CHRD 2024: Abstract Submission Form

Presenter Name
Mikaela Perron

Presenter Status
Masters Student

Role in the project
Write Abstract

Research Category
Basic Science

Title
Investigating the role of FAN1 and MecP2 in Autism Spectrum Disorder

Background
The DNA repair gene FAN1 affects the onset of Huntington disease (Wright et al., 2020) and has been shown to improve health and lifespan in mice with Mecp2 null mutations, suggesting a role in mitigating developmental disorders like Rett Syndrome (RTT) and Autism Spectrum Disorder (ASD) (Enikanolaiye et al., 2020). FAN1 is key in homology-directed repair (HDR), and its loss may shift DNA repair to alternative pathways like non-homologous end joining (NHEJ), important in neurons.

Objective
A loss of Fan1 in Mecp2-null mice may result in redirecting DNA damage repair to NHEJ and may act in a cell-type-specific manner.

Methods
Fan1 conditional-knockout (cKO) mice were combined with tissue-specific cre drivers, Nestin (for the central nervous system) and Emx1 (for the neocortex), targeting the deletion of Fan1 in neural stem cell progenitors. Brains were dissected on postnatal day 1 followed by nissl staining and immunohistochemistry to identify cortical structures and cell types. In parallel, ongoing analysis using Mosaic Analysis with Double Markers (MADM) generates Fan1 genetically mosaic mice. MADM permits single cell analysis in vivo by tracing wild-type and mutant cell lineages within the same organism, making it ideal for studying diseases like RTT and ASD.

Results
Preliminary analysis of Fan1-cKO mice at birth indicates minimal disruptions to the overall neocortex cytoarchitecture. Analysis using cell type-specific markers and MADM is ongoing to examine changes in the number of neurons and glia.

Conclusion
Initial analysis indicates that a loss of Fan1 does not cause gross-morphological changes in the cortex at birth. MADM provides a quantitative view of Fan1 and Mecp2 interactions in brain development, aiming to uncover the mechanisms of neuron and glia formation in neurodevelopmental disorders. Of direct relevance to child health in Manitoba, MADM identifies key molecular changes in each brain cell type as RTT and ASD develop.

Do you have a table/figure to upload?
No

Authors

Name	Email	Role	Profession
Mikaela Perron	perronm6@myumanitoba.ca	Presenting Author	Graduate
Hailey Therrien	therrieh@myumanitoba.ca	Co Author	Student
Paul Houston	housto15@myumanitoba.ca	Co Author	Student
Deborah Owoyemi	owoyemid@myumanitoba.ca	Co Author	Student
Galen Wright	galen.wright@umanitoba.ca	Co Author	Assistant Professor
Robert Beattie	robert.beattie@umanitoba.ca	Co Author	Assistant Professor