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Current Opinion in Plant Biology

Histone methylation in epigenetic regulation and temperature responses

Kaixuan He[1,2], Xiaofeng Cao[1,2] and Xian Deng[1]

Methylation of histones on different lysine residues is dynamically added by distinct writer enzymes, interpreted by reader proteins, and removed by eraser enzymes. This epigenetic mark has widespread, dynamic roles in plant development and environmental responses. For example, histone methylation plays a key role in mediating plant responses to temperature, including alterations of flowering time. In this review, we summarize recent advances in understanding the mechanism by which histone methylation regulates these processes, and discuss the role of histone methylation in temperature responses, based on data from *Arabidopsis thaliana*.

Addresses

[1] State Key Laboratory of Plant Genomics and National Center for Plant Gene Research, CAS Center for Excellence in Molecular Plant Sciences, Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Beijing 100101, China

[2] University of Chinese Academy of Sciences, Beijing 100049, China

Corresponding authors: Cao, Xiaofeng (xfcao@genetics.ac.cn), Deng, Xian (xdeng@genetics.ac.cn)

Current Opinion in Plant Biology 2021, **61**:102001

This review comes from a themed issue on **Epigenetics**

Edited by **Mary Gehring** and **François Roudier**

For a complete overview see the Issue and the Editorial

Available online 25th January 2021

https://doi.org/10.1016/j.pbi.2021.102001

Introduction

Epigenetic regulation, that is, heritable changes in gene expression without DNA sequence alteration, involves diverse molecular mechanisms, including DNA methylation, histone modification, histone variants, chromatin remodeling, and noncoding RNAs [1]. Nucleosome is the basic subunit of chromatin, which is composed of an octameric complex of the core histone proteins containing one H3/H4 tetramer and two H2A/H2B dimers wrapped with genomic DNA. Histone modification is one of the most important and complicated epigenetic regulatory mechanisms in eukaryotes. In this epigenetic mechanism, cellular enzymes place various post-translational modifications on core histones, including acetylation, methylation, phosphorylation, ubiquitination, sumoylation, and glycosylation [2]. These covalent modifications (and their crosstalk) play an indispensable role in chromatin-dependent processes such as chromatin structure, DNA replication, recombination, repair, transcriptional regulation, and mRNA processing, thus further affecting multiple aspects of various physiological and developmental processes [2–4].

Histone methylation is mainly deposited on lysine (K) and arginine (R) residues of core histone tails and is dynamically regulated by histone methyltransferases (writers), which add marks, and histone demethylases (erasers), which remove marks. Moreover, effector proteins (readers) bind to the histone modifications and interpret the information into functional outcomes [2]. Current research on histone methylation mainly focuses on histones H3 and H4, in which H3K4, K9, K27, and K36 are modified by mono-methylation, di-methylation, and tri-methylation, as identified by mass spectrometry [3,5]. Histone methylation provides unique and specific signals for gene expression, in which H3K4 and K36 tri-methylation are associated with transcriptional activation and H3K9me2 (mainly in plants) and K27me3 methylation are associated with transcriptional repression. Genome-wide epigenetic profiling has revealed how histone methylation is associated with gene expression, but the mechanism of dynamic regulation of histone methylation and their crosstalk remains an active area of research.

Environmental temperature has crucial effects on the growth and development of plants, and therefore on the yield and quality of crops. On the one hand, environmental temperature directly influences plant physiological activities and biochemical reactions, which further affect growth and development. On the other hand, temperature changes lead to changes in other factors, such as humidity, which induce additional physiological responses [6–9]. Plants have evolved multiple mechanisms to constantly sense environmental temperature and acclimate to natural daily and seasonal changes. Emerging research has highlighted the effect of environmental temperature on plant development and histone methylation has been reported to be involved in temperature responses and the resulting phenological adaptation.

