A G(enomic)PositioningS(system) for Plant RNAPII Transcription

Xueyuan Leng, Quentin Thomas, Simon Horskjær Rasmussen and Sebastian Marquardt

Copenhagen Plant Science Centre
Department of Plant and Environmental Sciences
University of Copenhagen
Bülowsvej 34, 1870 Frederiksberg C
Denmark

sebastian.marquardt@plen.ku.dk

https://cpsc.ku.dk/meet-the-scientists-page/sebastian-marquardts-group/

Twitter: @marquardtlab

Histone PTM, RNA Polymerase II, ChIP-seq, chromatin, epigenetics, transcriptional interference
ABSTRACT

Post-translational modifications (PTMs) of histone residues shape the landscape of gene expression by modulating the dynamic process of RNAPII transcription. The contribution of particular histone modifications to the definition of distinct RNAPII transcription stages remains poorly characterized in plants. Chromatin Immuno-precipitation combined with next-generation sequencing (ChIP-seq) resolves the genomic distribution of histone modifications. Here, we review histone PTM ChIP-seq data in *Arabidopsis thaliana* and find support for a Genomic Positioning System (GPS) that guides RNAPII transcription. We review the roles of histone PTM “readers”, “writers” and “erasers”, with a focus on the regulation of gene expression and biological functions in plants. The distinct functions of RNAPII transcription during the plant transcription cycle may in part rely on the characteristic histone PTMs profiles that distinguish transcription stages.
MAIN TEXT

Histones: the coordinates for transcription?

Gene expression relies on different functions of RNA Polymerase II (RNAPII) during transcription. The separation of these functions defines different stages of RNAPII transcription: initiation, elongation and termination. The question how RNAPII recognizes the right time and position to execute a needed function remains an exciting research opportunity. In eukaryotes, genomes are organized in the form of nucleosomes that comprise of two copies of histones H2A, H2B, H3 and H4 [1]. N-terminal histone tail residues undergo extensive post-translational modifications (PTMs), including methylation (me), acetylation (ac) and ubiquitination (ub), which are associated with functional consequences on chromatin organization and gene expression (reviewed in [2, 3]). The establishment and maintenance of histone PTMs requires recognition by “reader” effector enzymes, deposition by “writer” enzymes and removal by “eraser” enzymes. Histone acetylation is mainly read by bromodomain (BRD) proteins, written by histone acetyltransferases (HATs) and erased by histone deacetylases (HDACs). Histone methylation is read by proteins with plant homeodomain (PHD) finger domain and “Royal Family” domains (e.g. Chromodomain and Tudor domain), written by histone methyltransferases (HMTs) and erased by histone demethylases (HDMs) [4, 5]. Similarly, histone ubiquitination is read by proteins with ubiquitin-binding domain (UBD) and modulated by histone ubiquitin ligases (ULs) and deubiquitinases (DUBs) [6]. Trios of “reader-writer-eraser” enzymes define the genomic localization of histone PTMs connected to RNAPII transcription.

Chromatin profiling techniques such as ChIP-chip [7], ChIP-seq [8], CUT&RUN-seq and [9] and CUT&Tag-seq [10] (see Box 1) revealed the genomic distribution of histone PTMs and variants associated with different RNAPII transcription stages. However, the causality of histone PTM and transcriptional consequences is actively debated [11]. On the one hand, histone PTMs can be instructive for RNAPII transcription (reviewed in [12]). On the other hand, the act of RNAPII transcription can shape the chromatin landscape [13-15]. Perhaps these hypotheses can be unified by the idea that the interplay between chromatin state and transcription forms a feedback loop. Here, we focused on how histone PTMs and variants serve as coordinates during RNAPII to identify the current position of transcription and to execute appropriate functions. Our review includes a comprehensive assessment of histone PTM ChIP-seq data in wild type Arabidopsis. 

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 18 March 2020
*Arabidopsis thaliana* (Col-0). We provide comparable metagene profiles that visualize the interplay between histone PTMs and RNAPII transcription stages (Figure 1A). These ChIP-seq data reflect the localization of histone PTMs in the whole plant under normal growth condition, regardless of cell-, tissue- or condition-specific histone patterns [16-18]. This review covers recent advances in understanding how plant gene expression is underpinned by a histone PTM-based Genomic Positioning System (GPS) that guides RNAPII through transcription stages.

**Histone PTMs define transcription stages**

RNAPII transcribes the DNA sequence of genes into mRNA. Analyses of the genomic distribution of RNAPII reveals different stages of the transcription process, known to form the RNAPII transcription cycle [19] (Figure 1A). Studies of nascent RNAPII transcription in *Arabidopsis thaliana* have informed events linked to the RNAPII transcription cycle in plants [20, 21]. RNAPII initiates transcription from transcription start sites (TSSs) in promoter regions. After initiation, RNAPII enters the gene bodies and elongates nascent RNA chains (early elongation). RNAPII usually stalls near the 5’-end of genes after initiation, a phenomenon known as promoter proximal RNAPII stalling. RNAPII then enters the productive elongation stage to complete nascent RNA production of the full transcript. When RNAPII passes poly-(A) site (PAS) sequences at 3’-end of genes, RNAPII stalls again to assist transcriptional termination.

RNAPII thus performs different functions in transcription stages that are coordinated with different co-transcriptional molecular events (e.g. capping, splicing and poly-adenylation). These considerations raise the question: what molecular system informs RNAPII of the current transcription stage during transcriptional progression? Chromatin Immuno-precipitation followed by next-generation sequencing (ChIP-seq) resolved the genomic distribution profiles of many histone post-translational modifications (PTMs) and variants. Interestingly, the deposition of different histone PTMs or variants is spatially associated with different stages of transcription (Figure 1A). The profile of histone PTMs may thus be connected to the definition of transcription stages that define distinct RNAPII activities.

**Histone PTMs and transcription initiation**

Transcription initiation controls the recruitment of RNAPII to promoters, and regulates the polymerase flux into the gene bodies. Transcription initiation relies on the assembly of the pre-initiation complex (PIC) including RNAPII and general transcription factors (GTFs) at promoters.
In yeast, PIC formation is facilitated by highly conserved general transcription factor II D (TFIID) and Spt-Ada-Gcn5 acetyltransferase (SAGA) complex [22]. TFIID and SAGA complexes both contain subunits with histone acetyltransferase (HAT) activity [23]. Consistently, histone acetylation represents a characteristic genomic signature of transcription initiation. In Arabidopsis, a pioneering ChIP-chip study established the enrichment of histone acetylation at histone H3 lysine 9 (H3K9ac) and lysine 27 (H3K27ac) near transcription start sites (TSSs) for many genes [24]. Later, an enrichment of additional histone acetylation modifications at histone H3 lysine 14, 18, 23, 36 and 56 (i.e. H3K14ac, H3K18ac, H3K23ac, H3K36ac and H3K56ac) and at histone H4 lysine 5, 8, 12, 16 and 20 (i.e. H4K5ac, H4K8ac, H4K12ac, H4K16ac and H4K20ac) near TSSs was determined by ChIP-seq in Arabidopsis [25-27]. In Arabidopsis, HAF1 and HAF2 (Histone acetyltransferase of the TAFII250 Family 1 and 2), the homologues to metazoan TFIID largest subunit gene TAF1 (TATA-binding Protein-Associated Factors 1), promote H3K9ac, H3K27ac and H3K4ac in promoter regions [28]. The acetyltransferase activity of SAGA is derived from its HAT module, represented by the GCN5 (General Control Non-repressed Protein 5) subunit (reviewed in [29]). Loss of function of Arabidopsis AtGCN5 reduces H3K9ac levels at promoter regions and results in gene repression [30-33]. Arabidopsis histone acetylation reader BRAT1 (Bromodomain and ATPase domain-containing protein 1) binds to histone H4 acetylation (H4ac) and presumably facilitates transcription initiation by modulating the chromatin environment in the transcriptionally silenced regions [34]. Similarly, Arabidopsis SWR1 (SWI2/SNF2-Related 1) complex subunit MBD9 (Methyl CpG-BINDING DOMAIN 9) and NPX1 (Nuclear Protein X1) read histone H3 acetylation (H3ac) and contribute to histone variant H2A.Z deposition which further recruits DNA demethylation machinery to activate transcription [35]. These results collectively underscore the potential roles of histone acetylation in regulating transcription initiation through events facilitating PIC assembly in plants.

Tri-methylation on histone H3 lysine 4 (H3K4me3) characterizes a well-studied chromatin modification associated with transcription initiation (Figure 1A). In Arabidopsis, H3K4me3 density across transcription units peaks at 5'-end of genes, and high levels of H3K4me3 are often correlated with gene expression [36, 37]. Intriguingly, Arabidopsis H3K4me3 readers EBS (EARLY BOLTING IN SHORT DAY) and SHL (SHORT LIFE) can both read active H3K4me3 and repressive tri-methylation on histone H3 lysine 27 (H3K27me3) [38, 39]; and the H3K27me3 reader PRC1 (Polycomb Repressive Complex 1) is also shown to have H3K4me3 binding.
property. The dual specificity may facilitate chromatin state switching to control transcription activity [40]. In metazoans, H3K4me3 facilitates the formation of PICs through the interaction with the TFIID subunit TAF3 [41]. In Arabidopsis, PIC formation correlates with H3K4me3, yet a direct role in PIC recruitment remains unclear. Deposition of H3K4me3 requires the function of ATX1 (ARABIDOPSIS TRITHORAX 1)/COMPASS-like complex in Arabidopsis. While PIC formation is dependent on the ATX1/COMPASS-like complex, it is independent of the H3K4me3 level [42-45]. Interestingly, a catalytically inactive ATX1 mutant that distinguishes the effect of the ATX1/COMPASS-like complex and H3K4me3 reveals defects in RNAPII elongation rather than initiation, arguing for a role of H3K4me3 in transcription elongation instead of initiation [42]. These results support an indirect molecular connection between transcription initiation and H3K4me3 in plants. Perhaps this connection depends on the genomic context, since the SWI/SNF (Switch/Sucrose Non-Fermentable) chromatin remodeler complex controls the activation and repression of sense gene transcription and anti-sense non-coding transcription through PIC formation correlating with H3K4me3 levels at both gene ends [46]. In summary, H3K4me3 may promote PIC formation and RNAPII initiation in plants, yet the precise molecular mechanisms remain to be elucidated.

Histone PTMs and early transcriptional elongation

We sub-divide transcription elongation by RNAPII into early elongation and productive elongation [47]. Promoters coincide with nucleosome-depleted region (NDR) with resulting low levels of histone PTMs. In contrast, the first (i.e. +1) nucleosomes fall within the early elongation zone during RNAPII transcription. These nucleosomes dominate the genomic distribution of histone PTMs. In metazoans, early elongation refers the stage of RNAPII between transcription initiation and productive elongation linked to well-defined RNAPII promoter proximal pausing sites regulated by pausing factors such as negative elongation factor NELF (Negative Elongation Factor) [48]. Even though NELF is conspicuously absent in plants, RNAPII tends to stall at the position of the first nucleosome in gene bodies [20]. In addition, the distribution of RNAPII in plant promoter proximal regions is wider compared to metazoans, perhaps indicating an extension of the RNAPII early elongation stage in plants compared to metazoans. Di-methylation on histone H3 lysine 4 (H3K4me2) and tri-methylation on histone H3 lysine 36 (H3K36me3) peak slightly downstream of histone PTMs for transcription initiation [37, 49-52], thus could be associated with RNAPII early elongation and RNAPII stalling (Figure 1A)[20]. However, the
mechanistic connections between chromatin during early RNAPII elongation and RNAPII stalling are yet to be firmly established.

It is plausible to imagine a cross talk between transcription initiation and productive elongation that occurs during early elongation to facilitate progression further into the gene. In Arabidopsis, increased H3K4me2 levels by mutations in the H3K4me2/me3 demethylase FLD (FLOWERING LOCUS D) are associated with elevated H3K4me3 and H3ac levels near the 5'-end of the genes, and increased H3K36me3 level over the gene bodies [15]. In addition, reduced H3K4me2/me3 levels are associated with decreased levels of H3ac, H3K36me3 and a drop of RNAPII occupancy near promoters in Arabidopsis [53, 54]. Moreover, repression of plant transposable elements (TE) requires coordinated modulation of histone acetylation (i.e. H3ac and H4ac) and histone methylation (e.g. H3K4me2 and H3K4me3) [55]. However, H3K4me2 in rice and Arabidopsis may exhibit negative correlations with transcription activity [56]. This phenomenon could be attributed to the dynamic removal of H3K4me3 that may recruit H3K4me2 readers to facilitate repression. Interestingly, characterizations of histone PTMs during circadian oscillations revealed a sequential enrichment of H3ac, H3K4me3 and H3K4me2 [57]. These data may reflect an orchestrated progression through RNAPII transcription stages from initiation to early elongation. In conclusion, H3K4me2 during early RNAPII elongation might represent a molecular hub that coordinates the transition from transcription initiation to elongation through the interaction with histone acetylation.

