Preface

Now a popular and widely used term, "Epigenetics" has changed its meaning several times since "epigenesis" was debated by Greek philosophers as an alternative to existence of the homunculus (Aristotle, *On the Generation of Animals*). Waddington famously proposed that an "epigenetic landscape" underlies alternative cell fates, incorporating the idea, still novel at the time, that genes might contribute to this landscape. But it was the merging of embryology with non-Mendelian inheritance that ultimately led to the commonly accepted meaning of "Epigenetics" today. In this molecular age, we define epigenetics by what it is not – epigenetic changes are alterations in the hereditary material (usually chromosomes) that are not accompanied by changes in the DNA sequence. Certainly, epigenetics profoundly influences embryonic development, but equally it impacts chromosome organization, genome defense, heredity, gene expression and evolution.

Just as genetics allowed us the first glimpse of the genome in the form of linkage maps of genes and cytogenetic landmarks (Creighton and McClintock, 1931), so epigenetics allowed the first glimpse of the epigenome, with the discovery of widespread modifications of chromosomal material, including DNA and histones, associated with epigenetic regulation. Immunocytochemistry revealed striking correlations between, for example, histone H4 acetylation and dosage compensation, while molecular biology revealed correlations between, for example, DNA methylation and transposon inactivation. It was quickly realized that many of these modifications were conserved among most if not all eukaryotes, and were associated with a wide diversity of "epigenetic" phenomena. But it was only when the first whole genome sequences became available that the concept of the "epigenome" took hold. Just as DNA sequence can be aligned with the chromosome, so epigenetic modifications can be aligned with the DNA sequence. The epigenome has emerged at nucleosome and nucleotide resolution from genome profiling using high density programmable microarrays, chromatin immunoprecipitation and next generation DNA sequencing, as well as analytical procedures to detect and display significant associations. This volume commences with a section describing the current technologies employed in mapping epigenomes and the challenges associated with the analysis and visualization of these large datasets within their genomic context. The impact of the technology cannot be underestimated and as such, is recognised in many of the subsequent contributions.

In subsequent chapters, the current understanding of these epigenetic maps is reviewed within the context of epigenetic phenomena in eukaryotes. The role that model organisms have played in unveiling key conserved mechanisms is a general theme, as is the idea of an epigenetic "code", comprising histone and DNA modifications, guided by modifying enzymes, and in some cases RNA interference, and interpreted by histone and DNA binding proteins that recognize these modifications and signal their downstream effects. The relationship between epigenetic states, non-protein coding transcripts and sub-nuclear localization is also explored. The impact of these mechanisms on gene activity and repression, developmental memory, imprinting, X inactivation, genome defense and chromosome organization is reviewed in animals, plants and fungi. We also review the first glimpses of the human epigenome in differentiating cells and relate these mechanisms to human disease and development.

In the conclusion of his chapter describing the relevance of variant histones to epigenome function, Steven Henikoff reminds us that, since the completion of the draft human genome sequence, the 21st century is often referred to as the "post-genomics era". The combination of major advances in our understanding of model epigenetic processes and remarkable technological advances, as illustrated in this volume, have ushered in what he suggests might rather be considered an "epigenomics era". Whatever it is called, the integration of the epigenetic components required to consolidate DNA into its highly regulated chromatin context, is now recognized as profoundly important for understanding the functions of normal and compromised genomes. The development of effective new tools having the ability to modulate epigenetic states and influence genome function in clinical contexts, seems a realistic goal. We have witnessed the birth of a major new discipline in genetics that has taken us inside chromosomes to unfold multiple highly-regulated dynamic epigenetic landscapes within which a genome is parceled and to which it responds. We are grateful to all the authors of this volume for sharing their research, views and ideas, and for revealing these landscapes.

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