Here, we review the molecular mechanisms of histone methylation, demethylation, and recognition in *Arabidopsis* discovered in recent years, and the role histone methylation plays in environmental temperature responses. Understanding the dynamics of histone methylation and its role in thermosensory responses is an important

stepping stone towards mechanistic insight into the complexity of the epigenetic landscape.

Mechanisms regulating histone methylation

H3K4 methylation

As one of the most widespread histone modifications in *Arabidopsis*, H3K4 methylation covers more than two-thirds of the genes in the genome, and H3K4me3 and H3K4me2 usually associates with gene activation [10]. H3K4me2 and H3K4me3 are mainly located in promoters and 5′ genic regions, while H3K4me1 is concentrated within the gene body [10].

TRITHORAX (TRX) and the SET families are responsible for H3K4me3 deposition in *Arabidopsis*. SET family member SET DOMAIN GROUP PROTEIN2 (SDG2) operates globally across the genome [11,12]. However, the TRX family members ARABIDOPSIS TRITHORAX 1 (ATX1) [13–16] and ATX2 [16] mediate locus-specific addition of H3K4me3 and H3K4me2, respectively. ATX1-mediated locus-specific H3K4me3 functions in multiple processes, such as floral organ development [17], flowering time control [18,19], and dehydration and endoplasmic reticulum (ER) stress responses [20,21]. ATX1-mediated H3K4me3 also affects transcript elongation by phosphorylated elongation factor [13,18]. Although work in *Drosophila* reported that TRX can be recruited to TrxG Repressive Elements (TREs) via DNA binding proteins [22], whether TREs exists in plants remains unclear.

The dynamic balance of H3K4 methylation in the genome is also regulated by the H3K4me3 demethylases [23]. In *Arabidopsis*, the jumonji domain-containing Lysine (K)-Specific Demethylase 5/Jumonji and ARID Domain Protein (KDM5/JARID) subfamily members JUMONJI14 (JMJ14) [24–26], JMJ15 [27,28], JMJ16 [29], JMJ17 [30•], and JMJ18 [31], demethylate H3K4 and function in various biological processes, such as flowering [25,28,31], gene silencing [32,33], leaf senescence [29], salt tolerance [27], and dehydration stress responses [30•]. Among the KDM5 subfamily members, the recognition and catalytic mechanisms of JMJ14 have been well studied. The C-terminal FYR domain of JMJ14 interacts with NAC050 and NAC052, two plant-specific NAC (NAM, ATAF, CUC) domain-containing transcription factors, facilitating its targeting to specific DNA motifs [26,34]. Structural analysis of the catalytic domain of JMJ14 revealed that H3R2 and H3Q5 are essential for substrate selectivity, suggesting a common substrate selection mechanism among plant and animal KDM5 subfamily demethylases [35••].

H3K36 methylation

Histone H3K36 can be mono-methylated, di-methylated, and tri-methylated. H3K36me3 is an important mark for transcriptional elongation, as it is positively correlated with the transcription rate [2,36]. Genome-wide analysis in *Arabidopsis* found H3K36me3 in the 5′ end of the gene body, peaking near the transcription start site (TSS), in contrast to its transcription terminal site (TTS) enrichment in animal genes [37], indicating the intricate and divergent mechanisms for H3K36 establishment during evolution.

Work in *Arabidopsis* identified some SDGs as responsible for H3K36 methylation. SDG4 [38] and SDG26 [39] specifically function in floral organ specification and flowering time control, respectively. The major H3K36 methyltransferase SDG8 [40] is involved in diverse biological processes, such as plant and seed size [41,42], flowering [43••] and fertility [40], light and carbon responses [44], shoot branching [45,46], pathogen defense [47], and nitrogen responses [48•].

