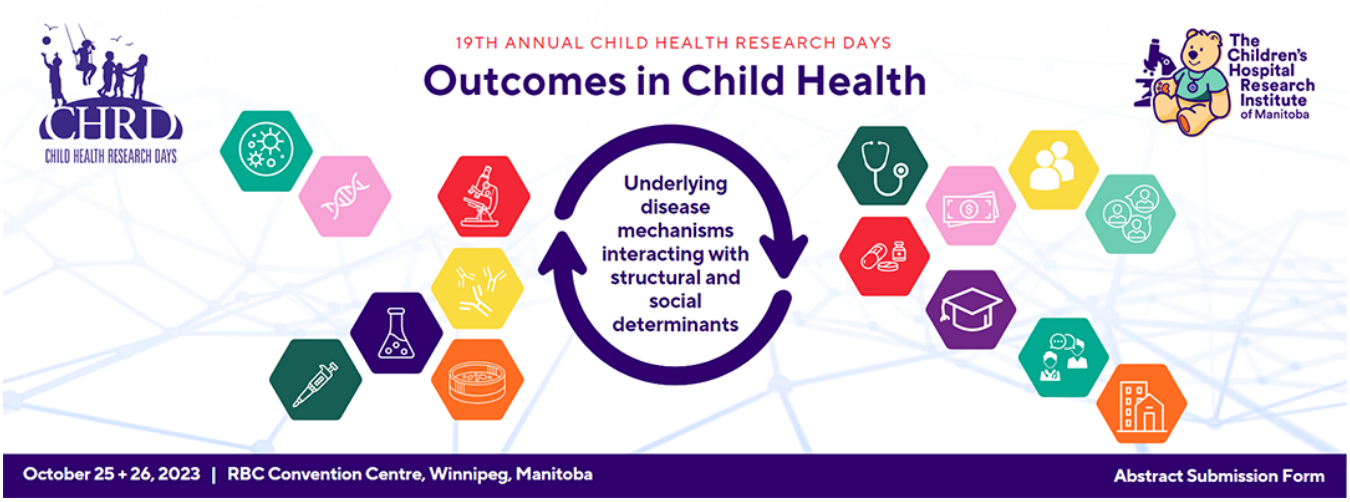


# CHRD 2023: Abstract Submission Form

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**Presenter Name**
Berardino Petrelli

**Presenter Status**
PhD Student

**Research Category**
Basic Science

**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 the world, affecting 1-5% of North Americans. The vitamin A hypothesis of FASD postulates ethanol-induced retinoic acid (RA) deficiency during development results in prenatal alcohol exposure (PAE) phenotypes. Accordingly, alcohol or RA-metabolic genes as well as RA-regulated developmental genes may represent risk or resilience variants influencing PAE outcomes. Additionally, many rare neurodevelopmental disorders which involve RA signaling phenocopy FASD. Taken altogether, allelic variants within the RA network genes may be genetic biomarkers influencing PAE outcomes.

**Objective**
The goal of this research was to identify enrichment of potential risk and resilience variants found within the RA-signaling network in FASD individuals when compared to controls.

**Methods**
To test this hypothesis, variant analysis using a gene candidate approach on RA-network genes was competed on whole exome sequencing data of 23 FASD diagnosed individuals, while allele frequencies obtained from NCBI served as controls. A chi-squared test was used to determine statistically significant variants ($p$-value $< 0.05$), followed by multiple testing correction using Bonferroni and Benjamin-Hochberg

methods.

**Results**
Overall, FASD individuals had higher risk allele frequencies within the RA network and were deficient in resilience alleles when compared to controls. Discovered risk variants in alcohol metabolism genes were associated with variations in alcohol consumption, dependence and clearance rate. Variants altering enzymatic activity of RA metabolism genes were also identified. PAE risk variants in several genes within RA controlled pathways, in addition to known pathogenic variants for neurodevelopmental disorders with shared phenotypes to FASD, were also enriched in the FASD cohort.

**Conclusion**
This research is the first to associate these variants with FASD, and may help identify new mechanisms of PAE and diagnostic tools.

# Authors


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