Transcriptional Repression by Histone Deacetylases in Plants

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ABSTRACT **Reversible histone acetylation and deacetylation at the N-terminus of histone tails play crucial roles in regulation of eukaryotic gene activity. Acetylation of core histones usually induces an 'open' chromatin structure and is associated with gene activation, whereas deacetylation of histone is often correlated with 'closed' chromatin and gene repression. Histone deacetylation is catalyzed by histone deacetylases (HDACs). A growing number of studies have demonstrated the importance of histone deacetylation/acetylation on genome stability, transcriptional regulation, and development in plants. Furthermore, HDACs were shown to interact with various chromatin remolding factors and transcription factors involved in transcriptional repression in multiple developmental processes. In this review, we summarized recent findings on the transcriptional repression mediated by HDACs in plants.**

Key words: histone deacetylases; transcriptional repression; plant development; abiotic and biotic stresses.

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INTRODUCTION

Eukaryotic DNA is organized into chromatin with nucleosomes as the basic building unit. A single nucleosome is composed of two H3–H4 histone dimmers bridged together as a stable tetramer that is flanked by two separate H2A–H2B dimmers and is typically enfolded by 147 bp of DNA (Luger et al., 1997). Each histone has a structured globular domain and an unstructured amino-terminal tail that extends from the core nucleosome. These histone tails provide sites for a variety of posttranslational modifications, such as acetylation, phosphorylation, methylation, ubiquitination, and ADP-ribosylation (Berger, 2007). All of these modifications are reversible and maintained by the controlled action of different histone modifying enzymes influencing chromatin structure. Histone modifications play an important role in the regulation of several biological processes involving DNA dynamics like transcription, DNA repair, and replication.

The acetylation state of the ε-amino group of conserved lysine residues within all four core histones was regulated by the opposing activities of histone acetyltransferases and histone deacetylases (HDACs). HDACs can remove acetyl groups from histone tail lysines and non-histone substrates including transcription factors and other proteins involved in DNA repair and replication, metabolism, cytoskeleton dynamics, apoptosis, and cell signaling (Yang and Seto, 2007). Based on sequence similarity and cofactor dependency, HDACs in all eukaryotes are grouped into three families: RPD3/HDA1 (Reduced Potassium Dependence 3/Histone Deacetylase 1), SIR2 (Silent Information Regulator 2), and HD2 (Histone Deacetylase 2)-related protein families (Pandey et al., 2002). Members of the SIR2 family (Sirtuins) have a catalytic domain that is characterized by the requirement for Nicotine Adenine Dinucleotide (NAD) as a cofactor (Haigis and Guarente,

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2006), while members of the RPD3/HDA1 superfamily share sequence homology in the HDAC domain and require Zn^{2+} cofactor for deacetylase activity (Yang and Seto, 2007). In addition, HD2 proteins are plant-specific HDACs (Pandey et al., 2002).

HISTONE DEACETYLASES IN PLANTS

In the past decade, plant HDACs have drawn considerable research attention and an increasing number of HDACs were identified and characterized from *Arabidopsis*, rice, and other plant species. Among 18 HDACs indentified in *Arabidopsis*, 12 of them belong to the RPD3/HDA1 superfamily (Hollender and Liu, 2008; Alinsug et al., 2009). Based on sequence similarity, the RPD3/HDA1 superfamily are further divided into three classes. Class I has four members: HDA19, HDA6, HDA7, and HDA9, representing the functionally best-characterized HDACs in *Arabidopsis*. Class II includes HDA5, HDA15, and HDA18. HDA2 and its two additional isoforms comprise class III. HDA8, HDA14, HDA10, and HDA17 are unclassified members of the RPD3-like superfamily (Pandey et al., 2002; Hollender and Liu, 2008).