Interestingly, H3K36me3 mediated by SDG8 also affects co-transcriptional RNA processing. The nuclear mRNA cap-binding complex interacts with SDG8 and ATX1, combining H3K36me3 and H3K4me3 with co-transcriptional mRNA processing and cap preservation of mRNA, resulting in high levels of mature mRNA [49]. SDG8-mediated H3K36me3 is required for nitrogen-responsive RNA processing and ambient temperature-induced alternative splicing, thus influencing plant responses to nitrogen [48•] and temperature [43••]. Although the H3K36 methyltransferases are well characterized, the demethylases acting on H3K36 methylation remain to be found. Therefore, identifying H3K36 demethylases will help us further understand the dynamic regulation of H3K36 methylation in plants.

H3K9 methylation

In *Arabidopsis*, the main form of H3K9 methylation is K3K9me2, with only low levels of H3K9me3 observed [50]. H3K9me2 is enriched in pericentromeric heterochromatin containing transposons and repeat clusters, and it co-regulates the silencing of transposons and genome stability with DNA methylation [51–54]. KRYPTONITE (KYP)/SUVH4, SUVH5, and SUVH6, three *Arabidopsis* homologs of *Drosophila* Su(var)3-9 containing an SRA domain, bind to methylated DNA and catalyze the addition of H3K9me2 in a self-reinforcing feedback pattern [50,55–58]. Distinct from other Su(var)3-9 homologs, the *Arabidopsis* Su(var)3-9 RELATED (SUVR) protein SUVR5 establishes the heterochromatic state by depositing H3K9me2 through directly recognizing DNA with its zinc finger domains, repressesing a subset of stimulus-response genes [59].

H3K9 methyltransferases and demethylases regulate the dynamics of H3K9 methylation. INCREASE IN BONSAI METHYLATION 1 (IBM1/JMJ25) is a JmjC domain-containing histone demethylase that catalyzes H3K9 demethylation [60,61]. IBM1 protects active genes from silencing caused by heterochromatin formation and

spreading H3K9 and DNA methylation from flanking transposons [61]. IBM1 regulates multiple aspects of plant development, such as leaf morphology and reproduction [61], suggesting it has an essential role in limiting heterochromatin formation and ensuring normal gene expression.

In eukaryotes from fission yeast to mammals, Heterochromatin Protein 1 (HP1) recognizes H3K9 methylation to maintain heterochromatin [62]. However, although H3K9 methylation exists in *Arabidopsis*, the genuine HP1 homologs that recognize this modification have remained elusive. However, recent work has solved this long-standing mystery. *Arabidopsis* AGENET DOMAIN CONTAINING PROTEIN 1 (ADCP1), a plant-specific protein containing three tandem Agenet domains, is a multivalent H3K9me2 reader that, mediates the maintenance of H3K9 and DNA methylation, and transposon silencing. Interestingly, similar to human and fly HP1, ADCP1 participates in heterochromatin phase separation, in which molecules condense to form membraneless organelles and compartmentalize biochemical reactions, which is crucial for heterochromatin formation [63••,64••].

H3K27 methylation

In *Arabidopsis*, H3K27 can be mono-methylated, di-methylated and tri-methylated, and H3K27me1 and H3K27me3 have been intensively studied. ARABIDOPSIS TRITHORAX-RELATED PROTEIN 5 (ATXR5) and ATXR6 catalyze H3K27 mono-methylation (H3K27me1) [65], which is usually present in heterochromatin. H3K27me1 participates in inhibiting transcription and preventing abnormal DNA replication in heterochromatin [65,66]. By contrast, H3K27me3, a facultative repressive chromatin mark mediated by Polycomb repressive complexes (PRCs), is mostly distributed in the transcribed regions within euchromatin, covering more than 7000 genes. H3K27me3 is crucial for tissue-specific gene expression and developmental regulation [67–69].

