Intraocular pressure reduction and neuroprotection conferred by bone marrow-derived mesenchymal stem cells in an animal model of glaucoma

Roubeix C (1,2,3) , Godefroy D (4,5,6) , Mias C (7) , Sapienza A (8,9,10) , Riancho L (11,12,13) , Degardin J (14,15,16) , Fradot V (17,18,19) , Ivkovic I (20,21,22) , Picaud S (23,24,25) , Sennlaub F (26,27,28) , Denoyer A (29,30,31,32) , Rostene W (33,34,35) , Sahel JA (36,37,38,39) , Parsadaniantz SM (40,41,42) , Brignole-Baudouin F (43,44,45,46,47,48) , Baudouin C (49,50,51,52,53,54)

1 INSERM, U968, Paris, F-75012, France. chris.roubeix@gmail.com. 2 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. chris.roubeix@gmail.com. 3 CNRS, UMR_7210, Paris, F-75012, France. chris.roubeix@gmail.com. 4 INSERM, U968, Paris, F-75012, France. david.godefroy@inserm.fr. 5 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. david.godefroy@inserm.fr. 6 CNRS, UMR_7210, Paris, F-75012, France. david.godefroy@inserm.fr. 7 Institut des Maladies Métaboliques et Cardiovasculaires, INSERM UMR 1048, 31432 Toulouse cedex 4, France, Toulouse, France. celine.mias@inserm.fr. 8 INSERM, U968, Paris, F-75012, France. anais.sapienza@inserm.fr. 9 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. anais.sapienza@inserm.fr. 10 CNRS, UMR_7210, Paris, F-75012, France. anais.sapienza@inserm.fr. 11 INSERM, U968, Paris, F-75012, France. luisa.riancho@inserm.fr. 12 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. luisa.riancho@inserm.fr. 13 CNRS, UMR_7210, Paris, F-75012, France. luisa.riancho@inserm.fr. 14 INSERM, U968, Paris, F-75012, France. julie.degardin@inserm.fr. 15 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. julie.degardin@inserm.fr. 16 CNRS, UMR_7210, Paris, F-75012, France. julie.degardin@inserm.fr. 17 INSERM, U968, Paris, F-75012, France. valerie.fradot@inserm.fr. 18 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. valerie.fradot@inserm.fr. 19 CNRS, UMR_7210, Paris, F-75012, France. valerie.fradot@inserm.fr. 20 INSERM, U968, Paris, F-75012, France. ivana.ivkovic@inserm.fr. 21 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. ivana.ivkovic@inserm.fr. 22 CNRS, UMR_7210, Paris, F-75012, France. ivana.ivkovic@inserm.fr. 23 INSERM, U968, Paris, F-75012, France. serge.picaud@inserm.fr. 24 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. serge.picaud@inserm.fr. 25 CNRS, UMR_7210, Paris, F-75012, France. serge.picaud@inserm.fr. 26 INSERM, U968, Paris, F-75012, France. florian.sennlaub@inserm.fr. 27 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. florian.sennlaub@inserm.fr. 28 CNRS, UMR_7210, Paris, F-75012, France. florian.sennlaub@inserm.fr. 29 INSERM, U968, Paris, F-75012, France. alexandre.denoyer@gmail.com. 30 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. alexandre.denoyer@gmail.com. 31 CNRS, UMR_7210, Paris, F-75012, France. alexandre.denoyer@gmail.com. 32 Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, INSERM-DHOS CIC 503, Paris, F-75012, France. alexandre.denoyer@gmail.com. 33 INSERM, U968, Paris, F-75012, France. william.rostene@inserm.fr. 34 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. william.rostene@inserm.fr. 35 CNRS, UMR_7210, Paris, F-75012, France. william.rostene@inserm.fr. 36 INSERM, U968, Paris, F-75012, France. jose.sahel@institut-vision.org. 37 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. jose.sahel@institut-vision.org. 38 CNRS, UMR_7210, Paris, F-75012, France. jose.sahel@institut-vision.org. 39 Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, INSERM-DHOS CIC 503, Paris, F-75012, France. jose.sahel@institut-vision.org. 40 INSERM, U968, Paris, F-75012, France.

stephane.melik-parsadaniantz@inserm.fr. 41 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. stephane.melik-parsadaniantz@inserm.fr. 42 CNRS, UMR_7210, Paris, F-75012, France. stephane.melik-parsadaniantz@inserm.fr. 43 INSERM, U968, Paris, F-75012, France. frbaudouin@aol.com. 44 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. frbaudouin@aol.com. 45 CNRS, UMR_7210, Paris, F-75012, France. frbaudouin@aol.com. 46 Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, INSERM-DHOS CIC 503, Paris, F-75012, France. frbaudouin@aol.com. 47 University Paris Descartes, Sorbonne Paris Cité, Paris, F-75006, France. frbaudouin@aol.com. 48 Faculté de Pharmacie de Paris, University Paris Descartes, Sorbonne Paris Cité, Paris, F-75006, France. frbaudouin@aol.com. 49 INSERM, U968, Paris, F-75012, France. cbaudouin@quinze-vingts.fr. 50 UPMC Université Paris 06, UMR_S 968, Institut de la Vision, Paris, F-75012, France. cbaudouin@quinze-vingts.fr. 51 CNRS, UMR_7210, Paris, F-75012, France. cbaudouin@quinze-vingts.fr. 52 Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, INSERM-DHOS CIC 503, Paris, F-75012, France. cbaudouin@quinze-vingts.fr. 53 Department of Ophthalmology, Hôpital Ambroise Pare, AP HP, Boulogne, F-92100, France. cbaudouin@quinze-vingts.fr. 54 University Versailles St Quentin en Yvelines, Montigny-Le-Bretonneux, F-78180, France. cbaudouin@quinze-vingts.fr.

METHODS: Ocular hypertension model was performed by cauterization of 3 episcleral veins (EVC) of Long-Evans male rat eyes. MSCs were isolated from rat bone marrow, amplified in vitro and tagged with quantum dot nanocrystals. Animals were distributed as 1) MSCs group receiving 5.10(5) cells/6μl Minimum Essential Medium and 2) MEM group receiving 6μl MEM (n = 10 each) . Injections were performed into the anterior chamber of 20 days-hypertensive eyes and IOP was monitored twice a week for 4 weeks. At the end of experiment, cell distribution in the anterior segment was examined in confocal microscopy on flat mounted corneas. Moreover, we tested in vitro effects of MSCs conditioned medium (MSC-CM) on primary human trabecular meshwork cells (hTM cells) using Akt activation, myosin phosphorylation and TGF-β2-dependent profibrotic phenotype in hTM cells.

RESULTS: We demonstrated a rapid and long-lasting in vivo effect of MSCs transplantation that significantly reduced IOP in hypertensive eyes induced by EVC. MSCs were located to the ciliary processes and the TM. Enumeration of RGCs on whole flat-mounted retina highlighted a protective effect of MSCs on RGCs death. In vitro, MSC-CM promotes: (i) hTM cells survival by activating the antiapoptotic pathway, Akt, (ii) hTM cells relaxation as analyzed by the decrease in myosin phosphorylation and (iii) inhibition of TGF-β2-dependent profibrotic phenotype acquisition in hTM cells.

CONCLUSIONS: MSCs injection in the ocular anterior chamber in a rat model of OHT provides neuroprotective effect in the glaucoma pathophysiology via TM protection. These results demonstrate that MSCs constitute promising tool for treating ocular hypertension and retinal cell degeneration.

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