CHRD 2022: Abstract & Poster Submission Form

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Presenter Status
- ○ Undergraduate Students
- ◉ Masters Student
- ○ PhD Student
- ○ Post-Doctoral Fellows
- ○ Residents
- ○ Non-Trainee

Research Category
- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

Role in the project
- ☐ Design
- ☑ Perform Experiments
- ☐ Analyze Data
- ☑ Write Abstract
- ☑ Msc. project proposal

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 thirty cases have been published. Additionally, IRF2BPL missense variants are associated with autism. Little is known about IRF2BPL function, but it is important in nervous system development and maintenance.

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 the majority of the gene (Δ17-651). 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

We observed that Irf2bpl KO mice are born at lower Mendelian ratios, close to 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% (standard error of the mean) for males and 76% +/- 5.6% (SEM) 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 where nearly all WT and HET mice could successfully hang onto the grid.

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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Authors

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