Characterization of *HDAC* mutants in *Arabidopsis* indicated that the members of the RPD3/HDA1 family HDACs play a vital role in regulating gene expression in various biological processes. For instance, *HDA6* mutant alleles, *axe1-1* and *axe1-5*, displayed increased expression of the auxin-responsive reporter genes (Murfett et al., 2001). Another *HDA6* allele, *rst1*, was shown to have reduced DNA methylation in centromeric and rDNA repeats, indicating that HDA6 may act to maintain DNA methylation (Aufsatz et al., 2002), while *HDA19*, the closest homolog of *HDA6*, was shown to be important for proper vegetative development as *hda19* mutants displayed various developmental abnormalities (Tian and Chen, 2001; Tian et al., 2005; Zhou et al., 2005; Long et al., 2006). Loss-of-function of *HDA18* resulted in alterations in the cellular patterning in the root epidermis in *Arabidopsis* (Xu et al., 2005; Liu et al., 2013a). In addition, HDA7 is crucial for female gametophyte development and embryogenesis in *Arabidopsis* (Cigliano et al., 2013). Furthermore, HDA14 is an α-tubulin decetylase associated with α/β-tubulin and enriched in microtubule fractions by direct association with the PPP-type phosphatases PP2A (Tran et al., 2012).

Arabidopsis has four members of the plant-specific HD2 family proteins, namely HD2A/HDT1, HD2B/HDT2, HD2C/HDT3, and HD2D/HDT4. Silencing of *HD2A* in *Arabidopsis* resulted in aborted seed development (Wu et al., 2000), while overexpression of *HD2A* caused morphological defects of leaves and flowers as well as delayed flowering and aborted seed development (Zhou et al., 2004). HD2A and HD2B were found to act independently with ASYMMETRIC LEAVES1 (AS1) and AS2 to control miR165/166 distribution and the development of adaxial–abaxial leaf polarity (Ueno et al., 2007). Furthermore, HD2A also functions in the postembryonic establishment of nucleolar dominance (Pontes et al., 2007).

The function of SIR2 family HDACs was also been investigated in *Arabidopsis*. The *Arabidopsis* genome encodes two SIR2 family HDACs: SRT1 and SRT2. SRT2 resides predominantly at the inner mitochondrial membrane and interacts with a small number of protein complexes mainly involved in energy metabolism and metabolite transport (Koenig et al., 2014). Further analysis indicated that SRT2 plays an important role in fine-tuning mitochondrial energy metabolism.

Compared to *Arabidopsis*, relatively few HDACs were characterized in other plant species. HD2-type HDACs was first discovered in maize as an acidic nucleolar phosphoprotein in a high-molecular-weight complex (Lusser et al., 1997). The maize RPD3/HDA1-type HDAC, HDA101, is involved in sequence-specific modulation of histone modifications to regulate gene transcription and plant development (Rossi et al., 2007). The rice HD2-type HDAC, HDT701, was found to be a histone H4 deacetylase that negatively regulates plant innate immunity by modulating histone H4 acetylation of defense-related genes (Ding et al., 2012). Furthermore, down-regulation of rice *HDT702* led to the production of narrowed leaves and stems (Hu et al., 2009). In contrast, down-regulation of *RPD3/HDA1*-type *HDACs* by RNAi or amiRNA in rice led to various developmental defects. For examples, down-regulation of *HDA703* by amiRNA reduced rice peduncle elongation and fertility, while inactivation of a closely related homolog *HDA710* by RNAi affected vegetative growth (Hu et al., 2009). Overexpression of *OsHDAC1* leads to increased growth rate and altered plant architecture in rice (Jang et al., 2003). Further analyses indicated that OsHDAC1 regulates the expression of *OsNAC6* that controls seedling root growth in rice (Chung et al., 2009). Taken together, these findings suggested that various HDACs play distinct roles in plant developmental processes. More recently, *Arabidopsis* HDACs were shown to interact with various transcription factors and chromatin remolding factors involved in repression of gene expression in multiple development processes (Table 1 and Figure 1).

TRANSCRIPTION REPRESSION IN PLANT DEVELOPMENT

Histone acetylation and deacetylation play key roles in the regulation of flowering time in *Arabidopsis* (He et al., 2003). Loss-of-function *HDA6* mutants exhibit a late-flowering phenotype, suggesting that HDA6 is involved in control of flowering time by histone deacetylation (Wu et al., 2008). HDA6 directly interacts with the histone demethylase, FLOWERING

Table 1 List of Interaction Proteins of HDACs in *Arabidopsis*.

