Engineering the retinal microenvironment to improve donor neuron integration post-transplantation

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Neuron transplantation is an exciting solution for replacing retinal ganglion cells (RGCs) lost in glaucoma and other optic neuropathies. However, one significant barrier to successful donor RGC integration is their migration into the ganglion cell layer (GCL). To address this, we developed an approach to control donor neurons in vivo by engineering their microenvironment post-transplantation.

Using an in silico analysis of the developing human retina and a functional in vitro assay, we evaluated receptor-ligand candidates for their potential to control RGC migration. Among these, SDF1 emerged as our lead molecule. By establishing an SDF1 gradient in vivo, we increased donor RGC integration into the GCL nearly threefold. While this strategy has not yet restored vision, only donor RGCs that migrated into the GCL extended neurites toward the optic nerve head and expressed mature RGC markers.

This work establishes a framework for controlling donor cell function through tissue microenvironment engineering, laying the foundation for future advancements in stem cell-based therapies for vision restoration.

ABOUT the SPEAKER

Jonathan Soucy is a postdoctoral research fellow in the Ophthalmology Department at Harvard Medical School and the Schepens Eye Research Institute of Mass. Eye and Ear. He earned his PhD in Chemical Engineering from Northeastern University under the mentorship of Dr. Ryan Koppes, where he developed organ-chip models of the cardiac nervous system. Before that, Jon completed his undergraduate studies in Chemical Engineering at Rensselaer Polytechnic Institute. Jon's postdoctoral research in Dr. Petr Baranov's lab focuses on improving retinal neuron survival and integration post-transplantation. Leveraging his training in neural tissue engineering and vision science, Jon aims to uncover mechanisms of retinal neuron plasticity and develop new stem cell-based therapies for restoring vision lost to glaucoma and other optic neuropathies. Jon holds multiple patents, has received several national fellowships and awards, and was recently recognized as a 2024 Rising Star in Engineering and Health.

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