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Introduction: Reviews on Gene Expression 2000

This issue of *Gene Expression* brings together a collection of review articles covering the broad topic of regulation of gene expression in animal cells. We begin this volume with a review of Phosphorylation in Transcription: the CTD and More, by Reidl and Egly. This review focuses on the role of phosphorylation of components of the basal transcription machinery (the general transcription factors—GTFs), the carboxyl-terminal domain (CTD) of RNA polymerase II, and activator proteins in regulating gene expression in the transcription cycle and in RNA processing. Recent evidence has provided clues as to how transcription and the various steps in RNA processing (capping, splicing, and polyadenylation) are tied together by phosphorylation of the CTD. In the next review, White and coauthors review the basic concepts of RNA polymerase III transcription, its regulation during the cell cycle and control by tumor suppressor proteins such as p53 and Rb, and its deregulation by viral transforming proteins. The authors propose an important link between regulated pol III transcription and oncogenic transformation of cells.

Van Orden and Nyborg review the role of the coactivator CBP (CREB binding protein) in cellular and viral gene expression and how the tumor suppressor function of CBP is manifested through interactions with the viral oncoprotein Tax in human T-cell leukemia virus-infected cells. CBP is an important cellular coactivator that is brought to promoters by sequence-specific transcription factors and, once tethered to the promoter, CBP elicits its activator function by recruiting GTFs and through its histone and transcription factor acetyltransferase activity. In the next review, Annunziato and Hansen focus on the roles of histone acetylation in two important chromatin processes, replication-coupled nucleosome assembly and reversible transitions in chromatin higher order structures. Histone acetylation likely plays an important active role in regulating chromatin folding and hence in the accessibility of DNA to transcription factors, DNA repair enzymes, and the replication machinery. The converse side of this story is covered by El-Osta and Wolffe, who review the important link between DNA methylation and histone deacetylation. It has long been known that active regions of the genome are enriched in acetylated histones while acetylated histones are absent or underrepresented in transcriptionally silent domains of the genome. Likewise, DNA methylation has been correlated with epigenetic silencing of gene expression. El-Osta and Wolffe tie these two observations together into a coherent picture of how DNA methylation recruits histone deacetylases through methyl-CpG binding proteins and how defects in these processes can affect development and lead to oncogenic transformation of cells.

Finally, we turn to chemical approaches to control gene expression as reviewed by Gottesfeld, Turner, and Dervan. Chemical strategies—utilizing either natural products or synthesized small molecules—have been devised to manipulate gene expression at both the level of transcription and translation. Using these approaches, both activation and repression of gene expression has been achieved. These studies offer promise for the development of therapeutic agents for treating human diseases, such as viral diseases and cancer. While every attempt has been made to present a contemporary overview of the field, many important aspects of gene regulation will not be covered in depth in this volume, and citations to other reviews or the primary literature can be found in these reviews.

Joel Gottesfeld
Guest Editor