
Preface

In 1870, Eduard Pfluger demonstrated that respiration takes place in cells and around a full century ago, in 1910, Kingsbury postulated that respiration takes place in “mitochondria.” However, Carl Benda coined the term “mitochondria” (thread granules) in 1898 to describe these ubiquitous cellular structures. After the initial discovery of mitochondria, the respiratory chain was conceptualized by Keilin, Warburg, Hartree, and others in between the 1910s and 1930s. From the 1920s to 1950s, key aspects of aerobic metabolism were elucidated. The chemiosmosis hypothesis for ATP generation was then proposed by Peter Mitchell in 1961. This era was followed by mitochondrial isolation and the publication of first high-resolution images of mitochondria by George Palade and Fritiof Sjostrand. In the 1960s and 1970s, much of the focus remained on ATP synthesis, electron transport chain (ETC), and anion translocators. With the sequence of the human mitochondrial genome in 1981, a new era of mitochondrial biology was initiated resulting in the recognition of mitochondrial inheritance. In 1998, the first mitochondrial proteome was published, and eventually by 2008, the complete catalog of mitochondrial proteins, “MitoCarta,” was unveiled. The ever growing interest in mitochondria and pharmacology, as well as the physiology associated with them, is widely discussed in several scientific meetings and literature.

Classically, mitochondria were defined as the key regulators of cellular energy. However, now it is universally accepted that they are dynamic, interconnected, and integrated with other cellular organelles. In addition to their role in the generation of ATP by oxidative phosphorylation, mitochondria are involved in controlling cell metabolism and are key players in cellular calcium signaling, free radical homeostasis, lipid transport and biosynthesis, apoptosis, cell cycle and differentiation, and cellular aging. They also participate in retrograde signaling with nucleus and cross talk with endoplasmic reticulum either directly or via mitochondria-associated membranes. *Pharmacology of Mitochondria*, the focus of this handbook, is a unique effort by leading experts and researchers to assimilate information on pharmacology and physiology of mitochondria. Topics covered in the handbook expand beyond canonical roles assigned to mitochondria. The information presented will be highly useful for mitochondrial biologists and researchers working in physiology, medicine, and plant sciences.

In the *Handbook of Pharmacology*, information is delineated from mitochondrial genetics to mitochondrial diseases and physiology. Even though mitochondria possess their own genes, the majority of proteins imported into mitochondria are encoded by nuclear DNA and a chapter in our book titled “Nuclear Transcription Factors in the Mitochondria: A New Paradigm in Fine-Tuning Mitochondrial Metabolism” provides an overview of nuclear-encoded factors. Ionic homeostasis plays a major role in maintaining the structural and functional integrity of mitochondria. The majority of the proteins involved in maintaining the mitochondrial ionic homeostasis are encoded by the nuclear DNA; however, information on these proteins responsible for transporting ions is still in its infancy. Several ion channels and transporters involved in mitochondrial ionic homeostasis have been shown to present by either pharmacological or genetic approaches. In this handbook, chapters titled “The Mitochondrial Permeability Transition Pore and ATP Synthase”; “The Roles of Mitochondrial Cation Channels Under Physiological Conditions and in Cancer”; “Anion Channels of Mitochondria”; “Guide to the Pharmacology of Mitochondrial Potassium Channels”; and “The Mitochondrial Ca^{2+} Uniporter: Structure, Function, and Pharmacology” provide an overview of different classes of ion channels and transporters present in mitochondria, pharmacology associated with them, and their roles in diseases.

Mitochondrial structural and functional dynamics are associated with human physiological and pathological conditions. To maintain the structural and functional integrity of mitochondria, they continuously undergo fission, fusion, and trafficking, regulate lipid transportations, modulate reactive oxygen species production, and regulate cellular metabolism. Any deviation or abnormality from mitochondrial structural and functional integrity can result in human pathological conditions and diseases. Several chapters titled “Mitochondrial Fission in Human Diseases”; “Mitochondrial Cholesterol and the Paradox in Cell Death”; “Mitochondrial Changes in Cancer”; “The Emerging Role of Mitochondrial Targeting in Kidney Disease”; “Mitochondrial Dynamics as a Therapeutic Target for Treating Cardiac Diseases”; “Mitochondria in Alzheimer’s Disease and Diabetes-Associated Neurodegeneration: License to Heal!”; “Leber Hereditary Optic Neuropathy: A Mitochondrial Disease Unique in Many Ways”; and “Leber Hereditary Optic Neuropathy: Exemplar of an mtDNA Disease” summarize the association of mitochondrial structural and functional integrity with human diseases.

Pharmacologically, mitochondria have undergone a renaissance in the last two decades. Several novel approaches at pharmacological and genetic levels have been incorporated to the mitochondrial medicine. The recent first live birth of three-parent baby carrying mitochondria from donor mother is the spectacular breakthrough in treating mitochondrial diseases. However, several new approaches and treatments are required to treat mitochondrial diseases and disorders. Chapters discussing new as well as existing therapeutic approaches in this handbook “Mitochondria-Targeted Agents: Mitochondriotropics, Mitochondriotoxics, and Mitocans”; “Mitochondrial Flashes: Elemental Signaling Events in Eukaryotic Cells”; “Role of Mitochondrial Reactive Oxygen Species in the Activation of Cellular Signals, Molecules, and Function”; “MITO-Porter for Mitochondrial

Delivery and Mitochondrial Functional Analysis”; and “Toxicity of Antiepileptic Drugs to Mitochondria” provide highly useful overview on mitochondria in pharmacology. In the current era the amount of data generated by multidisciplinary approaches on a daily basis, there is an urgent need of integrating the big data to derive useful information and a chapter focused on understanding the complexity of mitochondrial phenome titled “Equipping Physiologists with an Informatics Tool Chest: Toward an Integrated Mitochondrial Phenome” provides an excellent platform for the same.

The authors and editors of the *Pharmacology of Mitochondria* hope that the chapters presented herein will provide extremely beneficial and inspiration information to mitochondrial enthusiasts, researchers, students, and clinicians. The chapters contributed by leading mitochondrial researchers in the *Handbook of Pharmacology* will take us through the novel pharmacological strategies via mitochondria to understand their physiological and pathological role as well as present them as therapeutic targets. We hope that the handbook will motivate the current and new generation of researchers to pursue the unanswered questions and understand the pharmacological and physiological implications of this fascinating and complicated organelle, “mitochondrion.”

Philadelphia, PA, USA

Harpreet Singh
Shey-Shing Sheu

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Singh, H.; Sheu, S.-S. (Eds.)

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