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Mitochondria: From Basic Biology to Cardiovascular Disease

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This is an exciting time in mitochondrial research. Mitochondria have long been known as the “powerhouse” of the cell and the organelle responsible for generating ATP. In recent years there has been a resurgence of interest in mitochondria as controller of cell death. Mitochondria and metabolism have long been a major focus of the JMCC, the journal of the International Society for Heart Research (ISHR). Indeed the ISHR grew from its roots as the “International Study Group for Research in Cardiac Metabolism”. The JMCC has published many seminal papers on mitochondria and metabolism^{1–9}. Thus, this Special Issue on mitochondria demonstrates the continuing commitment of the JMCC to this exciting and fundamentally important area of research.

The mitochondrial permeability transition pore (MPT) is usually attributed a key role in regulating cell death. In fact one of the seminal papers showing that inhibition of the MPT could reduce post-ischemic reperfusion injury was published in JMCC by Drs. Griffiths and Halestrap¹, who are each authors of review articles in this Special Issue^{10, 11} (add reference for Griffiths and reference for Halestrap). However as discussed in three focused reviews in this issue, the molecular composition of the MPT is still largely unknown and the topic of intense debate (12 and add Reference – Halestrap¹¹, and Di Lisa¹³). With the recent understanding that mitochondria can modulate cell death has come the realization that alterations in mitochondria are therefore exciting targets of cardioprotection, as discussed in reviews by Brookes¹⁴ and Garlid¹⁵ and modifiers of disease as discussed by Sack¹⁶. Mitochondria, which were originally thought of as static organelles have recently been shown to under go fission and fusion. Whether fission and fusion are active processes in a post mitotic cell such as a cardiomyocyte is a hot topic of debate and is the focus of a review by Sheu¹⁷.

Although mitochondria have long been known to be the site of ATP generation, we still do not fully understand how energy needs in the cytosol are signaled to the mitochondria and precisely how mitochondrial oxidative phosphorylation is regulated. This important area is the focus of a review by Balaban¹⁸ and several original articles. The review by Balaban¹⁸ suggests that Ca²⁺ and inorganic phosphate (Pi) are key regulators of oxidative phosphorylation. Interestingly these same regulators, Ca and Pi, are key regulators of the MPT¹³ (ref Di Lisa). Although Ca²⁺ is recognized as a key regulator of oxidative phosphorylation and is suggested to be an important signal from the cytosol to the mitochondria to activate oxidative phosphorylation, there is considerable debate as to whether Ca²⁺ transients in the cytosol result in mitochondrial Ca²⁺ transients or whether the mitochondria integrate the Ca²⁺ transients. This topic is discussed in a point counterpoint by O’Rourke and Blatter¹⁹ and is also discussed in a two review articles^{10, 20} (Rizzuto and Griffiths) and is the topic of 2 original papers²¹,

²² (reference Kettleworth and Bers). It is interesting that mitochondria were originally thought to control cytosolic Ca^{2+} ²³, but this hypothesis was later discounted^{24, 25} because mitochondrial Ca^{2+} transporter were shown to not be active at cytosolic Ca^{2+} levels. However, recent work showing the generation of microdomains of high Ca^{2+} in the proximity of mitochondria has led to a resurgence of the hypothesis that mitochondrial Ca^{2+} may promptly respond to cytosolic Ca^{2+} increases and modify their amplitude and diffusion across the cell^{26, 27}.

It is hoped that this Special Issue on Mitochondria will spur new research and insight into the important role for this organelle in basic biology and its role in cardiovascular disease.

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