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Editorial

Recent progress in the epigenetics and chromatin field

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Guest editors
Yi Zhang[1]
[1]*Howard Hughes Medical Institute, Dept. of Biochemistry & Biophysics, Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC 27599-7295, USA*
yi_zhang@med.unc.edu

In eukaryotic cells, the genome is packaged into chromatin by wrapping DNA around histones. Studies in the past decade revealed that chromatin is not a static structure. In response to developmental and environmental cues, chromatin structure has to be dynamically regulated to accommodate the requirements for many basic DNA-templated biological processes, such as transcription, replication, recombination, and repair. Therefore, the interplay between the sequence information encoded in the DNA and the factors controlling the dynamics of chromatin is at the heart of many nuclear processes. Indeed, chromatin not only stores heritable genetic information, but also carries heritable modifications independent of DNA sequence. Since epigenetics encompasses the heritable changes that do not involve change in DNA sequences, chromatin is a major subject for epigenetic studies.

Studies in the past decade have revealed that chromatin dynamics can be regulated by several classes of enzymes, including histone modifying enzymes and ATP-dependent nucleosome remodelers. In addition, various histone variants also play a role in this process. Since currently evidence demonstrating the inheritance of each of the chromatin modifications is still lacking, it is still debatable which modification can be considered epigenetics. However, there is little doubt that Polycomb silencing, which involves histone modifications, and DNA methylation are classical epigenetic events. Technological advancement, particularly the use of high-throughput sequencing and live cell imaging in the studies of chromatin and epigenetic modifications has not only advanced our knowledge of the epigenetic machineries, but also their biological functions. These advances are nicely summarized in this collection of reviews that focus on the enzymes and "readers" of the various modifications, histone variants, DNA methylation and genomic imprinting, as well as the role of epigenetic modifications in reprogramming and cancer.

As a starting point to understanding epigenetic and chromatin modifications, we have to first identify the enzymes responsible for the modifications. Bannister and Kouzarides discuss the various histone modifications, the responsible enzymes that deposit the modifications, their genomic distribution, and their known functions, particularly their role in transcription. Hargreaves and Crabtree review the four major families of ATP-dependent chromatin remodeling complexes, including their genomic distribution, mechanism of function, and their biological function in the context of the organism. In addition to histone modifications and ATP-dependent chromatin remodelers, recent studies suggest that chromatin dynamics can also be regulated by the incorporation of various histone variants. One of the best characterized histone variant is H3.3, a histone H3 variant associated with actively transcribing regions. Although this histone variant was originally proposed to participate in the epigenetic transmission of active chromatin states, recent studies indicated that this variant also accumulates in pericentric heterochromatin and telomeres. In light of these findings, Szenker, Ray-Gallet and Almouzni review the known properties of H3.3 and the various modes of deposition by different histone chaperones, as well as the role of H3.3 in germline formation and early development.

One important question in the studies of histone modifications is how histone modifications affect chromatin dynamics and various DNA-templated processes. Accumulating evidence suggests that one of the

ways that histone modifications impact downstream events is to serve as a binding site for the recruitment of the downstream effectors who in turn mediate the function of the modification. Yun, Wu, Workman, and Li review the known "readers" and how the histone modification language is interpreted. Despite the fact that histone modifications and histone variants are believed to carry important epigenetic information, little is known about the molecular mechanism by which the epigenetic information is inherited. Zhu and Reinberg review some recent studies and discuss several models concerning mitotic inheritance of some histone modifications.

Unlike histone modifications and histone variants, which still lack a defined mechanism of inheritance, DNA methylation is a well-studied epigenetic modification with a defined mechanism of inheritance. He, Chen, and Zhu compare the similarities and differences of the DNA methylation machinery in plants and animals. They also discuss recent progress in the studies of active DNA demethylation and the function of DNA methylation. As the best example of an epigenetic phenomenon, genomic imprinting is an epigenetic marking system responsible for parental-origin-specific gene expression. Genomic imprinting plays important roles in development and adult behavior. Its defect has also been known to be the cause of several human diseases. Li and Sasaki review some recent discoveries on the reprogramming and maintenance of genomic imprinting. They also discuss the epigenetic changes at the imprinted loci during the generation of induced pluripotent stem (iPS) cells.

In addition to regulating transcription, chromatin dynamics and nuclear organization are also important for the maintenance of genomic stability. Nagai, Davoodi, and Gasser review recent studies that connect nuclear organization and genome stability, particularly their connection through the evolutionarily conserved family of SUMO-targeted ubiquitin ligases. Given that epigenetic modifications have a great impact on transcription and genome stability, it is expected that epigenetic modifications affect many biological processes, including cell reprogramming and the development of cancer. The landmark discovery by Shinya Yamanaka and colleagues that terminally differentiated cells can be reprogrammed by a defined set of transcription factors leaves open the question how these transcription factors can induce the genome-wide epigenetic changes that accompany the reprogramming process. Papp and Plath review the studies characterizing global changes in the epigenetic landscape during the reprogramming process. Accumulating evidence suggests that dysregulation of epigenetic factors is an important contributor to the pathogenesis of cancer. Genome-wide profiling of PcG proteins and DNA methylation in normal and cancer cells revealed that epigenetic abnormality is a common feature of cancer. Tsai and Baylin review recent cancer-related epigenetic studies and suggest that the development of epigenetic biomarker and drugs targeting epigenetic factors may represent the future of cancer diagnosis and treatment.

In summary, this collection of excellent reviews covers the major topics in the epigenetic and chromatin field and provides up-to-date information in this rapidly-progressing field. I believe that it will serve as an excellent reference for the novice as well as the experts.