CHRD 2024: Abstract Submission Form

Presenter Name
Anna Shypilova

Presenter Status
Undergraduate Students

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
Muscle cell SIRT3 activation improves glucose utilization by offspring exposed to gestational diabetes.

Background
Intrauterine exposure to Gestational Diabetes Mellitus (GDM) is associated with an elevated risk of offspring obesity and type 2 diabetes (T2D) in later life. Skeletal muscle has an important role in regulating blood glucose levels since it is a major site of glucose utilization. Muscle mitochondrial dysfunction is a mechanism that precedes the development of T2D in adults, that is partially attributable to reduced expression of SIRT3, the main mitochondrial deacetylase protein. Protein acetylation is a major regulatory mechanism of mitochondria that regulates activity of metabolic enzymes.

Objective
We hypothesize that increasing SIRT3 in skeletal muscle tissue of offspring may provide protection against GDM-induced metabolic dysfunction.

Methods
To induce GDM female mice were fed a high fat and sucrose (HFS; 45% fat) diet for 6 weeks prior to mating and throughout pregnancy and lactation. Control lean dams were fed a low fat (LF; 10% fat) diet. Dams were mated to transgenic male sires overexpressing SIRT3 (SIRT3-TG) in skeletal muscle tissue to generate a mix of non-transgenic and transgenic offspring. Postweaning, offspring from Lean and GDM dams were fed LF or HFS diets. To evaluate metabolic differences, insulin and glucose tolerance tests were performed.

Results
Non-transgenic offsprings exposed to GDM and fed a postnatal HFS diet displayed significantly higher body weight, fasted blood glucose, impaired response to insulin, and impaired glucose tolerance; these differences were not observed in GDM-HF-SIRT3 TG offspring, suggesting a protective effect of SIRT3. Western blot analysis of gastrocnemius muscle revealed increased SIRT3 in our SIRT3-TG offspring compared to WT littermates. We found no differences in citrate synthase expression, a marker of mitochondrial content between groups.

Conclusion
Our results suggest a protective role of SIRT3 overexpression against metabolic dysfunction in offspring exposed to intrauterine GDM and postnatal HFS diet.

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No

Authors

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