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DIFFERENTIAL EXPRESSION OF GENES ENCODING ADHESION AND CELL-TO-CELL INTERACTION MOLECULES IN BONE MARROW NICHE UNDER SIMULATED MICROGRAVITY

Abstract

It is known that the functional condition of hematopoietic stem cells (HSCs) depends on the state of the bone marrow niche.

The bone marrow stroma includes endosteal osteoblasts, endothelial cells, reticular cells, smooth muscle cells, adipocytes, macrophages, osteoclasts, multipotent mesenchymal stromal cells (MMSCs), neural cells. These cells, embedded in an extracellular matrix (ECM), form a milieu for HSC maintenance. The cell functional activity is determined by external signals from the local microenvironment. These signals are presented by soluble mediators, cell-to-cell contacts and ECM. The coordinated action of these factors on HSCs allows them to maintain physiological resting or differentiation.

HSC-supportive stromal cells are known to be gravisensitive. The alteration of their functions were described both under real and simulated microgravity (SMG). Integrins, selectins, cadherins are the principal molecules determined the cell interaction with the milieu, change its expression under microgravity as well. A microgravity-induced change of bone marrow stromal cell functions including cell-to-matrix contacts can disrupt the interaction of stromal and hematopoietic cells and violation of hematopoiesis.

3D-clinorotation is widely used to simulate the effects of microgravity in vitro. It provides continuous random change of cell orientation relative to the gravity vector. The goal of our work was to study the influence of the SMG on the transcriptional activity of genes encoding adhesion and cell-to-cell interaction molecules in bone marrow microexplants.

Bone marrow from BALB/c male mice (19–20 weeks old) was used. After isolation, bone marrow samples were divided into 2 groups: static control and cells under SMG (Gravite device, Space Bio-Laboratories Co., Ltd, Japan) during 16 days. Differential expression of genes encoding cell-to-cell (E-cadherin, ICAM-1, VCAM-1), cell-to-matrix interaction (integrins, osteopontin, perostin, etc.), other adhesion molecules (fibronectin, vitronectin, PECAM-1, etc.), transmembrane receptors (CD44, CD39, synaptotagmin-1, etc.) was analysed.

After SMG, transcripts of adhesion molecules (Ncam1, Vcam1), integrins (Itgam, Itgb1), ECM components (perostin, versican, thrombospondin-1) were upregulated. Genes encoding integrins (Itga5, Itgax, Itgb2, Itgb3), cell-to-matrix interaction molecules (Tgfbi, thrombospondin-2, CD44, beta-catenin, Emilin1, osteopontin) were downregulated. The expression of other genes did not change.

It could be concluded from the data above, that SMG provoked the adhesion gene pattern alteration. Cell-to-cell interaction genes were upregulated, while cell-matrix interaction genes were downregulated. This may cause a decrease in HSC mobilization from the bone marrow, observing in space flight under real MG.

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