

Preface

Ever since the ancient bacteria entered a primitive eukaryotic host cell billions of years ago, the proto-mitochondrion and its host cells have entered into an intricate symbiosis relationship that has been constantly evolving. Mitochondria and their host cells depend on each other for maintenance and survival. For example, the majority of the components of the mitochondrial proteome are encoded by host nuclear DNA. On the other hand, mitochondria are essential for such diverse functions as energy metabolism, reactive oxygen species production, calcium buffering, and cell death control. As the name implied (*mito* and *chondrion* means threaded and grain, respectively, in Greek), the morphology of mitochondrion is dynamic, constantly undergoing fission and fusion processes *in vivo*, and these morphological changes are believed to be important for the essential mitochondrial functions mentioned above. Given the critical roles of mitochondria for the normal physiology and life and death decisions of its host cells throughout the body of a multicellular organism, it is not surprising that defects in mitochondrial dynamics are linked to human diseases. What is surprising is the relatively selective vulnerability of neurons to defective mitochondrial dynamics. This has fueled considerable efforts in neurodegenerative disease field to use mitochondrial dynamics as a new experimental paradigm for disease mechanism investigation.

Although many reviews and books have been written on the contribution of mitochondrial dysfunction to human diseases, this is the first book that integrates diverse topics such as the genetic control of mitochondrial dynamics, the relationship between mitochondrial dynamics and bioenergetics, the roles of mitochondrial dynamics in apoptosis, axonal transport, mitochondrial quality control, and the contribution of defective mitochondrial dynamics to the pathogenesis of neurodegenerative diseases. Focusing on the theme of mitochondrial dynamics and its role in neurodegeneration, this book brings together leading scientists and clinicians from around the world to deliver a comprehensive treatise on all aspects of mitochondrial dynamics. In Chap. 1, Dr. McQuibban and his colleagues present a comprehensive historical account of key discoveries in mitochondria research and those that lead to the identification of key molecular players involved in mitochondrial dynamics. They especially emphasize the role played by model organism genetics in these latter discoveries. In Chap. 2, Dr. Rossignol and colleagues describe the fundamental mechanisms by which mitochondrial dynamics and cellular energy status

can reciprocally regulate each other. Many thought-provoking hypotheses are proposed. In Chap. 3, Dr. Shirihi and colleagues discuss the regulation and interdependence of mitochondrial dynamics and mitochondrial autophagy (mitophagy) in mitochondrial quality control. This is a very timely topic as mitophagy is currently one of the heavily studied areas in neurodegenerative disease research. In Chap. 4, Dr. Youle and colleague highlights the importance of mitochondrial dynamics in the timely execution of apoptosis, one of the fundamental processes involved in neurodegeneration. In Chap. 5, Dr. Sheng and colleague discuss the molecular processes that lead to the transport and distribution of mitochondria to neuronal axons and synapses, arguably one of the most important aspects of neuronal physiology. Although disease relevance is not the main focus of this chapter, understanding the relationships among mitochondrial dynamics, transport, and neuronal plasticity will shed important insights into the disease conditions. In Chap. 6, Dr. Reynier and colleagues presents recent findings on the clinical diversity of diseases caused by mutations in the mitochondrial fusion machinery, the spectrum of mutations in the mitochondrial fusion genes and the corresponding pathophysiology, and the therapeutic perspectives. In Chap. 7, Dr. Chu and colleague summarize a rapidly growing body of literature focusing on the role of mitochondrial dynamics in the pathogenesis of Parkinson's disease, and they discuss unresolved controversies in the field in the context of a dynamic network of compensatory responses to mitochondrial stress, dysfunction and injury. In Chap. 8, Dr. Lipton and colleagues highlight the role of aberrant mitochondrial dynamics in the pathogenesis of Alzheimer's disease, and offer a molecular mechanism connecting disease-causing insults and post-translational modification of the mitochondrial fission machinery component Drp1. In Chap. 9, Dr. Monteiro and colleagues discuss the published literature linking mitochondrial dysfunction in Huntington's disease, focusing on the role that defects in mitochondrial dynamics might play in disease pathogenesis. These chapters discuss the central problems associated with the nascent but rapidly growing research field of mitochondrial dynamics in neurodegeneration. They should serve as an excellent reference book for students, clinicians, and researchers engaged or interested in mitochondria biology, neurobiology, and mechanisms of neurodegenerative diseases.

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