Preface

It hardly seems possible that we are approaching two decades since the discovery that DNA methyltransferases act by everting the target base out of the double helix Klimasauskas et al., HhaI methyltransferase flips its target base out of the DNA helix. Cell 1994 76:357–69. Since 1994, a very substantial body of work has emerged from the attempts to understand both the molecular mechanisms and biological roles of methylation, not only of DNA but also of the associated histone proteins.

As is typical of important biological questions, there is no good stopping point at which we can say that the basic answers are known. Nevertheless, we feel the time is right for a summing up that allows establishment of context. For that reason, we are delighted that colleagues who study chromatin methylation from a variety of perspectives have agreed to contribute to this volume.

This book is divided into five sections, following an introduction by us that is intended to consolidate the most basic background material into one chapter. The next five paragraphs should have appropriate section numbers.

Section I explores the evolution of the DNA- and histone-methylating (and demethylating) enzymes and of the biological roles of this methylation. The former is presented in two chapters by Iyer et al. and Aravind et al., while the latter involves chapters on chromatin methylation in *Drosophila* (Krauss and Reuter) and zebrafish (Goll and Halpern).

Section II is focused on the major mammalian DNA methyltransferases, Dnmt1 (Svedruzic) and Dnmt3/3L (Chédin). One of the take-home messages is that the division of labor between *de novo* and maintenance methylation is much less strict than had been thought earlier.

Section III examines the processes and control of DNA methylation and demethylation. There are chapters on recruitment of Dnmt1 (Sharif and Koseki) and modulation of its stability (Morey-Kinney and Pradhan), along with the functional linkages between demethylation of DNA and histones (Chen).

Section IV covers the association between DNA methylation and silencing of gene expression. This can occur via an RNA-directed process (Wutz) or the involvement of proteins bearing a methyl-binding domain (Defossez and Stancheva).

Finally, Section V describes biomedical and biotechnological aspects of these epigenetic processes. There are chapters on chromatin methylation and cancer (Toyota and Yamamoto) and diseases associated with imprinting

(Wilkins and Úbeda). The section, and the volume, is brought to a close by a description of the methods to determine, and the implications of knowing, the distribution of DNA methylation at the single-nucleotide level (Wong and Wei).

We are happy that these chapters will be available online in addition to the print format, so it will be possible to update them periodically.

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