McGill University - Imperial College London Student Exchange

Training opportunity within the Stifani Laboratory at the Montreal Neurological Institute at McGill University

Background

Motor neuron (MN) diseases are pathological conditions of severe morbidity and mortality. For instance, amyotrophic lateral sclerosis (ALS) results in severe paralysis and death, with no successful pharmacological treatment currently available. Recent progress in stem cell biology and regenerative medicine is highlighting the therapeutic potential of undifferentiated neural stem or progenitor cells to replace MN cells lost during disease. However, the successful application of stem cell-based cell replacement therapies requires a detailed characterization of the molecular mechanisms controlling the normal genesis, correct localization and target connectivity of the MNs that are lost in MN diseases.

Opportunity

Cell intrinsic mechanisms of transcriptional regulation play fundamental roles in neural cell development. In that regard, recent work has shown that transcriptional corepressors of the Groucho (Gro)/TLE family are expressed in MN progenitor cells in the developing spinal cord where they participate in the generation of the correct number and types of spinal MNs. Gro/TLE proteins are also expressed in post-mitotic MNs in the spinal cord, where they are hypothesized to form transcription complexes with one of their DNA-binding partners, the transcription factor Runx1. The Stifani lab has shown that Runx1 is important for the development of subtypes of postmitotic MNs that innervate specific forelimb muscles [lateral motor column (LMC) MNs] or that are critical for mastication and swallowing (hypoglossal MNs). Notably, those are among the MNs most susceptible to degeneration in ALS, which led us to hypothesize that Gro/TLE and Runx1 act as regulators of the development and/or target muscle connectivity of MNs affected in ALS. The visiting student will perform studies aimed at testing hypothesis. More specifically, s/he will conduct experiments that will determine precisely the pattern of axonal innervation of the MNs expressing Gro/TLE and Runx1.

These studies will provide new information on the mechanisms controlling the generation and target connectivity of different MN subtypes in the hindbrain and spinal cord and will help advance our understanding of cell replacement therapy for MN disease.

Contact:
Dr. Stefano Stifani
Montreal Neurological Institute
Email: stefano.stifani@mcgill.ca