HDAC	Partner	Function	Reference
HDA6	FLD	Flowering time	Yu et al., 2011
	FVE (MSI4), MSI5	Flowering time	Gu et al., 2011
	HOS1	Flowering time	Jung et al., 2013
	AHL22	Flowering time	Yun et al., 2012
	MET1	Transposon silencing	Liu et al., 2012
	HD2C	Salt and ABA stress response	Luo et al., 2012a
	AS1, AS2	Leaf development	Luo et al., 2012b
	JAZ1, JAZ3, JAZ9	Ethylene/jasmonate response	Zhu et al., 2011
	EIN3, EIL1	Ethylene/jasmonate response	Zhu et al., 2011
	TPL	Circadian clocks	Wang et al., 2013b
	COI1	Jasmonate response	Devoto et al., 2002
HDA15	PIF3	Chlorophyll biosynthesis	Liu et al., 2013b
HDA19	HSL1	Seed maturation	Zhou et al., 2013
	AP2, TPL	Floral organ identity	Krogan et al., 2012
	LEUNIG	Flower development	Gonzalez et al., 2007
	AFR1, AFR2	Flowering time	Gu et al., 2013
	AHL22	Flowering time	Yun et al., 2012
	TPR1	Immune responses	Zhu et al., 2010
	TPL	Circadian clocks	Wang et al., 2013b
	BZR1	Brassinosteroid signaling pathway	Wang et al., 2013a
	SNL1, SNL2	Seed dormancy	Wang et al., 2013c
	ERF7, SIN3	ABA and drought stress response	Song et al., 2005
	ERF3, ERF4, SAP18	Salt stress response	Song and Galbraith, 2006
	WKRY38, WKRY62	Basal defense	Kim et al., 2008
HD2B	RPS6	rRNA gene expression	Kim et al., 2014

LOCUS D (FLD), both *in vitro* and *in vivo* (Yu et al., 2011). FLD is a Lysine Specific Demethylase1 (LSD1)-type histone demethylase that remove methyl groups from mono- and dimethylated histone H3K4 (Jiang et al., 2007). Increased levels of histone H3 acetylation and H3K4 trimethylation at *FLC*, *MAF4*, and *MAF5*, the key repressors of flowering, were found in both *hda6* and *fld* mutant plants, suggesting functional interplay between histone deacetylase and demethylase in flowering control. These results support a scenario in which histone deacetylation and demethylation crosstalk is mediated by physical association between HDA6 and FLD. Additionally, HDA6 was also shown to associate with FVE (MSI4) and MSI5, two *Arabidopsis* homologs of the human histone-binding proteins RbAp46/48, to form HDAC complex in control of flowering time (Gu et al., 2011). More recently, it was found that the *Arabidopsis* functional relatives of the yeast SAP30, SAP30 FUNCTION RELATED 1 (AFR1), and AFR2, act as part of HDAC complexes to modulate the expression of the florigen gene *FT* (Gu et al., 2013). Furthermore, HDA9 regulates flowering time through repression of *AGL19*, which promotes flowering in a way that is independent of the *FLC* pathway (Kim et al., 2013). These findings suggest that different HDACs may play distinct roles in the regulation of flowering.

Meristem activity in the shoot apex is specified in part by the class I *KNOTTED-LIKE HOMOBOX* (*KNOX*) genes (Scofield and Murray, 2006). *KNOX* repression during organogenesis is mediated by the MYB domain protein AS1 in *Arabidopsis thaliana* (Guo et al., 2008). In addition, AS1 interacts with the LATERAL ORGAN BOUNDARIES (LOB) domain protein AS2 and directly represses the expression of *BP*/*KNAT1* and *KNAT2* (Xu et al., 2003; Guo et al., 2008). We found that HDA6 can interact with AS1 *in vitro* and *in vivo* (Luo et al., 2012c). The *KNOX* genes were up-regulated and hyperacetylated in the *hda6* mutant, indicating that HDA6 may regulate *KNOX* expression through histone deacetylation. Chromatin immunoprecipitation assays revealed that HDA6 and AS1 bind directly to the chromatin of *KNOX* genes, *KNAT1*, *KNAT2*, and *KNATM*. Taken together, these data indicate that AS1 recruits HDA6 to form a HDAC repressor complex involved in the regulation of *KNOX* expression in leaf development (Figure 1A).

