

5th World Congress on **Cell & Stem Cell Research**

March 23-25, 2015 DoubleTree by Hilton Chicago - North Shore, USA

Activated leukocytes alter allogeneic multipotent mesenchymal stromal cell functions

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Multipotent mesenchymal stromal cells (MSCs) have been assumed as a perspective tool for allogeneic application in cell therapy due to their immunotolerance. Recent findings reveal that MSCs are not totally invisible for host immune system but rather possess immuno-evasive properties. Here we evaluated the direct cell-to-cell and paracrine effects of PHA-activated mononuclear cells (MNCs) from peripheral blood on allogeneic MSCs at standard (20%) and tissue-related (5%) O₂ level. Interaction with MNCs had no effect on MSC stromal phenotype, but significantly increased soluble and membrane-associated ICAM-1 expression. Upon direct contact, MNCs modulated the functional activity of MSCs: The viability of MSCs with elevated ROS was reduced. ROS formation, mitochondrial trans-membrane potential and lysosome activity were increased. MSC proliferation and differentiation was slowed down. Paracrine regulation of MNC/MSCs interaction did not affect MSC intracellular parameters, but suppressed its migration. The global gene expression analysis showed that MSCs were more sensitive to the MNCs at 20% O₂. MSC “proinflammatory” activation was associated with increased expression of *IL-8*, *CCL5*, *IL-1b*, *COX-2*, *MCP-1*, *IL-1b*, *TRAF3IP2* were up regulated, and *IL-8*, *COX-2*, *IL-7R*—down regulated at 5% O₂ in comparison with 20% O₂. Upon interaction with MNCs the up-regulation of “immunosuppressive” genes: *HLA-B*, *-E*, *-F*, *-H*, *PTGIS*, *TGFBI*, *LIF*, *PTGS2* was detected. Increased expressions of genes whose products provide MSC proliferative activity, extracellular matrix remodeling (*MMP1*, *MMP3*) were also demonstrated. These data indicate that the interaction with MNCs significantly altered MSC gene profile and functional activity that can further facilitate the MSC participation in regenerative processes in tissues.

Biography

Elena R Andreeva received her Ph.D. at Russian Cardiology Research Center in 1996. She is a Leading Research Scientist in Cell Physiology Lab in the Institute of Biomedical Problems of Russian Academy of Sciences. The field of her scientific interests: Cell physiology of stem and progenitor cells, cellular and molecular mechanisms of adaptation, cell-to-cell interactions. She has published more than 60 papers in Russian and International Journals. She is a member of Russian Atherosclerosis Society, International Atherosclerosis Society.

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