The RPB / TGF Career Advancement Award

Matthew J. Van Hook, PhD –Assistant Professor, University of Nebraska

Specialty: Neuroscience of the retina and visual system

Research Interests: Retinal synapses and function in neurodegenerative disease.

Dr. Van Hook's lab explores synaptic transmission between neurons in the retina in health and during degenerative diseases.

They use a combination of patch-clamp electrophysiology, anatomical and histochemical techniques, calcium imaging, and two-photon microscopy to characterize unexplored retinal synapses with an eye toward the ways that synaptic function gives rise to the unique processing capabilities of retinal circuits.

They also make use of mouse genetic tools and models of retinal neurodegenerative diseases, such as glaucoma, to determine how retinal function is altered at the earliest stages of disease, before substantial loss of neurons.

Their research is intended to provide a basic understanding of how the retina encodes visual information as well as insight into disease mechanisms in order to inform novel diagnostic and therapeutic strategies for detecting and treating retinal disease.

Project:

The objective of the proposed research is to test the hypothesis that microglia, the immune cells of the central nervous system, are responsible for degeneration of retinal ganglion cell (RGC) outputs to the brain in glaucoma. Published work and preliminary data from the candidate's lab has probed the timing and mechanisms of synaptic dysfunction and degeneration in the dorsal lateral geniculate nucleus (dLGN).

This work is significant in its application of quantitative structural and functional circuit and single-neuron neuroscience tools to probe mechanisms of synapse loss in glaucoma. Moreover, much emphasis has historically been placed on degeneration of RGC cell bodies in the retina and effects of eye pressure on the axons in the optic nerve with less known about the timing and mechanisms of how glaucoma and eye pressure affect RGC outputs to the brain. Understanding this is critically important in establishing the link between eye pressure and vision loss in glaucoma. Thus, this work will (1) reveal the mechanisms of how eye pressure affects RGC outputs to visual centers in the brain; (2) shed light on the role(s) played by microglia in glaucoma, which are important regulators of central nervous system function; and (3) identify potential signaling pathways that might serve as targets for future vision-saving therapeutics. Additionally, this proposal involves development of several new mouse lines in order to identify and manipulate microglia in glaucoma and the candidate anticipates these will be useful resources for the field and his own future studies.

Innovation:

Complement deposition and synaptic loss is known for neurological diseases but has not been extensively studied in glaucoma. This is quite a novel application.

Comments from the RPB Scientific Advisory Panel:

This is a very good application from an excellent scientist with good training and excellent productivity at this stage of his career. He appears to be on a good trajectory. The proposal is interesting, with a feasible approach. The candidate has a solid experimental plan with good pilot data and appropriate tools and expertise to conduct the studies. The environment is very good and there is good support from the department.