manitoba neuroscience network

Molecular mechanisms regulating radial glia progenitor lineage progression in the neocortex

SEMINAR & VISITING SPEAKER SERIES

DATE

Friday, February 25, 2022
9:00AM

ZOOM LINK

https://us02web.zoom.us/j/83594461654?pwd=cGR6OW96WTVGSkFXRDE5MGRKaDNXZz09

MEETING ID
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PASSCODE
771772

SPEAKER

Robert Beattie, PhD

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BIO

Dr. Beattie is originally from Winnipeg and graduated from the University of Manitoba with a BSc Honours in Microbiology. After an internship at the National Microbiology Labs, he moved to Europe for his graduate studies. He received his PhD in Biomedical Sciences from the University of Sheffield, however his studies were primarily done in Basel, Switzerland. During his PhD, his supervisors' lab moved several times, beginning in Freiburg, Germany at the Max Planck Institute of Immunobiology and Epigenetics, relocating briefly to Sheffield, England and finally settling at the University of Basel in the Department of Biomedicine. After a brief postdoc at the University of Basel, Dr. Beattie moved to Vienna, Austria as a postdoctoral fellow at the Institute of Science and Technology (IST) Austria. Here he helped advance a genetic technology for studying health and disease at single-cell resolution called Mosaic Analysis with Double Markers (MADM). He is excited to return to the University of Manitoba and apply these novel tools to study developmental and neuropsychiatric disorders. His future work aims to understand the molecular origins of cellular heterogeneity in the brain and characterize the cell type specific contributions in these disorders.

RESEARCH

The mechanistic target of rapamycin (mTOR) signalling pathway is a central regulator that integrates intracellular signals in the developing cerebral cortex to control proliferation, differentiation, migration and dendrite formation and is thought to play a critical role in stem cell maintenance. mTOR acts through two large biochemical complexes, mTORC1 and mTORC2. Specific to mTORC1 is the regulator-associated protein of the mammalian target of rapamycin (Rptor). Here we dissected the cell-autonomous from the non-cell-autonomous role of Rptor in both cortical development and postnatal neuron maintenance. Using mosaic analysis with double markers (MADM) technologies, we generated genetic mosaics for Rptor in defined populations of cortical excitatory neurons. We observed distinct systemic phenotypes that accumulate and eventually give rise to observable embryonic microcephaly. Furthermore, we identify that Rptor is not cell-autonomously required for embryonic cortical development but instead in the maintenance and survival of defined populations of excitatory neurons. We then tested the pathway through which excitatory neurons are eliminated and discovered that some, but not all, could be rescued via ablation of Bax apoptotic signalling pathway and was independent of p53. More generally, our results suggest the functional relevance of mTORC1 signalling for generating cortical cell-type diversity.

OBJECTIVES

1. Provide an overview of Mosaic Analysis with Double Markers (MADM) technology and its applications for studying brain development and maintenance.

2. Discuss the importance of dissecting cell-autonomous and non-cell-autonomous gene function in vivo.

3. Demonstrate the cell-type-specific role of Rptor, a key component of the mTORC1 complex, in the development and maintenance of the neocortex.

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