The highly conserved Polycomb group proteins (PcGs) form two major multi-protein complexes, PRC1 and PRC2, which are important for plant development. The Enhancer of zeste (E(z)) subunit of PRC2 catalyzes the addition of H3K27me3, and the Polycomb (Pc) protein in PRC1 specifically binds H3K27me3 [70–74]. Distinct combinations of PcGs preferentially regulate different developmental processes by repressing tissue-specific gene expression, and specific transcription factors (TFs) modulate their target specificity [75]. In particular, the composition of the *Arabidopsis* PRC2 complex is also complicated, at least including EMBRYONIC FLOWER (EMF), VERNALIZATION (VRN) and FERTILISATION INDEPENDENT SEED (FIS) complexes, responsible for reproductive growth, flowering control, and embryonic development, respectively [76,77]. In addition, DNA methylation [78] and DNA replication [79] also affect PRC2-mediated H3K27me3 and cooperate in gene repression. These observations suggest that H3K27me3 mediated by specific PcGs and the chromatin environment is important for gene expression and plant development.

In flies and mammals, multiple TFs help recruit PRC2 to the Polycomb Repressive Elements (PREs) to regulate H3K27me3 spreading and gene repression [80–82]. Recent work has addressed the long-standing question of PRC2 recruitment in *Arabidopsis* [77,83]. Several classes of TFs recognize a number of sequence motifs, such as *GAGA* and *telobox cis*-elements, for PRC2 recruitment and H3K27me3 deposition [84,85]. Although this is an evolutionarily conserved model, the diverse composition of PRC2 and the natural variation of PREs among different ecotypes add complexity to this regulatory mechanism.

The dynamic balance of H3K27 methylation is regulated by PcGs and H3K27me3 demethylases, mainly EARLY FLOWERING 6 (ELF6/JMJ11), RELATIVE OF EARLY FLOWERING 6 (REF6/JMJ12), and JMJ13 [86,87,88••]. These demethylases restrict the H3K27me3 mark and promote gene activation spatially and temporally during plant development [89••]. Interestingly, these H3K27me3 demethylases have distinct targeting mechanisms. REF6 recognizes specific DNA motifs via its C_2H_2 zinc finger domains [90,91] and is required for recruitment of the chromatin remodeler BRAHMA at some loci [92]. Other chromatin factors also affect REF6 targeting, such as non-CG DNA methylation [93••] and open/closed chromatin status [90]. ELF6, by contrast, is recruited to a specific locus by the TF BRASSINAZOLE-RESISTANT1 (BZR1) to downregulate levels of H3K27me3 on the brassinosteroid (BR)-responsive element of *FLC* in the presence of BR [94•]. JMJ13 specifically recognizes H3K27me3 by hydrogen bonding and hydrophobic interactions, and the flanking residues between H3R26 and H3P30 are essential for H3K27me3 recognition and substrate selectivity [88••]. These distinct and diversified targeting mechanisms are tightly controlled to ensure the proper balance between repressive chromatin status and tissue-specific gene activation during plant development [87,88••,89••,90,94•,95,96].

Crosstalk between histone marks

Every chromatin mark has a characteristic genome-wide landscape and correlates with some kind of chromatin state, traditionally thought of as active or inactive. For instance, H3K4me3 occurs in active chromatin regions, while H3K27me3 is associated with developmentally repressed loci or downregulation of highly expressed genes. However, the discovery of bivalent chromatin carrying both active and repressive histone marks and the cross-talk between histone methylation and other chromatin marks (such as histone variants and DNA methylation) [97] have shown that this 'black or white' logic is too simple [1]. Indeed, many studies have shown the prevalence of bivalent chromatin in diverse cell types

and organisms, fine-tuning 'poised' genes to be active or inactive [98,99,100••].

In *Arabidopsis*, the bivalent chromatin marks H3K4me3 and H3K27me3 exist on individual genes across the whole genome [100••,101,102]. Interestingly, recent studies identified two plant-specific histone readers, EARLY BOLTING IN SHORT DAY (EBS) and SHORT LIFE (SHL), which recognize both H3K27me3 and H3K4me3 via their bromo-adjacent homology (BAH) and plant homeodomain (PHD) domains, respectively [103••,104••,105••]. The recognition of these two antagonistic histone marks by two distinct domains of a single reader protein can be regulated by certain developmental or environmental signals and may balance the chromatin landscapes to quickly fine-tune gene expression, thus playing crucial role in plant development and responses to environmental challenges.

