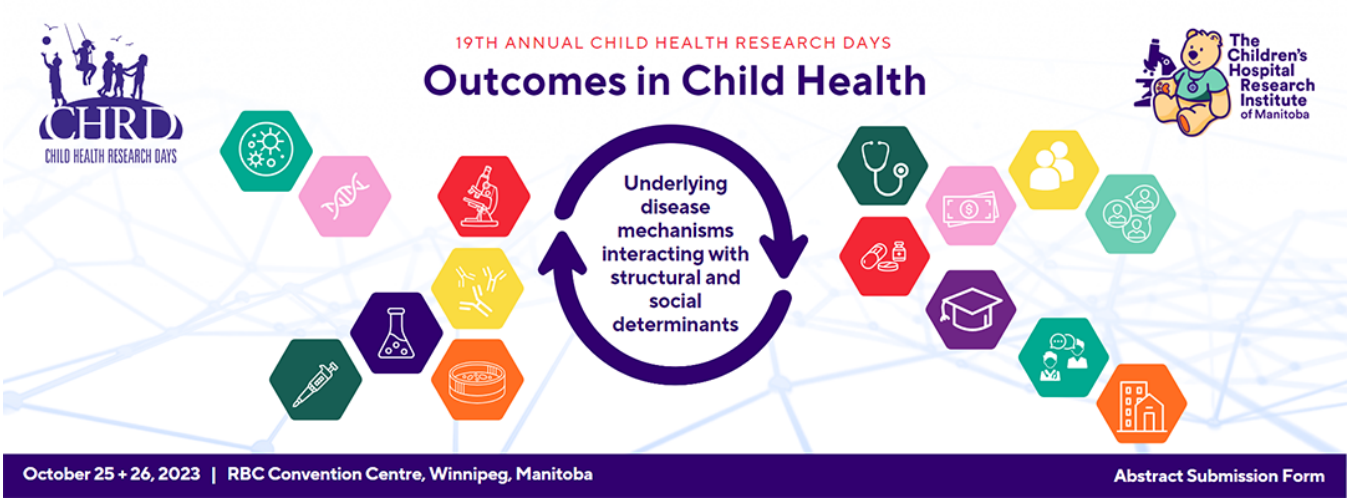

CHRD 2023: Abstract Submission Form

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Presenter Status
Non-Trainee

Research Category
Basic Science

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Title
In-utero Exposure to Maternal Diabetes and DNA Methylation Alterations in the Next Generation Birth Cohort

Background
The incidence of type 2 diabetes (T2D) in youth is increasing and in-utero exposure to maternal diabetes is a known risk factor, with higher risk associated with pregestational T2D exposure compared to GDM exposure. We hypothesize that this occurs through DNA methylation (DNAm) changes induced by in-utero exposure to maternal diabetes that predispose offspring to hyperglycemia.

Objective
This study presents an epigenome-wide investigation of DNAm alterations associated with in-utero exposure to maternal diabetes, and specifically compares maternal pregestational T2D and gestational diabetes mellitus (GDM), to determine whether the timing of prenatal diabetes exposure alters DNAm differently.

Methods
We performed an epigenome-wide analysis on cord blood from 50 newborns exposed to GDM, 72 exposed to pregestational T2D and 28 unexposed to diabetes in-utero from the Next Generation Birth Cohort.

Results
We identified 19 differentially methylated sites associated with exposure to GDM, 46 sites associated with exposure to T2D, and 11 sites associated with exposure to both GDM and T2D (adjusted p-value < 0.05

and effect size estimate > 0.01). DNAm changes associated with both T2D and GDM in the HACD4 gene were observed only in males. One site at SKAP1 and one site on an unannotated gene were previously associated with obesity. While we did not identify specific CpG sites previously associated with having diabetes, we identified a novel CpG site in the PTPRN2 gene, a gene previously associated with DNAm differences associated with diabetes.

Conclusion
Our findings suggest that in-utero exposure to maternal diabetes is associated with DNAm alterations in offspring. Moreover, the timing of maternal diabetes in-utero exposure (GDM or T2D) produces different DNAm patterns, suggesting that the widow of exposure to maternal diabetes produces different molecular modifications and may explain, at least in part, the difference in risk for youth onset T2D in offspring.

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