During early transcription elongation, H3K36me3 often correlates with H3K4me2 at positions just downstream of H3K4me3 (Figure 1). Roles of H3K4me3 and H3K36me3 in transcription initiation and elongation characterize these histone PTMs as excellent predictors for gene expression in plants [58]. In Arabidopsis, H3K36me3 acts in concert with other histone PTMs for active transcription (e.g. H3K4me3 and histone acetylation) to promote gene expression [59-62]. Moreover, H3K36me3 is highly enriched at temperature-regulated alternatively spliced genes, and a reduction of H3K36me3 affects alternative splicing outcomes in Arabidopsis [63]. Likewise, retained introns in the Arabidopsis spliceosome mutant brra2 often exhibit low H3K36me3 profiles [64]. These data link chromatin features during RNAPII transcription to pre-mRNA processing. Arabidopsis MRG (MORF Related Gene) proteins read H3K36me3 as well as H3K4me3 and mediate transcription activation by directing H4ac deposition near 5’-end of target
genes [65, 66]. The genomic distributions of H3K36ac and H3K36me3 overlap downstream of TSSs, albeit with antagonizing effects even though both are associated with active transcription [25]. Combinatorial effects on gene expression of histone PTMs of the same residue as suggested for H3K36 may increase the resolution to differentiate stages of RNAPII transcription. In summary, the H3K36me3 peak during early RNAPII elongation is linked to chromatin features ahead of the peak, and to pre-mRNA processing after the peak, supporting a role in bridging RNAPII initiation and elongation.

**Histone PTMs/variants and productive transcriptional elongation**

Eukaryotic transcription elongation, processivity and co-transcriptional histone PTMs are regulated by transcription elongation factors such as pTEF-b (positive transcription elongation factor b), PAF1-C (polymerase-associated factor 1 complex) and SPT4/5 (suppressor of Ty 4/5) [67-71]. In *Arabidopsis*, both PAF1-C and pTEF-b are part of RNAPII elongation complex [72]. The *Arabidopsis* pTEF-b subunit CDKC;2 regulates the global level elongating RNAPII (RNAPII-Ser2 Phosphorylation) transcription [73]. In addition, *Arabidopsis* SPT5 can be phosphorylated by CDKC;2, interact with PAF1C subunit VIP5 (VERNALIZATION INDEPENDENCE 5) and further influence H3K4me3 deposition on target loci [74]. During the productive transcriptional elongation stage, RNAPII translocates along the DNA template to synthesize a growing nascent RNA chain. In eukaryotes, the activity of elongating RNAPII is modulated by various elongation factors, including histone modifiers and splicing regulators [75]. RNAPII encounters few nucleosome barriers during transcription initiation and early elongation, while many nucleosomes need to be navigated during the productive elongation stage. The chromatin landscape shaped by histone PTMs on these intragenic nucleosomes thus provides the opportunity to regulate RNAPII elongation. In plants, a variety of histone PTMs localize to this stage and display nuanced distribution patterns. Histone PTMs that peaked at early elongation stage (i.e. H3K4me2 and H3K36me3) decline gradually towards 3'-end of genes. Mono-ubiquitination of histone H2B (H2Bub) and mono-methylation on histone H3 lysine 4 (H3K4me1) prominently cover most of the gene body without a clear peak. Di-methylation on histone H3 lysine 36 (H3K36me2) is gradually enriched towards the 3'-end of genes where it peaks, representing a histone PTM characterizing late stages of productive transcriptional elongation in plants (Figure 1A).
In *Arabidopsis*, H2Bub is deposited by E3 ubiquitin ligases for example HUB1 and HUB2 (HISTONE MONO-UBIQUITINATION 1 AND 2) [76]. Chromatin profiling determined a H2Bub profile covering gene bodies [52, 77]. In *Arabidopsis*, HUB1 genetically interacts with transcription elongation factor ELONGATOR complex and the FACT (Facilitates Chromatin Transcription) complex with synergistic effects on plant development [77, 78]. In addition, HUB2-mediated H2Bub functions with histone methyl-transferase SDG8 (SET DOMAIN GROUP 8)-mediated H3K36me3 to reinforce transcription activity at selected loci [79]. Furthermore, H2Bub is associated with rapid gene induction during environmental changes [80]. In rice, defects in H2Bub are associated with reduced global H3K4me2, suggesting a potential role of H2Bub promoting other histone elongation PTMs [81]. H2Bub and H3K4me3 both correlate with active transcription. In yeast and human cells, the deposition of H3K4me3 is mediated by H2Bub, suggesting a crosstalk between histone PTMs associated with elongation to this controlling transcription initiation [82, 83]. However, an equivalent mechanistic crosstalk awaits discovery in plants. In *Arabidopsis*, a reduction of H3K4me3 level has been observed at target genes in H2Bub defective mutants, but not globally [77, 84, 85]. Recent advances suggested that the establishment of H3K4me3 is largely independent of H2Bub [80, 86], arguing against the histone crosstalk model in plants. H2Bub is removed by the histone deubiquitination module (DUBm), which is part of the SAGA complex in yeast, but may be uncoupled from SAGA in plants [49, 87]. Interestingly, plant DUBm co-purifies with RNAPII subunits, mediator, histone chaperons and RNA processing factors, while HUB1 also co-purifies with transcription elongation factors. These data suggest a strong association of H2Bub biology and productive transcriptional elongation in plants [72, 87].

H3K4me1 shows a similar distribution profile over gene bodies to H2Bub, but with a trend to increase towards 3'-gene ends (Figure 1A). Interestingly, H3K4me1 may negatively correlate with initiation, potentially due to the dynamic conversion to the higher-order methylation states H3K4me2/me3 [37]. In gene bodies, H3K4me1 is enriched at cryptic intragenic TSSs that are repressed by the activity of the histone chaperone FACT complex in *Arabidopsis* [88]. The repressive effect of H3K4me1 on intragenic initiation appears to be distinct from H3K36 methylation, although SDG8, a H3K36 methyltransferase, has been proposed to read H3K4me1 as well as deposits H3K36me2/me3 [89]. In metazoans, H3K4me1 is classically associated with enhancers, whereas in plants, H3K4me1 is largely associated with RNAPII elongation and
antagonizes the repressing effect of di-methylation on histone H3 lysine 9 (H3K9me2) [90]. Intriguingly, the individual methylation states of H3K4 are associated with transcriptional initiation (H3K4me3), early elongation (H3K4me2) and productive elongation (H3K4me1) in Arabidopsis. It is tempting to speculate that the dynamics of H3K4 methylation-state conversion could guide the progression of plant RNAPII transcription.

H3K36me2 represents an additional key histone PTM for productive transcriptional elongation [88]. In Arabidopsis, the distribution of H3K36me2 spreads over gene bodies and peaks towards the 3’-end of genes [25, 91]. The distribution of H3K36me2 shifts further towards 3’-ends of genes in RNAPII elongation factor mutants [92]. Although direct evidence for a role of H3K36me2 in promoting RNAPII elongation is lacking, there is evidence to implicate H3K36 methylation in alternative splicing. In rice, the distributions of H3K36me2 or H3K36me3 correlate with differences in intron retention [93]. In addition, H3K36me2 showed a possible interaction with mRNA m^6^A modification in Arabidopsis [94]. Collectively, these studies support the co-transcriptional roles of H3K36me2 in modulating transcriptional elongation and RNA processing events such as splicing and RNA modification in Arabidopsis.

The histone variant H2A.Z is linked to transcriptional regulation in plants. On the one hand, H2A.Z is enriched near TSSs and anti-correlates with repressive DNA methylation [95]. On the other hand, H2A.Z is also enriched over gene bodies of lowly expressed genes [96]. H2A.Z may have the ability to activate or to repress transcription, depending on its genomic deposition. Curiously, H2A.Z can also regulate transcription by balancing the gene accessibility of +1 and -1 nucleosomes in Arabidopsis [97]. H2A and H2A.Z carry PTMs, for example ubiquitination. H2Aub co-localizes with repressive chromatin marks (e.g. H3K27me3), showing a profile peaking towards 5’-end of repressed genes [98] (Figure 1). In Arabidopsis, Polycomb Repressive Complex 1 (PRC1) and PRC2 mediates gene repression. Although the sequence of PRC1 and PRC2 recruitment during gene repression is actively debated, H2A.Zub deposition by PRC1 shows a strong correlation with PRC2-independent gene repression genome-wide in Arabidopsis [99, 100]. Interestingly, the Arabidopsis histone H3 reader YAF9 (YEAST ALL1-FUSED GENE FROM CHROMOSOME 9) proteins mediate the acetylation of H2A.Z and H4 at target loci potentially through the interaction with histone acetyltransferase HAM1 in Arabidopsis (HISTONE ACETYLTRANSFERASE OF THE MYST FAMILY 1) [101]. Collectively, the diversity
of PTMs on H2A.Z may help to explain the its dual roles in transcription regulation suggested for bulk H2A.Z. In conclusion, chromatin-based signatures linked to RNAPII elongation interact with pre-mRNA processing and transcriptional initiation, highlighting important aspects of plant gene expression.

**Genomic information for transcriptional termination**

The final stage of the transcription cycle represents transcriptional termination. RNAPII transcribes through the poly (A) sites (PAS) at 3’-end of genes. Here, RNAPII decelerates and stalls downstream of PASs, presumably to facilitate nascent RNA cleavage and poly-adenylation by CF/CPFs (Cleavage/Cleavage and Polyadenylation Factors) [102-104]. RNAPII elongates beyond PASs until the process of transcriptional termination releases RNAPII from the DNA template. RNAPII dissociation from the DNA template is presumably triggered when 5’-3’ exonucleases acting on the non-capped 5’-end reach RNAPII [20, 21, 105].

In plants, H3K36me2 marks late transcriptional elongation and peaks upstream of PASs. This profile may indicate a role for H3K36me2 in transcriptional termination. ChIP-seq analyses of the *Arabidopsis* histone H3 variant H3.3 revealed a positive correlation with transcription level [106-108]. Moreover, H3.3 density is low in gene bodies and enriched at gene boundaries, in promoter regions and close to PASs in *Arabidopsis*. The spatial correlation between PASs and H3.3 levels would be consistent with a role of H3.3 in transcriptional termination. Interestingly, the histone H3 variant H3.1, which differs from H3.3 by only 4 amino acid residues, preferentially marks heterochromatin represented by H3K9me2 and H3K27me3 [109, 110]. In conclusion, meta-genomic associations spatially connect chromatin marks to transcriptional termination, but experimental evidence testing these correlations are currently missing.

Transcriptional termination involves RNAPII stalling near PAS of genes [20, 21]. In mammals, PAS-associated RNAPII pausing can be achieved through local heterochromatin formation marked by H3K9me2 and the formation of R-loops [111]. R-loops are chromatin structures formed by DNA:RNA hybrids, which often correlate with RNAPII pausing during transcriptional termination in mammals [112]. Interestingly, another non-canonical DNA secondary structure G-quadruplex (G4) may interact with R-loops and facilitate transcriptional termination in human cells [113, 114]. However, in plants, genome-wide mapping of R-loops revealed a strong correlation with repressive histone PTMs (e.g. H3K9me2), whereas R-loop levels are low in
transcriptional termination regions, suggesting distinct regulatory mechanisms of R-loops in transcriptional termination in plants [115]. Curiously, *Arabidopsis* anti-sense R-loops and maize anti-sense G4s localize to 5’-UTR of genes [115, 116], perhaps indicating a role in transcriptional initiation in sense direction or transcriptional termination of anti-sense RNAPII transcription in plants. *Arabidopsis* BORDER proteins contribute to transcriptional termination, however the links to chromatin states remain elusive [117]. In summary, while transcription initiation and termination share key genomics features of RNAPII transcription, such as NDRs and RNAPII-stalling, our understanding of chromatin-based mechanisms affecting initiation greatly exceed those connected to termination. Whether this represents an opportunity for discovery, or whether RNAPII termination may rely less on chromatin-based signals awaits to be resolved in future studies.

**Mis-specification of the PTM-based GPS.**

Genome-wide analyses of histone PTMs reveal characteristic patterns indicative of histone-based regulatory mechanisms in plants. The integration of these epigenomic data yielded a database of histone states during gene expression for *Arabidopsis*, rice and maize [118]. The access for scientists to genome-wide experiments interrogating chromatin structures is improving through such databases (Box 1). The reproducible patterns of histone modifications over transcription units in various tissues raises the question of how they assist RNAPII transcription and gene expression [32]. Moreover, it is possible to identity genes deviating from this consensus pattern, perhaps highlighting gene regulation through mis-specification of the PTM GPS.

