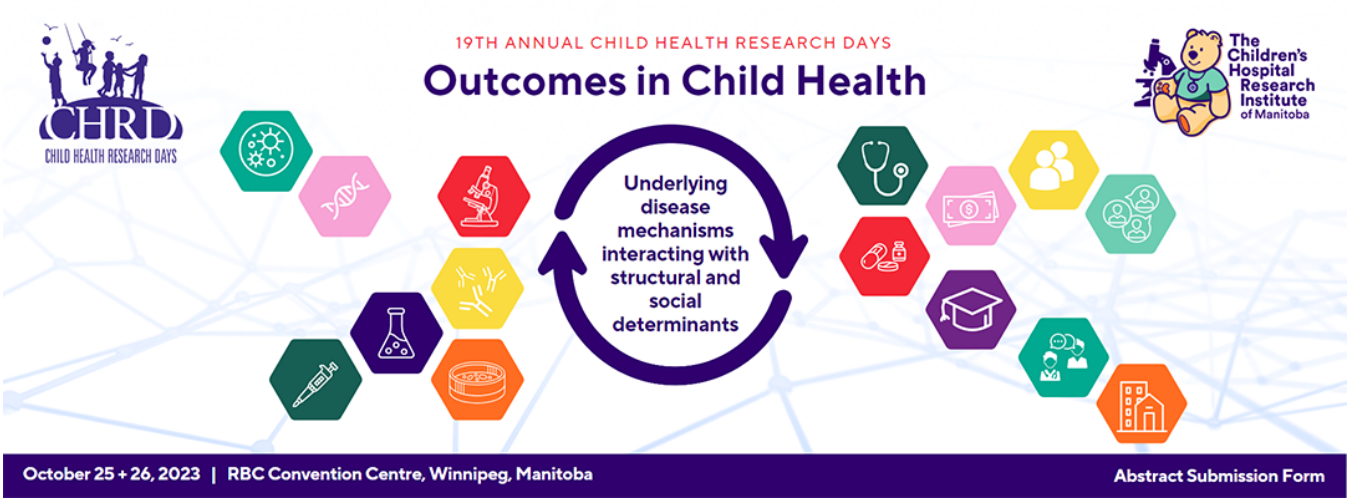

CHRD 2023: Abstract Submission Form

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Presenter Status
Undergraduate Students

Research Category
Basic Science

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Title
Dissecting the cell type-specific role of Fan1 in the developing neocortex

Background
The DNA repair gene FAN1 influences the age of onset of the neurodegenerative disease, Huntington disease (Wright et al., 2020). Further, Fan1 mutations have been shown to improve the health and life span of mice with Rett Syndrom (RTT), Mecp2 null mutations, indicating it may play a role in attenuating the severity of developmental neurological disorders (Enikanolaiye et al., 2020).

Objective
To better understand the mechanism of Fan1 in disease, this study aimed to measure the cell type-specific requirements of Fan1 in the developing neocortex.

Methods
A Fan1 conditional-knockout (cKO) mouse model was genetically linked to MADM-7-GT and TG cassettes. Tissue-specific cre drivers, Nestin (whole central nervous system) and Emx1 (neocortex) were introduced to facilitate cKO of Fan1 (increased somatic repeat instability) in neural stem cell progenitors in defined brain regions. Brains were dissected on postnatal day 1, fixed in paraformaldehyde, embedded in OCT, and cryosectioned before mounting on slides. Nissl staining and immunohistochemistry were performed to identify cortical structures and cell types.

Results
Preliminary analysis of Fan1-cKO mice at birth indicates minimal disruptions to the overall neocortex cytoarchitecture. Further analysis is required at later timepoints, including 1 and 3 months. Analysis using

cell type-specific markers is ongoing to examine changes in the number of neurons and glia.

Conclusion
This preliminary data indicates that a loss of Fan1 does not cause gross-morphological changes in the cortex at birth. However, further studies are required to determine if neural stem cell lineage progression is affected, resulting in specific cell populations of neurons or glia being gained or lost during embryonic and early postnatal development.

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