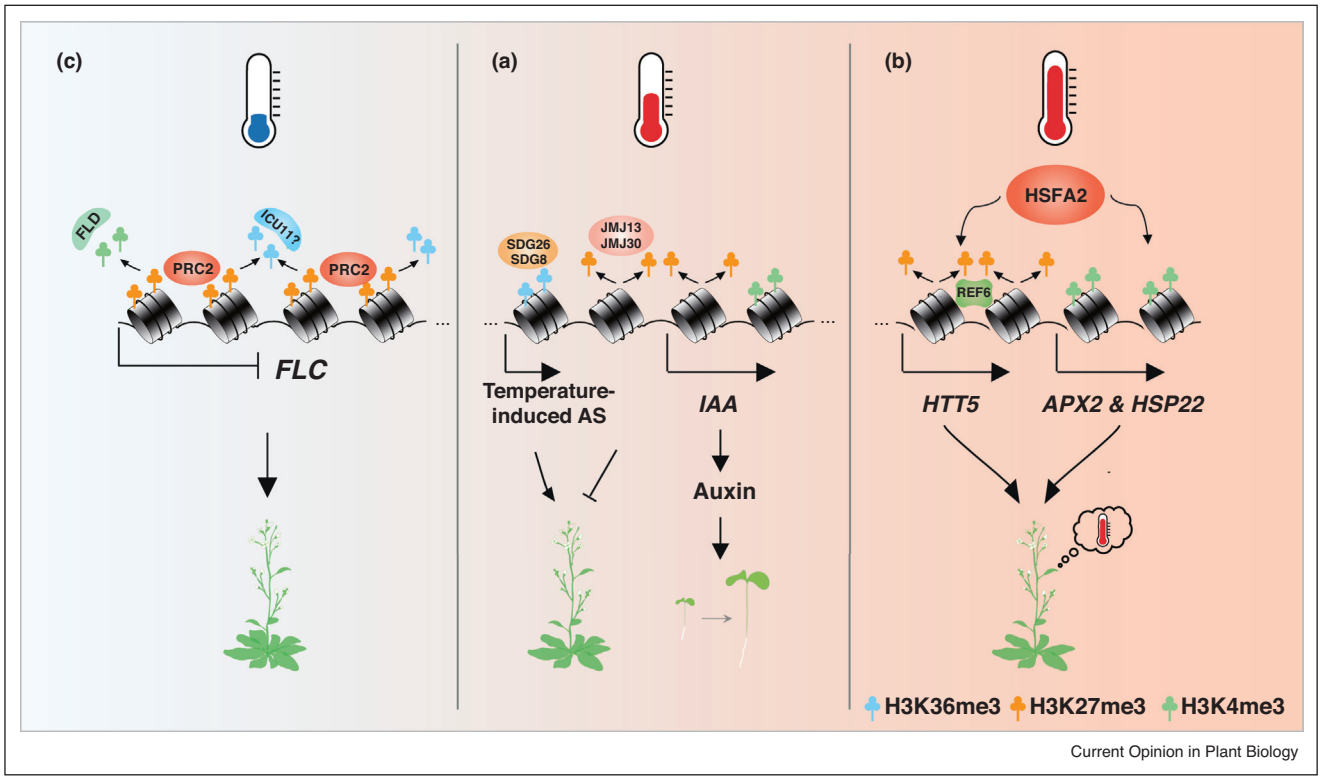
Histone methylation in temperature responses

Temperature is one of the major environmental signals controlling plant development, geographical distribution, and seasonal behavior. Being sessile organisms, plants are sensitive to daily and seasonal changes of ambient temperature, adjusting their growth and development accordingly to improve survival. Histone methylation is involved in the transcriptional response to temperature changes.