Chromatin-based effects during transcription elongation ensure the fidelity of gene expression [52, 72, 119]. In *Arabidopsis*, the H3K4me1, and H3K36me2 PTMs associate with productive elongation of transcription [52]. These two features of transcription elongation were recently associated with chromatin-based “repressive transcription” [47]. The *qua1-1* T-DNA allele represents an insertion upstream of the *QUASIMODO1 (QUA1)* promoter. In this allele, RNAPII elongation over the *QUA1* gene promoter results in a recessive loss-of-function phenotype. Transcription units within the T-DNA extend together with elongation PTMs into the genome and interferes with the consensus PTM profile at the downstream *QUA1* promoter. The *QUA1* promoter DNA sequence displays elevated elongation (H3K36me2) signatures, and consistently
reduced initiation and early elongation-associated histone PTMs H3K4me3 and H3K36me3. The underlying molecular mechanism is consistent with “transcriptional interference”, where the act of RNAPII transcription changes the chromatin state at gene promoters to repress functional transcriptional initiation (Figure 1B) [120]. In Arabidopsis, Genome-wide data support the idea that H3K36me2, when localized to promoters, correlates with negative gene expression. Perhaps through a similar mechanism to transcription repression associated with enrichment of H3K4me1 at human promoters [121, 122]. It will be instrumental to clarify the consequences and mechanisms that trigger mis-enrichment of elongation marks such as H3K36me2 and H3K4me1 at TSSs. The FACT complex, a known facilitator of chromatin-based transcriptional elongation [123], is required for transcriptional interference in qua1-1, as the mutant phenotype was partially restored in mutants of the FACT components SSRP1 and SPT16. Thus, in Arabidopsis, FACT can both facilitate RNAPII elongation by recycling nucleosomes and repress transcription initiation associated with H3K4 methylation dynamics [88]. More generally, FACT restricts the usage of TSSs located in intragenic positions in yeast, human and plants [88, 124-126]. In plants, the intragenic TSSs repressed by FACT displayed elevated H3K4me1, but the role of H3K4me1 and its connection to the FACT complex in transcriptional repression in plants awaits clarification. It appears that H3K4me1 role in transcription elongation is of interest to understand transcription elongation in plants. The H3K4 specific methyltransferase FAD family of FLD; LDL1,LDL2 and LDL3 (Table 1) appear to be important for erasing H3K4 methylation at highly regulated genes involved in flowering time and root elongation [127]. LDL2, one of the FAD family H3K4 methyltransferase is important for the maintenance of transcription-associated H3K4me1 in gene bodies and prevents deposition of the silencing H3K9me2 modification [90]. Interestingly, the LDL1 histone demethylase forms a complex with the deacetylation factor HDA6 (Table1) to repress transcription [128]. Characterizations of the chromatin-based gene repression through the act of RNAPII transcription in the qua1-1 mutant provided important first insights into the functional significance of histone PTM mis-specification of across gene bodies. The identification and characterization of additional examples where shifted histone GPS signals mediate transcriptional interference represent an exciting future research area.
Functional implications of plant-specific co-transcriptional chromatin profiles.

Plants and metazoans display an overall similar profile of histone PTMs across transcription units. However, some histone PTMs adopt deviant roles in the plant kingdom. In budding yeast, drosophila and human cells, H3K36me3 localizes to the 3′-end of gene bodies of expressed genes, and H3K36me2 to the 5′ region [7, 129-132]. The marks are deposited at chromatin during RNAPII transcription. In yeast, interactions of the RNAPII complex, histone chaperones, such as Spt6p FACT, and subunits of the PAF-I complex can maintain the characteristic pattern of H3K36me3/me2 during transcription. Depletion of the PAF-I complex shifted H3K36me3 towards the 5′-end of yeast genes [133]. In contrast, H3K36me3 localizes to the early transcriptional elongation zone in rice and Arabidopsis, while H3K36me2 peaks at the 3′-end of genes [25, 134-136]. These H3K36me2/me3 profiles thus characterize an intriguing difference between plants and metazoans, with implications for the RNAPII GPS, whereby plants progressively erase methyl groups from H3K36me3 to H3K36me1 during RNAPII transcription elongation (Box 2). The functional implications are presently unclear, yet it may indicate evolutionary adjustments of the chromatin-based GPS for RNAPII during the plant lineage. In mammals, H3K36m3 represses cryptic initiation through recruitment of histone deacetylases during elongation, whereas the repression of intragenic TSSs in Arabidopsis is linked to H3K4me1 [137]. In Arabidopsis, H3K36 methylation may repress natural antisense transcripts (NATs) at a subset of transcriptionally active genes [50]. In human, H3K36me3 mis-localization to gene promoters during RNAPII elongation of non-coding antisense transcription represses transcription initiation of the sense mRNA [138]. Finally, the role of the H3K36 methyltransferase SDG8 in splicing and capping of pre-mRNAs appears shared with the budding yeast homolog Set2p [139, 140]. However, several other transcription-associated chromatin PTMs appear under-studied in plants, for instance H4K20me3 is widely studied in animals and represents a heterochromatin-associated histone modification, whereas it would associated with transcription activation in Arabidopsis. [52, 141] It remains unclear which factors are involved in deposition, reading and erasing of the modification. Extending analyses to poorly explored PTMs in plants could improve our understanding of how the specifications of the chromatin-based RNAPII GPS in plants offer advantages, perhaps linked to a sessile life cycle.
Histone-based GPS service guides plant development and environmental responses

The chromatin states are dynamically regulated by the trios of histone “reader-writer-eraser” enzymes. Mutants defective in a particular histone modifying enzyme often profoundly affect gene expression and are associated with defects in plant growth, development and environmental response. We summarize the recent advances in understanding how histone PTM enzymes regulate biological processes in plants (Table 1 and Figure 2).

In plants, H2Aub is deposited by the “writer” enzyme ubiquitin E3 ligase (e.g. RING1A/RING1B and BMI1A/BMI1B) [142-145] and removed by “eraser” deubiquitinases (DUBs) (e.g. UBP12/UBP13) [146]. Writing and erasing H2Bub requires equivalent enzymatic activities. The E3 ubiquitin ligases HUB1/HUB2 and E2 ubiquitin-conjugating (UBC) enzymes (UBC1/UBC2) are involved in H2Bub deposition on target genes that control plant development and environmental responses [77, 81, 84, 147-149]. In plants, removal of H2Bub requires DUB activity for example from the DUB module (DUBm) of SAGA complex [49, 87] or other histone deubiquitinases [150, 151].

In *Arabidopsis*, methylation on histone lysine residues (i.e. H3K4 and H3K36) are added by the “writer” enzymes, SDG (SET Domain Group) proteins [152]. The histone methyltransferases (HMTs) SDG4 [153, 154], SDG8 [155, 156], SDG25 [157-162] and SDG26 [156, 159] can methylate both H3K4 and H3K36. SDG2 [57, 158, 163-165], SDG27 [42, 166, 167] and SDG30 [167] are specific writers for H3K4 methylation. SDG14, SDG16 and SDG19 represent additional putative HMTs for H3K4 methylation [168]. *Arabidopsis* histone lysine methylation is largely erased by enzymes harboring JmjC domains [169]. For example, MJM14 [164, 170, 171], MJM15 [172, 173], MJM16 [174], MJM17 [175] and MJM18 [176] are responsible for removing H3K4 methylation states, while MJM30 is involved in H3K36 demethylation [177, 178]. Additionally, H3K4 methylation can also be removed by cofactor FAD-dependent lysine-specific demethylases including FLD [179, 180] and LDL1/2/3 (LYSINE-SPECIFIC DEMETHYLASE 1-LIKE HISTONE DEMETHYLASES 1/2/3) [127, 128, 181, 182].

The dynamics of histone acetylation is maintained by histone acetyltransferases (HATs) and histone deacetylases (HDACs). *Arabidopsis* HATs classify into four families: the GNAT (GCN5-
RELATED ACETYL TRANSFERASE) family, the MYST (MOZ-YBF2/SAS3-SAS2/TIP60) family, the CREB-binding protein (CBP) family and the TAFII250 family [183, 184]. The GNAT family includes H3K14ac-specific HAT GCN5/HAG1 [30, 33, 185-187], H4K12ac-specific HAT HAG2 (HISTONE ACETYLTRANSFERASE OF THE GNAT FAMILY 2) [188] and HAG3 [189-192]. Arabidopsis HAM1 and HAM2 (HISTONE ACETYLTRANSFERASE OF THE MYST FAMILY 1 and 2) of the MYST family catalyze H4K5ac [188, 193]. The CPB family HATs, for example HAC (HISTONE ACETYLTRANSFERASE OF THE CBP FAMILY) 1, 2, 4, 5 and 12 are involved in general histone H3 and H4 acetylation [194-198]. The TAFII250 family includes HAF1 (HISTONE ACETYLTRANSFERASE OF THE TAFII250 FAMILY 1) and HAF2, which are the homologues to TAF1, the largest subunit of transcription initiation factor TFIID in metazoans [195, 199-201]. Arabidopsis HDACs are largely from Reduced Potassium Dependency 3 (RPD3)/Histone Deacetylase 1 (HDA1) family, that can be further divided into Class I and Class II [184]. The RPD3/HDA1 family Class I HATs include HDA6 [128, 202-205], HDA7 [206], HDA9 [207-211] and HDA19 [204, 212-217]. Class II contains HDA5 [218], HDA14 [219], HDA15 [212, 220-223] and HDA18 [200, 224]. Interestingly, Class I and Class II enzymes can have opposite roles in regulating particular plant biological functions [225, 226], suggesting antagonistic regulation by the same type of histone modifying enzymes. Another HDAC family in plant is the Silent Information Regulator 2 (SIR2) family including SRT1 and SRT2 (SIRTUIN 1 and 2) [227-229]. Additionally, the Histone Deacetylase 2 (HD2) family contains the plant-specific histone deacetylases HD2A, HD2B, HD2C and HD2D, which are also involved in various plant development processes [230-232] and environmental response [233-235].

Histone readers also contribute to the regulatory functions of histone PTMs. For example, Arabidopsis H3K4me3 reader EBS and SHL can read both H3K4me3 and H3K27me3 [38, 39]. The H3K36me3 reader MRG1 and MRG2 (MORF RELATED GENE 1 and 2) read H3K36me3 and interact with histone acetyltransferases (HATs) for the deposition of histone H4 acetylation (H4ac) [65, 66]. Histone acetylation readers MBD9 and NPX1 mediate the deposition of histone variant H2A.Z and further lead to DNA demethylation to activate gene transcription [35]. Thus, histone readers and effectors not only recognize particular histone PTMs, but also mediate the downstream regulation and contribute to the crosstalk between different histone PTMs. Trios of “reader-writer-eraser” enzymes collectively regulate gene expression through the dynamics of histone PTMs/variants. In general, loss-of-function mutant of a particular “writer”, “eraser” or
“reader” enzyme will directly or indirectly affect the local or global histone PTM/variant levels, which may further impair the RNAPII functions associated with transcription stages, reflected by changes of RNAPII occupancy or expression level of target genes. Even though the chromatin state profiles in many of the mutants listed in Table 1 is incomplete, it may be interesting to interpret the resulting phenotypic defects through the GPS model presented in this review. This view may reveal defects resulting in the mis-specification of transcription stages and associated defects in pre-mRNA processing. Future progress in this area would help to appreciate the biological significance of diverse spatially resolved effects chromatin modifications may have on gene isoform expression.

**Conclusion Remarks and Future Directions**

The roles of histone PTMs and associated factors in plant RNAPII transcription cycles remain largely uncharacterized. In this review, we summarized the current information on how histone PTMs appear to serve as coordinates to guide RNAPII transcription. Thus, histone PTMs can regulate progression through plant RNAPII transcription cycles. The act of transcription activity deposits histone PTMs throughout the cycle. It remains unclear for most histone modification and histone variants whether they affect transcription, are the result of transcription, or form a positive feedback loop. The number of possible combinations of histone PTMs and variants may build a complex chromatin-based regulation system for RNAPII transcription. Considering that some histone PTMs differ in their basic genomic distribution and functions from metazoans to plants, the epigenetic regulation of RNAPII transcription is largely unclear. The histone-based GPS associates the common histone PTM profiles at most expressed genes and aids the discovery of potentially regulatory “repressive transcription” events through dynamic mis-specification of histone PTMs. The combination of histone ChIP-seq experiments and emerging transcriptomics methods promises to stimulate future research to understand chromatin-based effects exerted through the act of RNAPII transcription in plant genomes (see Outstanding Questions).
REFERENCES

1. Luger, K., et al. (1997) Crystal structure of the nucleosome core particle at 2.8 angstrom resolution. *Nature* 389, 251-260

2. Bannister, A.J. and Kouzarides, T. (2011) Regulation of chromatin by histone modifications. *Cell research* 21, 381-395

3. Allis, C.D. and Jenuwein, T. (2016) The molecular hallmarks of epigenetic control. *Nature reviews. Genetics* 17, 487-500

4. Zhao, S., et al. (2018) Systematic Profiling of Histone Readers in Arabidopsis thaliana. *Cell Rep* 22, 1090-1102

5. Taverna, S.D., et al. (2007) How chromatin-binding modules interpret histone modifications: lessons from professional pocket pickers. *Nature structural & molecular biology* 14, 1025-1040

6. Dikic, I., et al. (2009) Ubiquitin-binding domains - from structures to functions. *Nature reviews. Molecular cell biology* 10, 659-671

7. Pokholok, D.K., et al. (2005) Genome-wide map of nucleosome acetylation and methylation in yeast. *Cell* 122, 517-527

8. Johnson, D.S., et al. (2007) Genome-wide mapping of in vivo protein-DNA interactions. *Science* 316, 1497-1502

9. Skene, P.J. and Henikoff, S. (2017) An efficient targeted nuclease strategy for high-resolution mapping of DNA binding sites. *Elife* 6

10. Kaya-Okur, H.S., et al. (2019) CUT&Tag for efficient epigenomic profiling of small samples and single cells. *Nature communications* 10

11. Henikoff, S. and Shilatifard, A. (2011) Histone modification: cause or cog? *Trends Genet* 27, 389-396

12. Gates, L.A., et al. (2017) Histone Marks in the 'Driver's Seat': Functional Roles in Steering the Transcription Cycle. *Trends in biochemical sciences* 42, 977-989

13. Soares, L.M., et al. (2017) Determinants of Histone H3K4 Methylation Patterns. *Mol Cell* 68, 773-785 e776

14. Fong, N., et al. (2017) RNA Pol II Dynamics Modulate Co-transcriptional Chromatin Modification, CTD Phosphorylation, and Transcriptional Direction. *Mol Cell* 66, 546-557 e543