Previous studies showed that HDA6 and HDA19 redundantly regulate the expression of *LEAFY COTYLEDON 1* (*LEC1*), *FUSCA 3* (*FUS3*), and *ABA INSENSITIVE 3* (*ABI3*) involved in embryogenesis (Tanaka et al., 2008). Recently, we demonstrated that HDA19

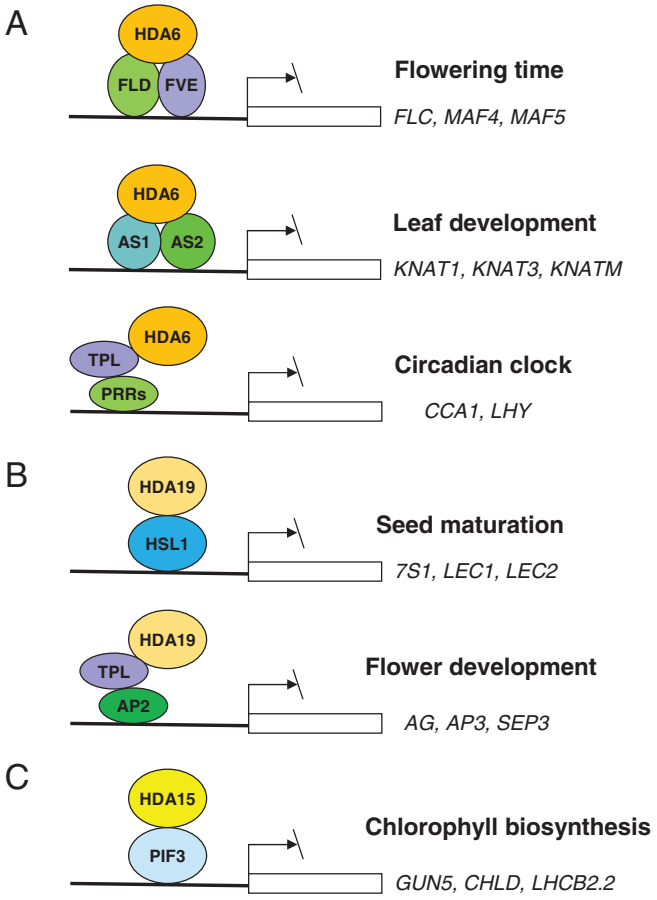

Figure 1 Transcriptional Repression Mediated by HDACs in *Arabidopsis*.

(A) HDA6 represses gene expression by interacting with various transcription factors and co-repressors involved in flowering time, leaf development, and circadian clock.

(B) HDA19 represses gene expression involved in seed maturation and flower development.

(C) PIF3 interacts with HDA15 to repress chlorophyll biosynthetic genes.

interacted with the HIGH-LEVEL EXPRESSION OF SUGAR-INDUCIBLE GENE2-LIKE1 (HSL1) to repress seed maturation genes, such as *7S1*, *OLEOSIN1* (*OLE1*), and *ABI3* during seed germination (Zhou et al., 2013). Mutations in *HDA19* resulted in the ectopic expression of seed maturation genes in seedlings, which was associated with increased levels of gene activation marks, such as histone H3 and H4 acetylation, and histone H3K4me3, but decreased levels of the gene repression mark histone H3K27me3 in the promoter and/or coding regions. Chromatin immunoprecipitation assays showed that HDA19 directly binds to the chromatin of the seed maturation genes. These results suggest that HDA19 and HSL1 may act together to repress seed maturation gene expression during germination (Figure 1B).

