

Preface

The transmission of mutated and deleted mitochondrial DNA (mtDNA) from one generation to another through the maternal lineage can result in a series of diseases that, if not severely debilitating, are lethal. These diseases primarily arise through the inability of the affected cells to generate sufficient cellular energy, ATP. The number of diseases described has been increasing steadily over the last 20 years. The first chapter in this book describes the various mitochondrial diseases, their aetiologies and prevalences and provides a clinical approach to their diagnosis.

We then concentrate on Complex I of the electron transfer chain and how deficiencies to this complex can lead to severe cases of disease. This chapter also describes how Complex I is assembled and how mutations to the assembly genes result in mitochondrial disease.

We progress to describe how embryonic stem cells function and how they can be mimicked by somatic cells that have been reprogrammed to behave like embryonic stem cells, namely induced pluripotent stem cells. This sets the scene for the following chapters, the first of which examines the role and need for mitochondria as they pass from the oocyte through to the pluripotent stem cells and into fully differentiated cells. This is followed by an account of how replication of the mitochondrial genome is strictly controlled from the oocyte and into undifferentiated pluripotent and differentiating embryonic stem cells and how this is a vital step during development. It also critically assesses whether induced pluripotent stem cells regulate their mtDNA copy number effectively during differentiation and whether they could thus have any therapeutic benefit. This is followed by a chapter discussing the role of mitochondria and mtDNA in tumor-initiating cells and during tumourigenesis and whether mtDNA defects can lead to cancer. Collectively, these chapters related to stem cell biology demonstrate that the processes of mitochondrial biogenesis, mtDNA replication, pluripotency and differentiation are tightly linked and interdependent.

Finally, we round off with an account of how mtDNA replication is regulated during development and how it is transmitted and segregated. We then discuss how certain assisted reproductive technologies can result in two populations of mtDNA being transmitted to the offspring. We discuss the pitfalls of some the

assisted reproductive technologies that have been proposed to prevent the transmission of mutant mtDNA from one generation to the next.

The contributing authors are experienced and accomplished scientists and clinicians. They have provided in depth accounts and state-of-the-art knowledge from their own specialized areas.



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