Modulation of telomerase gene expression of activated peripheral blood mononuclear cells is influenced by Ala16Val-Sod2 gene polymorphism

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The activation process of T and B-lymphocytes involves the increase in cellular proliferation and upregulation of telomerase activity, comparable to those observed in stem cells and transformed cell lines. However, aging decline of total number of T and B-lymphocytes (immunosenescence) due decrease in the telomerase activity that is responsible to telomeric DNA region restoration. As immunosenescence is a process that present individuals variation, the influence of genetic alteration of oxidative stress metabolism on telomerase gene expression of activated lymphocytes, need to be elucidated. Human beings present a superoxide dismutase manganese dependent (SOD₂) single nucleotide polymorphism (SNP) (rs4880 in 16 codon (Ala16Val-SOD₂) generating three genotypes. Both homozygous genotypes create imbalance in O₂– H₂O₂ levels due change in SOD₂ efficiency (VV = low efficiency; AA= high efficiency) and has been associated with chronic diseases and differential response to drug and toxicants exposition. Therefore, we evaluated the effect of SOD2-SNP cell expansion, viability and telomerase expression of peripheral blood mononuclear cells (PBMCs) from subjects with different Ala16Val-SOD₂ genotypes (n=12). PBMCs were cultured in RPMI 1340 in controlled conditions (CO₂ 5%-37oC) and the viability/cells proliferation was evaluated by MTT assay and flow cytometry (cell cycle and apoptosis induction) after 1, 3, 7 and 14 days. The telomerase modulation was analyzed by qRT-PCR and telomere shortening by ELISA immunoassay. Whereas, after 3 days exposition AA-PBMCs presented high proliferative rate than other genotypes, from this period also occur a fast loss of proliferation and apoptosis processes. After 15 days just VV genotype presented up regulation of telomerase gene. The present study corroborate the hypothesis that proliferation-immunosenece is broadly regulated by O₂– H₂O₂ mitochondrial levels.