CHRD 2024: Abstract Submission Form

Presenter Name
Caitlin Menzies

Presenter Status
PhD Student

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Gestational Diabetes Mellitus Induced Cardiac Hypertrophy and Altered Mitochondrial Protein Acetylation in the Offspring Heart and the Protective Role of SIRT3

Background
Exposure to gestational diabetes mellitus (GDM) increases risk of cardiovascular disease in offspring later in life. Intrauterine GDM exposure also induced abhorrent protein acetylation in cardiac mitochondria of offspring, which may underlie cardiac dysfunction. Protein acetylation is a major mechanism in cardiac mitochondria that regulates activity of metabolic enzymes. Sirtuin-3 (SIRT3), the main mitochondrial deacetylase, is downregulated in GDM and chronic high-fat diet conditions.

Objective
We hypothesize that increasing SIRT3 in offspring cardiac tissue protects from GDM-induced cardiac dysfunction.

Methods
To induce GDM, female mice were fed a high-fat and sucrose (HFS; 45% fat) diet for 6 weeks prior to mating. Control lean dams were fed a low-fat (LF; 10% fat) diet. Dams were mated to transgenic male sires overexpressing SIRT3 in cardiac tissue to generate a mix of non-transgenic and transgenic offspring. Postweaning, offspring were fed LF or HFS diets. Echocardiography was performed in 15-week-old offspring. Acetylated mitochondrial peptides were extracted from offspring hearts via immunoprecipitation and quantified by mass spectrometry.

Results
Non-transgenic male offspring exposed to GDM and postnatal HFS-diet displayed cardiac hypertrophy; this phenotype was not observed in transgenic offspring suggesting a protective role of SIRT3. Similarly, GDM exposure altered acetylation of mitochondrial peptides in non-transgenic male offspring which was exacerbated by a postnatal HFS diet (GDM-HF vs Lean-LF 88 peptides, $p<0.05$). Functional classification revealed prominent representation of acetylated proteins in fatty acid oxidation, electron transport, and mitochondrial biogenesis pathways.

Conclusion
Cardiac mitochondrial enzyme acetylation contributes to cardiac hypertrophy in male offspring exposed to intrauterine GDM and postnatal HFS diet. Our preliminary results support SIRT3 overexpression as a novel protective mechanism within this context.

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No

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