect, plants in nature are usually challenged simultaneously by different kinds of stresses. Responses to these stress combinations are largely controlled by different signalling pathways that can interact in a non-additive manner, producing effects that could not have been predicted from the study of either stress individually [151, 152]. The occurrence of simultaneous biotic and abiotic stresses introduces an added degree of complexity that requires stresses to be imposed simultaneously and to treat each set of environmental conditions as an entirely new stress. For this reason and to clarify the mechanism behind the regulation of stress responses by histone methylation changes, there is a strong necessity to intensify our investigations. For instance, the correlation between histone methylation/demethylation and stress responses remains elusive and clarifications will require in-depth dynamic approaches based on comparative analyses of both epigenomes and transcriptomes during stress responses. In parallel, current knowledge about the corresponding histone-modifying enzymes is still largely missing. This lack of knowledge is pending on the identification of different stress-responsive histone modifiers and will require large-scale screens and genetic analyses for the sensitivity of different histone methyltransferases/demethylases mutants to various stresses, combined or not. Among other factors governing stress-induced chromatin changes, almost nothing is known about the specific reader/effector that will recognize particular histone methylation sites in order to determine their functional and structural outcome. An effort in this direction will most likely benefit the comprehensive understanding of the fundamental mechanisms connecting histone methylation changes with the modulation of transcription of stress-responsive genes, subsequently enabling plant to withstand stress. Higher-resolution chromatin studies are undoubtedly required to reveal the targeted stress-responsive genes and the specific sites of histone methylation/demethylation. Nevertheless, investigation of the direct effects of histone methylation/demethylation in plants is difficult. One reason is that plant genomes harbour high-copy number of histone genes (e.g. the *Arabidopsis* genome comprises 47 genes that encode 33 different core histone proteins; www.chromdb.org) and the incorporation/modification of such variants can result in the formation of chromatins with particular properties and functions [153–155]. Although ChIP assays have proven valuable in helping to identify histone methylation changes, many antibodies used to detect these changes have been so far unable to distinguish between different variants. New technologies (e.g. generation of mutants with point mutations targeting amino acid in the N-terminal tail of histone using the clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPER-associated (Cas) system) [156] will need to be explored to unravel histone methylation changes of specific histone variants and their functions. Another challenge is that plants consist of many functionally specialized tissues and cell types, each with its own unique epigenome, transcriptome and proteome. Until now, histone methylation changes induced by stresses were exclusively addressed in entire plant or organs, meaning that the obtained profiles most likely reflect the consensus of multiple tissue- or cell-specific profiles that may differ. New methods allowing the mapping of chromatin features in specific tissue/cell types such as the one described by Wang and Deal [157] will be decisive for determining the cell-/tissue-specific chromatin alterations involved

in a particular stress response. Finally, as plants have finite resources that must be balanced between growth and defence against stresses, often resulting in a growth or yield penalty, histone methylation changes in response to stress should be integrated in a more global developmental view, taking into account the involvement of several histone methyltransferases/demethylases in various processes such as root growth, flowering time, floral organogenesis, gametophyte or embryo formation [33]. Finally, understanding such regulatory network is an essential step to provide both novel paradigms and potential tools for further exploitation towards sustainable agriculture.

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