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
- ☐

Title

Risk and Resilience Variants in the Retinoic Acid Network and Developmental Pathways Influence FASD Outcomes

Background

Fetal Alcohol Spectrum Disorder (FASD) is the most common neurodevelopmental disorder in children, with a prevalence of 1-5% in Canada. Prenatal alcohol exposure (PAE) studies have shown maternal and fetal genetic background influence PAE outcomes, but the nature of the exact genetic variation remains unknown. In this study, we focused on the connection between PAE and retinoic acid (RA) synthesis during development.

Objective

We hypothesize variants in RA metabolism and RA-dependent developmental signalling pathways genetically link acute PAE with FASD outcomes.

Methods

Whole exome sequencing (WES) data from 23 FASD diagnosed individuals was acquired. A gene candidate approach variant analysis on the WES data using R software was completed, using frequencies downloaded from NCBI as a reference population. Our gene list of interest included genes composing alcohol and RA metabolic pathways, known FASD susceptibility genes and causative genes of genetic disorders that result in similar FASD phenotypic outcomes. Allelic frequencies of the FASD cohort were compared to the reference using a chi-squared test, where a p-value smaller than 0.05 was considered significant.

Results

Variant analysis revealed a genetic tolerance for increased alcohol consumption and reduced rates of alcohol clearance in the genes composing the RA and alcohol metabolic pathways. Enrichment of potential PAE susceptibility variants were found in important developmental pathways, as well as genes associated with causative-genes of genetic developmental disorders in the FASD cohort.

Conclusion

Overall, variant analysis revealed enrichment of PAE-sensitizing variants, and a lack of protective variants for the FASD cohort compared to the reference population. The identification of risk alleles underlying a PAE-induced RA deficiency during development provides a new molecular etiology driving FASD outcomes, including neural tube, brain and craniofacial defects. These results identify potential new predictive biomarkers and novel therapeutic targets for prevention or reduction of FASD outcomes following acute PAE.

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Authors

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