Advances in Experimental Medicine and Biology 942

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Advances in Mitochondrial Medicine

Springer

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ISSN 0065-2598
ISBN 978-94-007-2868-4 e-ISBN 978-94-007-2869-1
DOI 10.1007/978-94-007-2869-1
Springer Dordrecht Heidelberg London New York

Library of Congress Control Number: 2011945106

Preface

Mitochondria are far more than the "powerhouse" of the cell as they have classically been described. In fact, mitochondria biological activities have progressively expanded to include not only various bioenergetic processes but also important biosynthetic pathways, calcium homeostasis and thermogenesis, cell death by apoptosis, several different signal transduction pathways mainly related to redox control of gene expression and so on. This functional and structural complexity may undergo important derangements so to justify the definition of 'mitochondrial medicine', which should include all the clinical consequences of congenital or acquired mitochondrial dysfunctions. There are actually a growing number of studies which assign a significant pathogenic role to damaged mitochondria in different diseases: ischemia/reperfusion injury, neurodegenerative diseases, metabolic syndrome, hyperlipidemias, just to mention a few of the most important pathologies.

In this context, a further aspect that should not be disregarded is the interaction of pharmacological agents with mitochondria, not only in regard of the toxicological aspects but, above all, of the potential therapeutic applications. In fact, it is interesting to note that, while the properties of different so-called "mitoxicants" are well-known from a physical, chemical and biochemical point of view, the often subtle linkages between drugs and mitochondria is still in need of a real pharmacological and therapeutic control at the clinical level.

This lack of consideration can often lead to an underestimation of unwanted toxic effects but also of desirable therapeutic activities, both diverging outcomes resulting from drug induced modification of mitochondrial homeostasis.

The aim of this book is to stimulate a re-evaluation of the potential clinical role of mitochondria that could shed new light on some yet debated aspects of human pathophysiology.

Roberto Scatena

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Part I
Physiology and Structure of Mitochondria

Chapter 1
The Oxidative Phosphorylation System in Mammalian Mitochondria

Sergio Papa, Pietro Luca Martino, Giuseppe Capitanio, Antonio Gaballo, Domenico De Rasmo, Anna Signorile, and Vittoria Petruzzella

Abstract The chapter provides a review of the state of art of the oxidative phosphorylation system in mammalian mitochondria. The sections of the paper deal with:

(i) the respiratory chain as a whole: redox centers of the chain and protonic coupling in oxidative phosphorylation
(ii) atomic structure and functional mechanism of protonmotive complexes I, III, IV and V of the oxidative phosphorylation system
(iii) biogenesis of oxidative phosphorylation complexes: mitochondrial import of nuclear encoded subunits, assembly of oxidative phosphorylation complexes, transcriptional factors controlling biogenesis of the complexes.

This advanced knowledge of the structure, functional mechanism and biogenesis of the oxidative phosphorylation system provides a background to understand the pathological impact of genetic and acquired dysfunctions of mitochondrial oxidative phosphorylation.

Keywords F_1F_o ATP synthase • Mitochondrial biogenesis • Mitochondrial protein import • Oxidative phosphorylation • Respiratory chain complexes

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R. Scatena et al. (eds.), *Advances in Mitochondrial Medicine*, Advances in Experimental Medicine and Biology 942, DOI 10.1007/978-94-007-2869-1_1,