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REVERSIBLE CHANGES IN HUMAN BONE MARROW MMSC GENE EXPRESSION UNDER
SIMULATED MICROGRAVITY**Abstract**

Numerous experiments have shown that altered gravity affects embryonic and adult stem cells. Perhaps, inappropriate commitment of MMSCs in microgravity is one of the reasons for the emergence of osteopenia in human after long space flights and unloading. We have previously demonstrated remodeling of the cytoskeleton and fast up-regulation of α -actin expression that became more significant after 48 hrs of simulated microgravity (SMG). Moreover the up-regulation of beta-tubulin, cofilin and small GTPase RhoA gene expression was also detected. The purpose of this investigation was to identify other "target genes" of human bone marrow MMSCs that are sensitive to gravity changes using the Random Positioning Machine (RPM). RNA was isolated from MMSCs and amplified using the Illumina® TotalPrep™ RNA Amplification Kit and then hybridized on microchips Human-Ref8 gene expression array (Illumina, USA). It was found that only 7 genes were significantly up-regulated (at least 2 fold) after 30 min of SMG. These genes were mainly so-called "early response genes" and genes that cause non-specific reactions to stressful factors (growth factors, glucocorticoids, radiation, heat stress et al.): DUSP1, EGR1, EGR2, NFKBIZ, PTGS2, SGK. More pronounced changes (≥ 2 folds) in the expression of 35 genes were observed after 48 hrs of SMG: 16 genes were up-regulated and 19 were down-regulated. Group of genes with more elevated expression (HLA-II, HMGCR, MTSS1, OLFML2A, SREBF1) included those controlled of cell activity and markers of different tissue types. The same was true for the most down-regulated genes (BNIP3, COL1A1, ENC1, JUN, SERPINE1, THRA). After 120 hrs of SMG, the number of genes with altered expression decreased: only 4 genes were up-regulated and 2 – down-regulated at least. It suggests the activation of mechanisms responsible for progenitor cell adaptation to the altered gravity. In general, our findings revealed that the reversible changes in the transcriptional activity of MMSCs occur during short-term SMG. The genes with fast "gravity up-regulation" under SMG mostly belong to the so-called "early response genes" and genes that contribute to the universal cell response to stress of any kind. Longer effects of microgravity selectively modulate the expression of genes involved in various aspects of progenitor cell physiology and is likely to perform the function of "gravity/mechanical-sensitive genes".

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