Supervisor Name: Dr Michael Fehlings

Hospital/Research Institution: Krembil Research Institute at UHN

Email: Michael.fehlings@uhn.ca

Field of Research (2 keywords): Spinal cord injury / Stem cells

Department: Genetics and Development / Neurosurgery

School of Graduate Studies Appointment (IMS, LMP, IHPME etc)? Yes:

If YES, please name: IMS

Project Title: The establishment of a novel treatment for cervical spinal cord injury using directly reprogrammed human neural precursor stem cells.

Brief Project Description (<300 words):

I have previously shown that directly reprogrammed Neural Precursor Cells (drNPCs) are a promising stem cell source for treatment of thoracic SCI (manuscript under review). I now propose to determine the ability of drNPCs to facilitate regeneration of the injured cervical spinal cord. Over half of all traumatic SCI occurs at the cervical level (C1 to C7-T1) and patients with cervical injuries suffer the most devastating neurological impairment. A central rationale for employing a cervical model of SCI is that significant differences in the anatomy of cervical versus thoracic regions of the spinal cord result in different pathophysiological responses to injury. drNPCs will be transplanted into a cervical SCI (cSCI) rat model and their integration, differentiation and survival will be tested. We will conduct our studies in a level 6 cSCI model developed in the Fehlings lab. At 2 weeks following injury, drNPC stem cells will be injected
under isoflurane inhalation anesthesia at 4 locations rostral and caudal to the injury epicenter. Rats will receive cell transplantation 2 weeks (subacute) following cSCI, which is a relevant time window for clinical interventions. During the 10-week post-injury period, rats from each experimental group will undergo weekly neurobehavioral testing to assess forelimb strength, digital dexterity, trunk stability and hind limb function. The aim of this application is to generate Proof of Concept (POC) data that will meet the IND requirements of the Federal Drug Administration (FDA) and Health Canada to proceed to Phase I/II clinical trials for the use of directly reprogrammed NSCs (drNSCs), to treat SCI. Determining the regenerative potential of drNPCs in a cervical model of SCI is a critical step that both the Federal Drug Administration and Health Canada have indicated is required for the transfer of drNPC technology to a Phase I/II clinical trial.