Fernanda Barbisan, J Cell Sci Ther 2015, 6:2
http://dx.doi.org/10.4172/2157-7013.S1.033

OMICS International
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5th World Congress on
Cell & Stem Cell Research

March 23-25, 2015 DoubleTree by Hilton Chicago - North Shore, USA

Genetic influence of oxidative metabolism on lymphocyte telomerase modulation

Fernanda Barbisan
Universidade Federal de Santa Maria, Brazil

The activation process of T and B-lymphocytes involves an increase in cellular proliferation and up regulation 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 is responsible for telomeric DNA region restoration. As immunosenescence is a process that presents individual 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 O^{-2}–H_2O_2 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 exposure. 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 (CO_2 5%-37°C) 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 three days exposition AA-PBMCs presented higher 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-imunosenescence is broadly regulated by O^{-2}–H_2O_2 mitochondrial levels.

Biography

Fernanda Barbisan is a biologist by Western Santa Catarina University and pharmacologist by Federal University of Santa Maria. Currently, she is Ph.D. student and assistant researcher at Biogenomics Laboratory Federal University of Santa Maria, Brazil. She investigates the pharmacogenetic influence on immunosenescence, as well as drug response of lymphocytes and adult stem cells using *in vitro* experimental models.

fernandabarbisan@gmail.com

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