MITOCHONDRIAL DISEASES: A NEW CONCISE REPORT ON THE ISSUE

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Mitochondrial diseases (MDs) are a group of heterogenic systemic disorders stipulated by mutations in both mitochondrial and nuclear genome. Such disorders affect primarily the nervous system (neurons) and myocytes of skeletal and cardiac muscle. Pancreatic β cells are also very sensitive to defects in mitochondria leading to lowering of their energetic status.

The mitochondrial proteins are encoded partly in cyclic double-stranded mtDNA as well as in nuclear genes, and play a key part in the functioning of these organelles. So 13 genes out of total 37 in the human mitochondrial chromosome encode the protein subunits present in the respiratory chain ensembles, but the information of other 1,100 structural and functional mitochondrial proteins is stored in nuclear genome.

Mitochondria are the main producers of reactive oxygen species (ROS) in the cell. The very ROS forms (e.g. superoxide anion $-\cdot O^{2-}$) mostly damage the structure and functions of the mitochondrion, and an excessive ROS production is connected primarily with complexes I and III of the respiratory chain. ROS negatively influence on mtDNA causing appearance of mutations in it. Such mutations in turn lead to formation of ineffective proteins and low level of ATP synthesis in the mitochondrion. For example, insulin production and release into the blood are largely dependent on the ATP level in pancreatic β cells. If it rises over a certain threshold, then after K^+ channel closing, membrane depolarizing and Ca^{2+} entering, insulin is released from the cell. If the threshold was not reached, insufficient insulin secretion would lead to diabetes. Alzheimer, Parkinson, and Huntington diseases, heart failure, aging are consequences of the mtDNA damage by ROS. Links between damage and diseases have yet been shown.

There were some classifications of MDs proposed in the past, as too many factors could cause disorders in the mitochondrion. So, amongst most significant of them are such as: defects of mitochondrial substrate transport, defects of substrate utilization, defects of the respiratory chain, defects of accumulation and transformation of energy. Then come some syndromes which nature is tightly bound to mitochondria – encephalomyopathies. Syndromes of Barth, Kearns-Sayre, Pearson; syndrome MELAS, syndrome MERRF are typical MDs caused by gene mutations. Diversity of MDs is revealed not only in their clinical manifestations, but also in age variations when first symptoms of such pathologies appear, as well as in presence or absence of classical signs of dysmorphogenesis, lactate acidosis, myopathy. The visual muscle injury outcome is described as a ragged-red muscle fibre appearance. Thus, a widespread opinion concludes that critical decrease in energy supply of the cell by mitochondria, and ROS production in them are the main reasons for pathology development.