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TRANSCRIPTOMIC CHANGES IN ENDOTHELIAL AND MESENCHYMAL STROMAL CELLS UNDER SIMULATED MICROGRAVITY

Abstract

The endothelium and stroma play an important role in maintaining the integrity and are the basis for regenerative processes. Therefore, the study of the effects of microgravity is an important aspect in understanding the changes occurring during space flight. Cultured endothelial cells (ECs) and mesenchymal stromal cells (MSCs) are a well recognized models for studying the molecular mechanisms of gravisensitivity. The effects of microgravity on these cells was assessed both in ground-based model experiments and in a real space flight. However, the study of transcriptomic changes in microgravity is essential for understanding the mechanisms of cell adaptation. The aim of our study was to analyze gene expression in ECs and MSCs in response to simulation of microgravity effects. Transcriptome analysis of samples was performed using the GeneChip Human Gene 1.0 ST Array microarray (Affymetrix, United States). A significant changes in the expression of 177 genes that can be classified into several functional clusters was detected. Among the genes with over expression, clusters of cell response to external stimuli and regulation of cell motility and proliferation can be reliably distinguished. Among down-regulated genes, clusters of transcription factors with the "zinc fingers" domain and factors involved in the regulation of morphogenesis and angiogenesis were observed. The overlapping of signaling pathways involved in mechanotransduction and inflammatory changes is discussed. More pronounced changes (more 2 folds) in the expression of 35 genes in MSCs were observed after simulated microgravity: 16 genes were up-regulated and 19 were down-regulated. Group of genes with more elevated expression (HLA-II, HMGCR, MTSS1,SREBF1) included those controlled of cell activity and markers of different tissue types. It was shown also the up-regulation genes responsible for proliferation, adhesion, cell interaction. Down-regulated genes were responsible for self-renewal and markers of differentiation. It is interesting that transcripts involving in Wnt- and Notch-signaling pathways demonstrated the opposite dynamics. This work was supported by the Russian Science Foundation (project no. 16-15-10407).