15. Wu, Z., et al. (2016) Quantitative regulation of FLC via coordinated transcriptional initiation and elongation. *Proc Natl Acad Sci U S A* 113, 218-223
16 You, Y., et al. (2017) Temporal dynamics of gene expression and histone marks at the Arabidopsis shoot meristem during flowering. *Nature communications* 8

17 Lee, L.R., et al. (2019) Cell-type-specific transcriptome and histone modification dynamics during cellular reprogramming in the Arabidopsis stomatal lineage (vol 116, pg 21914, 2019). *P Natl Acad Sci USA* 116, 24376-24376

18 Rosa, S., et al. (2014) Cell Differentiation and Development in Arabidopsis Are Associated with Changes in Histone Dynamics at the Single-Cell Level. *The Plant cell* 26, 4821-4833

19 Buratowski, S. (2009) Progression through the RNA Polymerase II CTD Cycle. *Mol Cell* 36, 541-546

20 Kindgren, P., et al. (2019) Native elongation transcript sequencing reveals temperature dependent dynamics of nascent RNAPII transcription in Arabidopsis. *Nucleic Acids Res*

21 Zhu, J., et al. (2018) RNA polymerase II activity revealed by GRO-seq and pNET-seq in Arabidopsis. *Nature plants* 4, 1112-1123

22 Rhee, H.S. and Pugh, B.F. (2012) Genome-wide structure and organization of eukaryotic pre-initiation complexes. *Nature* 483, 295-301

23 Antonova, S.V., et al. (2019) Epigenetics and transcription regulation during eukaryotic diversification: the saga of TFIID. *Genes & development* 33, 888-902

24 Charron, J.B., et al. (2009) Dynamic landscapes of four histone modifications during deetiolation in Arabidopsis. *The Plant cell* 21, 3732-3748

25 Mahrez, W., et al. (2016) H3K36ac Is an Evolutionary Conserved Plant Histone Modification That Marks Active Genes. *Plant Physiol* 170, 1566-1577

26 Stroud, H., et al. (2014) Non-CG methylation patterns shape the epigenetic landscape in Arabidopsis. *Nature structural & molecular biology* 21, 64-72

27 Chen, C., et al. (2017) Cytosolic acetyl-CoA promotes histone acetylation predominantly at H3K27 in Arabidopsis. *Nature plants* 3, 814-824

28 Benhamed, M., et al. (2006) Arabidopsis GCN5, HD1, and TAF1/HAF2 interact to regulate histone acetylation required for light-responsive gene expression. *The Plant cell* 18, 2893-2903

29 Moraga, F. and Aquea, F. (2015) Composition of the SAGA complex in plants and its role in controlling gene expression in response to abiotic stresses. *Frontiers in plant science* 6, 865

30 Hu, Z.R., et al. (2015) Histone acetyltransferase GCN5 is essential for heat stress-responsive gene activation and thermotolerance in Arabidopsis. *Plant J* 84, 1178-1191
31 Wang, T.Y., et al. (2016) Histone acetyltransferase general control non-repressed protein 5 (GCN5) affects the fatty acid composition of Arabidopsis thaliana seeds by acetylating fatty acid desaturase3 (FAD3). *Plant J* 88, 794-808

32 Wang, T., et al. (2019) GCN5 modulates trichome initiation in Arabidopsis by manipulating histone acetylation of core trichome initiation regulator genes. *Plant cell reports* 38, 755-765

33 Wang, T., et al. (2019) Histone acetyltransferase GCN5-mediated regulation of long non-coding RNA At4 contributes to phosphate-starvation response in Arabidopsis. *Journal of experimental botany*

34 Zhang, C.J., et al. (2016) The Arabidopsis acetylated histone-binding protein BRAT1 forms a complex with BRP1 and prevents transcriptional silencing. *Nature communications* 7, 11715

35 Nie, W.F., et al. (2019) Histone acetylation recruits the SWR1 complex to regulate active DNA demethylation in Arabidopsis. *Proc Natl Acad Sci U S A* 116, 16641-16650

36 Zhang, X., et al. (2009) Genome-wide analysis of mono-, di- and trimethylation of histone H3 lysine 4 in Arabidopsis thaliana. *Genome biology* 10, R62

37 van Dijk, K., et al. (2010) Dynamic changes in genome-wide histone H3 lysine 4 methylation patterns in response to dehydration stress in Arabidopsis thaliana. *BMC plant biology* 10, 238

38 Yang, Z.L., et al. (2018) EBS is a bivalent histone reader that regulates floral phase transition in Arabidopsis. *Nat Genet* 50, 1247+

39 Qian, S., et al. (2018) Dual recognition of H3K4me3 and H3K27me3 by a plant histone reader SHL. *Nature communications* 9, 2425

40 Peng, L., et al. (2018) Structural Analysis of the Arabidopsis AL2-PAL and PRC1 Complex Provides Mechanistic Insight into Active-to-Repressive Chromatin State Switch. *J Mol Biol* 430, 4245-4259

41 Lauberth, S.M., et al. (2013) H3K4me3 interactions with TAF3 regulate preinitiation complex assembly and selective gene activation. *Cell* 152, 1021-1036

42 Ding, Y., et al. (2012) ATX1-generated H3K4me3 is required for efficient elongation of transcription, not initiation, at ATX1-regulated genes. *PLoS genetics* 8, e1003111

43 Fromm, M. and Avramova, Z. (2014) ATX1/AtCOMPASS and the H3K4me3 marks: how do they activate Arabidopsis genes? *Curr Opin Plant Biol* 21, 75-82

44 Song, Z.T., et al. (2015) Transcription factor interaction with COMPASS-like complex regulates histone H3K4 trimethylation for specific gene expression in plants. *P Natl Acad Sci USA* 112, 2900-2905
Huang, D., et al. (2018) WHIRLY1 Occupancy Affects Histone Lysine Modification and WRKY53 Transcription in Arabidopsis Developmental Manner. *Frontiers in plant science* 9, 1503

Archacki, R., et al. (2017) Arabidopsis SWI/SNF chromatin remodeling complex binds both promoters and terminators to regulate gene expression. *Nucleic Acids Res* 45, 3116-3129

Jonkers, I. and Lis, J.T. (2015) Getting up to speed with transcription elongation by RNA polymerase II. *Nature reviews. Molecular cell biology* 16, 167-177

Gilmour, D.S. (2009) Promoter proximal pausing on genes in metazoans. *Chromosoma* 118, 1-10

Nassrallah, A., et al. (2018) DET1-mediated degradation of a SAGA-like deubiquitination module controls H2Bub homeostasis. *Elife* 7

Luo, C., et al. (2013) Integrative analysis of chromatin states in Arabidopsis identified potential regulatory mechanisms for natural antisense transcript production. *Plant J* 73, 77-90

Zhang, X.Y., et al. (2009) Genome-wide analysis of mono-, di- and trimethylation of histone H3 lysine 4 in Arabidopsis thaliana. *Genome biology* 10

Roudier, F., et al. (2011) Integrative epigenomic mapping defines four main chromatin states in Arabidopsis. *Embo Journal* 30, 1928-1938

Le Masson, I., et al. (2012) Mutations in the Arabidopsis H3K4me2/3 demethylase JMJ14 suppress posttranscriptional gene silencing by decreasing transgene transcription. *The Plant cell* 24, 3603-3612

Butel, N., et al. (2017) sgs1: a neomorphic nac52 allele impairing post-transcriptional gene silencing through SGS3 downregulation. *Plant J* 90, 505-519

Liu, X., et al. (2012) HDA6 directly interacts with DNA methyltransferase MET1 and maintains transposable element silencing in Arabidopsis. *Plant Physiol* 158, 119-129

Liu, Y.H., et al. (2019) H3K4me2 functions as a repressive epigenetic mark in plants. *Epigenet Chromatin* 12

Malapeira, J., et al. (2012) Ordered changes in histone modifications at the core of the Arabidopsis circadian clock. *P Natl Acad Sci USA* 109, 21540-21545

Wu, Z., et al. (2019) Chromatin Signature and Transcription Factor Binding Provide a Predictive Basis for Understanding Plant Gene Expression. *Plant & cell physiology* 60, 1471-1486
59 Yang, H.C., et al. (2014) Antagonistic Roles for H3K36me3 and H3K27me3 in the Cold-Induced Epigenetic Switch at Arabidopsis FLC. *Curr Biol* 24, 1793-1797

60 Csorba, T., et al. (2014) Antisense COOLAIR mediates the coordinated switching of chromatin states at FLC during vernalization. *P Natl Acad Sci USA* 111, 16160-16165

61 Cheng, L., et al. (2018) EARLY FLOWERING IN SHORT DAYS (EFS) regulates the seed size in Arabidopsis. *Science China. Life sciences* 61, 214-224

62 Yang, H.C., et al. (2016) Physical coupling of activation and derepression activities to maintain an active transcriptional state at FLC. *P Natl Acad Sci USA* 113, 9369-9374

63 Pajoro, A., et al. (2017) Histone H3 lysine 36 methylation affects temperature-induced alternative splicing and flowering in plants. *Genome biology* 18, 102

64 Mahrez, W., et al. (2016) BRR2a Affects Flowering Time via FLC Splicing. *PLoS genetics* 12, e1005924

65 Xu, Y.F., et al. (2014) Arabidopsis MRG domain proteins bridge two histone modifications to elevate expression of flowering genes. *Nucleic Acids Res* 42, 10960-10974

66 Bu, Z., et al. (2014) Regulation of arabidopsis flowering by the histone mark readers MRG1/2 via interaction with CONSTANS to modulate FT expression. *PLoS genetics* 10, e1004617

67 Chen, F.X., et al. (2015) PAF1, a Molecular Regulator of Promoter-Proximal Pausing by RNA Polymerase II. *Cell* 162, 1003-1015

68 Pirngruber, J., et al. (2009) Insights into the function of the human P-TEFb component CDK9 in the regulation of chromatin modifications and co-transcriptional mRNA processing. *Cell Cycle* 8, 3636-3642

69 Wu, L.P., et al. (2014) H2B Ubiquitylation Promotes RNA Pol II Processivity via PAF1 and pTEFb. *Mol Cell* 54, 920-931

70 Tomson, B.N. and Arndt, K.M. (2013) The many roles of the conserved eukaryotic Paf1 complex in regulating transcription, histone modifications, and disease states. *Bba-Gene Regul Mech* 1829, 116-126

71 Martinez-Rucobo, F.W. and Cramer, P. (2013) Structural basis of transcription elongation. *Bba-Gene Regul Mech* 1829, 9-19

72 Antosz, W., et al. (2017) The Composition of the Arabidopsis RNA Polymerase II Transcript Elongation Complex Reveals the Interplay between Elongation and mRNA Processing Factors. *The Plant cell* 29, 854-870

73 Wang, Z.W., et al. (2014) Antisense-mediated FLC transcriptional repression requires the P-TEFb transcription elongation factor. *Proc Natl Acad Sci U S A* 111, 7468-7473
74 Lu, C., et al. (2017) Phosphorylation of SPT5 by CDKD2 Is Required for VIP5 Recruitment and Normal Flowering in Arabidopsis thaliana. The Plant cell 29, 277-291
75 Chen, F.X., et al. (2018) Born to run: control of transcription elongation by RNA polymerase II. Nat Rev Mol Cell Bio 19, 464-478
76 Feng, J. and Shen, W.H. (2014) Dynamic regulation and function of histone monoubiquitination in plants. Frontiers in plant science 5, 83
77 Himanen, K., et al. (2012) Histone H2B monoubiquitination is required to reach maximal transcript levels of circadian clock genes in Arabidopsis. Plant J 72, 249-260
78 Lolas, I.B., et al. (2010) The transcript elongation factor FACT affects Arabidopsis vegetative and reproductive development and genetically interacts with HUB1/2. Plant J 61, 686-697
79 Zhao, W., et al. (2019) Interactive and noninteractive roles of histone H2B monoubiquitination and H3K36 methylation in the regulation of active gene transcription and control of plant growth and development. The New phytologist 221, 1101-1116
80 Bourbousse, C., et al. (2012) Histone H2B Monoubiquitination Facilitates the Rapid Modulation of Gene Expression during Arabidopsis Photomorphogenesis. PLoS genetics 8
81 Cao, H., et al. (2015) Histone H2B Monoubiquitination Mediated by HISTONE MONOUBIQUITINATION1 and HISTONE MONOUBIQUITINATION2 Is Involved in Anther Development by Regulating Tapetum Degradation-Related Genes in Rice. Plant Physiol 168, 1389-U1514
82 Kim, J., et al. (2009) RAD6-Mediated Transcription-Coupled H2B Ubiquitylation Directly Stimulates H3K4 Methylation in Human Cells. Cell 137, 459-471
83 Sun, Z.W. and Allis, C.D. (2002) Ubiquitination of histone H2B regulates H3 methylation and gene silencing in yeast. Nature 418, 104-108
84 Cao, Y., et al. (2008) Histone H2B monoubiquitination in the chromatin of FLOWERING LOCUS C regulates flowering time in Arabidopsis. The Plant cell 20, 2586-2602
85 Gu, X., et al. (2009) Repression of the floral transition via histone H2B monoubiquitination. Plant J 57, 522-533
86 Fiorucci, A.S., et al. (2019) Arabidopsis S2Lb links AtCOMPASS-like and SDG2 activity in H3K4me3 independently from histone H2B monoubiquitination. Genome biology 20, 100
87 Pfab, A., et al. (2018) The Adaptor Protein ENY2 Is a Component of the Deubiquitination Module of the Arabidopsis SAGA Transcriptional Co-activator Complex but not of the TREX-2 Complex. J Mol Biol 430, 1479-1494
Nielsen, M., et al. (2019) Transcription-driven chromatin repression of Intragenic transcription start sites. *PLoS genetics* 15, e1007969

