Book Reviews

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Genetics of Mitochondrial Diseases. Edited by Ian J. Holt. New York: Oxford University Press, 2003. Pp. 350. $89.50.

Ian Holt has put together an outstanding book on the genetics of mitochondrial disorders. The book offers much more than clinical correlations of genetic abnormalities. The chapters were contributed by the best minds in the field, and, although it is a multiauthor book, the chapters were assembled in well-designed sections to cover the basic biology of mitochondria; a description of mitochondrial and nuclear DNA mutations in clinical disorders; the role of mitochondrial dysfunction in cellular function; neurodegenerative disorders and aging; and, finally, discussions on therapy, experimental models, and genetic counseling. The editor has clearly put a great deal of effort into making the chapters complementary and keeping a seamless thematic flow. Because the book approaches its topics in depth, it will be an excellent reference book, not only for physicians and genetic counselors but also for students and scientists interested in any aspect of mitochondrial biology and genetics.

Genetics of Mitochondrial Diseases has a very comprehensive segment on the basic biology of mitochondria and mitochondrial DNA (mtDNA), including new concepts on mtDNA replication, maintenance, repair, recombination, and expression. It also summarizes very recent findings on the protein biosynthetic and proteolytic systems inside mitochondria. All these aspects are quickly evolving and not yet completely understood. An update on the mechanisms of protein import into mitochondria is also provided, as defects in this process have been associated with deafness and dystonia in Mohr-Tranebjaerg syndrome. The chemical aspects of oxidative phosphorylation are described, but in such a clear framework that even the non–chemically inclined could follow the intricacies of the chemiosmotic theory of ATP synthesis.

The second and third sections deal specifically with diseases caused by both mitochondrial and nuclear DNA mutations. This area has advanced tremendously in the past few years, and the chapters incorporate the most recent findings. Both point mutations and rearrangements of the mtDNA are described, including the most recent thoughts on their pathogeneses. The molecular bases of autosomal dominant multiple mtDNA deletions and autosomal recessive mtDNA depletions are examples of mechanisms of mitochondrial diseases involving nuclear-mitochondrial communication, unveiled in the past few years, that are included in these sections. Identifications and characterizations of specific nuclear-coded genes implicated in infantile forms of mitochondrial disorders (e.g., Leigh syndrome) are also extensively discussed.

The fourth section addresses the cellular consequences of oxidative phosphorylation defects and how these alterations—such as increased reactive oxygen species production and decreased calcium buffering capacity—can have a fundamental role in cellular function. The chapter by Aubrey de Grey feels like a scholars' debate in a traditional Cambridge college, where the involvement of mitochondria in aging is spiritedly argued and theories are defended, attacked, and proposed. Did you know that a cell with heteroplasmic mtDNA could have homochondrous organelles and still maintain a heterokairotic state?

The fifth and final section deals with important aspects of disease management and future therapies. mtDNA segregation is quite complex and has important implications about pathogenesis. Mitochondrial genomes complementation and dominant effects are other examples of these complex interactions. In recent years, several animal models of mitochondrial diseases have been created, including a few with mutated mtDNA. Such models should accelerate the development of new therapies. Current therapies are not discussed in this book. Such therapies are basically vitamin supplementations that have not been shown to be effective. They are in the category of "If it does not harm, why not?" The editor chose instead to present the state of the art of new therapeutic approaches, particularly emerging genetic and pharmacogenetic concepts. Prenatal diagnosis and genetic management of mitochondrial diseases are arguably the most important practical consequences of the scientific advancements in this field. These are discussed in detail and should guide genetic counselors when they are faced with these mysterious disorders.

CARLOS T. MORAES
Department of Neurology and Cell Biology & Anatomy
University of Miami School of Medicine
Miami

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