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THE EXTRACELLULAR MATRIX OF STROMAL LINEAGE CELLS AS A TARGET FOR MICROGRAVITY

Abstract

During space missions and ground-based experiments, the mechanism of mechanotransduction, which provides an urgent cell response to microgravity by transmitting a signal from the extracellular space to the cytoskeleton via integrins and further to the nucleus, has been studied in detail. At the same time, the effect of gravity deprivation on extracellular matrix (ECM) has been investigated to a much lesser extent. As evidenced from real space and ground-based observations the ECM-reach skeleton is the mostly affectable system under microgravity. The above makes ECM structures of stromal lineage cells responsible for skeleton metabolism a first point of interest. Most available data are focused on transcriptional/translational activity of stromal cells under the real and simulated microgravity, while only few observations describing changes in ECM structures under microgravity are presented. In our hands mesenchymal stromal cells and their osteocommitted progeny were exposed to simulated microgravity at random positioning machine (RPM). The results suggest the existence of complex time-dependent changes in transcriptional activity of matrix-associated genes. At first stage, an upregulation of MSC collagen and proteoglycan encoding genes was observed. With a longer exposure (10 days), the number of ECM genes with altered transcription decreased. Only collagenA1, laminin, and tenascin were upregulated. At the same time, osteomodulin was downregulated, while the expression of osteocalcin had no differences vs static control. In addition to the MSC transcriptional activity, the features of ECM per se were analyzed. After 10-days of RPM, the collagenous and non-collagenous proteins decreased in ECM of MSCs. After 20 days, an attenuated mineralization of ECM was detected. After RPM exposure, a significant enhancement of both intracellular (catepsins) and extracellular (MMPs) ECM-remodeling proteases was revealed. These alterations can trigger the attenuation of ECM remodeling in the skeleton. In whole, the direction of above described changes do not depend on the commitment levels of stromal precursors. Meanwhile, based on our and others' data, it could be concluded that microgravity affects all steps of ECM remodeling – synthesis and degradation as well. This study was supported by the Program of Basic Research of IBMP RAS 65.3.