

MSc DEFENCE Wednesday, September 19th, 2018

Student: Cameron Oram

Title: GRANZYME B: ROLE IN SPINAL CORD INJURY AND IMPEDED REPAIR

Time and location: 10:00 am PST; Blusson Spinal Cord Center (iCORD), First Floor Lecture Hall, 818 West 10th Avenue, Vancouver, BC

Supervisor: Dr. David Granville

ABSTRACT

The inflammatory cascade following spinal cord injury (SCI) involves multiple cellular and molecular responses that can both aid and impede recovery. A large component of the wound response is the infiltration of immune cells that secrete pro-inflammatory cytokines and proteases. Granzyme B (GzmB) is a serine protease released by immune cells that negatively affects wound healing through its intracellular and extracellular protease activity. GzmB is abundant in neuroinflammatory conditions and contributes to neuron and oligodendrocyte cell death. In this study we investigate the role of GzmB in tissue injury, inflammation, repair, and functional recovery following SCI. Thoracic SCI was induced in wild-type (WT) and GzmB knockout (GzmB-KO) mice. Mice were observed over the course of 6 weeks using three locomotive recovery tests (Basso mouse scale, rotarod and horizontal ladder). Lesions were harvested for histological analysis and sections stained with markers for neurons and myelin. A second cohort of mice were maintained for 1 week after SCI and probed for GzmB expression and cellular localization. GzmB-KO mice exhibited significantly improved motor scores, increased myelin and neural survival compared to WT controls. GzmB expression co-localized to macrophages at 7 days post injury. In summary, GzmB is elevated and contributes to neurotoxicity, myelin loss and impaired functional recovery following SCI.