THE THERAPEUTIC POTENTIAL OF PRECONDITIONED MESENCHYMAL STEM CELLS IN ATHEROSCLEROSIS

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Atherosclerosis (AS) is a multifactorial and inflammatory disease the cause of which is the formation of lipid and cholesterol plaques on the inner wall of blood vessels. Experimental and clinical studies have shown that the pathogenesis of atherosclerosis is, in particular, connected with inflammatory reactions. Recent studies reported that preconditioned mesenchymal stem cells (MSCs) possess an enhanced immunomodulatory potential. The purpose of the study was to investigate the therapeutic potential of preconditioned MSCs in the development of atherosclerosis.

MSCs were isolated from the compact bone of mice by standard protocol. The characterization was conducted using flow cytometry, CFU assay and three-lineage differentiation. Cells were preconditioned with different combinations of cytokines and the optimal concentrations were determined by ELISA and by analysis of co-culturing with lymphocytes. The cytokine-preconditioned MSCs were administrated to mice with induced atherosclerosis. The lipids analysis, measuring of mouse spleens' weights, ELISA and histological analysis of the aorta sections were done after 8-th weeks.

We isolated MSCs and then confirmed the possession of the immunomodulatory properties. Preconditioning with the TNF-α cytokine effectively increased the immunomodulatory properties of MSCs compared to untreated MSCs in vitro. The results of in vivo study that the use of TNF-α-preconditioned MSCs reduced the development of atherosclerosis in mice compared to untreated MSCs: it increased the level of Treg cells in the spleen of mice; significantly reduced the levels of TNF-α and IFN-γ in blood serum; significantly reduced the spleen weights of mice; slightly decreased the total cholesterol levels and also increased HDL levels. Administration of TNF-α-preconditioned MSCs reduced the size of atherosclerotic plaques in the aorta of mice.

The results of this study demonstrated the effect of cytokine-preconditioned MSCs in the inhibition of the development of atherosclerosis in a mouse model. However, for application as a therapy for suffered patients additional studies are needed. Besides, using of TNF-α preconditioned MSCs can be considered in other preclinical studies of the different diseases.