Preface

Although their scopes definitely overlap, the terms epigenesis and epigenetics are commonly used in different contexts. Epigenesis is etymologically derived from genesis and as such includes everything that touches upon development. Its scope is extremely wide and covers not only somatic, but also mental development. It is not surprising that its oldest and most rudimentary formulation dates back to early embryologists. The term epigenetics is a more recent and apparently more focused concept since it explicitly refers to genes and chromosomes and via which mechanisms this genetic information can be heritably repressed, or activated, in specific lineages or transmitted from one generation to the next.

In parallel with our increasing understanding of gene function, it became overwhelmingly obvious that not everything, albeit hereditary, is defined by the DNA sequences of our genes as we can now read them in complete genomic databanks. In the limited context of this book, we will examine how modifications of DNA and associated proteins can heritably impinge on its packaging into chromatin and subsequently on fundamental DNA transactions – replication and transcription – which marks the first step towards gene expression.

The first chapter by P. Varga-Weisz gives a comprehensive survey of the already highly documented field of chromatin assembly and remodeling factors which accompany DNA replication and the deposition of new nucleosomes. It also emphasizes the key role of PCNA in the general problem of epigenetic inheritance and reviews the role of some of the above factors in the hereditary transmission of chromatin states. This same issue is tackled by Déjardin and Cavalli who question how Polycomb- and trithorax-induced chromatin states can be maintained across a specific differentiation program, allowing cells to remember their identity throughout.

The next chapter by Caron and coworkers addresses the specific problems posed by sperm chromatin, histone modification and histone variants, the role of transition proteins in histone removal and subsequent protamine deposition, and the reorganization of chromatin after meiosis.

Chromatin modifications are central to the problem of dosage compensation raised by the presence of two copies of the X chromosome in females. There are three known epigenetic mechanisms which can compensate for this

allelic imbalance and thus achieve comparable levels of X chromosome genes in males and females. In mammalian organisms, a mechanism has evolved to inactivate one copy of the X chromosome and this very peculiar mechanism is reviewed by Cohen and coworkers. The reciprocal possibility is to upregulate the single X copy in males. This is the mechanism chosen by *Drosophila* where hypertranscription is achieved by an RNA protein-containing compensation complex which is described in detail in the chapter by Taipale and Akhtar. The intermediate possibility, i.e., downregulating to 50 % expression both X copies in females, as is the case in the nematode *Caenorhabditis elegans*, has not been considered in this book.

In many instances, be they physiological or pathological, DNA methylation is the causal event in gene silencing. Razin and Kantor give a general survey of the various facets of this mechanism and its involvement in genomic imprinting and in disease, of which cancer provides many well-documented examples. The chapter by Ballestar and Esteller follows along this latter line and focuses on epigenetic mechanisms leading to cancer and raises the possibility of therapeutic reactivation of silenced genes.

Developmental regulation of the β-globin gene cluster has been a long-standing, highly relevant model to study the influence of chromatin structure on gene expression. However, the recognition of epigenetic control of developmental β-globin gene expression has only recently emerged and this new aspect is reviewed by Chakalova and coworkers.

The last two chapters cover genomic imprinting, i.e., the fact that some (few) genes are expressed from only one parental allele, and this is the last, but not least, facet of epigenetic regulation. Weber and coworkers give an in-depth analysis of this mechanism in mammals which they adequately place in an evolutionary perspective. Köhler and Grossniklaus conclude with a comprehensive review of this phenomenon in plants.

Philippe Jeanteur