

Preface

Human genomic DNA is the ultimate blueprint of our heredity and holds the key to our most fundamental questions about human biology of health and disease. Remarkable advance in genomics research made since the human genome was sequenced a decade ago has greatly increased our understanding of the capacity of the human genome to store, release, and inherit biological information. Gene expression of the human genome is governed not only by the information encoded in the DNA sequence but also influenced by environmental factors—*the essence of epigenetics*. One prime example is of stem cells in that a balance between self-renewal and lineage commitment of a stem cell lies at the heart of how the gene transcriptional program dictates pluripotent cell behavior and identity.

Gene expression in response to physiological and environmental stimuli is directed by posttranslational modifications (PTMs) of DNA-packing histones including acetylation, methylation, phosphorylation, sumoylation, and ubiquitination in addition to DNA methylation. Distinct nuclear activities such as chromatin structure change associated with gene activation or silencing are defined by chromatin-modifying enzymes and directed by chromatin and transcription regulatory proteins that interact with the chromatin in a modification-sensitive manner through the evolutionarily conserved epigenome reader domains embedded in them including the acetyl-lysine binding bromodomain, the methyl-lysine-binding chromodomain, and the PHD finger. Given a large number of different histone PTMs operational in a combinatorial fashion, how they function in concert with direct gene expression is quite complex.

The goal of this book is to introduce to readers the current knowledge on the role of histone modifications in the epigenetic control of gene transcription in chromatin. The book consists of multiple chapters that collectively cover four major topics: (1) Basic mechanisms of molecular recognition of histone PTMs are covered in Chaps. 1–6; (2) combinatorial readout of histone PTMs by tandem epigenome reader modules is described in Chap. 7; (3) genome-wide profiling of histone PTM interactions is presented in Chap. 8; and (4) small-molecule modulation of histone PTM interactions in human biology and disease is illustrated in Chaps. 9–12. Each chapter is authored by leading scientists in the field

who have made the key original discoveries of the structure and mechanisms of histone PTM-mediated molecular interactions in gene transcription. Collectively, this book provides a comprehensive understanding of the structural and molecular bases and mechanisms of how histone modifications endow the regulatory capability of chromatin to direct gene silencing and “on demand” expression in an orderly manner. Finally, the book discusses the promise and potential of small molecule modulation of histone PTM-mediated protein–protein interactions in gene expression as a new approach to therapeutic interventions of human disorders including cancer and inflammation.

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Ming-Ming Zhou

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Zhou, M.-M. (Ed.)

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