Top Ten Things to Know
Mitochondrial Function, Biology, and Role in Disease

1. Primary mitochondrial diseases include a broad spectrum of disorders affecting multiple tissues and organ systems. These disorders affect an estimated 1 in 5000 people, although it is suspected that this may be an underestimate since many cases go undiagnosed.

2. The continuous energy requirements of the heart are sustained by the consumption of a mass of adenosine triphosphate (ATP) daily that is estimated to exceed cardiac weight itself by 5- to 10-fold.

3. Cardiomyocytes have among the highest concentrations of mitochondria of any human cell, and because of the high ATP demands of the heart, relatively subtle defects in the generation of ATP by mitochondria can affect cardiac function.

4. Evidence has shown that mitochondria play a key role in cardiovascular disease, particularly in response to ischemia and the transition to heart failure.

5. Mutations in mitochondrial proteins can lead to defects in mitochondrial quality control, leading to additional mitochondrial defects and errors in metabolic signaling, bioenergetics, calcium transport, reactive oxygen species generation, and activation of cell death pathways.

6. Protocols for the clinical diagnosis of mitochondrial diseases are often invasive, are labor-intensive, and have variable rates of success, warranting additional research on mitochondrial biomarkers.

7. It has become apparent that there is cross talk among the mitochondria, the cytosol, and the nucleus. Posttranslational modifications have been identified as a primary mechanism for this communication between the mitochondria and the rest of the cell.

8. Although the uptake of small amounts of calcium by the mitochondria is thought to regulate its metabolism and ATP production, mitochondria can take up much larger levels of calcium during calcium overload of the cytosol. This leads to the opening of the mitochondrial permeability transition pore; the sustained opening of this pore is a trigger for cell death.

9. A number of gaps remain in our understanding of mitochondrial function and its role in disease. These include a better understanding of the effects of posttranslational modifications on protein function, the mechanisms by which mitochondria regulate cell death – including regulation of the mitochondrial permeability transition pore, and pathways that regulate mitochondrial turnover.

10. Increased knowledge of how mitochondrial function and pathophysiology integrate with other intracellular compartments and structures will also be crucial in order to ultimately enable the modulation of quality-control programs to maintain cardiomyocyte homeostasis.