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EDITORIAL

The regulation and control of mitochondrial homeostasis in changing cardiac tolerance to ischemia-reperfusion injury: a focused issue

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The resurgence of investigation into mitochondrial biology stems, in part, from the realization that the regulation of mitochondrial content, turnover, and function to maintain diverse homeostatic demands are driven by exquisite biochemical and molecular controls. In the last decade the regulatory programs governing mitochondrial biogenesis [1], dynamics [2], responses to stressors, and post-translational regulatory control programs [3] have become more clearly defined. In the heart, this 'fine-tuning' of mitochondrial biology is proposed to modulate cardiac susceptibility to oxidative stress, ischemia-reperfusion injury, metabolic syndromes, and heart failure [4–7]. The National Heart Lung and Blood Institute, together with the Office of Rare Diseases of the National Institutes of Health and the Society of Heart and Vascular Metabolism funded an international conference held in Bethesda, MD, USA, to review these recent advances. In this focused issue of Basic Research in Cardiology, the highlights of this scientific program pertaining to the role of mitochondrial biology in modulating tolerance to ischemic stress are published. The studies examine advances in our understanding regarding the following: (1) modulating electron transfer flux to modulate ischemia-reperfusion tolerance [8, 9]; (2) identification of novel sights of mitochondrial generation of cytotoxic reactive oxygen species within the mitochondrion [10]; (3) signaling pathways and the modulation of mitochondrial membrane channels and pores to modulate mitochondrial tolerance to ischemia and reperfusion injury [11, 12]; (4) the more recently characterized mitochondrial homeostatic regulatory program of autophagy/mitophagy is explored in the context of cardiomyocyte ischemia/reperfusion stress and the modulation of mitophagy by a pharmacological cardioprotective agent [13, 14]; (5) the controversial aspects of our understanding of the function and structure of the mitochondrial permeability transition pore [15, 16] and finally (5) the evaluation of how molecular targeting of cardiac substrate utilization can alter ischemic stress tolerance [17]. These original studies and review articles identify novel regulatory programs that control mitochondrial biology and identify new targets to pursue in the development of therapeutic strategies to potentially augment cardiac tolerance against ischemia and reperfusion stress. Future advances in the role of post-translational regulation on mitochondrial functioning on the interaction of the mitochondria with other intracellular organelles such as the sarcoplasmic reticulum [18] and additional programs modulating mitochondrial homeostasis [19] may additionally modulate cardiac stress tolerance. We look forward to further investigations into these arenas that should enhance our understanding of the role and place of mitochondria in cardiac stress tolerance.

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