From ambient temperature to heat stress

Ambient temperature, especially warm ambient temperatures (22–28°C) below the heat-stress range for *Arabidopsis*, induces dramatic morphological changes in plants. These changes, such as hypocotyl and petiole elongation, leaf hyponasty, early flowering, and modulation of the circadian clock and immunity, are collectively termed thermomorphogenesis [106]. Thermomorphogenesis involves interconnected epigenetic, transcriptional, and co-transcriptional regulation mechanisms [106]. For instance, H3K36me3 is involved in regulating temperature-induced alternative splicing and temperature-dependent flowering time control in *Arabidopsis* (Figure 1a) [43••]. H3K36me3 links chromatin modifications, transcription rate, and co-transcriptional

Figure 1



The role of histone methylation in temperature responses.
(a) Warm ambient temperature leads to the deposition of H3K36me3 by SDG8 and SDG26 on flowering-related genes, regulating temperature-induced alternative splicing (AS) and temperature-dependent flowering time control. Warm ambient temperature induces JMJ13 and JMJ30 to remove H3K27me3 and repress flowering. Warm ambient temperature also affects histone methylation levels of auxin biosynthetic and responsive genes, resulting in warm temperature-induced hypocotyl elongation.
(b) Heat stress induces HSFA2, which forms a heritable feedback loop with REF6 to activate transgenerational thermomemory for flowering. Heat stress-induced HSFA2 also promotes the deposition of H3K4me3 at heat memory genes.
(c) During vernalization, H3K4me3 and H3K36me3 are removed from *FLC* locus, and H3K27me3 is deposited by PRC2 to repress *FLC* expression.

regulation in the context of fluctuating ambient temperature [107]. High ambient temperature-induced hypocotyl elongation depends on local auxin biosynthesis and intercellular transport [108,109], in which chromatin remodeling factors, transcription factors, and RNA binding proteins affect the histone methylation levels of auxin biosynthetic and responsive genes (Figure 1a) [108,110,111].

Increased ambient temperatures accelerate flowering in *Arabidopsis* and dynamic histone methylation functions in high ambient temperature-mediated flowering control. JMJ13 acts as a temperature and photoperiod-dependent flowering repressor, and *JMJ13* expression is induced by long-day conditions and high ambient temperatures (Figure 1a) [88••]. JMJ30 also functions as a H3K27 demethylase, removing H3K27me3 on the *FLC* promoter and thus preventing the extreme precocious flowering caused by high ambient temperature (Figure 1a) [112]. These observations suggest that chromatin modifications tightly control the balance between vegetative growth and reproductive growth at high ambient temperature.

When the temperature is above 30°C, plants induce a series of heat responses to limit heat-related damages, such as membrane disruption, protein unfolding, and oxidative damage [113]. The HEAT SHOCK TRANSCRIPTION FACTOR (HSF) family is activated immediately after heat stress and is responsible for the heat responses [114]. After a nonlethal heat exposure, plants can acquire heat stress memory, an active process that enables plants to better response subsequent heat stress (priming). In this priming process, the HSFA2 and REF6 activate each other, forming a heritable feedback loop that plays an important role in transgenerational thermomemory for flowering (Figure 1b) [115,116••].

HSFA2 is also required for the regulation of heat stress memory genes, such as those encoding small HSPs and ASCORBATE PEROXIDASE 2 (APX2), which are reinduced by a recurring heat stress (Figure 1b) [117]. Interestingly, these heat stress memory genes are decorated with H3K4me2/3 during the memory process; this requires HSFA2 and renders the target loci more sensitive to subsequent heat stress [117,118]. In addition to heat stress, H3K4me2 and H3K4me3 are also associated with transcriptional memory in systemic acquired resistance and drought stress [119]. This suggests that the stress-primed H3K4me2/3 deposition at memory-related genes is common and crucial for the activation of stress-responsive genes after stress. However, further study will be required to reveal whether the relationship between histone marks and stress responses is causal or correlational.