Members of the plant Groucho/Tup1 co-repressor family, LEUNIG (LUG) and TOPLESS/TOPLESS-RELATED (TPL/TPR), are associated with HDACs involved in plant development (Gonzalez et al., 2007; Krogan et al., 2012; Wang et al., 2013b). The expression of the core clock genes *CIRCADIAN CLOCK ASSOCIATED 1* (*CCA1*) and *LATE ELONGATED HYPOCOTYL* (*LHY*) was regulated by PSEUDO RESPONSE REGULATOR 5 (PRR5), PRR7, and PRR9 (Wang et al., 2013b). TPL interacts with PRR5, PRR7, and PRR9 to repress *CCA1* and *LHY* transcription and alter circadian period. In addition, PRR9 and TPL forms a complex with HDA6, acting as a central repressor of circadian gene expression (Wang et al., 2013b). Furthermore, APETALA2 (AP2) recruits the co-repressor TPL and HDA19 to regulate the expression floral organ identity genes involved in flower development (Krogan et al., 2012). More recently, HDA19 was shown to be associated with BRASSINAZOLE RESISTANT1 (BZR1), the key transcriptional factor in BR sigaling in a tandem affinity purification assay (Wang et al., 2013a). Taken together, these data indicate that *Arabidopsis* HDACs such as HDA6 and HDA19 can be recruited by different transcriptional factors and form multiple protein complexes involved in various developmental proecess (Figure 1A and 1B).

Light is an important environmental factor governing plant growth and development. Previous studies suggest an involvement of histone acetylation and deacetylation in the regulation of light-responsive genes (Chua et al., 2001, 2003; Benhamed et al., 2006). More recently, we gained insight into the molecular mechanisms of HDAC functions in modulation of light-responsive gene expression. We found that HDA15 specifically interacts with PHYTOCHROME INTERACTING FACTOR 3 (PIF3), a key transcription factor involved in photomorphogenesis in *Arabidopsis* (Liu et al., 2013b). Loss-of-function *hda15* mutants showed increased proto-chlorophyllide contents similar to *pif3* mutants. In addition, HDA15 and PIF3 co-repress the gene expression involved in chlorophyll biosynthesis and photosynthesis. Furthermore, PIF3 recruits HDA15 to the promoters of the light-responsive genes and represses their expression by histone deacetylation. Our finding revealed that PIF3 and HDA15 form a repression complex, which plays a critical role in the regulation of light-responsive genes (Figure 1C). Further phenotypic analyses showed that *hda15* mutant seedlings exhibited relative longer hypocotyls compared to the wild-type under red light (RL) and far-red light (FR) conditions, indicating that HDA15 might positively regulate Phytochrome A (PHYA)- and PHYB-mediated inhibition of hypocotyl elongation. In contrast, mutations of *HDA19* in *Arabidopsis* resulted in a short-hypocotyl phenotype under RL and FR (Benhamed et al., 2006). Genetic analyses showed that HDA15 and HDA19 may act antagonistically in the regulation of hypocotyl growth (Liu et al., 2013b). These observations indicate that HDA15 and HDA19 play distinct roles in the regulation of photomorphogenesis in *Arabidopsis*.

