Metabolic and Structural Retinal Vulnerabilities Following Traumatic Brain Injury

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Project Description:

Traumatic brain injury (TBI) frequently leads to lasting visual and circadian disturbances, implicating secondary neurodegeneration within retinal ganglion cells (RGCs) and their central projections. The retina offers a unique, accessible model to investigate neurodegenerative processes after TBI, as it mirrors central nervous system (CNS) pathology while allowing for precise visualization and molecular interrogation of axonal and synaptic alterations.

Emerging evidence indicates that TBI disrupts mitochondrial metabolism, autophagy, and inflammatory signaling within retinal neurons—pathways central to both degeneration and repair. Metabolic dysregulation and impaired cellular clearance may contribute to progressive RGC loss, glial activation, and synaptic remodeling long after the initial injury. This project investigates how distinct TBI mechanisms—controlled cortical impact (CCI) and jet-flow overpressure (JFO)—differentially affect retinal structure, function, and metabolic gene expression.

Using histological, molecular, and electrophysiological assays, this study aims to define the extent and regional specificity of RGC and glial changes across dorsal–ventral retinal zones following injury. Additional experiments will evaluate the therapeutic efficacy of metabolic and autophagy-enhancing compounds in mitigating post-TBI retinal degeneration. This work seeks to elucidate shared molecular pathways linking CNS trauma, metabolic compromise, and impaired regeneration—thereby identifying potential targets for neuroprotective intervention.

Student Training and Mentoring Plan:

Students will participate in all phases of the project, including: TBI Model and Drug Administration: Assisting in controlled cortical impact or jet-flow overpressure procedures, post-surgical monitoring, and intraperitoneal/intravitreal drug delivery. Tissue Collection and Histology: Performing perfusion, retinal flat-mount preparation, immunohistochemistry, and fluorescence imaging to quantify RGC subtypes and glial activation. Molecular and Functional Analysis: Conducting Western blot, qPCR, or spatial gene expression studies; assisting in visual electrophysiology (PERG/VEP) recordings; and contributing to data curation and analysis. . All training will occur in RGE 400 at NEOMED,

under the direct supervision of Dr. Smith and advanced graduate researchers. Advanced CITI and in-lab training will required for individuals wanting to be involved in animals based experiments. However, a student can still contribute greatly to advance project without engaging in animal experiments.

Scholarly Development: Students will attend weekly Smith Lab meetings, receive one-on-one mentoring with the PI, and be encouraged to present progress during BTB student seminars.