

## **Abstract**

Mesenchymal stem cells (MSC) represent a heterogeneous population of multipotent stem cells that can be isolated from various tissues of adult organism. Due to their immunomodulatory, antiapoptotic, cytoprotective and differentiation capabilities, MSC hold a great promise for treatment of many inflammatory diseases and for use in regenerative medicine.

We aimed to analyze the therapeutic effect of MSC in a model of skin transplantation. In our research, nanofiber scaffolds were used for application of MSC. Allogeneic skin grafts were transplanted from C57BL/6 mice to BALB/c mice and they were subsequently covered with nanofiber scaffolds prepared from poly-L-lactic acid (PLA) by the original needleless electrospun Nanospider technology. Some animals remained untreated, others were treated by specific therapies that combined usage of nanofiber scaffolds with cultivated MSC and nanofiber scaffolds with or without incorporated cyclosporin A (CsA). We used various methods, including FACS analysis, ELISA, PCR, immunohistochemistry and Griess reaction to determine effect of MSC on immune response.

It has been reported that MSC home preferentially to sites of inflammation within damaged tissues and can be localised also in lymphatic organs. Six days after transplantation and local MSC application we detected MSC mainly in the skin graft and also in lymph nodes and spleen. According to our results MSC suppress both local and systemic immune inflammatory reactions. We found that specific therapies reduced number of macrophages in skin allograft, nitric oxide production and also altered the profile of gene expression of the cells in grafted tissue. Depending on the therapy, we also detected changes in distribution of leukocyte populations and in interleukin 10 and interferon gamma production by lymph node cells.

Based on these results, we conclude that CsA-loaded MSC-seeded nanofibres represent a suitable delivery system which combines advantages of cell-based therapy with local administration of immunosuppressive drug. This treatment has a beneficial effect on modulation of inflammatory reaction and could subsequently inhibit rejection of the allografts.

**Keywords:** mesenchymal stem cells, skin graft transplantation, nanofiber scaffold