Introduction to the Thematic Minireview Series on Epigenetics*

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The past decade has witnessed rapid advances in our understanding of the biochemistry of “epigenetics,” as exemplified by the articles in this minireview series. Epigenetics is usually defined as the study of inherited changes in the phenotype of an organism or cell caused by changes in gene expression that do not result from changes in the underlying DNA sequence. Epigenetic modifications of DNA and chromatin are essential for development of an adult organism from a fertilized egg. Each cell type in an organism expresses a distinct set of genes, but, with minor exceptions, all cells have the same DNA or genes. A fertilized egg, or zygote, changes into the numerous cell types of an organism, i.e. neurons, muscle, blood cells, etc., by activating some genes and inactivating others. Similarly, the cells within an organism respond to various stimuli by the programmed expression or repression of classes of genes.

Two major mechanisms are responsible for epigenetic regulation of gene expression, namely modifications to DNA, such as methylation of the 5-position of cytosines at particular sites in the genome, and post-synthetic modifications of the histone proteins, both at gene control regions (promoters and enhancers) and within the coding regions of genes. DNA methylation is usually a mark of gene repression, whereas histone post-synthetic modifications can be associated with either active gene expression or repression, depending upon the amino acid residues that are modified in each of the histone proteins. Emerging evidence also points to a role for small noncoding RNAs in epigenetic gene regulatory mechanisms.

In our first minireview, Zhao-xia Chen and Arthur D. Riggs describe recent advances in our understanding of the mechanisms responsible for DNA methylation and demethylation in mammals. DNA methylation patterns are established during early development for each of the cell types in an embryo. To understand just how DNA methylation affects tissue/cell type-specific gene expression, it is essential to understand the mechanisms that are responsible for establishing methylation of particular cytosine residues in genomic DNA and how demethylation can be achieved for gene activation. Although the enzymes responsible for both de novo DNA methylation and maintenance of methylation patterns during cell divisions are very well characterized, how these activities function in the context of cellular chromatin is less understood. The links between DNA methyltransferases and chromatin-associated proteins and post-synthetic modifications are discussed in this minireview. Likewise, the enzymes responsible for demethyla-

* The last article in this thematic minireview series will be published in a later issue. This minireview will be reprinted in the 2011 Minireview Compendium, which will be available in January, 2012.

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2 The abbreviation used is: PTM, post-translational modification.
PTMs are “translated” by the chromatin readers into biological outcomes.

Histone PTMs also direct the recruitment of other chromatin-associated proteins and enzymes that serve to regulate gene expression. These include chromatin “remodelers,” enzymes that can change either the conformation of nucleosomes or their position relative to the underlying DNA sequence, and histone “chaperones,” proteins that directly bind histones and function during transcription. One member of the histone chaperone family is a two-subunit complex known as FACT (facilitates chromatin transcription). FACT is a histone chaperone critical for nucleosome reorganization during replication, transcription, and DNA repair. Duane D. Winkler and Karolin Luger review the structural and biophysical basis for FACT-mediated nucleosome reorganization in their minireview entitled “The Histone Chaperone FACT: Structural Insights and Mechanisms for Nucleosome Reorganization.” They discuss recent models for FACT function and how FACT allows the passage of RNA polymerase through nucleosome-bound DNA.

In the last minireview of the series (to be published in a later issue), Xizhe Zhang and John Rossi consider “RNAi and Transcriptional Gene Silencing and Activation.” The RNAi pathway in post-transcriptional gene regulation is very well established; however, recent studies have implicated small noncoding RNAs in both positive and negative aspects of gene regulation at the level of transcription initiation and elongation. Both antisense and promoter-proximal RNAs have been identified, and these RNAs have been shown to recruit chromatin-modifying enzymes, including histone deacetylases, to regulate gene expression. This minireview links these small RNAs to epigenetic regulation.

Although the Journal of Biological Chemistry recognizes that these minireviews provide only a limited snapshot of the field of epigenetics, the topics were chosen to highlight recent successes in our understanding of the mechanisms involved in establishing and maintaining patterns of DNA methylation and the histone PTMs and the function of the histone code in gene regulation and cellular development. We are confident that future advances in the field will be highlighted in other minireviews and published in research articles in the Journal.

REFERENCES