Preface

Special issue: Mitochondria in diseases and therapeutics

The appreciation of how mitochondrial dysfunction plays a critical role in a range of clinical disease processes has encouraged us to compile this special issue titled Mitochondria in Diseases and Therapeutics. The paper by Carmen A. Mannella introduces the important concept of the critical role of mitochondrial membrane topology in influencing mitochondrial functions such as energy metabolism, mitochondrial biogenesis, and apoptosis. One of the intriguing aspects of mitochondrial membrane topology is the formation of contact sites between the outer and the inner membrane. This brings up an important question: what are the biological consequences of the protein–protein interactions in the contact site complexes? This topic is addressed in the paper by Dieter Brdiczka et al. One of the familiar protein complexes in the contact sites is the outer membrane voltage-dependent anion channel (VDAC), inter-membrane mitochondrial creatine kinase (MtCK), and inner membrane adenine nucleotide translocase (ANT). By its localization in contact site complexes, MtCK serves as a key signaling protein in regulating bioenergetics channeling, Ca²⁺ homeostasis, and apoptosis. Therefore, functional abnormality of this protein is involved in several human diseases, as is described in the paper by Uwe Schlattner et al. Mitochondrial outer membrane serves as a barrier to filter the information trafficking between the mitochondrial and the cytosolic milieu. The article by John Lemasters suggests that VDAC is a gatekeeper for such communication and that VDAC closure may cause global suppression of mitochondrial function in pathophysiological states. The other protein in the outer mitochondrial membrane controlling the release of cytochrome c is the mitochondrial apoptosis-induced channel (MAC). The article by Laurent Dejean et al. discusses the regulation of MAC by Bcl-2 family proteins and how this regulation influences apoptosis. The ion channels in the inner membrane of mitochondria also play a critical role in mitochondrial energy metabolism, reactive oxygen species (ROS) generation, and apoptosis. The article by Heberty Facundo et al. describes physiological functions of K⁺ channels in the inner membrane of mitochondria and the mechanisms whereby they protect against ischemia–reperfusion injury. The electron transport complexes also participate in the regulation of mitochondrial functions. Defects in activity in the enzymes of the oxidative phosphorylation system can cause serious diseases. Brigit Schilling et al. have developed techniques that make possible rapid and in-depth analysis of all five complexes of the oxidative phosphorylation. The paper by Andrew Tompkins et al. evaluates the involvement of the mitochondrial complex I in the formation of ROS during ischemia–reperfusion injury. The perturbation in the spatial and temporal profiles of ROS can translate into cellular excitability and associated lethal cardiac arrhythmia, as discussed in the paper by Miguel Aon et al. To visualize the importance of mitochondrial ROS in causing cell death, Tsung-I Peng et al. used two-photon confocal microscopy to monitor mitochondrial ROS formation during the progression of cell death at single-cell levels. The review by Shey-Shing Sheu et al. summarizes recent strategies for synthesizing mitochondrially targeted antioxidants and their future promise for disease treatment. Although this issue cannot encompass all aspects of mitochondria and disease, we hope the reader will find that these articles illustrate well the breadth and significance of mitochondrial function and dysfunction in pathophysiological processes.

Shey-Shing Sheu
Departments of Pharmacology and Physiology, of Anesthesiology, of Medicine, School of Medicine and Dentistry, University of Rochester, 601 Elmwood Avenue, Box 711, Rochester, NY 14642, USA
E-mail address: sheyshing_sheu@urmc.rochester.edu.
Corresponding author.

John J. Lemasters
Department of Cell and Developmental Biology, University of North Carolina, CB #7090, 236 Taylor Hall, Chapel Hill, NC 27599, USA
E-mail address: lemaster@med.unc.edu.