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Epigenetic Modifications and Plant Hormone Action

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ABSTRACT

The action of phytohormones in plants requires the spatiotemporal regulation of their accumulation and responses at various levels. Recent studies reveal an emerging relationship between the function of phytohormones and epigenetic modifications. In particular, evidence suggests that auxin biosynthesis, transport, and signal transduction is modulated by microRNAs and epigenetic factors such as histone modification, chromatin remodeling, and DNA methylation. Furthermore, some phytohormones have been shown to affect epigenetic modifications. These findings are shedding light on the mode of action of phytohormones and are opening up a new avenue of research on phytohormones as well as on the mechanisms regulating epigenetic modifications.

Key words: epigenetics, auxin, plant hormones, gene expression, chromatin regulation, DNA methylation

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INTRODUCTION

Epigenetic modifications regulate mitotically or meiotically heritable gene expression without altering any changes in the genomic DNA sequences, and therefore contribute to flexible and reversible regulation of gene expression. Epigenetic modifications involve histone modification, chromatin remodeling, non-coding RNAs, and DNA methylation. Each of these modifications alone, or in combination with one another, and the interplay between different epigenetic modifications, controls gene expression patterns. Numerous studies show that genetic programming can be overridden by altering epigenetic modifications in response to environmental conditions, thus contributing to flexible survival strategies of sessile plants (Kim et al., 2008; Dowen et al., 2012). Intriguing underexplored aspects in this field of research include the biochemical signals that alter the epigenome and the transduction of these signals to control the downstream epigenetic pathways. An increasing number of studies suggest a tight link between epigenetic regulation and plant hormone signaling (Zhu, 2010). The plant hormone auxin is perceived by the nuclear auxin receptors TRANSPORT INHIBITOR RESPONSE1 (TIR)/AUXIN SIGNALING F BOX PROTEINS (AFBs), leading to the activation of AUXIN RESPONSE FACTORS (ARFs), the transcriptional factors that activate auxin-induced gene expression (Salehin et al., 2015). Emerging evidence indicates that the ARF-dependent induction of auxin-responsive genes is modulated by microRNAs (miRNAs) as well as by multiple epigenetic factors, such as histone modifications and the chromatin remodeling factor PICKLE (PKL) (Rhoades et al., 2002; Jones-Rhoades and Bartel, 2004; Mallory et al., 2005; Long et al., 2006; Navarro et al., 2006; Wu et al., 2006; Chen et al., 2010; Zhu, 2010; Weiste and Dröge-Laser, 2014). Interestingly, auxin has also been implicated in the regulation of changes in the epigenome, suggesting an auxin-linked epigenetic regulation loop. In this review, we discuss recent literature on the interconnection between epigenetic control and phytohormone signaling, with a focus on auxin signaling.

HISTONE MODIFICATION MACHINERY AND PLANT HORMONE SIGNALING

Histone Acetylation and Plant Hormones

Eukaryotic chromatin is a highly organized complex of DNA and proteins, and is composed of the basic repeat element, the nucleosome. Each nucleosome contains two copies of the histone protein H2A, H2B, H3, and H4, and is typically enfolded by 147 bp of DNA. Modifications of histone tails such as acetylation, methylation, phosphorylation, and ubiquitination play an important role in epigenetic regulation. One major histone modification, which occurs at the ε-amino group of conserved lysine residue, is

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acetylation mediated by the reversible activity of histone acetyltransferases (HATs) and histone deacetylases (HDACs). Both histone acetylation and deacetylation play an important role in gene regulation and have been implicated in hormone signaling (Sieberer et al., 2003; Zhou et al., 2005; Long et al., 2006; Chen and Wu, 2010; Chen et al., 2010; Zhu, 2010). Acetylation neutralizes the positive charges of lysine residues on the histone N-terminal tail, thereby decreasing the interaction between histone protein and negative charged DNA, leading to a more open and loose chromatin conformation (Shahbazian and Grunstein, 2007). There are four HAT families. GCN5 (general control nonderepressible 5) belongs to the Gcn5 *N*-acetyltransferase (GNAT) subfamily and is the best characterized HAT in yeast, mammals, and plants (Baker and Grant, 2007; Chen and Tian, 2007; Lee and Workman, 2007). *Arabidopsis* GCN5 acetyltransferase and the transcription factor (TF) adaptor proteins ADA2a and ADA2b (also known as PROPORZ1) interact with each other, and are the subunits of the transcriptional adaptor complex SAGA (Spt-Ada-Gcn5-Acetyltransferase) (Servet et al., 2010). GCN5's HAT activity is modulated by ADA2b in *Arabidopsis* (Mao et al., 2006). Genome-wide analysis showed that the expression of ~5% of all genes is changed in *gcn5* and *ada2b*/*prz1* mutants (Benhamed et al., 2008). However, some reports indicate that specific genetic pathways are controlled by *GCN5* or *ADA2*.

gcn5/*hag1* mutants have a short root phenotype with defects in the columella differentiation layer and in QC marker gene expression (Vlachonasios et al., 2003; Kornet and Scheres, 2009), implicating the GCN5 complex in the maintenance of root stem cell niche in *Arabidopsis*. *PLT1* and *PLT2* genes encode AP2 domain TFs induced by auxin in an ARF-dependent manner, and play a major role in the specification of root stem cells (Aida et al., 2004; Galinha et al., 2007). Interestingly, *GCN5* acts in the same genetic pathway as the *PLT* genes, and the short root phenotype *of gcn5*/*hag1* mutant results from severely reduced expression of *PLT* genes, suggesting a chromatin modification-based mechanism that underlies the PLT-dependent stem cell specification. However, whether the GCN5 acetylase complex is recruited to the promoter of *PLT* genes directly to activate *PLT* gene expression remains obscure (Kornet and Scheres, 2009).

