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IL-8 PRODUCTION IS INCREASING IN MESENCHYMAL STROMAL CELLS DURING 10-DAYS OF SIMULATED MICROGRAVITY

Abstract

Long-term space flights cause adverse changes in many human physiological systems, despite of countermeasures. To understand the mechanisms of these changes, the cellular effects of microgravity are being actively studied. Special attention is paid to mesenchymal stromal cells (MSCs) that are mechanosensitive precursors of structural tissue and therefore can determine their properties. One of MSC function is the secretion of cytokines that control a wide range of processes: cell migration, differentiation, functional activity and survival. The aim of this study is to estimate effect of microgravity on MSC cytokine secretion. MSCs were isolated from human adipose tissue and cultured in standard conditions. To simulate the effects of microgravity, the Random Positioning Mashine (RPM) was used. After a 10-day exposure, cytokine level in conditioned media of exposed and control cultures were measured by Human VEGF, IL-8, IL-6 and MCP Quantikine ELISA Kits (RD, USA). Simulated microgravity (SMG) led to increase of IL-8 secretion by 3.5 times compared with the static control. IL-8 is a pro-inflammatory cytokine recruiting monocytes and macrophages, the precursors of osteoclasts. Such reaction in vivo can be one of the bone resorption accelerated factors in microgravity, since there is a connection between resorption and the pro-inflammatory cytokine profile. In addition, IL-8 can stimulate the production of certain extracellular matrix proteases. SMG stimulated the secretion of angiogenesis stimulating factor (VEGF) up to 20%. No changes in the secretion of cytokines IL-6 and MCP-1 were observed. Earlier we have shown that RPM exposure during 6 and 24 hours caused increase in IL-8 secretion; 6-hour exposure caused increase the IL-6 level, and exposure for 96 hours also caused increase in the secretion of VEGF and IL-8. These results demonstrate that MSC secretion during SMG is shift in time dependent manner. Thus, a 10-day simulation of microgravity effects causes an increase of IL-8 production by MSCs, which may be the reason for the accelerated degradation of the extracellular matrix by the autocrine mechanism and activation of bone resorption. Funding: The reported study was funded by RFBR, project number 19-315-90005