206 Optic nerve regeneration: Barriers past and future - Minisymposium
Monday, May 08, 2017 8:30 AM–10:15 AM
Ballroom 4 Minisymposium
Program #/Board # Range: 1191–1194
Organizing Section: Glaucoma
Contributing Section(s): Anatomy and Pathology/Oncology, Biochemistry/Molecular Biology, Eye Movements/Strabismus/ Amblyopia/Neuro-Ophthalmology, Retina, Retinal Cell Biology, Visual Neuroscience

Program Number: 1191
Presentation Time: 8:40 AM–9:00 AM
Zebrafish as a model system for uncovering mechanisms underlying optic nerve and retina regeneration
Daniel Goldman. Molecular & Behavioral Neuroscience Inst, University of Michigan, Ann Arbor, MI.
Presentation Description: Unlike mammals, zebrafish can regenerate a damaged optic nerve and retina. Because of their robust regenerative powers, zebrafish provide an ideal system for uncovering mechanisms underlying these processes. In this presentation, I will discuss how zebrafish have been used to study optic nerve and retina regeneration and how these studies can inform us of strategies that may stimulate optic nerve and retina regeneration in mammals.
Commercial Relationships: Daniel Goldman, None
Support: NIH, NEI R01 EY018132

Program Number: 1192
Presentation Time: 9:00 AM–9:20 AM
Amacrine cells regulate the survival and regenerative potential of retinal ganglion cells
Larry Benowitz[2, 1]. [1]Neurosurgery and Ophthalmology, Harvard Medical School, Boston, MA; [2]Neurosurgery; Neurobiology, Boston Children's Hospital, Boston, MA.
Presentation Description: Retinal ganglion cells (RGCs) normally cannot regenerate their axons once the optic nerve has been injured and soon begin to die, precluding visual recovery after traumatic or ischemic injury to the optic nerve or in neurodegenerative disorders such as glaucoma. Although prior work has identified numerous pathological changes that occur in RGCs after nerve injury, the mechanisms that initiate these changes are unknown. In addition, neuroprotective treatments generally result in only transient RGC protection, or enable RGCs to survive in a compromised state and/ or unable to regenerate axons. Further, whereas studies from our lab and others have identified strategies to stimulate some injured RGCs to regenerate injured axons from the eye to the brain, the number of RGCs that do so successfully is small. These observations point to the existence of other major unknown suppressors of cell survival and axon growth. We report here that the dysregulation of mobile zinc (Zn2+) in the retina is one previously unknown key factor. Within an hour after the optic nerve is injured, Zn2+ increases dramatically in synaptic contacts between amacrine cells and RGC dendrites of the inner plexiform layer (IPL) of the retina. Zn2+ elevation is triggered by a rise in nitric oxide, whereas the loading of Zn2+ into synaptic vesicles requires the transporter protein ZnT3. After a delay of 2-3 days, Zn2+ is released across the synapse and taken up by RGCs. Chelating Zn2+ leads to the persistent survival of many RGCs and extensive axon regeneration, and amplifies the effects of certain other pro-regenerative treatments. Importantly, chelation is effective even if delayed for a few days after nerve injury. Thus, Zn2+ chelation may represent a promising therapy to protect RGCs after optic nerve damage.
Commercial Relationships: Larry Benowitz, None
Support: NEI R01EY024481, Dept. of Defense/CDMRP W81XWH-14-10-0488; W81XWH-14-10-0488; Adelson Medical Research Foundation

Program Number: 1193
Presentation Time: 9:20 AM–9:40 AM
Electrical activity and compartmented signaling of survival and axon growth
Jeffrey L. Goldberg. Ophthalmology, Stanford University, Palo Alto, CA.
Presentation Description: Retinal ganglion cells degenerate in optic neuropathies including glaucoma; discovering the signaling pathways responsible for survival and axon growth may lead to new approaches to prevent degeneration or promote regeneration. Here we discuss advances in our understanding of how electrical activity signals RGCs to enhance responsiveness to neurotrophic factor signaling, and how these may be manipulated to promote neuroprotection in retinal ganglion cells in vivo.
Commercial Relationships: Jeffrey L. Goldberg, None
Support: NIH EY026766

Program Number: 1194
Presentation Time: 9:40 AM–10:00 AM
Challenges from axon regeneration to functional recovery
Zhigang He. Neurology, Boston Children's Hospital, Boston, MA.
Presentation Description: After optic nerve injury in the adult mammals, majority of injured retinal ganglion cells (RGCs) will die and no spontaneous regeneration will occur. Our previous studies identified a number of signaling pathways that are critical in regulating the intrinsic regenerative ability of RGCs. We also attempted to test whether the induced regenerating axons are able to form functional synapses and mediate functional recovery. We found that in both juvenile and adult mice, either PTEN and SOCS3 co-deletion, or co-overexpression of osteopontin (OPN)/ insulin-like growth factor 1 (IGF1)/ciliary neurotrophic factor (CNTF), induces regrowth of retinal axons and formation of functional synapses in the superior colliculus (SC), but not significant recovery of visual function. Further analyses suggest that regenerated axons fail to conduct action potentials from the eye to the SC due to lack of myelination. Consistent with this idea, administration of voltage-gated potassium channel blockers restores conduction and results in increased visual acuity. Thus, while our results reveal the myelination as an additional barrier for functional recovery, we also demonstrated that enhancing both regeneration and conduction effectively improves function after optic nerve injury.
Commercial Relationships: Zhigang He, None
Support: NIH EY026939

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