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Angiogenic and Immunomodulatory Properties and Phenotype of Mesenchymal Stromal Cells Can Be Regulated by Cytokine Treatment

Authors : Ekaterina Zubkova, Irina Beloglazova, Iurii Stafeev, Konsyantin Dergilev, Yelena Parfyonova, Mikhail Menshikov

Abstract : Mesenchymal stromal cells from adipose tissue (MSC) currently are widely used in regenerative medicine to restore the function of damaged tissues, but that is significantly hampered by their heterogeneity. One of the modern approaches to overcoming this obstacle is the polarization of cell subpopulations into a specific phenotype under the influence of cytokines and other factors that activate receptors and signal transmission to cells. We polarized MSC with factors affecting the inflammatory signaling and functional properties of cells, followed by verification of their expression profile and ability to affect the polarization of macrophages. RT-PCR evaluation showed that cells treated with LPS, interleukin-17, tumor necrosis factor α (TNF α), primarily express pro-inflammatory factors and cytokines, and after treatment with polyninosin polycytidic acid and interleukin-4 (IL4) anti-inflammatory factors and some proinflammatory factors. MSC polarized with pro-inflammatory cytokines showed a more robust pro-angiogenic effect in fibrin gel bead 3D angiogenesis assay. Further, we evaluated the possibility of paracrine effects of MSCs on the polarization of intact macrophages. Polarization efficiency was assesed by expression of M1/M2 phenotype markers CD80 and CD206. We showed that conditioned media from MSC preincubated in the presence of IL-4 cause an increase in CD206 expression similar to that observed in M2 macrophages. Conditioned media from MSC polarized in the presence of LPS or TNF-α increased the expression of CD80 antigen in macrophages, similar to that observed in M1 macrophages. In other cases, a pronounced paracrine effect of MSC on the polarization of macrophages was not detected. Thus, our study showed that the polarization of MSC along the pro-inflammatory or anti-inflammatory pathway allows us to obtain cell subpopulations that have a multidirectional modulating effect on the polarization of macrophages. (RFBR grants 20-015-00405 and 18-015-00398.)

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