CHRD 2024: Abstract Submission Form

Presenter Name
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Presenter Status
Masters Student

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Cell-Type-Specific Analysis of the Genetic and Environmental Contributions to Autism Spectrum Disorder

Background
Autism spectrum disorder (ASD) affects about 1-2% of Manitoban children and results from the convergence of genetic and environmental risk factors leading to altered neuron function. 16p11.2 deletion syndrome is among the most frequent copy number variants in humans, affecting up to 1 in 2,000 live births. 16p11.2 deletions include approximately 27-29 protein-coding genes and are among the strongest genetic associations for ASD, resulting in motor and developmental delays in carriers.

Objective
Our working hypothesis is that the 16p11.2 locus is critical for producing and maintaining defined classes of neurons and glia in the brain.

Methods
This study measures the dosage-dependent requirements of 16p11.2 by applying Mosaic Analysis with Double Markers (MADM). MADM is a lineage tracing approach that allows cells with two different genotypes (wild-type and knockout) to be generated within the same tissue and for cells of each genotype to be identified with a different fluorescent marker.

Results
To test the hypothesis that 16p11.2 is required in a cell-type-specific manner, MADM-based mouse models were combined with tissue-specific cre drivers, Nestin (for the central nervous system) and Emx1 (for the neocortex), targeting the deletion of 16p11 in neural stem cell progenitors. 16p11-MADM mosaic mice were successfully generated, and analysis is ongoing. Brains will be dissected on postnatal day 1, 14 and 21 followed by immunohistochemistry to identify cortical structures and cell types. To identify populations of cells requiring 16p11.2, we will compare the ratio of green to red cells in defined brain regions.

Conclusion
Gaining deeper insights into ASD neurobiology is crucial for improving diagnosis and developing targeted treatments. MADM technology permits the identification of key molecular changes in each brain cell type as ASD progresses. This understanding is vital for validating future therapies before clinical trials.

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No

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