2018 Talent Development Competition Awardees

Title: Impact of miR137 point mutation on neural development of the cerebral cortex and hippocampus in a novel transgenic preclinical model for schizophrenia

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Abstract: Schizophrenia (SCZ) is a neurodevelopmental disorder with a strong genetic component typically manifesting during adolescence. Disruptions in how neurons (brain cells) grow and mature have been shown to be the underlying mechanisms for SCZ development. The development and maturation of neurons is controlled by small molecules known as microRNAs (miRNA). A recent study has identified one such microRNA, miR137, as one of the important genes responsible for development of SCZ. MiR137 is highly enriched in the brain, particularly in the parts of a neuron that send and receive signals. This suggests that miR137 has an important role in how neurons are born, grow and specialize in function. Studies have also shown that miR137 is directly involved in the regulation of numerous well-known genes related to SCZ. However, little is known regarding miR137 function in neurodevelopment and its role in the pathophysiology of SCZ. We have developed a mutant preclinical model to better understand the role of miR137 in the development of SCZ. Our preliminary data suggests that miR137 expression is decreased in brain regions including cerebral cortex and hippocampus in our mutant preclinical model. We propose to perform a variety of behavioural and histological screening experiments to characterize the mutant preclinical SCZ model. We will perform biochemical/molecular assays to identify genes that interact with miR137, thereby giving us a better understanding of what pathways are affected by miR137 and how they contribute to SCZ. Finally, these candidate genes of miR137 will be studied in schizophrenic patients and healthy controls and compared to our mutant preclinical model studies. This will help validate the usefulness of the mutant preclinical model to study miR137 related SCZ. These studies will potentially provide insight into the mechanisms of SCZ disease and identify potential targets for intervention.