102. THE ROLE OF MITOCHONDRIA DYSFUNCTION IN METABOLIC AGING

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Introduction. Although mitochondria are considered the main cellular energy generators, their functions are far more extensive. Mitochondria also provide biosynthetic precursors for macromolecule synthesis, generates metabolites required for the maintenance of redox homeostasis, participates in cellular quality-control processes, including the recycling of damaged components. The age-associated decline in mitochondrial function represents a physiological process, analyzed in this study.

Aim of study. To elucidate the physiological mechanisms involved in mitochondrial degradation, which are essential for maintaining cellular homeostasis.

Methods and materials. For this study, recent scientific literature was analyzed, from databases such as: PubMed, Google Scholar, Scopus, Web of Science, published between 2021-2025.

Results. The results of the literature analysis indicates that mitochondrial dysfunction plays a crucial role in the development of metabolic aging through several complex molecular mechanisms. ATP production decreases due to reduced activity of respiratory chain complexes I, III, and IV, leading to diminished efficiency of oxidative phosphorylation. ROS production increases, amplifying cellular oxidative stress, damaging cellular structures, and contributing to metabolic decline. mtDNA mutations further impair the synthesis of respiratory chain proteins. Mitochondrial biogenesis is reduced through the downregulation of key regulatory factors (PGC-1α, NRF1, and TFAM), a process exacerbated by decreased AMPK activity, which normally stimulates mitochondrial biogenesis. Reduced activity of sirtuins (SIRT1/3) and hyperactivation of the mTOR signaling pathway inhibits autophagy. Mitochondrial dysfunction promotes the activation of cell-cycle regulators such as p53 and p21. Decreased fatty-acid oxidation leads to intracellular lipid accumulation, increasing the risk of common metabolic disorders, such as insulin resistance, impaired glucose metabolism, obesity, dyslipidemia, sarcopenia, and chronic low-grade metabolic inflammation (inflammaging).

Conclusions. Mitochondrial dysfunction plays a fundamental role in metabolic aging, contributing to the disruption of cellular energy homeostasis and metabolic functions. Impaired mitophagy, reduced efficiency of oxidative phosphorylation, increased production of ROS and the accumulation of dysfunctional mitochondria lead to decreased ATP synthesis and altered carbohydrate and lipid metabolism. Mitochondrial integrity and the quality-control mechanisms that regulate mitochondrial turnover are essential for maintaining physiological metabolic homeostasis and for slowing the progression of metabolic aging.

Keywords. Mitochondria dysfunction, Mitochondrial turnover, Metabolic disorders, Mitophagy.

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