
AA.56 — Alterations in mtROS and reduced glutathione production don't influence viability of atherosclerosis-associated cells

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Atherosclerosis(A) has a multifactorial nature that leads to the development of systemic disorders including oxidative stress. An increase in the generation of reactive oxygen species (ROS) is frequently associated with dysfunctions in the electron transport chain (ETC) 13 subunits of which are encoded in mitochondrial DNA (mtDNA). [1]. But exact role of mitochondrial DNA (mtDNA) mutations in the pathogenesis of A remains relatively understudied. This field of study may offer promising ways for the identification of novel molecular markers and the potential discovery of new therapeutic targets [2].

The cytoplasmic hybrid lines investigated in this study were derived from THP-1 and exhibited mitochondrial DNA mutations associated with A [3]. In experiments utilizing the MitoTracker Red dye, an increase in the rate of mtROS production was observed in the majority of cell lines. The determination of reduced glutathione (GSH) content in mitochondria using monochlorobimane fluorescence colocalized with TMRM demonstrates a reduction in thiol content in the majority of cell lines (from 61,9 to 90 % of THP-1) with increase to 114,2-119 % in three others. The absence of oxidative stress was indicated by the comparable to THP1 level of cell viability determined by Hoechst 33342 and Propidium iodide.

The data may indicate the presence of mechanisms regulating GSH levels in mitochondria, thereby maintaining redox balance. The maintenance of GSH in mitochondria relies on nicotinamide adenine dinucleotide phosphate (NADPH) as an electron donor for glutathione reductase (GR). The maintenance of NADPH homeostasis is primarily controlled by a network of metabolic pathways and enzymes, including malic enzymes (ME) (ME3 in mitochondria), the nicotinamide nucleotide transhydrogenase (NNT), cytosolic or mitochondrial NADP-dependent isocitrate dehydrogenase (IDH), glutamine metabolism and fatty acid oxidation (FAO) [4]. It is essential to maintain an elevated mitochondrial membrane potential ($\Delta\Psi_m$) in order to sustain the function of NNT. In some studied cell lines, the elevated level of $\Delta\Psi_m$ (from 103,9 to 116,6 %) was clearly demonstrated, which indirectly indicates that this mechanism may contribute to the maintenance of NADPH. Furthermore, an elevated contribution of NNT is observed when mtNADH content is increased. In some cell lines the lev-

el was 101 to 129%. Furthermore, elevated IDH activity was observed in cells with active production of pro-inflammatory cytokines, a phenomenon that was also evident in cells with a pro-atherogenic profile. At the same time, glutaminolysis and FAO are reduced in pro-atherogenic cells [5] that make these pathways are less probable sources of NADPH. But the role of exact routes of NADP reduction and GSH pool maintenance need to be further studied.

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AA.57 — Calculation of the kinetic isotope effect for the dissociation of polyglycine dimers as a model system for protein denaturation

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The influence of isotopic substitution on the kinetics of chemical reactions is called the kinetic isotope effect (KIE). The KIE has a significant effect on the kinetics of unfolding of the secondary structure of proteins, which leads to their denaturation (loss of activity) in biological systems. Recent studies confirm the effect of KIE on the metabolic kinetics of aging in simple and complex organisms and the effect of KIE on the longevity of microorganisms [1]. The use of deuterium oxide as a solvent allows to increase the lifetime of vaccines, which is associated with the KIE during protein denaturation. Thus, the estimation of