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Mitochondria as sensitive indicator and early predictor of the efficiency of cardiac shock wave therapy

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T n the heart, mitochondrial alterations play a major role in cell injury, including ischemia-reperfusion (IR), heart failure, oxidative stress, etc. Severe impairment of mitochondrial oxidative phosphorylation during IR dramatically decreases cardiac energy status (ATP and phosphocreatine) leading to cellular energy stress. Cardiac IR is associated with specific damage to mitochondria. This was confirmed also in in vitro studies in cultured cardiac cells showing severe changes in energy metabolism and mitochondria under conditions of hypoxia or simulated ischemia. Also, function of mitochondrial creatine kinase (CKmit) in the heart can be used as sensitive biomarker for evaluation of the efficiency of cardiac repair, regeneration, remodeling. In various pathologies like cardiomyopathy, heart failure, ischemia-reperfusion injury, CKmit functional coupling correlates well with the parameters of cardiac function, such as left ventricular ejection fraction and end-diastolic pressure. Thus, multiple mitochondrial damages are considered for determining factor causing loss of cardiomyocytes function and viability through apoptosis and necrosis. Based on these findings, an assessment of mitochondrial properties and function can be suggested for the evaluation of organ recovery and efficiency of various therapies of the heart, including post-ischemic shock wave therapy (SWT). Models and methods used were: Cardiac tissue; Permeabilized myocardial fibers (from left ventricle); Cell cultures; simulated ischemia-reperfusion; HL-1 and H9c2 cardiomyocytes. In vitro and in situ methods are: Fluorescent confocal in vivo imaging; High-resolution respirometry of myocardial fibers and cardiac cells; FACS analysis; and luminescent determination of cellular ATP levels. To better understand the mechanisms of SWT, various IR models are frequently used. In our studies, the correlation of cardiac performance and mitochondrial function in animal IR models indicates the potential of mitochondrial analysis for quantitative assessment of the recovery of myocardial energy metabolism and organ function upon SWT. Also, in vitro models using cardiomyocytes we show that after IR cell viability correlates with the loss of mitochondrial respiratory capacity, membrane potential and cellular ATP. SWT significantly improves mitochondrial function in H9c2 cardiomyocytes upon IR. Therefore, detailed mitochondrial analysis can offer a sensitive tool to evaluate efficiency of SWT and tissue regeneration. Furthermore, mitochondria are major source for ROS, which in turn may directly or indirectly stimulate angiogenesis. Mitochondrially generated ROS thus can be considered as potential targets for promoting myocardial angiogenesis in cardiac SWT. Summarizing, the advances of modern approaches in mitochondrial research and applications of these methods to recently established experimental in vivo and in vitro models can provide sensitive estimation of SWT efficiency, as well as new insights into shock wave associated mechanisms.

Biography

Andrey V Kuznetsov has worked on the problems of delicate mechanisms of energy metabolism in the heart and their changes under pathophysiological conditions. He has studied mitochondrial function and regulation in normal cells and in various pathological states, in particular in the field of mitochondrial cardiac system, mitochondrial interactions with other intracellular structures and systems, performing analysis of mitochondria *in situ* and in vivo. Also, he studied the roles of mitochondrial damage in ischemia reperfusion injury, apoptosis, calcium homeostasis, oxidative stress, mitochondrial ROS production, cardiac and muscle diseases with imaging of mitochondria and mitochondrial function, mitochondrial dynamics (fission, fusion, motility) in various living cells. He has extensive knowledge in cardiac bioenergetics and mitochondrial physiology and experience in optical imaging (fluorescent, two-photon) of single cell and single mitochondria, imaging of mitochondrial Ca2+, ROS, membrane potential, mitochondrial dynamics for basic science and in clinically oriented studies.

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