TRANSCRIPTION REPRESSION IN ENVIRONMENTAL STRESS RESPONSES

The involvement of HDACs in plant responses to abiotic stresses has been demonstrated (Luo et al., 2012a; Yuan et al., 2013). In rice, the expression of *HDAC* genes is regulated by stress-related hormones such as salicylic acid (SA), jasmonic acid (JA), or abscisic acid (ABA) (Fu et al., 2007; Hu et al., 2009). In *Arabidopsis*, the expression of *HDA6* and *HDA19* is induced by JA (Zhou et al., 2005), whereas the expression of *HD2A*, *HD2B*, *HD2C*, and *HD2D* is repressed by ABA and NaCl (Sridha and Wu, 2006; Luo et al., 2012b). The *hda6* mutant plants are hypersensitive to ABA and salt stress, and the expression of ABA-responsive genes including *ABA INSENSITIVE 1* (*ABI1*), *ABI2*, *3-KETO-ACYL-COA THIOLASE 1* (*KAT1*), *KAT2*, *DEHYDRATION-RESPONSIVE ELEMENT-BINDING PROTEIN 2A* (*DREB2A*), *RESPONSIVE TO DESICCATION 29A* (*RD29A*), and *RD29B* is reduced in *hda6* mutants (Chen et al., 2010). Furthermore, cold-acclimated *hda6* mutant plants showed a freezing-sensitive phenotype compared with cold-acclimated wild-type plants, due to the reduced expression of genes involved in cold stress, such as fatty acid desaturase and lipid transfer protein genes (To et al., 2011b). We also showed that *hd2c* mutants displayed increased sensitivity to ABA and NaCl during germination and decreased tolerance to salt stress (Luo et al., 2012b). Moreover, HD2C physically interacts with HDA6 and represses the expression of abiotic stress-responsive genes, *ABI1*, *ABI2*, and *ERF4.* Our studies indicated that HD2C functionally associates with HDA6 and regulates gene expression through histone modifications.

Arabidopsis HDA19 has been found to be associated with the ERF transcriptional repressors, ERF3, ERF4, and ERF7, to regulate gene expression in response to abiotic stresses (Song et al., 2005; Song and Galbraith, 2006). ERF3, ERF4, and ERF7 are EAR-motif-containing transcriptional repressors involved in regulating ABA and abiotic stress responses in *Arabidopsis* (Yang et al., 2005). ERF7 interacts with the *Arabidopsis* homolog of a human global co-repressor, Sin3, which in turn interacts with HDA19 (Song et al., 2005). On the other hand, ERF3 and ERF4 can interact with SAP18, an ortholog of human SAP18 (Song and Galbraith, 2006). Both Sin3 and SAP18 are subunits of the human HDAC complex. Therefore, ERF repressors may form a transcriptional repression complex with SAP18, Sin3, and HDA19 to regulate gene expression in ABA and abiotic response through chromatin modifications mediated by histone deacetylation.

In addition, HDACs were reported to paticipate in the transcription regulation of plant defense responses (Zhou et al., 2005; Choi et al., 2012). A coimmunoprecipitation assay showed that HDA6 assocaites with COI1, an essential component of the JA siganling pathway (Devoto et al., 2002). Recent studies showed that JAZ proteins directly interact and recruit HDA6 to repress EIN3/EIL1-dependent transcription (Zhu et al., 2011). The *Arabidopsis* resistance protein SNC1 activates immune responses through association with the transcriptional co-repressor TPR1 and HDA19 (Zhu et al., 2010). Furthermore, HDA19 can also interact with two type III WRKY transcription factors: WRKY38 and WRKY62 (Kim et al., 2008). WRKY38 and WRKY62 act as negative regulators of plant basal defense, whereas HDA19 prevents activation of transcription mediated by WRKY38 and WRKY62. Taken together, these findings indicated that HDAC-mediated gene repression plays a key regulatory role in plant responses to environmental stress responses.