Liu, Y. and Huang, Y. (2018) Uncovering the mechanistic basis for specific recognition of monomethylated H3K4 by the CW domain of Arabidopsis histone methyltransferase SDG8. *The Journal of biological chemistry* 293, 6470-6481

Inagaki, S., et al. (2017) Gene-body chromatin modification dynamics mediate epigenome differentiation in Arabidopsis. *The EMBO journal* 36, 970-980

Wang, C.M., et al. (2015) Genome-wide analysis of local chromatin packing in Arabidopsis thaliana. *Genome Res* 25, 246-256

Oh, S., et al. (2008) Genic and global functions for Paf1C in chromatin modification and gene expression in Arabidopsis. *PLoS genetics* 4, e1000077

Wei, G., et al. (2018) Position-specific intron retention is mediated by the histone methyltransferase SDG725. *Bmc Biol* 16

Shim, S., et al. (2020) H3K36me2 is highly correlated with m(6) A modifications in plants. *Journal of integrative plant biology*

Zilberman, D., et al. (2008) Histone H2A.Z and DNA methylation are mutually antagonistic chromatin marks. *Nature* 456, 125-U114

Coleman-Derr, D. and Zilberman, D. (2012) Deposition of Histone Variant H2A.Z within Gene Bodies Regulates Responsive Genes. *PLoS genetics* 8

Dai, X., et al. (2018) H2A.Z Represses Gene Expression by Modulating Promoter Nucleosome Structure and Enhancer Histone Modifications in Arabidopsis. *Molecular plant* 11, 635

Zhou, Y., et al. (2017) H2A monoubiquitination in Arabidopsis thaliana is generally independent of LHP1 and PRC2 activity. *Genome biology* 18

Gomez-Zambrano, A., et al. (2019) The repressive role of Arabidopsis H2A.Z in transcriptional regulation depends on AtBMI1 activity. *Nature communications* 10, 2828

Yang, X., et al. (2017) Governing the Silencing State of Chromatin: The Roles of Polycomb Repressive Complex 1 in Arabidopsis. *Plant & cell physiology* 58, 198-206

Crevillen, P., et al. (2019) Arabidopsis YAF9 histone readers modulate flowering time through NuA4-complex-dependent H4 and H2A.Z histone acetylation at FLC chromatin. *New Phytologist* 222, 1893-1908

Nagarajan, V.K., et al. (2013) XRN 5'--3' exoribonucleases: structure, mechanisms and functions. *Biochimica et biophysica acta* 1829, 590-603
103 Kurihara, Y. (2017) Activity and roles of Arabidopsis thaliana XRN family exoribonucleases in noncoding RNA pathways. *Journal of plant research* 130, 25-31

104 Hunt, A.G., *et al.* (2012) Plant polyadenylation factors: conservation and variety in the polyadenylation complex in plants. *BMC genomics* 13, 641

105 Proudfoot, N.J. (2016) Transcriptional termination in mammals: Stopping the RNA polymerase II juggernaut. *Science* 352, aad9926

106 Shu, H., *et al.* (2014) Arabidopsis replacement histone variant H3.3 occupies promoters of regulated genes. *Genome biology* 15, R62

107 Stroud, H., *et al.* (2012) Genome-wide analysis of histone H3.1 and H3.3 variants in Arabidopsis thaliana. *Proc Natl Acad Sci U S A* 109, 5370-5375

108 Wollmann, H., *et al.* (2012) Dynamic deposition of histone variant H3.3 accompanies developmental remodeling of the Arabidopsis transcriptome. *PLoS genetics* 8, e1002658

109 Lu, L., *et al.* (2018) The plant-specific histone residue Phe41 is important for genome-wide H3.1 distribution. *Nature communications* 9

110 Jacob, Y., *et al.* (2014) Selective methylation of histone H3 variant H3.1 regulates heterochromatin replication. *Science* 343, 1249-1253

111 Skourtis-Stathaki, K., *et al.* (2014) R-loops induce repressive chromatin marks over mammalian gene terminators. *Nature* 516, 436-439

112 Sanz, L.A., *et al.* (2016) Prevalent, Dynamic, and Conserved R-Loop Structures Associate with Specific Epigenomic Signatures in Mammals. *Mol Cell* 63, 167-178

113 Zheng, K.W., *et al.* (2014) A competitive formation of DNA:RNA hybrid G-quadruplex is responsible to the mitochondrial transcription termination at the DNA replication priming site (vol 42, pg 10832, 2014). *Nucleic Acids Res* 42, 12960-12960

114 Wanrooij, P.H., *et al.* (2012) A hybrid G-quadruplex structure formed between RNA and DNA explains the extraordinary stability of the mitochondrial R-loop. *Nucleic Acids Res* 40, 10334-10344

115 Xu, W., *et al.* (2017) The R-loop is a common chromatin feature of the Arabidopsis genome. *Nature plants* 3, 704-714

116 Andorf, C.M., *et al.* (2014) G-Quadruplex (G4) Motifs in the Maize (Zea mays L.) Genome Are Enriched at Specific Locations in Thousands of Genes Coupled to Energy Status, Hypoxia, Low Sugar, and Nutrient Deprivation. *J Genet Genomics* 41, 627-647

117 Yu, X., *et al.* (2019) BORDER proteins protect expression of neighboring genes by promoting 3' Pol II pausing in plants. *Nature communications* 10, 4359
118 Liu, Y., et al. (2018) PCSD: a plant chromatin state database. *Nucleic Acids Res* 46, D1157-D1167

119 Herz, M.A.G. and Kornblihtt, A.R. (2019) Alternative Splicing and Transcription Elongation in Plants. *Frontiers in plant science* 10

120 Ard, R., et al. (2017) Emerging Properties and Functional Consequences of Noncoding Transcription. *Genetics* 207, 357-367

121 Luo, C.Y. and Lam, E. (2010) ANCORP: a high-resolution approach that generates distinct chromatin state models from multiple genome-wide datasets. *Plant J* 63, 339-351

122 Cheng, J., et al. (2014) A role for H3K4 monomethylation in gene repression and partitioning of chromatin readers. *Mol Cell* 53, 979-992

123 Belotserkovskaya, R., et al. (2003) FACT facilitates transcription-dependent nucleosome alteration. *Science* 301, 1090-1093

124 Kaplan, C.D., et al. (2003) Transcription elongation factors repress transcription initiation from cryptic sites. *Science* 301, 1096-1099

125 Carvalho, S., et al. (2013) Histone methyltransferase SETD2 coordinates FACT recruitment with nucleosome dynamics during transcription. *Nucleic Acids Res* 41, 2881-2893

126 Mason, P.B. and Struhl, K. (2003) The FACT complex travels with elongating RNA polymerase II and is important for the fidelity of transcriptional initiation in vivo. *Molecular and cellular biology* 23, 8323-8333

127 Martignago, D., et al. (2019) The Four FAD-Dependent Histone Demethylases of Arabidopsis Are Differently Involved in the Control of Flowering Time. *Frontiers in plant science* 10, 669

128 Hung, F.Y., et al. (2018) The Arabidopsis LDL1/2-HDA6 histone modification complex is functionally associated with CCA1/LHY in regulation of circadian clock genes. *Nucleic Acids Res* 46, 10669-10681

129 Barski, A., et al. (2007) High-resolution profiling of histone methylations in the human genome. *Cell* 129, 823-837

130 Bell, O., et al. (2007) Localized H3K36 methylation states define histone H4K16 acetylation during transcriptional elongation in Drosophila. *The EMBO journal* 26, 4974-4984

131 Kuo, A.J., et al. (2011) NSD2 links dimethylation of histone H3 at lysine 36 to oncogenic programming. *Mol Cell* 44, 609-620
132 Wagner, E.J. and Carpenter, P.B. (2012) Understanding the language of Lys36 methylation at histone H3. Nature reviews. Molecular cell biology 13, 115-126

133 Fong, N., et al. (2017) RNA Pol II Dynamics Modulate Co-transcriptional Chromatin Modification, CTD Phosphorylation, and Transcriptional Direction. Mol Cell 66, 546-+

134 Liu, B., et al. (2019) The transcription factor OsSUF4 interacts with SDG725 in promoting H3K36me3 establishment. Nature communications 10, 2999

135 Zhang, T., et al. (2018) A variant NuRD complex containing PWWP2A/B excludes MBD2/3 to regulate transcription at active genes. Nature communications 9, 3798

136 Liu, B., et al. (2016) SET DOMAIN GROUP 708, a histone H3 lysine 36-specific methyltransferase, controls flowering time in rice (Oryza sativa). The New phytologist 210, 577-588

137 Neri, F., et al. (2017) Intragenic DNA methylation prevents spurious transcription initiation. Nature 543, 72-77

138 Loos, F., et al. (2015) Chromatin-Mediated Reversible Silencing of Sense-Antisense Gene Pairs in Embryonic Stem Cells Is Consolidated upon Differentiation. Molecular and cellular biology 35, 2436-2447

139 Li, Z., et al. (2016) Coupling of histone methylation and RNA processing by the nuclear mRNA cap-binding complex. Nature plants 2, 16015

140 Sorenson, M.R., et al. (2016) Histone H3K36 methylation regulates pre-mRNA splicing in Saccharomyces cerevisiae. Rna Biol 13, 412-426

141 Sanchez, M.D. and Gutierrez, C. (2009) Arabidopsis ORC1 is a PHD-containing H3K4me3 effector that regulates transcription. P Natl Acad Sci USA 106, 2065-2070

142 Qin, F., et al. (2008) Arabidopsis DREB2A-interacting proteins function as RING E3 ligases and negatively regulate plant drought stress-responsive gene expression. The Plant cell 20, 1693-1707

143 Yang, C., et al. (2013) VAL- and AtBMI1-Mediated H2Aub Initiate the Switch from Embryonic to Postgerminative Growth in Arabidopsis. Curr Biol 23, 1324-1329

144 Shen, L.S., et al. (2014) The putative PRC1 RING-finger protein AtRING1A regulates flowering through repressing MADS AFFECTING FLOWERING genes in Arabidopsis. Development 141, 1303-U1238

145 Li, J., et al. (2017) Polycomb Group Proteins RING1A and RING1B Regulate the Vegetative Phase Transition in Arabidopsis. Frontiers in plant science 8, 867

146 Derkacheva, M., et al. (2016) H2A deubiquitinases UBP12/13 are part of the Arabidopsis polycomb group protein system. Nature plants 2
147 Liu, Y.X., et al. (2007) The absence of histone H2B monoubiquitination in the Arabidopsis hub1 (rdo4) mutant reveals a role for chromatin remodeling in seed dormancy. The Plant cell 19, 433-444

148 Xu, L., et al. (2009) The E2 ubiquitin-conjugating enzymes, AtUBC1 and AtUBC2, play redundant roles and are involved in activation of FLC expression and repression of flowering in Arabidopsis thaliana. Plant J 57, 279-288

149 Hu, M., et al. (2014) Histone H2B Monoubiquitination Is Involved in Regulating the Dynamics of Microtubules during the Defense Response to Verticillium dahliae Toxins in Arabidopsis(1[OPEN]). Plant Physiol 164, 1857-1865

150 Schmitz, R.J., et al. (2009) Histone H2B Deubiquitination Is Required for Transcriptional Activation of FLOWERING LOCUS C and for Proper Control of Flowering in Arabidopsis. Plant Physiol 149, 1196-1204

151 Krichevsky, A., et al. (2011) Involvement of KDM1C histone demethylase-OTLD1 otubain-like histone deubiquitinase complexes in plant gene repression. Proc Natl Acad Sci U S A 108, 11157-11162

152 Ng, D.W., et al. (2007) Plant SET domain-containing proteins: structure, function and regulation. Biochimica et biophysica acta 1769, 316-329

153 Cartagena, J.A., et al. (2008) The Arabidopsis SDG4 contributes to the regulation of pollen tube growth by methylation of histone H3 lysines 4 and 36 in mature pollen. Dev Biol 315, 355-368

154 Kumpf, R., et al. (2014) The ASH1-RELATED3 SET-domain protein controls cell division competence of the meristem and the quiescent center of the Arabidopsis primary root. Plant Physiol 166, 632-643

155 Cazzonelli, C.I., et al. (2014) A chromatin modifying enzyme, SDG8, is involved in morphological, gene expression, and epigenetic responses to mechanical stimulation. Frontiers in plant science 5

156 Liu, B., et al. (2016) Interplay of the histone methyltransferases SDG8 and SDG26 in the regulation of transcription and plant flowering and development. Biochimica et biophysica acta 1859, 581-590

157 Tamada, Y., et al. (2009) ARABIDOPSIS TRITHORAX-RELATED7 Is Required for Methylation of Lysine 4 of Histone H3 and for Transcriptional Activation of FLOWERING LOCUS C. The Plant cell 21, 3257-3269

