



Editorial overview: COPB issue 2022 on “epigenetics and gene regulation”

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Plant epigenetics and chromatin dynamics: From programmed nuclear processes to protection against genomic parasites

Molecular activities in the nucleus are essential for translating information encoded in genomes into phenotypic outputs. Highly complex processes interpret the DNA sequence in a spatiotemporal manner to regulate gene expression and associated features of cells, tissues, and whole organisms. Motifs in the DNA sequence provide specificity for binding transcription factors (TFs) to initiate transcription regulation, yet their accessibility often depends on chromatin states. Chromatin is the combination of DNA, nucleosomes, and other associated proteins that modify DNA packaging, accessibility to DNA-interacting proteins, and compartmentalization in the nucleus. Chromatin states differentiate genomic regions roughly into three types of packaging: (1) constitutively densely packed heterochromatin containing repeats and transposons, (2) largely expanded euchromatin including active genes and their associated cis-regulatory elements, and (3) regions that change their chromatin state in a dynamic mode, depending on intranuclear location, cell type, developmental state, or environmental input. Advances in sequencing, microscopy, genetics, biochemistry, and structural biology have uncovered numerous subspecies of chromatin states and how they are interpreted by chromatin-associated proteins. Specialized pathways that often result in self-reinforcing feedback loops provide the basis for the maintenance of either condensed or relaxed chromatin states. In fact, some of these pathways lead to stable states that are inherited from cell to cell or even across generations, creating epigenetic variation that causes inherited changes to gene expression without changing the DNA sequence.

Although chromatin is a feature of all eukaryotes, plants possess a range of chromatin components and epigenetic regulatory pathways that exceeds that of many other organisms. This diversification, the need for environmental adaptation of plants by their sessile lifestyle, and the late separation of the germline from somatic cells have suggested that epigenetic information could contribute to the diversity of phenotypes. In addition, a lot of our insight into chromatin and RNA-based epigenetic regulation and inheritance stems from experimental work with plants. This collection of

review articles aims at capturing some of the key nuclear processes in plants that are essential to maintain genome stability and translate DNA sequence into gene expression patterns and phenotypes in response to developmental and/or environmental cues.

Chromatin organization and structure

Central elements of chromatin are the nucleosomes built of histone octamers that are comprised of four different histone proteins. Histones are among the most conserved proteins across eukaryotes. Nevertheless, plant histones encompass specific variants. In this issue, the contribution by [Probst](#) provides an overview about histone variants in plants, their modification, and their deposition and eviction, resulting in different chromatin states. It also describes how histone variants contribute to the maintenance of the acquired states, while providing a platform for dynamic reprogramming. [Hu and Du](#) focus on histone methylation, one type of post-translational modification that distinguishes chromatin states in a fundamental way. They also summarize information about the antagonistically acting enzymes that install or remove the covalently bound methyl residues. An important role for other histone modifications is also emerging, but less extensively investigated. Intranuclear arrangement of the chromatin and the components of active transcription and RNA export result in a complex three-dimensional higher order structure, and novel insight into these connections is summarized by [Liu, Simmons, and Zhong](#). The contributions around structural aspects of chromatin point to novel questions and the need for additional methodology to capture these dynamic processes in high resolution.

Chromatin dynamics in development and reproduction

Maintenance of genetic and epigenetic information is especially important at the transition from one generation to the next. At the same time, sexual reproduction is associated with substantial changes in nuclear genome organization, when going through reduction in meiosis, duplication and combination of maternal and paternal genomes upon fertilization, and the seed plant-specific triplication upon endosperm formation. With a focus on the period between gamete formation and seed development, [Tiroit and Jullien](#) summarize the balance in epigenetic regulation between keeping transposons under control in this sensitive phase, while allowing the necessary transcriptional changes. [Sato and Köhler](#) focus on epigenetic gene regulation via imprinting, installing a parent-of-origin-determined and/or dosage dependent gene expression pattern. This is especially relevant for the development of the endosperm, and this tissue decides about the viability of seeds and their germination capacity. While the consequences of epigenetic

imprints are limited to the lifetime in these terminally differentiated cells, the reprogramming of parent-specific changes is reset after fertilization in the embryo. In contrast to most animals, where all organs are largely determined in early embryogenesis, plants continuously form new roots and shoots, due to primary and secondary meristems. The bridge to the next sexual generation is formed by stem cells in the shoot apical meristem that give rise to floral buds and gametes. [Nguyen and Gutzat](#) summarize insight into the epigenetic control in these important cells along plant development, discuss specific mechanisms of transposon control and the potential for changes in response to external cues. In addition to a germline that originates from stem cells in the shoot meristems, many cell types in different plant species have been proven to have the potential for de- and redifferentiation into organs, or embryos and whole plants, allowing the process of somatic cloning with frequencies and reproducibility way beyond this procedure in mammalian animals. [Aflaki, Gutzat, and Mozgova](#) describe the current insight into transcriptional reprogramming and chromatin changes during regain of pluripotency in plants. They further point to the potential for incomplete or alternative installation of epigenetic information that can go along with phenotypic differences and cause somaclonal variation.

