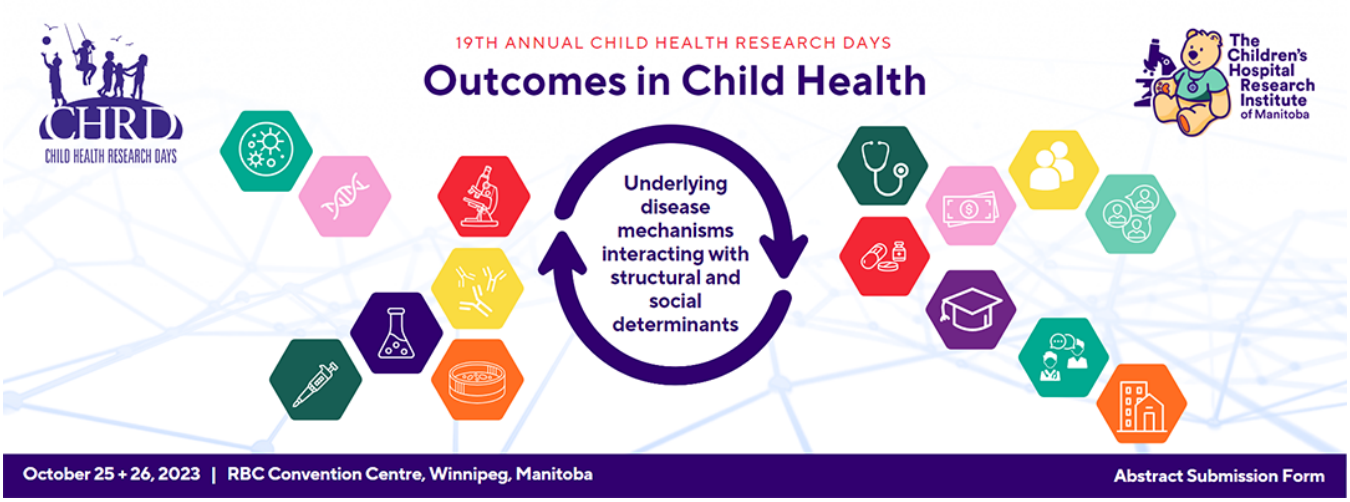

CHRD 2023: Abstract Submission Form

Submitter Name
Caitlin Menzies

Presenter Name
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Presenter Status
PhD Student

Research Category
Basic Science

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Title
Gestational Diabetes Mellitus Induces Cardiac Dysfunction and Increases the Acetylation of Metabolic Enzymes in the Offspring Heart

Background
Exposure to gestational diabetes mellitus (GDM) increases risk of cardiovascular disease in offspring later in life. Previously, our lab found that GDM exposure impaired mitochondrial respiration by the cardiomyocytes of fetal offspring that was associated with cardiac dysfunction. Protein lysine acetylation is a post-translational modification that regulates activity of metabolic enzymes within the mitochondria.

Objective
To determine how GDM exposure affects protein lysine acetylation in the offspring heart.

Methods
GDM was induced by feeding female mice a high fat sucrose (HFS; 45% fat) diet for 6 weeks prior to mating and throughout pregnancy. Control lean dams were fed a low fat (LF; 10% fat) diet. Offspring from Lean and GDM dams were fed LF and HFS diets. Echocardiography was performed in 15-week-old offspring. Mitochondria were isolated from offspring hearts and acetylated peptides were extracted via immunoprecipitation and quantified by mass spectrometry.

Results
GDM and HFS diet induced cardiac hypertrophy (Lean-LF vs. GDM-HFS p=0.015) and diastolic dysfunction (Lean-HFS vs GDM-HFS p=0.006) in 15-week aged offspring . GDM exposure differentially

altered the acetylation of mitochondrial peptides, which was exacerbated by a postnatal HFS diet (GDM-HFS vs Lean-LF 88 peptides, $p<0.05$). Functional classification revealed prominent representation of acetylated enzymes involved in the TCA cycle, fatty acid oxidation, respiratory electron transport, and mitochondrial biogenesis pathways in the hearts of GDM offspring.

Conclusion
GDM-induced cardiac hypertrophy and diastolic dysfunction in the offspring. These impairments in cardiac structure and functions were found in tandem with increased acetylation of cardiac mitochondrial enzymes regulation energy metabolism. Cardiac mitochondrial enzyme acetylation represents a novel molecular mechanism that contributes to GDM-induced mitochondrial dysfunction and cardiomyopathy in the offspring.

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