Multidisciplinary Research Program in Medicine Project*: Characterization of the Neurodegenerative Features in the Retina Associated with Eye and Brain Diseases*

Hypothesis or Research Question(s): During development, the retina and brain derive from the same embryological tissues and display molecular and cellular similarities. Our hypothesis is: In vivo imaging of cellular and subcellular changes in the retina can be used as diagnostic features for tracking the development and progression of age-related neurodegenerative diseases of the eye (e.g., AMD) and brain (e.g., Alzheimer's disease).

PROJECT BACKGROUND & SUMMARY

Rationale and Context:

The objective of our project is to develop a high-reward technology to assess degenerative diseases of the brain and eye. Our research approach will be undertaken by an interdisciplinary group of bioengineers, vision- and neuro-scientists to develop novel, advanced biomedical retinal imaging for in vivo assessment of cellular changes associated with brain and eye disease first in mouse models and later for clinical translation.

Background:

During development, the retina and brain derive from the same embryological tissues and display molecular, cellular and anatomical similarities. As the retina is readily imaged via the pupillary axis, while the bony skull prohibits non-invasive imaging of the brain, we will use the retina to assess neurodegenerative changes associated with brain disease. By imaging the retina we will address questions such as: What are the very first molecular and cellular events that trigger brain cells to degenerate and lose synaptic activity?

In vivo imaging of the retina is in a "golden-era" with many devices being developed that can potentially capture cellular and synaptic activity and sub-cellular structure and function in real time and in three dimensions. Proof-of-principle imaging methods have been obtained by our group by identifying key retinal features associated with age-related macular degeneration (AMD) a neurodegenerative eye disease. Our long-term goal is to develop high resolution retinal imaging methods to further understand eye disease and to use the retina as a surrogate tissue bed, to track pathological changes in the brain that underlie neurodegenerative diseases, such as Alzheimer's (AD).

Proposed Multidisciplinary Research Approach: This study combines the talents of neurosciences with bioengineering. Bioengineers will develop novel, high resolution in vivo imaging methods to acquire unique "retinal signatures" specific for brain (AD) and eye (AMD) disease. Neuroscientists will determine the biological correlates of the "retinal signatures" using established mouse models of AD and AMD. This multidisciplinary approach is essential to our goal to develop a transformative method of non-invasive retinal imaging to diagnose, follow and treat human neurodegenerative diseases of the brain and eye. Expected Outcomes: The expected outcomes of the proposed study include 1) hardware and software development to support bioengineering methods of adaptive optics and polarization diversity/contrast as it relates to ophthalmic imaging in mouse models; 2) the in vivo characterization of the image-based "retinal signature" associated with AD and AMD and 3) the ex vivo characterization of the cellular and molecular features that are the biological correlates of the "retinal signature."

BENEFIT TO THE STUDENTS

GAIN UNDERSTANDING OF CONDUCTING HIGH QUALITY RESEARCH

TS will learn how to conduct a high quality research project by several remote and hands-on methods.

TS will read selected, relevant scientific papers and discuss/critique experimental design with both supervisors.

TS will learn the ethical considerations of using animals in research and safety methods for using biohazard by taking online UBC courses.

TS will learn basic statistics to identify the value of a power calculation to estimate sample size in animal studies, and how to develop a testable hypothesis, and appropriate statistical tests for studies.

TS will learn to problem solve and trouble-shoot experimental methods and data collection as the situation requires.

TS will submit weekly progress reports to both supervisors to summarize the development towards the outcome and propose ideas for troubleshooting as required.

DEVELOP NEW SKILLS:

In this multidisciplinary project TS will develop skills in cellular/molecular methods as well as in bioengineering, optics and in vivo retinal imaging. Cellular/molecular skills will include confocal microscopy, advanced image analysis, protein assays (immunohistochemistry, ELISA and western blots). Bioengineering/optics skills will include understanding the basics of optics of the eye, adaptive optics technology, optical coherence tomography, principles of confocal microscopy and super-resolution microscopy.

INTERACTIONS WITH OTHER RESEARCHERS

TS will collaborate and work with both supervisors and their respective lab members, which will include postdoctoral fellows, graduate students, medical students, undergraduate students, research associates and technical staff. TS will attend weekly lab meetings to discuss and network with other lab members, participate in journal club presentations.

TS will give progress reports on their data every two weeks.

AVAILABLE RESOURCES

TS will work in an established basic science laboratory fully equipped for proposed studies using protein assays, tissue culture, bright and dark-field microscopes, paraffin and cryostat microtomes.

TS will work in the in vivo imaging lab situated in the Jack Bell animal facility, equipped with both commercial ophthalmic imaging and custom-designed imaging devices for rodents.

Departmental group equipment will be available to TS including Zeiss 800 confocal microscope and 880 super-resolution microscope are available on a sign-up basis.

WORKLOAD AND SPECIFIC TASKS The workload and specific tasks will largely depend on the background skills of each student in consultation with students and supervisors. Ideally, one student will be assigned to the cellular/molecular ex-vivo analysis of brain and eye tissues, while the other student will be assigned to the in vivo imaging of the retina. There will be opportunity for each student to develop new skills in bioengineering and neurosciences.