PREFACE

In 2004, when we edited the last three-volume series on *Chromatin and Chromatin Remodeling Enzymes*, remarkable progress had been made accessing the enzyme complexes that serve to remodel or modify histones and DNA, giving molecular insights into what might be considered "epigenetic landscapes" that lead to stable, and potentially heritable, states of gene expression. Clearly, that was only the tip of the iceberg. Over the past 8 years, interest in chromatin biology, and epigenetics in general, has sky-rocketed, in part due to numerous disease links to dysfunction in most, if not all, of the general classes of chromatin proteins, leading to the misactivation or mis-silencing of gene targets. Moreover, chromatin protein motifs such as bromodomains that recognize histone acetyl-lysine marks have now proven to be effective drug targets in several types of human disorders, lending support to the general view that modulating nonenzymatic, protein–protein interactions in chromatin-associated proteins can lead to therapeutically useful outcomes in humans. Researchers, in some cases, armed now with molecular insights gained from X-ray and NMR structures, are beginning to unravel the "rules" of effector recruitment to the chromatin template.

As well, the complexities of epigenetic landscapes have now been explored in the context of whole genomes, by combining RNA and chromatin immunoprecipitation with deep sequencing approaches. Importantly, this work is being done examining normal and disease states, stimulated by a flurry of recent findings of missense mutations in epigenetic-modifying activities, including the histone proteins themselves. Challenges remain such as determining "cause versus effect" in bringing about pathological disease states, even to the point of knowing whether histones and or methylated DNA are the physiologically relevant substrates for many of these activities. In addition, there remains a wide gap between reductionist, biochemical (vertical) approaches and the now-popular "omic" (horizontal) approaches, providing an excellent opportunity for clever new strategies to help "connect the dots" underlying these different scientific styles.

With the unquestioned importance of chromatin structure and function in human biology and disease, a wealth of new researchers are entering the field, bringing with them new expertise, methods, and approaches. This updated, two-volume series aims to bring many of these advances to the community, including exposure to genome-wide approaches,

single-molecule microscopy methods, and peptide array-based assays. We are most grateful to our colleagues for their efforts in contributing to these volumes. The popularity of the field has also spawned numerous other sources of chromatin methods that the reader may refer to. If the speed of discovery and technology development in prior years is any guide, we anticipate that this volume set will soon require updating. However, we are confident that each of the series devoted to chromatin over the years continues to provide an enduring and evolving set of tools for many newcomers who seek to address the most fundamental problems in chromatin biology.

In closing, we wish to make a special note in appreciation of Jonathan Widom, who passed away in 2011. Jon was the foremost practitioner of chromatin biophysics in our era and contributed on many occasions to *Methods in Enzymology*. We owe him a debt of gratitude for leaving a legacy of key concepts in nucleosome dynamics, robust biophysical techniques, and invaluable reagents that he and his laboratory provided to the chromatin field for decades. It is fitting that the closing chapter of these volumes honors his most recent contribution—a new method for mapping nucleosome positions *in vivo* at base pair resolution. Jon will be greatly missed.

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