158 Yun, J.Y., et al. (2012) ARABIDOPSIS TRITHORAX-RELATED3/SET DOMAIN GROUP2 is Required for the Winter-Annual Habit of Arabidopsis thaliana. Plant and Cell Physiology 53, 834-846
Berr, A., et al. (2015) The trxG family histone methyltransferase SET DOMAIN GROUP 26 promotes flowering via a distinctive genetic pathway. *Plant J* 81, 316-328

Liu, Y.X., et al. (2011) Identification of the Arabidopsis REDUCED DORMANCY 2 Gene Uncovers a Role for the Polymerase Associated Factor 1 Complex in Seed Dormancy. *Plos One* 6

Xia, S.T., et al. (2013) Regulation of Transcription of Nucleotide-Binding Leucine-Rich Repeat-Encoding Genes SNC1 and RPP4 via H3K4 Trimethylation. *Plant Physiol* 162, 1694-1705

Nojima, T., et al. (2015) Mammalian NET-Seq Reveals Genome-wide Nascent Transcription Coupled to RNA Processing. *Cell* 161, 526-540

Berr, A., et al. (2010) Arabidopsis SET DOMAIN GROUP2 Is Required for H3K4 Trimethylation and Is Crucial for Both Sporophyte and Gametophyte Development. *The Plant cell* 22, 3232-3248

Song, Q.X., et al. (2019) Diurnal regulation of SDG2 and JMJ14 by circadian clock oscillators orchestrates histone modification rhythms in Arabidopsis. *Genome biology* 20

Pinon, V., et al. (2017) SDG2-Mediated H3K4me3 Is Crucial for Chromatin Condensation and Mitotic Division during Male Gametogenesis in Arabidopsis. *Plant Physiol* 174, 1205-1215

Napsucialy-Mendivil, S., et al. (2014) ARABIDOPSIS HOMOLOG of TRITHORAX1 (ATX1) is required for cell production, patterning, and morphogenesis in root development. *Journal of experimental botany* 65, 6373-6384

Saleh, A., et al. (2008) The highly similar Arabidopsis homologs of trithorax ATX1 and ATX2 encode proteins with divergent biochemical functions. *The Plant cell* 20, 568-579

Chen, L.Q., et al. (2017) ATX3, ATX4, and ATX5 Encode Putative H3K4 Methyltransferases and Are Critical for Plant Development. *Plant Physiol* 174, 1795-1806

Chen, X.S., et al. (2011) Epigenetic gene regulation by plant Jumonji group of histone demethylase. *Bba-Gene Regul Mech* 1809, 421-426

Lu, F.L., et al. (2010) JMJ14 is an H3K4 demethylase regulating flowering time in Arabidopsis. *Cell research* 20, 387-390

Greenberg, M.V.C., et al. (2013) Interplay between Active Chromatin Marks and RNA-Directed DNA Methylation in Arabidopsis thaliana. *PLoS genetics* 9

Yang, H., et al. (2012) Overexpression of a histone H3K4 demethylase, JMJ15, accelerates flowering time in Arabidopsis. *Plant cell reports* 31, 1297-1308
173 Shen, Y., et al. (2014) Over-expression of histone H3K4 demethylase gene JMJ15 enhances salt tolerance in Arabidopsis. *Frontiers in plant science* 5, 290

174 Liu, P., et al. (2019) The Histone H3K4 Demethylase JMJ16 Represses Leaf Senescence in Arabidopsis. *The Plant cell* 31, 430-443

175 Huang, S., et al. (2019) Arabidopsis histone H3K4 demethylase JMJ17 functions in dehydration stress response. *The New phytologist* 223, 1372-1387

176 Yang, H., et al. (2012) A companion cell-dominant and developmentally regulated H3K4 demethylase controls flowering time in Arabidopsis via the repression of FLC expression. *PLoS genetics* 8, e1002664

177 Yan, Y.Y., et al. (2014) A MYB-Domain Protein EFM Mediates Flowering Responses to Environmental Cues in Arabidopsis. *Dev Cell* 30, 437-448

178 Wu, J.F., et al. (2019) Histone demethylases control root elongation in response to stress-signaling hormone abscisic acid. *Plant Signal Behav* 14

179 Singh, V., et al. (2014) Arabidopsis flowering locus D influences systemic-acquired-resistance- induced expression and histone modifications of WRKY genes. *Journal of biosciences* 39, 119-126

180 Banday, Z.Z. and Nandi, A.K. (2018) Arabidopsis thaliana GLUTATHIONE-S-TRANSFERASE THETA 2 interacts with RSI1/FLD to activate systemic acquired resistance. *Mol Plant Pathol* 19, 464-475

181 Jiang, D., et al. (2007) Arabidopsis relatives of the human lysine-specific demethylase1 repress the expression of FWA and FLOWERING LOCUS C and thus promote the floral transition. *The Plant cell* 19, 2975-2987

182 Zhao, M., et al. (2015) Arabidopsis histone demethylases LDL1 and LDL2 control primary seed dormancy by regulating DELAY OF GERMINATION 1 and ABA signaling-related genes. *Frontiers in plant science* 6, 159

183 Hu, Y.F., et al. (2019) Histone Acetylation Dynamics Integrates Metabolic Activity to Regulate Plant Response to Stress. *Frontiers in plant science* 10

184 Pandey, R., et al. (2002) Analysis of histone acetyltransferase and histone deacetylase families of Arabidopsis thaliana suggests functional diversification of chromatin modification among multicellular eukaryotes. *Nucleic Acids Res* 30, 5036-5055

185 Kim, J.Y., et al. (2015) Epigenetic control of juvenile-to-adult phase transition by the Arabidopsis SAGA-like complex. *Plant J* 83, 537-545

186 Poulilos, S. and Vlachonasios, K.E. (2018) Synergistic action of GCN5 and CLAVATA1 in the regulation of gynoecium development in Arabidopsis thaliana. *The New phytologist* 220, 593-608
187  Kim, J.Y., et al. (2018) Epigenetic reprogramming by histone acetyltransferase HAG1/AtGCN5 is required for pluripotency acquisition in Arabidopsis. *Embo Journal* 37

188  Earley, K., et al. (2006) Erasure of histone acetylation by Arabidopsis HDA6 mediates large-scale gene silencing in nucleolar dominance. *Genes & development* 20, 1283-1293

189  Fina, J.P. and Casati, P. (2015) HAG3, a Histone Acetyltransferase, Affects UV-B Responses by Negatively Regulating the Expression of DNA Repair Enzymes and Sunscreen Content in Arabidopsis thaliana. *Plant and Cell Physiology* 56, 1388-1400

190  Kojima, S., et al. (2011) Asymmetric leaves2 and Elongator, a histone acetyltransferase complex, mediate the establishment of polarity in leaves of Arabidopsis thaliana. *Plant & cell physiology* 52, 1259-1273

191  Silva, K.J.P., et al. (2017) The Arabidopsis ELP3/ELO3 and ELP4/ELO1 genes enhance disease resistance in Fragaria vesca L. *BMC plant biology* 17, 230

192  Woloszynska, M., et al. (2016) Plant Elongator-mediated transcriptional control in a chromatin and epigenetic context. *Biochimica et biophysica acta* 1859, 1025-1033

193  Latrasse, D., et al. (2008) The MYST histone acetyltransferases are essential for gametophyte development in Arabidopsis. *BMC plant biology* 8, 121

194  Hinckley, W.E., et al. (2019) The HAC1 histone acetyltransferase promotes leaf senescence and regulates the expression of ERF022. *Plant direct* 3, e00159

195  Fina, J.P., et al. (2017) HAC1 and HAF1 Histone Acetyltransferases Have Different Roles in UV-B Responses in Arabidopsis. *Frontiers in plant science* 8

196  Li, C., et al. (2014) Involvement of Arabidopsis histone acetyltransferase HAC family genes in the ethylene signaling pathway. *Plant & cell physiology* 55, 426-435

197  Singh, P., et al. (2014) Environmental History Modulates Arabidopsis Pattern-Triggered Immunity in a HISTONE ACETYLTRANSFERASE1-Dependent Manner. *The Plant cell* 26, 2676-2688

198  Li, C., et al. (2014) Involvement of Arabidopsis HAC family genes in pleiotropic developmental processes. *Plant Signal Behav* 9, e28173

199  Lee, K. and Seo, P.J. (2018) The HAF2 protein shapes histone acetylation levels of PRR5 and LUX loci in Arabidopsis. *Planta* 248, 513-518

200  Chen, W.Q., et al. (2016) One additional histone deacetylase and 2 histone acetyltransferases are involved in cellular patterning of Arabidopsis root epidermis. *Plant Signal Behav* 11
201 Waterworth, W.M., et al. (2015) Arabidopsis TAF1 is an MRE11-interacting protein required for resistance to genotoxic stress and viability of the male gametophyte. *Plant J* 84, 545-557

202 Wang, Y., et al. (2017) HISTONE DEACETYLASE 6 represses pathogen defence responses in Arabidopsis thaliana. *Plant, cell & environment* 40, 2972-2986

203 Yu, C.W., et al. (2017) HISTONE DEACETYLASE6 Acts in Concert with Histone Methyltransferases SUVH4, SUVH5, and SUVH6 to Regulate Transposon Silencing. *The Plant cell* 29, 1970-1983

204 Ning, Y.Q., et al. (2019) The HDA19 histone deacetylase complex is involved in the regulation of flowering time in a photoperiod-dependent manner. *Plant J* 98, 448-464

205 Nelson, S.K., et al. (2017) Biology in the Dry Seed: Transcriptome Changes Associated with Dry Seed Dormancy and Dormancy Loss in the Arabidopsis GA-Insensitive sleepy1-2 Mutant. *Frontiers in plant science* 8

206 Cigliano, R.A., et al. (2013) Histone Deacetylase AtHDA7 Is Required for Female Gametophyte and Embryo Development in Arabidopsis. *Plant Physiol* 163, 431-440

207 Zeng, X.L., et al. (2020) HISTONE DEACETYLASE 9 Functions with Polycomb Silencing to Repress FLOWERING LOCUS C Expression. *Plant Physiol* 182, 555-565

208 Zheng, Y., et al. (2016) Histone deacetylase HDA9 negatively regulates salt and drought stress responsiveness in Arabidopsis. *Journal of experimental botany* 67, 1703-1713

209 Yang, L.Y., et al. (2020) HOS15 and HDA9 negatively regulate immunity through histone deacetylation of intracellular immune receptor NLR genes in Arabidopsis. *New Phytologist*

210 Park, H.J., et al. (2019) HOS15 Interacts with the Histone Deacetylase HDA9 and the Evening Complex to Epigenetically Regulate the Floral Activator GIGANTEA. *The Plant cell* 31, 37-51

211 Mayer, K.S., et al. (2019) HDA9-PWR-HOS15 Is a Core Histone Deacetylase Complex Regulating Transcription and Development. *Plant Physiol* 180, 342-355

212 Shen, Y., et al. (2019) Arabidopsis histone deacetylase HDA15 directly represses plant response to elevated ambient temperature. *Plant J*

213 Chen, W.Q., et al. (2019) Histone Deacetylase HDA19 Affects Root Cortical Cell Fate by Interacting with SCARECROW. *Plant Physiol* 180, 276-288

214 Gao, M.J., et al. (2015) SCARECROW-LIKE15 interacts with HISTONE DEACETYLASE19 and is essential for repressing the seed maturation programme. *Nature communications* 6
van Zanten, M., et al. (2014) HISTONE DEACETYLASE 9 represses seedling traits in Arabidopsis thaliana dry seeds. *Plant J* 80, 475-488

Niu, D., et al. (2019) SIZ1-Mediated SUMOylation of TPR1 Suppresses Plant Immunity in Arabidopsis. *Molecular plant* 12, 215-228

Ueda, M., et al. (2018) Versatility of HDA19-deficiency in increasing the tolerance of Arabidopsis to different environmental stresses. *Plant Signal Behav* 13

Luo, M., et al. (2015) Regulation of flowering time by the histone deacetylase HDA5 in Arabidopsis. *Plant J* 82, 925-936

Tran, H.T., et al. (2012) Arabidopsis thaliana histone deacetylase 14 (HDA14) is an alpha-tubulin deacetylase that associates with PP2A and enriches in the microtubule fraction with the putative histone acetyltransferase ELP3. *Plant J* 71, 263-272

Zhao, L., et al. (2019) HY5 Interacts with the Histone Deacetylase HDA15 to Repress Hypocotyl Cell Elongation in Photomorphogenesis. *Plant Physiol* 180, 1450-1466

Tang, Y., et al. (2017) Arabidopsis NF-YCs Mediate the Light-Controlled Hypocotyl Elongation via Modulating Histone Acetylation. *Molecular plant* 10, 260-273

Lee, H.G. and Seo, P.J. (2019) MYB96 recruits the HDA15 protein to suppress negative regulators of ABA signaling in Arabidopsis. *Nature communications* 10

Gu, D.C., et al. (2017) Identification of HDA15-PIF1 as a key repression module directing the transcriptional network of seed germination in the dark. *Nucleic Acids Res* 45, 7137-7150

Liu, C., et al. (2013) HDA18 Affects Cell Fate in Arabidopsis Root Epidermis via Histone Acetylation at Four Kinase Genes. *The Plant cell* 25, 257-269

Ueda, M., et al. (2017) The Distinct Roles of Class I and II RPD3-Like Histone Deacetylases in Salinity Stress Response. *Plant Physiol* 175, 1760-1773