The *prz1* (*proporz1*) mutant was isolated based on the phenotype of ectopic callus tissue formation in root under auxin treatment (Sieberer et al., 2003). The *PRZ1* gene encodes for ADA2b, and the observed phenotype in *prz1* mutant is at least partially caused by misexpression of *KIP RELATED PROTEIN* (*KRP*) family genes (Sieberer et al., 2003). Auxin treatment did appear to have an impact on histone acetylation at the whole chromatin level. However, chromatin immunoprecipitation (ChIP) experiments showed that ADA2b/PRZ1 is associated with the KRP7 locus, and auxin treatment decreased histone H3Kac9 and H3Kac14 levels in the *KRP7* locus, which correlated with the reduction in expression of the KRP7 gene. Interestingly, the auxin-mediated reduction in *KRP7* expression was more obvious in the *prz1* mutant. Furthermore, constitutively reduced histone H3Kac9 and H3Kac14 levels were observed in the *KRP7* locus in *prz1* mutant. Collectively these studies support the hypothesis that auxin reduces histone acetylation level, whereas ADA2b/PRZ1 oppose the auxin-mediated suppression signal to control appropriate *KRP7* expression (Anzola et al., 2010). Future areas of research will involve auxin regulation of histone acetylation at a specific locus.

Elongator was first identified as an RNA polymerase II-associated protein complex in yeast (Otero et al., 1999). This elongator protein complex consists of six subunits (ELP1–ELP6), with ELP3 containing a HAT domain (Wittschieben et al., 1999). Some publications reported that mutations in elongator subunits cause pleiotropic phenotypes including abscisic acid (ABA), auxin, ethylene, and jasmonic acid (JA)-related phenotypes (Nelissen et al., 2005; Chen et al., 2006; Ding and Mou, 2015). ChIP experiments indicated that the SHORT HYPOCOTYL 2 (SHY2)/IAA3 and auxin influx carrier LIKE AUXIN RESISTANT 2 (LAX2) genes were direct targets of elongator HAT activity. Interestingly, SHY2/IAA3 is also a target of the GCN5 HAT (Benhamed et al., 2006), thus indicating a complex regulatory mechanism whereby two different HATs modulate SHY2/IAA3 gene expression.

HDACs and Plant Hormone Responses

Histone deacetylation has also been implicated in the regulation of hormone responses in plants. Histone deacetylation is mediated by the HDAC complex, which is composed of HDAC and other components. The *Arabidopsis* genome encodes 18 HDACs, and the largest and most characterized HDAC family is RPD3/HDA1, which can be divided into three classes (I–III) based on sequence similarity (Hollender and Liu, 2008; Alinsug et al., 2009). HDA6, 7, 9, and 19 belong to the class I family of RPD3/HDA1. Class II has three members, HDA5, HDA15, and HDA18. Class III comprises the plant-specific HD2A, HD2B, and HD2C (Pandey et al., 2002; Hollender and Liu, 2008). In contrast to HATs, HDACs repress transcription activity. Similarly to HATs, the recruitment of HDACs to DNA seems to occur both globally and at specific gene loci. For example, *hda19* knockout and knockdown mutants show pleiotropic phenotypes, implicating HDA19 in the regulation of various developmental processes, such as seed dormancy and embryo, leaf, and flower development (Tian and Chen, 2001; Tian et al., 2003, 2005; Long et al., 2006). The observed pleiotropic effects suggest a global role for HDA19 in gene regulation. However, HDA19 is also implicated in the specific regulation of auxin signaling (more details on this point are discussed later).

Several studies suggest an important role for *HDA6* and *HDA19* in the regulation of plant hormone responses. The expression of *HDA6* and *HDA19* is induced by plant hormones ethylene and JA (Zhou et al., 2005), and knocking out *HDA6* and *HDA19* causes ABA hypersensitivity (Chen and Wu, 2010; Chen et al., 2010). The transcriptional repressors (JASMONATE ZIM-DOMAIN) JAZ proteins and the TFs ETHYLENE INSENSTIVE 3 (EIN3) and its homolog EIN3-LIKE 1 (EIL1) act as master regulators for JA and ethylene signaling, respectively (Alonso et al., 2003; Chini et al., 2007; Thines et al., 2007; Yan et al., 2007; Zhong et al., 2009; An et al., 2010). JAZ inhibits the EIN3/EIL1 function, thus JAZ2 and EIN3 act at the crosstalk point of JA-inducible ethylene-regulated gene expression. HDA6 interacts with both EIN3 and JAZ proteins, and act as a repressor for EIN3-mediated transcription and JA signaling through HAT activity (Zhu et al., 2011). This evidence highlights a mechanism whereby HDAC can be