BCHM 421/422 – 2023/2024

Project Title: Neuroinflammation of spinal cord injury

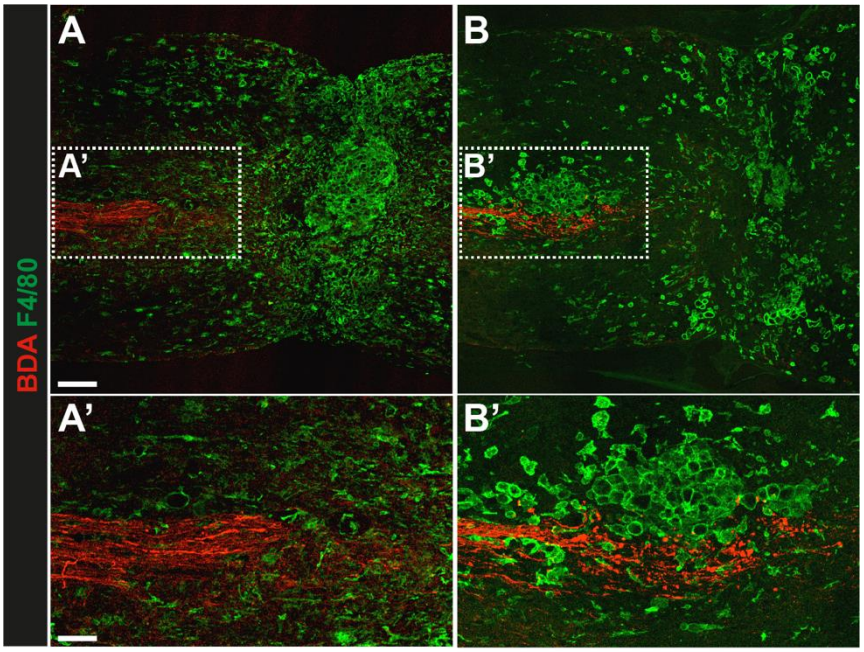
Supervisor: Dr. Faith Brennan https://dbms.queensu.ca/faculty/faith-brennan

Keywords:

1. **Macrophage**
2. **Axon loss**
3. **Neuropathology**

Project Outline:

Neurological disorders represent a major public health burden in Canada. Understanding the cellular and molecular drivers of neuropathology and poor outcomes will accelerate the development of novel therapeutics. Injury or disease to the brain or spinal cord triggers a robust neuro-inflammatory response. This immune response is dominated by macrophages, making them candidate cells to target for repair. However, macrophages have the potential to promote tissue repair and axon regeneration, or to spread tissue damage into neighboring intact neural tissue. This research program seeks to understand the molecular mechanisms that govern macrophage functional diversity and co-opt these mechanisms to reduce neuropathology and improve functional outcomes. The student will use molecular and cellular approaches to investigate how deficiency or overexpression of inflammation-related genes specifically within macrophages alters macrophage phenotype and shapes intraspinal neuro-inflammatory pathology and functional recovery.



Investigating macrophage interactions with degenerating axons. A, A': In an injured spinal cord (28 d post-injury), macrophages (F4/80$^+$ cells, green) cluster to the edge of degenerating corticospinal tract axons, labelled using an anterograde tracer (BDA, red). **B, B'**: In a mouse with altered macrophage phenotype, macrophages actively attack degenerating CST axons, causing axon 'blebbing'. This project aims to manipulate key macrophage genes to boost spinal cord axon repair/regeneration.

Project Goals:

1. Assess expression of macrophage inflammatory markers and lesion pathology in the injured spinal cord using histopathology and immunochemistry
2. Assess changes in intraspinal and circulating immune mediators using molecular assays
3. Perform motor testing of hindlimb function in groups with and without macrophage gene manipulation

Experimental Approaches:

- Tissue processing & histopathology techniques
- Immunochemistry and immunofluorescence staining
- Microscopy and high magnification image analysis
- Biochemical assays (e.g. ELISA, flow cytometry)
- In vivo behavioral testing
- Possible – basic surgical techniques

References:

Brennan, F.H., Li, Y., Wang, C., Ma, A., Guo, Q., Li, Y., Pukos, N., Campbell, W.A., Witcher, K.G., Guan, Z., Kigerl, K.A., Hall, J.C.E, Godbout, J.P., Fischer, A.J., McTigue, D.M., He, Z., Ma, Q. and Popovich, P.G. 2022. Microglia coordinate cellular interactions during spinal cord repair in mice. ***Nature Communications***, 13, 4096

Please visit www.brennanresearchlab.com for a full list of publications and related literature