Metabolic challenges for cardiac mitochondria: from womb to tomb

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Mitochondrial metabolism has long been recognized as central to sustaining the energy requirements of myocardial work and other cellular processes, with mitochondrial volume varying from 30% to 60% depending on the type of heart cell. Key elements of our latest understanding of how mitochondrial delivery of energy is intertwined with intracellular signaling between all cell compartments, indicate that the role of mitochondria extends well beyond mere energy delivery and includes regulatory roles in the cell cycle, growth and development, maintenance of cell and organ level homeostasis, apoptosis and cell death.

The most current view is that mitochondria form a crucial nexus of multiple intracellular signal transduction pathways, participating in bi-directional exchange of signaling between intracellular components. Such centrality not only ensures that changes in energy demand and metabolism are rapidly and efficiently met, it constantly permits adaptation to a lifetime of stress due to high work demand, acute and chronic disease, and senescence.

Mitochondria form a contiguous integrated reticulum which is morphologically plastic and undergoes continuous remodeling/movement, especially in development and adaptation. Mitochondrial morphology is regulated by fission, fusion and motility of the reticulum in response to changes in myocardial state set by function and energy demand. Mitochondrial respiration and metabolism is closely regulated according to mitochondrial shape, location and signaling. Thus the location, function and biogenesis of mitochondria closely reflect critical mitochondrial response to the demands of change on the cell such as in growth, cell division, development, pathological stress, ageing or cell death.

It is not surprising then that during development, advanced age or cardiovascular disease, heart dysfunction is associated with abnormal mitochondrial structure and function. Mitochondrial dysfunction may involve genetic defects and/or the consequences of post-metabolic perturbations. The severity of heart dysfunction will depend on the adaptive reserve capacity of mitochondria and their ability to activate or suppress alternative metabolic pathways and related gene expression.