Ueda, M., et al. (2019) Transcriptome Analysis of the Hierarchical Response of Histone Deacetylase Proteins That Respond in an Antagonistic Manner to Salinity Stress. *Frontiers in plant science* 10

Konig, A.C., et al. (2014) The Arabidopsis Class II Sirtuin Is a Lysine Deacetylase and Interacts with Mitochondrial Energy Metabolism. *Plant Physiol* 164, 1401-1414

Liu, X., et al. (2017) Histone Deacetylase AtSRT1 Links Metabolic Flux and Stress Response in Arabidopsis. *Molecular plant* 10, 1510-1522

Zhang, F., et al. (2018) Histone Deacetylases SRT1 and SRT2 Interact with ENAP1 to Mediate Ethylene-Induced Transcriptional Repression. *The Plant cell* 30, 153-166
230 Zhang, Y.Z., et al. (2019) Histone Deacetylase HDT1 is Involved in Stem Vascular Development in Arabidopsis. *Int J Mol Sci* 20

231 Li, H.C., et al. (2017) Plant-Specific Histone Deacetylases HDT1/2 Regulate GIBBERELLIN 2-OXIDASE2 Expression to Control Arabidopsis Root Meristem Cell Number. *The Plant Cell* 29, 2183-2196

232 Farhi, J., et al. (2017) Histone deacetylase HD2D is involved in regulating plant development and flowering time in Arabidopsis. *Plant Signal Behav* 12

233 Latrasse, D., et al. (2017) MAPK-triggered chromatin reprogramming by histone deacetylase in plant innate immunity. *Genome biology* 18, 131

234 Han, Z., et al. (2016) AtHD2D Gene Plays a Role in Plant Growth, Development, and Response to Abiotic Stresses in Arabidopsis thaliana. *Frontiers in plant science* 7, 310

235 Park, J., et al. (2018) Epigenetic switch from repressive to permissive chromatin in response to cold stress. *P Natl Acad Sci USA* 115, E5400-E5409

236 Shi, H., et al. (2015) Arabidopsis DET1 degrades HFR1 but stabilizes PIF1 to precisely regulate seed germination. *Proc Natl Acad Sci U S A* 112, 3817-3822

237 Li, K., et al. (2015) Arabidopsis DET1 represses photomorphogenesis in part by negatively regulating DELLA protein abundance in darkness. *Molecular plant* 8, 622-630

238 Liu, F.Q., et al. (2007) The Arabidopsis RNA-Binding protein FCA requires a lysine-specific demethylase 1 homolog to downregulate FLC. *Mol Cell* 28, 398-407

239 Xu, L., et al. (2008) Di- and tri- but not monomethylation on histone H3 lysine 36 marks active transcription of genes involved in flowering time regulation and other processes in Arabidopsis thaliana. *Molecular and cellular biology* 28, 1348-1360

240 Berr, A., et al. (2009) SET DOMIAN GROUP25 Encodes a Histone Methyltransferase and Is Involved in FLOWERING LOCUS C Activation and Repression of Flowering. *Plant Physiol* 151, 1476-1485

241 Peng, M., et al. (2006) AtMBD9: a protein with a methyl-CpG-binding domain regulates flowering time and shoot branching in Arabidopsis. *Plant J* 46, 282-296

242 Potok, M.E., et al. (2019) Arabidopsis SWR1-associated protein methyl-CpG-binding domain 9 is required for histone H2A.Z deposition. *Nature communications* 10

243 Zhang, T., et al. (2016) PlantDHS: a database for DNase I hypersensitive sites in plants. *Nucleic Acids Res* 44, D1148-1153

244 Cheneby, J., et al. (2020) ReMap 2020: a database of regulatory regions from an integrative analysis of Human and Arabidopsis DNA-binding sequencing experiments. *Nucleic Acids Res* 48, D180-D188
245 Xu, Y., et al. (2017) WERAM: a database of writers, erasers and readers of histone acetylation and methylation in eukaryotes. *Nucleic Acids Res* 45, D264-D270

246 Chow, C.N., et al. (2019) PlantPAN3.0: a new and updated resource for reconstructing transcriptional regulatory networks from ChIP-seq experiments in plants. *Nucleic Acids Res* 47, D1155-D1163

247 Turberfield, A.H., et al. (2019) KDM2 proteins constrain transcription from CpG island gene promoters independently of their histone demethylase activity. *Nucleic Acids Res* 47, 9005-9023
FIGURE LEGENDS

Figure 1 Key Figure. Histone-based genomic positioning system (GPS) for RNAPII transcription.

(A). (Top) A combined metagene plot illustrating the profiles of histone post-translational modifications (PTMs) during RNAPII transcription of *Arabidopsis thaliana* genes. The metagene plots are derived from reanalysis of published ChIP-seq data (Summarized in Table S1).The Y-axis represents the normalized ChIP-seq signal of histone PTMs. The raw values to plot these data are provided in (Table S2). The X-axis indicates the relative position across a gene (grey), from transcription start site (TSS) to polyadenylation site (PAS) with flanking regions. Colored curves represent the genomic distributions of indicated histone PTMs. mono-, di- and tri-methylation (me1/me2/me3) at histone H3 residues lysine 4 (K4) and lysine 36 (K36); ubiquitination of H2A and H2B (H2Aub and H2Bub); grouped profile of all lysine acetylation modifications on H3 and H4 (H3ac/H4ac). (Bottom) Schematic illustration of plant transcription cycle by RNAPII includes transcriptional initiation (light red), early elongation (light green), productive elongation (light blue) and termination (light purple) across a gene. PIC: preinitiation complex; GTFs: general transcription factors; P-TEFb: positive transcription elongation factor b; PAF1-C: polymerase-associated factor 1 complex; FACT: facilitates chromatin transcription; SPT4/5: suppressor of Ty 4/5; CFs/CPFs: cleavage factors/cleavage and poly-adenylation factors; XRN s: exoribonuclease [72, 102-104]. All histone PTMs are positively correlated with RNAPII transcription, yet their localization to different positions has functional implications for RNAPII.

(B). Mis-specification of histone-PTM-based GPS indicates potential genomic transcription conflicts. In plant genome, most of transcription events are restrained within their own genomic territories. In the case of tandem transcription interference (TI), where upstream transcription represses the transcription initiation from downstream promoter through the function of FACT complex, thus setting transcription elongation associated histone PTMs in transcription initiation region.

Figure 2 Histone-based GPS guides gene expression in various biological process in plants.

A histone octamer consists of 2 copies of histone H2A (green cycles), H2B (yellow circles), H3...
(blue circles) and H4 (purple circles), wrapped by DNA (black curve). Lysine residues (grey circles, numbers denote the residue positions from C-terminals) on histone tails are subject to intensive post-translational modifications (PTMs), for example ubiquitination (ub, green rectangles), methylation (me, blue rectangles) and acetylation (ac, red rectangles). Histone residues can be mono-, di- and tri-methylated (double and triple blue rectangles). Histone PTMs regulate gene expression that control various biological processes in plants, including plant growth, germination, flowering, defense, environmental responses and circadian rhythm.

Figure Box 1

In chromatin immunoprecipitation (ChIP, left), plant tissues are first cross-linked to stabilize the histone-DNA interaction. Then, the cross-linked chromatin is fragmented by sonication or MNase digestion. Specific antibodies are used to target certain histone PTM or variants (red triangle) and for further precipitation. DNA that binds to histones is released by reverse cross-linking. Purified DNA can be used in microarray (ChIP-chip) or library construction and followed by next-generation sequencing (NGS, ChIP-seq). When using CUT&RUN technology (right), antibodies control the digestion *in situ* by linking to protein A-MNase fusion. Chromatin fragments generated after MNase digestion can be used for further DNA purification. Purified DNA can be used for library construction and followed by next-generation sequencing (NGS, CUT&RUN-seq). CUT&tag represents an updated version of CUT&RUN. Instead of using protein A-MNase fusion, CUT&tag uses protein A-Transposase Tn5 fusion which mediates the tagmentation of NGS sequencing adapters to the targeted loci. Purified DNA can be PCR-amplified and directly used in NGS sequencing.
# TABLE

Table 1 Summary of Histone PTM readers/writers/erasers and related biological functions in *Arabidopsis*.

