ABSTRACT

Stem cells, in general, represent the potential for treating many diseases and disorders that are currently difficult to treat or the therapy has many side effects. One of the stem cells widely investigated these days are mesenchymal stem cells (MSCs). MSCs have the considerable immunomodulatory and regenerative potential for treating degenerative disorders and severe damage to various parts of the eye or other organs. Likewise, their application could serve as supportive therapy in corneal transplantation and other eye inflammatory conditions. In this study of immunomodulatory properties of MSCs, we have focused mainly on their ability to differentiate into cells of different tissue types (in our case, corneal epithelium and retina), their production of immunomodulatory molecules in the inflammatory environment, their ability to migrate to the site of the injury, and their local anti-inflammatory, regenerative, and anti-apoptotic effects. In addition, we tested the therapeutic effects of MSCs in a mouse model of ocular surface injury and a model of retinal degeneration. Finally, we investigated the mechanism of this effect in *in vitro* models with explants of these tissues.

Limbal stem cells (LSCs) are already used to treat severe corneal damage as limbal stem cell deficiency. However, this treatment is only suitable for a small percentage of patients in whom these stem cells need to be isolated from a healthy second eye or possibly from a donor, and immunosuppressive drugs are required. In this case, autologous MSCs, derived from the patient's bone marrow could be used. We have shown that MSCs are able to differentiate into cells expressing corneal epithelium markers in the corneal environment under the influence of insulin-like growth factor I. We further showed that MSCs, when transplanted onto chemically damaged cornea using a nanofibrous scaffold, migrate to the site of inflammation and there inhibit the expression of the pro-apoptotic genes for BCL-2-associated X protein and p53, increasing the expression of the anti-apoptotic gene B-cell lymphoma 2, and decrease the percentage of apoptotic cells in the cornea via a paracrine mechanism.

MSCs can also be used for the treatment of retinal degenerative diseases. In our work, we have shown that these cells can differentiate into cells expressing retinal-specific markers in the environment of inflammation, especially under the influence of interferon-γ. Furthermore, we have demonstrated that MSCs produce various growth and neurotrophic

factors in an inflammatory environment, and their application reduces the expression of proinflammatory molecules in the retina.