"Transplanting human-derived induced-pluripotent stem cells into rodent hippocampi to generate an animal model of bipolar disorder"

Treatment options for patients with bipolar disorder are limited, and one key obstacle that has slowed the development of new therapies is the lack of animal models that accurately recapitulate key features of this neuropsychiatric condition. One possible solution for this issue is to explore new technologies for disease modelling, such as induced-pluripotent stem cells (iPSCs), which are embryonic-like stem cells generated from human somatic cell samples. The Lalonde lab has previously used these cells to create neural progenitor cells, the precursor to neurons, from bipolar patients to investigate how calcium signaling and neurodevelopment is altered in this disorder. Indeed, neural progenitor cells derived from bipolar patients showed reduced calcium signaling, premature neural differentiation, and abnormal neurogenesis. Neurogenesis, which is creation of new neurons, occurs in the adult brain in two locations: the subventricular zone and the dentate gyrus of the hippocampus. Adult hippocampal neurogenesis is proposed to play a role in mood regulation, and when disrupted, could result in psychopathology. I hypothesize that bipolar disorder etiology includes the abnormal activity of neural progenitor cells within the hippocampus, which results in the manifestation of affective, behavioural, and cognitive deficits frequently associated with the disease. I will use this proposed pathological mechanism to accomplish the goal of my project, which is to create an animal model of bipolar disorder that encapsulates essential features of the disorder that are not represented in the current animal models. To achieve this, I will implant human iPSCs into the hippocampus of immunodeficient mice.