CROSSTALK OF HISTONE MODIFICATIONS AND DNA METHYLATION MEDIATED BY HDACS

DNA methylation and histone acetylation are two major epigenetic marks that contribute to the stability of gene expression status. Histone deacetylation and DNA methylation can act synergistically to repress genes in *Neurospora* and in mammalian cells (Momparler, 2003). In mammalian cells, crosstalk between DNA methylation and histone deacetylation can be mediated through either direct interactions between HDACs and DNA methyltransferases (DMTs) (Datta et al., 2003) or the recruitment of HDACs to methylated DNA via methyl CpG-binding proteins (MBPs) (Zemach and Grafi, 2007). Previous studies reported that HDA6 is an essential component in RNA directed DNA methylation (RdDM) (Aufsatz et al., 2002, 2007; Earley et al., 2010). In addition, HDA6 is also required for transposon and rRNA gene silencing via cytosine methylation maintenance (Lippman et al., 2003; Earley et al., 2006, 2010). Our study indicates that HDA6 directly interacts with the DNA methyltransferase MET1 both *in vitro* and *in vivo* (Liu et al., 2012). In addition, HDA6 and MET1 co-regulate a large subset of transposons and repeat sequences (To et al., 2011a). A subset of transposons transcriptionally reactivated in *hda6* mutants is associated with elevated histone H3 and H4 acetylation as well as increased H3K4Me3 and H3K4Me2 (Liu et al., 2012). Decreased DNA methylation of the transposons was also detected in *hda6* mutants, suggesting that HDA6 silences the transposons by regulating histone acetylation and methylation as well as the DNA methylation status. Similarly, transcripts of some of these transposons were also increased in the *met1* mutant, with decreased DNA methylation (Liu et al., 2012). These results indicate that HDA6 and MET1 interact directly and act together to silence transposons by modulating DNA methylation, histone acetylation, and histone methylation status.

MSI5 acts redundantly with FVE to silence various loci targeted by siRNAs, including *FLC* and RdDM target loci

(Gu et al., 2011). Both FVE and MSI5 form protein complexes with HDA6 to mediate histone deacetylation in their target loci. Furthermore, the nuclear matrix protein TEK associates with the FVE/MSI5 complex and binds to various target sites of transposons and repeat-containing genes, leading to histone deacetylation and gene silencing (Xu et al., 2013). These findings indicate that FVE and MSI5 act in the context of HDA6-containing repressor complexes to mediate chromatin silencing of developmental genes as well as transposable and repetitive elements.

Crosstalk between histone deacetylation and demethylation has previously been suggested to modulate gene expression in mammalian cells (Lee et al., 2006). The mammalian histone demethylase, LSD1, is an integral component of histone deacetylase co-repressor complexes, in which HDACs and LSD1 may cooperate to remove activating acetyl and methyl histone modifications (Shi et al., 2005; Lee et al., 2006). HDAC inhibitors can diminish histone demethylation activity, whereas LSD1 mutations can also affect deacetylation activity (Lee et al., 2006), indicating that the enzymatic activities of HDACs and LSD1 are closely linked. Our study indicates that *Arabidopsis* HDA6 is physically associated with the LSD1-type histone demethylase FLD (Yu et al., 2011), suggesting that histone deacetylases and demethylases may crosstalk and mutually affect each other's activities to coordinate regulate gene expression. Taken together, these findings indicate that HDA6 may act as a part of large co-repressor complexes with histone deacetylation and demethylation as well as DNA methylation activities.

HDA19 is associated with HSL1, a B3 domain transcription factor containing the zinc-finger CW (zf-CW) domain (Zhou et al., 2013). The deletion analysis of HSL1 indicated that the zf-CW domain of HSL1 is required for the interaction between HDA19 and HSL1. Since the zf-CW domain acts as a new histone modification reader by binding to methylated histone H3K4 (He et al., 2010; Hoppmann et al., 2011), the association of a CW domain protein and a HDAC may mediate the crosstalk between histone methylation and histone deacetylation in gene regulation. Further analysis is required to reveal how HDA19 and HSL1 interaction is involved in the crosstalk of different histone modifications.

CONCLUSIONS AND PERSPECTIVES

Reversible histone deacetylation and acetylation changes play crucial roles in regulation of gene expression involved in multiple developmental processes. Analysis of various *HDAC* mutants has uncovered distinct roles of different HDACs in *Arabidopsis*. Furthermore, identification of the interacting proteins of HDACs has gained insight into the molecular mechanisms of the function of HDACs in various biological processes (Table 1). Further research is required to investigate the function of other HDACs and identify their interaction proteins and targets. In mammalian cells, HDACs were found to catalyze the deacetylation of histones as well as non-histone substrates. It remains to be determined whether the plant HDACs can also modify non-histone proteins such as transcriptional factors and other chromatin remolding factors. Analysis of the components of HDAC-containing protein complexes will also be useful to reveal the molecular mechanisms of transcriptional repression mediated by HDACs in plants.

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