

Mesenchymal stem cells and their regenerative and immunomodulatory potential

Abstract

Mesenchymal stem cells (MSCs) possess multidirectional regenerative ability, which, together with their immunomodulatory potential, makes them promising cell type for therapy of wide variety of diseases. Despite ongoing research, which proved MSCs application to be safe, reported effect of MSCs administration on patients is not convincingly beneficial yet.

In our work we focused on elucidation of MSCs role in regeneration of vital organs, heart and liver, where a large damage is life threatening for patients and any improvement in therapy would save many lives. Similar situation is in Graft versus host disease (GVHD), where MSCs immunomodulatory properties could be beneficial.

Role of MSCs in heart regeneration was examined *in vitro*. Primary adult swine cardiomyocytes (CMCs) were co-cultured with or without swine MSCs for 3 days and morphological and functional parameters (contractions, current, respiration) of CMCs were measured. MSCs showed supportive effect on CMCs survival, especially at day 3 of the experiment, where in co-culture was significantly higher number of viable CMCs with physiological morphology and maintained function.

Effect of MSCs on liver regeneration was observed in swine model of chronic liver disease. Piglets underwent liver lobe resection followed by MSCs administration (1×10^6 cells/kg) into portal vein. Cytokines and growth factors quantification was performed in selected time points. The morphometry of regenerated liver tissue was analyzed by quantitative histology. Results showed the insignificantly increased connective tissue volume in liver parenchyma after MSCs administration and other measured parameters were not significantly influenced by MSCs.

Immunomodulatory effect of MSCs on GVHD was evaluated first *in vitro*, on mixed lymphocyte culture, where, according to metabolic activity measurement test, MSCs suppressed lymphocyte activity. Second, MSCs were administered in one dose to patients with severe GVHD and for three months levels of regulatory T – lymphocytes together with helper T-lymphocytes were measured as an evidence of MSCs immunomodulation. Statistics of obtained data showed no significance, but clinical condition of patients significantly improved.

Our work showed that MSCs have supportive and immunomodulatory effect on cells in *in vitro* culture, where conditions can be controlled easily. After MSCs administration into living organism many more variables influence results of the research, and the outcomes are usually promising, but not convincing. More experiments on large groups of participants need to be done to transfer MSCs transplantation from the research field into clinical practice.