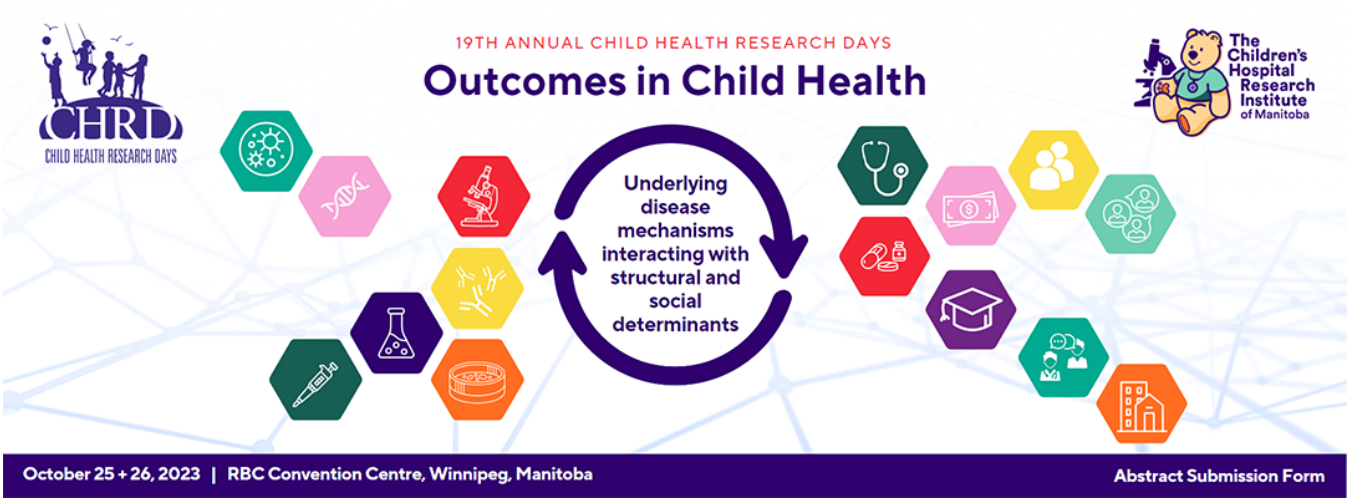

CHRD 2023: Abstract Submission Form

Submitter Name
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Presenter Name
Danielle Pascual

Presenter Status
PhD Student

Research Category
Basic Science

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Title
Modelling IRF2BPL-related pediatric neuroregression in mice

Background
De novo truncating variants in the gene IRF2BPL cause severe childhood-onset ataxia termed NEDAMSS (Neurodevelopmental disorder with abnormal movements, loss of speech and seizures). Since 2018, over forty cases have been published. Additionally, IRF2BPL is associated with autism. IRF2BPL function is not clear and remains to be explored.

Objective
We generated the first Irf2bpl knockout mice and hypothesize that Irf2bpl heterozygous mice show deficits in motor function, mimicking haploinsufficiency in NEDAMSS.

Methods
We generated an Irf2bpl null allele by removal of most of the single-exon gene. We performed heterozygous crosses to assess viability, mass, and motor function by vertical pole test and inverted grid test in wild-type (WT), heterozygous (HET), and homozygous (KO) littermates.

Results
Irf2bpl KO mice are born at lower Mendelian ratios as 33% of expected animals survive until weaning. Although WT and HET mice did not have a significant difference in mass, KO mice were 68% +/- 4.2% for males and 76% +/- 5.6% for females at three months of age. Three-month-old Irf2bpl KO mice display motor defects on the vertical pole test and inverted grid test. Specifically, Irf2bpl KO mice took about 1.7X longer than WT or HET mice to descend a vertical pole and half of the KO mice failed to hang onto the

inverted grid as all WT and HET mice could successfully hang onto the grid. Preliminary data also shows that cortical thickness is ~10-15% decreased in KO mice than WT mice.

Conclusion
Although we hypothesized Irf2bpl HET mice would display motor phenotypes, we only observed motor deficits in KO mice. Aging studies should be performed to determine if Irf2bpl HET mice display a progressive behavioural defect at later stages. Regardless, the Irf2bpl KO mice display motor defects reminiscent of NEDAMSS and may serve as an informative model.

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