Abstract

Mesenchymal stem cells (MSCs) have the potential to differentiate into various cell types, possess potent immunomodulatory properties and can influence various functions of immune cells. Since the immunomodulatory properties of MSCs can be modified by cytokines, we compered the effect of unstimulated MSCs and MSCs pretreated with interleukin (IL)-1, interferon (IFN)-γ, transforming growth factor (TGF)-β and IL-10 on the development of regulatory T cells (Treg) and T helper 17 (Th17) cells *in vitro* and on the inflammatory environment in the eye.

MSCs can produce significant levels of TGF-β and IL-6. These cytokines represent the key factors that reciprocally regulate the development of naive T cells into Treg and Th17 cells. Unstimulated MSCs produce TGF-β, but not IL-6, and the production of TGF-β can be further enhanced by IL-10 or TGF-β. In the presence of IL-1, MSCs secrete significant levels of IL-6, in addition to spontaneous production of TGF-β. MSC producing TGF-β induced preferentially expression of Foxp3 and activation of Treg lymphocytes, whereas MSCs supernatants containing TGF-β together with IL-6 supported RORγt expression and development of Th17 cells. We demonstrated that MSCs and their products effectively control the development of Tregs and Th17 cells in a population of alloantigen-activated mouse spleen cells.

We also investigated the effects of systemically administered MSCs on the early acute phase of inflammation in the alkali-burned eye. The results show that intravenously injected MSCs specifically migrate to the damage eye and that IFN-γ pretreated MSCs are superior in inhibiting the acute phase of inflammation, decreasing leukocyte infiltration, and attenuating the early inflammatory environment. We also show, that nanofibers prepared from polymer PA6/12 or containing Cyclosporine A represent a conventional scaffold for growth of MSCs and for their transfer to treat ocular surface injuries.