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## Preface

Mitochondria are double membrane-bound organelles present in nearly every eukaryotic cell. Thought to originate from a primitive bacterial endosymbiont, mitochondria generate most of the cellular supply of ATP and are therefore often referred to as the power plant of the cell. In addition to their central role in metabolism, mitochondria generate and sequester reactive oxygen species, serve as high capacity buffers of intracellular calcium, and mediate programmed cell death (apoptosis).

Neurons are particularly dependent on proper mitochondrial function, because of the high energy demands associated with the maintenance of ionic gradients during action potential firing and synaptic transmission, the principal components of neuronal computation. As well, adult neurons are difficult to replace and have a complex cytoarchitecture with dendrites and axons extending over considerable distances. For these reasons, mitochondrial quality control and transport are of unique importance in the nervous system.

Mounting evidence indicates that mitochondrial dysfunction is an essential contributing factor in several common neurodegenerative disorders, including Alzheimer disease, amyotrophic lateral sclerosis, Huntington disease, and Parkinson disease. Moreover, impaired mitochondrial dynamics and energetics have been implicated in peripheral diabetic neuropathy, chemotherapy-induced peripheral neuropathy, Charcot-Marie-Tooth disease, and several other types of acquired and inherited peripheral neuropathies. A better understanding of mitochondrial structure and function is therefore paramount to the development of effective therapies for many major CNS and PNS diseases.

This book is intended as a laboratory manual for a wide range of researchers who study mitochondria in the nervous system. The 16 chapters of this volume combine contributions of leading investigators in the field and describe a broad spectrum of experimental approaches for investigating structure, function, and transport of neuronal mitochondria in health and disease. Many of these approaches were only recently developed and, to the best of our knowledge, have never been assembled in book form. The state-of-the-art techniques compiled in this volume range from electron tomography-based 3D reconstruction of mitochondrial cristae to patch clamp recording from mitochondria in intact neurons. Several chapters describe optical approaches based on the use of genetically engineered fluorescent sensors for monitoring synaptic ATP and axonal ROS generation, mitochondrial  $\text{Ca}^{2+}$  cycling and pH changes, and mitochondrial dynamics and axonal trafficking in live neurons in real time. With recent advancements in mass spectrometry, this book also includes a chapter that details the use of mass spectrometry for mitochondrial proteomics analysis in neurons. Additional chapters in this volume describe respirometry, NADH imaging, and methods for studying pyruvate transport and mitophagy.

Each chapter focuses on a specific method for studying neuronal mitochondria and is prefaced with an introduction to its underlying scientific principles and areas of implementation. The main sections of each chapter describe specific materials, reagents, tools, and equipment required for a given technique, which is followed by a step-by-step protocol and practical details for employing the method. Each chapter also contains a section that

discusses potential problems and their solutions associated with a specific method as well as provides examples of results and outcomes for the described method.

We hope that this book will be a valuable practical resource for a broad range of investigators interested in the function of neuronal mitochondria in health and disease states and would like to thank all the authors for their contribution to this book.

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