

Intravitreal injections of neurotrophic factors secreting mesenchymal stem cells are neuroprotective in rat eyes following optic nerve transection

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PURPOSE: To evaluate the neuroprotective effect of intravitreal injections of neurotrophic factors secreting mesenchymal stem cells (NTF-SCs) on the survival of retinal ganglion cells (RGCs) in rat eyes after optic nerve transection (ONT) .

METHODS: Rat and human bone marrow-derived mesenchymal stem cells (MSCs) were induced to secrete high levels of NTF. The neuroprotective effect from intravitreally injected untreated MSCs or NTF-SCs was compared with that from PBS injections using an ONT model in 146 rats. RGCs were labeled by applying rhodamine dextran to the orbital optic nerve or by injecting Fluorogold into the superior colliculus. Cell- and saline-treated eyes were compared 8 days after ONT. For tracking, MSCs and NTF-SCs were labeled with PKH26 and analyzed at 2 hours and at 10, 17, and 24 days using immunohistochemistry and RT-PCR.

RESULTS: Mean RGC survival at 8 days after transection increased significantly after intravitreal injections of human NTF-SCs (69% \pm 3%) or of untreated human MSCs (66% \pm 5%) versus PBS (46% \pm 3%; $P = 0.0005$ and $P = 0.03$, respectively) . In an additional set of experiments, human NTF-SCs versus PBS were significantly neuroprotective, but bone marrow-derived rat NTF-SCs were not ($P = 0.001$ and $P = 0.1$, respectively) . Immunohistochemistry demonstrated that human-derived MSCs, human NTF-SCs, and rat-derived NTF-SCs survived at least 24 days after intravitreal injection.

CONCLUSIONS: Bone marrow-derived MSCs can deliver NTFs by intravitreal injection and can be neuroprotective after ONT. This approach might be further studied to deliver NTFs by autotransplantation in glaucomatous eyes.

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