Defense against and utilization of transposons

Many plant genomes contain more transposon-derived sequences than those encoding plant genes, reflecting a very successful amplification of mobile elements in evolutionary history, and indicating their nature as genetic parasites. On the other hand, present active transposition seems to be restricted to very limited conditions, revealing that plants possess effective defense mechanisms. In fact, a lot of insight into epigenetic mechanisms in plants, but also beyond, was derived by using transposons or other repetitive sequences as reporters to study pathways and components of epigenetic gene expression control. This is described by [Klein and Anderson](#), and they also highlight the ambiguous interaction between transposons and their host genomes: the potential to hijack regulatory elements of mobile elements for plant gene regulation in connection with stress or development of phenotypic diversity. One specialty of transposon amplification is the intermediate state between excision and reintegration of the “cut and paste” type, or between reverse transcription and integration in case of the “copy and paste” mechanism. [Peng, Mirouze, and Bucher](#) summarize information about these extrachromosomal DNA and a technology to capture it. They show that this non-integrated, circular DNA is not restricted to transposon-derived sequences and may have a role in stress response.

Natural epigenetic variation

Plants are ideal models for studies of natural variation due to their broad geographical distribution and their extensive genetic and phenotypic variation. One source of potential expression variation underlying these traits are epigenetic alleles (epialleles), which are usually associated with variation in DNA methylation in plants. [To and Kakutani](#) describe recent discoveries about the molecular mechanisms of how novel DNA methylation states form by way of chromatin-mediated establishment or by way of small RNA-directed DNA methylation pathways. Curiously, there has been extensive evolution of genes required for small RNA-directed DNA methylation across angiosperms. [Chakraborty, Payne, and Mosher](#) describe how core components required for double-stranded RNA production, processing of double-stranded RNAs into small RNAs or targeting of small RNAs to genomic loci have expanded, contracted and specialized repeatedly throughout evolution of flowering plants, often resulting in different DNA methylation states. Recognizing the importance of epigenetic variation, [Lieberman-Lazarovich](#) describe opportunities to incorporate this source of variation into breeding programs for crop improvement.

Understanding transcription factor targets, their associated networks and synthetic biology applications

Chromatin states and epigenetic pathways alone do not create gene expression patterns as such, although they do reflect the spatial landscape of chromatin composition and accessibility of genes. Although epigenetic differences are a source of variation within plant genomes, most processes are encoded in the genome and driven by TFs and their associated networks. However, mapping of TF binding sites in plant genomes has significantly lagged efforts in animals. [Hajheidari and Huang](#) discuss the current state-of-the-art methods of mapping TF binding sites in plants and how they can be used in plants to identify TF networks. [Heisler, Jonsson, Wenkel, and Kaufmann](#) show how studying TFs underlying floral development have uncovered complex regulatory mechanisms that are aided with the use of modeling and/or singlecell genomic data. TFs are also important components required for responses to the environment. [Xiong, Zhou, and Mas](#) describe the essential role of TFs and their interaction with chromatin remodelers in mediating responses to circadian cues. Knowledge of TF binding sites and how their function together and with chromatin remodeling complexes is instrumental to our ability to leverage TFs to improve crop performance and bioproduct development. [Yaschenko, Fenech, Mazzoni-Putman, Alonso, and Stepanova](#) show how discovery and characterization of cis-regulatory elements using experimental evidence in combination with machine learning will be important for

future efforts to use cell-type-specific control of gene expression in synthetic biology applications.

The role of regulatory RNAs in nuclear processes

Studies of epigenetics and chromatin dynamics are especially focused on DNA-related processes, yet RNA is vital to many of these nuclear processes such as post-transcriptional gene silencing, long non-coding RNA biology and small RNAs. During the last decade there has been an explosion of new technologies and discoveries that are revealing novel roles for RNAs and their associated base modifications in regulatory processes. [Bhatia, Prall, Sharma, and Gregory](#) discuss the emerging evidence supporting the role of the epitranscriptome and its crosstalk with epigenetic regulation of gene expression. [Zhai](#) summarizes advances in both short- and long-read technologies that are enabling the discovery of RNAs that result from transcription initiation, co-transcriptional splicing, polyadenylation, termination, or post-transcriptional splicing. The ability to identify these RNA products at high-resolution is aiding in our understanding of nuclear related RNA-dependent processes.

Future directions

The rate of high-quality reference plant genomes and gene annotations is continually expanding and revealing an evolutionary conserved group of chromatin associated proteins important to chromatin remodeling, transposon and repeat silencing, gene regulation, and RNA processing. These reference genomes are facilitating the identification of distinct chromatin states that underlie distinct genomic features of different repeat types, genes, and their associated cis-regulatory elements. How sequence information is used to coordinate gene expression while maintaining genome stability is becoming clearer. Some examples even reveal how, in rare cases, these transposons and repeats have been co-opted by the genome for gene regulation. Mapping of TF targets in plant genomes is emerging along with cell-type resolved defined molecular phenotypes. Yet, comprehending gene regulatory networks, in a cell-type-specific manner, and how they are rewired during evolution, is a complex endeavor. Fortunately, single-cell genomics and new tools to engineer the genome and gene expression are emerging. Genome editing of chromatin-related proteins in non-model species will test conservation of functions as well as how different genomes adopt different strategies for regulating genome stability and gene regulation. Similarly, advances in epigenome editing methods will lead to better understanding the basic biology of how these chromatin-related proteins function and how they can be used to engineer chromatin states to produce desired outcomes. Collectively, reference genome assemblies, knowledge of chromatin-related processes, and new tools for

genome engineering provide the basis for plant synthetic biology to comprehend the diverse, fascinating adaptation and differentiation processes in many plants and to leverage plants for use in bioproduction.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could

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