From vernalization to cold acclimation

Flowering regulation includes powerful genetic and epigenetic control loops. Winter-annual plants must go through vernalization, a long-term cold exposure (months to weeks), to repress floral repressor genes thus accelerate the transition to flowering [120]. Vernalization is needed for *Arabidopsis* in the vegetative stage, and the rapidly dividing cells, such as shoot apical meristem and young leaves, are sensitive to vernalization [58].

How plants respond to vernalization provides a well characterized example of how dynamic histone methylation affects this developmental transition [121]. The floral repressor gene *FLC* (encoding a MADS box-containing protein), is the key locus that perceives and responds to seasonal cues and determines the floral transition [122]. *FLC* is regulated at diverse levels, including the chromatin, transcription, co-transcription, and RNA metabolism levels. The expression of *FLC* mainly depends on the switch between opposing histone states of *FLC* chromatin (Figure 1c) [121,123,124].

In winter-annual *Arabidopsis* before vernalization, FRIGIDA (FRI) is as the major contributor to *FLC* activation [125]. FRI acts in a supercomplex, binds to the *FLC* chromatin, and enhances the binding of COMPASS-like (ATX1) and EFS, which deposit the active histone marks H3K4me3 and H3K36me3, respectively [14,126–128]. The FRI supercomplex establishes a local active environment at *FLC*, leading to high *FLC* expression levels [129].

During vernalization, prolonged cold exposure induces plant homeodomain protein (PHD)–PRC2 mediated H3K27me3 enrichment at *FLC* and thus quantitative silencing of *FLC* [121,130]. *Cis*-elements, *trans*-acting factors and long noncoding RNAs (lncRNAs) ensure the targeting of the Polycomb machinery to *FLC* for H3K27me3 deposition (Figure 1c) [83,121,131]. In detail, when winter is coming, a PRC2 containing SWINGER (SWN) [132••], the PRC2 accessory protein INCURVATA11 (ICU11, a candidate histone demethylase) [133••], and the PHD proteins VERNALIZATION INSENSITIVE 3 (VIN3) [134,135••] and VERNALIZATION 5 (VRN5) [136], produce a reversible, metastable silenced state at *FLC* by locally increasing the H3K27me3 levels in a small region (nucleation region) within *FLC* [132••]. This specific PRC2 induces this state at *FLC* with the assistance of a *cis*-regulatory DNA element named the cold memory element [137,138], the B3 transcriptional regulators VAL1 and VAL2 [137–139], and three kinds of lncRNAs, *COOLAIRs* [140,141], *COLDAIR* [142], and *COLDWRAP* [143].

After winter, CURLY LEAF (CLF) and the PHD protein LIKE HETEROCHROMATIN PROTEIN 1 (LHP1) establish long-term, stable silencing of *FLC* by spreading H3K27me3 across the *FLC* locus [132••]. *FLC* expression can be reset during embryo development by the H3K27me3 demethylase EARLY FLOWERING 6, the

H3K36 methyltransferase SDG8 [87,144], and the B3 domain transcription factors LEAFY COTYLEDON 1, LEAFY COTYLEDON 2, and FUSCA3 [145,146]. Therefore, the transitions from *FLC* activation to vernalization-mediated *FLC* silencing and *FLC* resetting in the next generation provide an elegant stepwise paradigm emphasizing the key roles of chromatin state switches in plant local adaption, phenological period, and geographical distribution.

