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CHANGES IN GENE EXPRESSION IN HUMAN BONE MARROW MESENCHYMAL STROMAL CELLS UNDER SIMULATED MICROGRAVITY

Abstract

Mesenchymal stromal cells are the population of multipotential precursors of adult bone marrow stroma able to differentiate into osteogenic, adipogenic and chondrogenic lineages. Recent studies have demonstrated that multipotential mesenchymal stromal cells can be the real candidates to gravity responding cell type that are involved into space flight induced osteopenia. These findings determine the necessity of more detailed study of its unique biology. We have studied the expression of genes in human bone marrow mesenchymal stromal cells (bmMSC) during different terms of simulated microgravity provided by Random Positioning Machine (RPM, manufactured by Dutch Space, The Netherlands). Cells were grown in OptiCell culture system and transferred into RPM for 48 and 120 hours. The Human Stem Cell RT Profiler^{TM} PCR Array (Assay Biosciences) profiles the expression of 84 genes related to the identification, growth and differentiation of stem cells. Stem-cell specific markers are included as well as stem cell differentiation markers, genes in signaling pathways important for stem cells maintenance are also contained on this array.

The results have shown that the expression of only nine genes were slightly changed (6 genes - down-regulated, 3 - up-regulated) after 48 hours of simulated microgravity. More pronounced and significant changes in gene expression were observed in bmMSC after 120 hours of simulated microgravity. Among 84 investigated genes 30 were no less than 5-fold up-regulated and 24 were down-regulated. The most up-regulated genes (more than 10-fold) generally included regulators and participants in cell proliferation (CCND2, CCND1, CDK1, CDC42, HSPA9, FGF2, NOTCH2, NUMB), cell adhesion (CD44, CD56, CDH2, CTNNA1, GJA1) and signaling pathways (ADAR, APC, FZD1, NOTCH2, NUMB). The most down-regulated (more than 50-100-fold) genes included such important regulators of stem cells self-renewal and differentiation like ALPI, WNT-1, MYOD1, BMP-3, DHH, DLL3, FGF4, PDX1, NEUROG2, SOX-2, COL9A1, COL2A1.Thus obtained results can clarify the genomic mechanisms of osteogenic differentiation reduction of bmMSC that was shown in our previous studies.

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