| Histone PTMs | Role          | Enzyme (Gene locus)                        | Functions                                                                                   |
|--------------|---------------|--------------------------------------------|---------------------------------------------------------------------------------------------|
| H2Aub        | Writer        | RING1A (AT5G44280) RING1B (AT1G03770)      | Part of PRC1, double mutant exhibits globally reduced H2AUb, curly leaves and late flowering [144, 145]. |
|              |               | BMI1A (AT2G30580) BMI1B (AT1G06770)        | Part of PRC1, mutants regulates and drought responses Part of PRC1, mutants exhibits globally reduced H2AUb, regulates cotyledon and root development [143] and drought responses [142]. |
|              | Eraser        | UBP12 (AT5G06600) UBP13 (AT3G11910)        | Interact with polycomb protein LHP1, prevent autonomous endosperm development during seed development [146]. |
| H2Bub        | Reader/Effector | DET1 (AT4G10180)                      | Mutant exhibits reduced bulk H2Aub, DET1 regulates the light-dependent degradation of DUBm [49], represses light-induced seed germination [236] and light induced photomorphogenesis [237]. |
|              | Writer        | HUB1 (AT2G44950) HUB2 (AT1G55250)         | Mutants exhibit reduced seed dormancy [147], early flowering Mutants exhibit reduced seed dormancy [147], early flowering [84], changes in plant defense [149] and circadian clock gene expression , changes in plant defense [149] and circadian clock gene expression [77]. |
|              | Eraser        | SGF11 (AT5G58575)                       | Part of DUBm of *Arabidopsis* SAGA-like complex [87].                                      |
|              |               | UBP22 (AT5G10790)                       | Part of DUBm of *Arabidopsis* SAGA-like complex, function as a major H2Bub deubiquitinase [49, 87]. |
|              |               | ENY2 (AT3G27100)                        | Part of DUBm of *Arabidopsis* SAGA-like complex [87].                                      |
|              |               | UBP26 (AT3G49600)                       | Mutant exhibits early flowing phenotype and high rate of seed abortion [150].                |
|              |               | OTLD1 (AT2G27350)                       | Erases H2Bub, work with KDM1C to repress gene expression [151].                           |
| H3K4me1      | Reader        | EBS (AT4G22140)                        | Reads H3K4me3 and H3K27me3, mutant exhibits early flowering phenotype [38].                |
| Effector | Reads H3K4me3 and H3K27me3, mutant exhibits early flowering phenotype [39]. |
|---|---|
| SHL (AT4G39100) | Writes H3K4me3, mutant exhibits global development defects, early flowering phenotype [158, 163], changes in circadian clock gene expression [57, 164] and defects in gametogenesis [165]. |
| SDG2/ATXR3 (AT4G15180) | Writes H3K4me3 (can also write H3K36 methylation, listed below), mutant exhibits growth defects [155] and early flowering phenotype [156]. |
| SDG8/ASHH2 (AT1G77300) | Writes H3K4me1/me2/me3, mutant exhibits early flowering phenotype [157-159], reduced seed dormancy [160] and changes in plant defense [161, 162]. |
| SDG25/ATXR7 (AT5G42400) | Writes H3K4me3, mutant exhibits late flowering phenotype [156, 159]. |
| SDG4/ASHR3 (AT4G30860) | Writes H3K4me2/me3 (can also write H3K36 methylation, listed below), mutant exhibits reproductive defects in ovules [153] and unsynchronized DNA replication and cell division, further leading to defects in root development [154]. |
| SDG27/ATX1 (AT2G31650) | Writes H3K4me3 [42], mutant exhibits defects in root developments [166] and early botting [167]. |
| SDG30/ATX2 (AT1G05830) | Writes H3K4me2, mutant displays no clear phenotypes [167]. |
| SDG14/ATX3 (AT3G61740) SDG16/ATX4 (AT4G27910) SDG29/ATX5 (AT5G53430) | Write H3K4me2/me3, triple mutants display drastic defects in seed development and plant growth [168]. atx4/5 double mutant showed drought tolerance in seed development [168]. |
| FLD (AT3G10390) | Erases H3K4me2, mutant exhibits late flowering [238] and defects in plant systemic acquired resistance [179, 180]. |
| LDL1 (AT1G62830) LDL2 (AT3G13682) LDL3 (AT4G16310) | Erase H3K4me2/me3, mutants exhibit late flowering phenotype [127, 181], increased seed dormancy [182] and changes in circadian clock gene expression [128]. |
| JMJ14 (AT4G20400) | Erases H3K4me1/me2/me3, mutant exhibits early flowering phenotype [170], changes in RNA-directed DNA methylation [171] and circadian clock gene expression [164]. |
| Reader/Effector | Writer | Eraser | H3K36me1 | H3K36me2 | H3K36me3 |
|-----------------|--------|--------|-----------|-----------|-----------|
| **H3K36me3**    |        |        | JMJ15 (AT2G34880) | Erases H3K4me3, overexpression leads to early flowering [172] and increased salt tolerance [173]. | |
| **JMJ16 (AT1G08620)** | Erases H3K4me1/me2/me3, mutants display leaf senescence phenotype [174]. | |
| **JMJ17 (AT1G08620)** | Erases H3K4me1/me2/me3, mutants exhibit enhanced resistance to dehydration [175]. | |
| **JMJ18 (AT1G30810)** | Erases H3K4me2/me3, mutant shows late flowering phenotype while overexpression leads to early flowering phenotype [176]. | |
| **H3K36me1**    | MRG1 (AT4G37280) | Bind H3K36me3 and interact with HATs to mediate H4 acetylation. Double mutant is late flowering under long day condition [65, 66]. | |
| **MRG2 (AT1G02740)** |        |        | |
| **SDG4/ASHR3 (AT4G30860)** | Writes H3K36me1/me2, mutant displays unsynchronized DNA replication and cell division, further leading to defects in root development [154]. | |
| **SDG8/ASHH2 (AT1G77300)** | Writes H3K36me2/me3 [239]. | |
| **SDG25/ATXR7 (AT5G42400)** | Writes H3K36me2 [240]. | |
| **SDG26/ASHH1 (AT1G76710)** | Writes H3K36me3 [159]. | |
| **SDG25/ATXR7 (AT5G42400)** | Writes H3K36me2 [240]. | |
| **SDG26/ASHH1 (AT1G76710)** | Writes H3K36me3 [159]. | |
| **JMJ30 (AT3G20810)** | Erases H3K36me2/me3, regulates circadian clock related flowering gene expression [177], root development and response to auxin [178]. | |
| **YAF9A (AT5G45600)** | Read acetylated and unmodified H3, regulates H4 and H2A.Z acetylation. Mutant shows late flowering phenotype [101]. | |
| **YAF9B (AT2G18000)** |        |        | |
| **MBD9 (AT3G01460)** | Binds to acetylated histone H3 and H4, mutants exhibit enhanced shoot branching and early flowering phenotype [241]. MBD9 also regulates SWR1 complex mediated H2A.Z deposition and DNA demethylation. Binds to acetylated histone H3 and H4, mutants exhibit enhanced shoot branching and early flowering phenotype [241]. MBD9 also regulates SWR1 complex mediated H2A.Z deposition and DNA demethylation [35, 242]. | |
| **NPX1 (AT5G63320)** | Binds acetylated histone H3 and regulates SWR1 complex mediated H2A.Z deposition and DNA demethylation [35]. | |
| Writer/Effector | Writer | Reader/Eraser |
|----------------|--------|--------------|
| GCN5/HAG1 (AT3G54610) | GCN5/HAG1 (AT3G54610) | GCN5/HAG1 (AT3G54610) |
| Writes H3K14ac, globally associated with growth and developmental defects [33, 185, 186]. Regulates plant heat tolerance [30], plant regeneration [187]. | Writes H3K14ac, globally associated with growth and developmental defects [33, 185, 186]. Regulates plant heat tolerance [30], plant regeneration [187]. | Writes H3K14ac, globally associated with growth and developmental defects [33, 185, 186]. Regulates plant heat tolerance [30], plant regeneration [187]. |
| H4ac | H4ac | H4ac |
| BRAT1 (AT1G05910) | BRAT1 (AT1G05910) | BRAT1 (AT1G05910) |
| Reads H4K5/K8/K12ac. Functions as an anti-silencing factor that prevents gene silencing at methylated loci [34]. | Reads H4K5/K8/K12ac. Functions as an anti-silencing factor that prevents gene silencing at methylated loci [34]. | Reads H4K5/K8/K12ac. Functions as an anti-silencing factor that prevents gene silencing at methylated loci [34]. |
| Involved in plant response to UV [189], leaf growth [190], plant defense [191] and associated with RNAPII elongation [192]. | Involved in plant response to UV [189], leaf growth [190], plant defense [191] and associated with RNAPII elongation [192]. | Involved in plant response to UV [189], leaf growth [190], plant defense [191] and associated with RNAPII elongation [192]. |
| Involved in circadian clock gene expression [199], response to UV [195], root development [200] and male gamete development [201]. | Involved in circadian clock gene expression [199], response to UV [195], root development [200] and male gamete development [201]. | Involved in circadian clock gene expression [199], response to UV [195], root development [200] and male gamete development [201]. |
| H4ac | H4ac | H4ac |
| HAG2 (AT5G56740) | HAG2 (AT5G56740) | HAG2 (AT5G56740) |
| Writes H4K12ac [188]. | Writes H4K12ac [188]. | Writes H4K12ac [188]. |
| HAM1 (AT5G64610) | HAM1 (AT5G64610) | HAM1 (AT5G64610) |
| HAM2 (AT5G09740) | HAM2 (AT5G09740) | HAM2 (AT5G09740) |
| Write H4K5ac [188] and is involved in gametophyte development [193]. | Write H4K5ac [188] and is involved in gametophyte development [193]. | Write H4K5ac [188] and is involved in gametophyte development [193]. |
| Involved in circadian clock gene expression [128], plant defense [202], transposon silencing [203], flowering [204] and seed dormancy [205]. | Involved in circadian clock gene expression [128], plant defense [202], transposon silencing [203], flowering [204] and seed dormancy [205]. | Involved in circadian clock gene expression [128], plant defense [202], transposon silencing [203], flowering [204] and seed dormancy [205]. |
| Involved in the development of female gametophyte and embryo [206]. | Involved in the development of female gametophyte and embryo [206]. | Involved in the development of female gametophyte and embryo [206]. |
| HDA5 (AT5G61060) | HDA5 (AT5G61060) | HDA5 (AT5G61060) |
| Interacts with other histone modifying enzymes, such as HDA6 and FLD. Mutant displays late flowering phenotype [218]. Quadruple mutant hda5/14/15/18 exhibits hypersensitivity towards salt [225]. | Interacts with other histone modifying enzymes, such as HDA6 and FLD. Mutant displays late flowering phenotype [218]. Quadruple mutant hda5/14/15/18 exhibits hypersensitivity towards salt [225]. | Interacts with other histone modifying enzymes, such as HDA6 and FLD. Mutant displays late flowering phenotype [218]. Quadruple mutant hda5/14/15/18 exhibits hypersensitivity towards salt [225]. |
| HDA6 (AT5G63110) | HDA6 (AT5G63110) | HDA6 (AT5G63110) |
| Involved in circadian clock gene expression [128], plant defense [202], transposon silencing [203], flowering [204] and seed dormancy [205]. | Involved in circadian clock gene expression [128], plant defense [202], transposon silencing [203], flowering [204] and seed dormancy [205]. | Involved in circadian clock gene expression [128], plant defense [202], transposon silencing [203], flowering [204] and seed dormancy [205]. |
| HDA7 (AT5G35600) | HDA7 (AT5G35600) | HDA7 (AT5G35600) |
| Involved in the development of female gametophyte and embryo [206]. | Involved in the development of female gametophyte and embryo [206]. | Involved in the development of female gametophyte and embryo [206]. |
| HDA9 (AT3G44680) | HDA9 (AT3G44680) | HDA9 (AT3G44680) |
| Mediates the H3K27 deacetylation and further leads to FLC gene repression by H3K27me3 [207]. Mutants also display differential responses to salt and drought [208]; enhanced pathogen resistance by activating NLR genes [209]. HDA9 also involves the regulation of flowering [210] and leaf development [211]. | Mediates the H3K27 deacetylation and further leads to FLC gene repression by H3K27me3 [207]. Mutants also display differential responses to salt and drought [208]; enhanced pathogen resistance by activating NLR genes [209]. HDA9 also involves the regulation of flowering [210] and leaf development [211]. | Mediates the H3K27 deacetylation and further leads to FLC gene repression by H3K27me3 [207]. Mutants also display differential responses to salt and drought [208]; enhanced pathogen resistance by activating NLR genes [209]. HDA9 also involves the regulation of flowering [210] and leaf development [211]. |
| HDA14 (AT4G33470) | HDA14 (AT4G33470) | HDA14 (AT4G33470) |
| Potentially links to protein acetylation to phosphorylation [219]. | Potentially links to protein acetylation to phosphorylation [219]. | Potentially links to protein acetylation to phosphorylation [219]. |
| Gene Name | Biological Functions |
|-----------|----------------------|
| HDA15 (AT3G18520) | Regulates temperature sensing [212], cell elongation [220, 221], response to auxin [222] and light [223]. |
| HDA18 (AT5G61070) | Involved in cell fate control in root epidermis [200, 224]. |
| HDA19 (AT4G38130) | Regulates photoperiod-dependent flowering time [204], temperature sensing [212], root development [213], germination [214, 215], plant defense [216] and plant stress responses [217]. Quintuple mutant hda5/14/15/18/19 exhibits salt tolerance [226]. |
| HD2A (AT3G44750) | Plant-specific histone deacetylases, involved in stem vascular development [230], root meristem development [231], flowering [232], plant defense [233], heat and cold stress response [234, 235]. |
| HD2B (AT5G22650) | |
| HD2C (AT5G03740) | |
| HD2D (AT2G27840) | |
| SRT1 (AT5G55760) | Involved in mitochondrial metabolite transport [227, 228] and ethylene signaling pathway [229]. |
| SRT2 (AT5G09230) | |

Table 1. Summary of Histone PTM readers/writers/erasers and related biological functions in *Arabidopsis*. Enzymes are clustered by their roles (column 2) as histone PTM (column 1) readers, writers and erasers. Gene name and ID are shown in column 3. The biological functions of corresponding enzymes are shown in column 4.
TEXT BOX

Box 1

ChIP-chip: Chromatin immunoprecipitation (ChIP) followed by microarray (chip) to determine the protein-DNA interaction in genome-wide,

ChIP-seq: ChIP sequencing (ChIP-seq) is the combination of chromatin immuno-precipitation (ChIP) and next-generation sequencing (NGS). The DNA-bound protein is immune-precipitated by antibody and the associated DNA is then fragmented, purified and sequenced. ChIP-seq analyzes the protein-DNA interaction and reveals the genomic distribution of a particular DNA-bound protein by NGS.

CUT&RUN-seq: CUT & RUN (Cleavage Under Targets and Release Using Nuclease) followed by next-generation sequencing is a technology to study DNA-protein interaction. DNA-protein complex is separated by the antibody-targeted in situ MNase cleavage and the DNA is subsequently purified and sequenced.

PCSD: a Plant Chromatin State Database providing information of chromatin states across the genomes of Arabidopsis thaliana, Oryza sativa and Zea mays based on various epigenomic sequencing data sets [118]. Based on Hidden Markov model, the genomes where clustered in relation with their chromatin environment. It is possible to download genome browser files for various ChIP-Seq experiments (i.e transcription factors, histones PTMs, or chromatin associated factors).

PlantDHS: a Plant DNase I Hypersensitive Site database also including the genomic information of histone PTMs, nucleosome positioning and transcription factor binding sites in plants [243]. The database provides downloadable ChIP-Seq files to load into a genome browser for several nucleosome related sequencing methods.

ReMap: A large database including integrative analysis of Arabidopsis ChIP-seq and DAP-seq data sets, providing the distribution information of histone PTM/variants, transcription regulators and factors [244].

WERAM: a database for writers, erasers and readers of histone acetylation and methylation in eukaryotes including many plant species [245].
PlantPAN3.0: A database exploring transcription factors from ChIP-Seq experiments from 78 plant species [246].

Box 2

In plants, the intragenic distribution profiles of H3K36me3 and H3K36me2 differs from many other higher organisms. Perhaps, H3K36me3 is progressively de-methylated in plants, where H3K36 is thought to be progressively methylated during RNAPII elongation in animals. These differences may result in plant-specific chromatin states [247]. The molecular mechanism responsible for the specific positioning of H3K36me3 and H3K36me2 along genes bodies in plants remains unclear. In yeast, a single H3K36 methyltransferase (Set2p) is responsible for all methylation states of H3K36. There are around eight H3K36 methyltransferases in mammals, but many more histone methyltransferases in Arabidopsis. H3K36-specific histone methyltransferase in plants, such as Arabidopsis SDG8 and SDG26 or SDG725 in rice, currently represent the main candidates responsible for these H3K36me patterns [134]. Since the H3K36me3 and H3K36me2 distributions along genes are opposite in plants compared to the distribution in animals, it remains to be investigated how this effects H3K36 methylation-associated events such as splicing and intragenic transcription initiation. A focus on the plant equivalents of H3K36me3, H3K36me2 and rarely studied H3K36me1 (peaking at the extreme 3’ end of genes in rice) in association with transcription elongation, termination and gene regulation promises to instruct intriguing lessons about plant-specific transcription regulation mechanisms.
GLOSSARY

Histone

A histone is a basic protein component of eukaryotic chromosomes, packaging DNA into ordered structures named nucleosomes. Core histones include histone H2A, H2B, H3 and H4.

Histone PTM

A histone post-translational modification (PTM) describes the chemical modification on histone residues, such as acetylation of histone H3 lysine 4 (H3K4ac). The common histone PTMs include methylation (me), phosphorylation (ph), acetylation (ac) and ubiquitination (ub). A histone residue can be modified in different states. For example, lysine residues can be mono-, di- and tri-methylated (me1, me2 and me3), expanding the diversity and functionality of histone PTMs.

RNAPII

DNA dependent RNA polymerase II (RNAPII or Pol II) is a multiprotein complex including 12 subunits. It is responsible for the transcription of messenger RNA (mRNA), long non-coding RNA, snRNA and microRNA.

PIC

A transcription preinitiation complex (PIC) is an assembly of RNAPII, co-factors and transcription factors in gene promoter region that facilitates RNAPII transcription initiation.