Cellular therapy for open angle glaucoma: tissue regeneration by mesenchymal stem cells

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But / *Goal*: Elevated intraocular pressure (IOP) in open angle glaucoma is often related to a dysfunction of the trabecular meshwork (TM) of the anterior chamber angle. A large number of studies involving multipotent meshenchymal stem cells (MSC) have demonstrated their ability to nduce regeneration of damaged tissues and organs. Our goal is to evaluate the ability of MSCs toinduce regeneration of the trabecular meshwork and to assess their ability to lower IOP in open angle glaucoma.

Methode / *Methodology*: MSC obtained from B6 mouse bone marrow were co-cultured with rat TM cells to study their differentiation potential. MSC (1X106 cells) were also injected into the anterior chamber of rat eyes harbouring experimental glaucoma caused by laser photocoagulation to the TM. Control rats received a similar injection of mouse T lymphocytes (1X106 cells) or no injection at all. The homing and repair potential of these cells and their ability to restore baseline IOP was assessed using immunohistochemistry and tonometry over 6 weeks.

Résultats / *Results*: After 7 days *in vitro*, MSC were not found to upregulate TM cell markers, such as Aquaporin-1, Pax-6, Laminin and Fibronectin, to a level similar to that of TM cells. *In vivo*, MSC were found scattered throughout the anterior chamber angle, but migrated in significantly higher numbers towards the area of laser damage (N=15). The MSCs remained in the eye for 4 days as detected by immunofluorescence. Interestingly, the IOP of rats who received an MSC graft (1X106 cells) in the anterior chamber began to decrease significantly on day 4 when compared to the control rats ($p<0.01$) in a blinded study. This drop in IOP continued until ocular pressure was restored to baseline at the end of the first week in the MSC treated group ($p<0.001$). Baseline IOP was attained only at day 30 in the control groups. Additionally, the anterior chamber histology was restored to normal after 1 month in the MSC treated group, while demonstrating clear signs of scarring in the control groups at the same time period.

Conclusion.s: The impressive regenerative effects of MSC, along with their apparent lack of differentiation and their rapid clearance out of the anterior chamber implies a mechanism of action that is probably linked to secreted factors. This could represent a novel approach in the management and treatment of open angle glaucoma.

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