

Abstract

Due to their immunomodulatory and regenerative potential, mesenchymal stem cells (MSCs) represent a promising therapeutic tool for cell-based therapy, organ transplantation or tissue engineering. To improve clinical applicability of MSCs, new methods to increase their delivery and efficacy have been tested in the latest years but the mechanism of observed alterations has not yet been described.

In the present project we focused on studying the effect of several factors that can significantly affect the therapeutic success of MSC-based treatment. Initially, we analysed the therapeutic effect of MSCs applied locally on nanofiber scaffold with incorporated cyclosporine A (CsA) in a mouse model of allogeneic skin transplantation. Our results indicate that application of MSCs in the presence of CsA direct M1/M2 macrophage polarization towards regulatory phenotype. This phenotype switching is accompanied by decreased production of nitric oxide (NO) and interferon γ (IFN- γ) and increase production of interleukin 10 (IL-10), and may result in suppression of the local inflammatory reaction.

The next goal of proposed study was to analyse the effect of the treatment based on MSCs combined with immunosuppressive drugs with different mechanism of action on the balance among distinct T cell subpopulations. We demonstrated that MSCs attenuate the adverse effects of immunosuppressive drugs, and in combination with these drugs modulate cell activation and apoptosis. This combining treatment favourably influence immune balance by harnessing the T helper 1 (Th1), Th2, Th17 and cytotoxic T lymphocyte phenotype while preserving the anti-inflammatory regulatory T cell-related response.

We have also shown that systemically administered MSCs specifically migrate to the alkali-burned eye and attenuate the early inflammatory environment. From all tested types of MSCs (untreated or pretreated with IFN- γ , transforming growth factor- α or IL-1), MSCs pretreated with IFN- γ were the most potent in inhibiting the acute phase of inflammation, decreasing infiltration by myeloid and lymphoid cells, and the local production of IL-1 α , IL-6 and NO.