CHRD 2024: Abstract Submission Form

Presenter Name
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Presenter Status
PhD Student

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Determining the role of IRF2BPL in neurological disease

Background
De novo, heterozygous truncating mutations in the single-exon gene, IRF2BPL cause a serious pediatric brain condition. Children are born developing typically, but at around age five, they develop a progressive ataxia, lose milestones such as speech, and develop seizures. This disorder gradually worsens until they are immobile in their teens. Some missense variants in this gene are also linked to autism spectrum disorders and Parkinsonism.

Objective
We have created the first Irf2bpl knockout mice and we expect our preliminary characterization of Irf2bpl KO mice to reveal phenotypes across the brain with key areas being affected: cortex, cerebellum, and potentially the basal ganglia, all areas relevant to ataxia, autism spectrum disorder, and Parkinson's disease. Additionally, we aim to learn more about Irf2bpl function by identifying where it binds in the genome and what other genes it controls.

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. They also display cortical thinning.

Conclusion
Although this is a rare disease, understanding this gene can help those with this condition and provide insights into common neurological disorders like autism and Parkinson's disease.

Do you have a table/figure to upload?
No

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