The requirement for vernalization in winter-annual plants resulted from long-term adaptation to different locations. Extensive natural variation at the *FLC* locus across diverse *Arabidopsis* accessions facilitates fine-tuning of the vernalization requirement and responses and adaptation to the local environment [147,148]. *FLC cis* and noncoding polymorphisms in the nucleation region in the Northern Swedish accession Lov-1 results in instability of long-term Polycomb-mediated silencing and thus *FLC* reactivation after cold exposure [149,150]. Quantitative regulation of gene expression through *cis* polymorphism-mediated chromatin state variation could be a general mechanism explaining the evolutionary adaption across plants. In-depth studies of this system may provide mechanistic insights on epigenetic regulation in eukaryotes.

In contrast, the role of histone methylation in cold acclimation, a process that differs from vernalization and can be effectively achieved in several days, has been rarely reported. One example of histone methylation in cold acclimation is the regulation of two cold-responsive genes (*COR15A* and *ATGOLS3*) by H3K27me3, in which cold exposure leads to decrease of H3K27me3 on *COR15A* and *ATGOLS3* in both histone occupancy–dependent and –independent ways [151]. Further studies of histone methylation in cold responses will make it prominent in plant adaptability.

Perspective

Researchers around the world have made great progress in exploring the molecular mechanisms of epigenetic regulation, with far-reaching implications for understanding the complexity and flexibility of epigenetic control, and normal development and adaptation. These covalent modifications and their cross talk are crucial for chromatin-dependent processes, such as chromatin structure, DNA replication, recombination, repair, transcriptional regulation, and mRNA processing. New discoveries and approaches have widely expanded our understanding of epigenetic regulatory mechanisms. For instance, phase separation, a physicochemical process in which molecules condense to form membraneless organelles and compartmentalize biochemical reactions, has given us another understanding of dynamic cellular processes, human diseases, and stress responses [152]. The spatiotemporal dynamics of three-dimensional (3D) chromatin architecture defined by high-throughput chromosome conformation capture (Hi-C) has also attracted much attention and provided insight into epigenetic regulation [153]. In addition, studies using transposase-accessible chromatin sequencing (ATAC-seq) [154], Cleavage Under Targets and Tagmentation (CUT and TAG) [155], global RNA interactions with DNA by deep sequencing (GRID-seq) [156], and native elongation transcript sequencing (NET-seq) [157•] will improve our understanding of the epigenetic landscape at more specific levels. It is worthy to note that epigenetic modification is highly dynamic in different developmental stages, diverse cell types and response to environmental stimuli. However, most of the datasets were a complex landscape from mixed tissues of *Arabidopsis*, resulting in the potential of nonspecific and misleading results. Application of single-cell strategies for epigenomic profiling will provide insight into the complexity and variability of epigenetic regulation, and help to identify the specific cells or tissues that most sensitive to temperature changes, thus improving our understanding on epigenetic regulation in response to temperature [5,158].

We also note that histone methylation is highly dynamic during plant development and in response to environmental signals, thus requiring multifunctional mechanisms for the complexity and flexibility of epigenetic regulation. Besides directly activating or repressing gene expression, histone methylation is also involved in many other cellular processes, such as alternative splicing [43••], RNA modification (e.g. m^6A) [159], and interaction with other histone modifications. This reveals cross talk between histone methylation and co-transcriptional events, thus adding another layer of complexity to the regulation of gene expression in normal and adaptive biological processes.

Recent studies on the regulatory mechanisms of plant responses to temperature changes have suggested the essential role of complex epigenetic regulatory networks in these processes. In the context of global climate change, studying whether and how stress memory is transmitted through cell divisions and across generations will be of interest for rationally breeding well-adapted crops prepared for unexpected stresses.

Conflict of interest statement

Nothing declared.

Acknowledgements

We apologize to all of our colleagues whose work could not be cited due to the size limitations of this manuscript. This work was supported by the National Natural Science Foundation of China (grants 31788103 to X. C., 31770323 and 31970193 to X. D.), the Chinese Academy of Sciences (Strategic Priority Research Program XDB27030201 and QYZDY-SSW-SMC022 to X.C.), the Youth Innovation Promotion Association, CAS (2018131), and the State Key Laboratory of Plant Genomics.

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Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

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