

CHRD 2024: Abstract Submission Form

Presenter Name

Jewel Paskaruk

Presenter Status

Undergraduate Students

Role in the project

Design
Perform Experiments
Analyze Data
Write Abstract

Research Category

Basic Science

Title

SIRT3 Deficiency in the Liver Results in Hepatic Steatosis and Adipocyte Expansion in Gestational Diabetes

Background

Gestational diabetes mellitus (GDM) is the most common pregnancy complication, affecting around 15-25% of pregnancies at the time of delivery in Canada, with obesity being a major risk factor. Fat accumulation in the liver contributes to insulin resistance, which is characteristic of GDM. White adipose tissue expands during pregnancy; however, adipocyte hypertrophy can have negative implications for insulin sensitivity. This project investigates the role of Sirtuin 3 (SIRT3), a mitochondrial protein deacetylase that is important in energy pathways such as fatty acid oxidation during pregnancy.

Objective

We hypothesize that SIRT3 deficiency in the liver induces hepatic steatosis and adipocyte expansion during pregnancy.

Methods

Mice with liver-specific-deletion of SIRT3 (SIRT3-LKO) were generated by crossing Sirt3^{tm1.1Auw} mice from Jackson Labs with loxP sites flanking exons 2-3 of the Sirt3 gene with Cre-recombinase mice with an albumin-promoter. SIRT3-LKO mice and Cre-negative controls fed either low fat diet (10% kcal fat) or high fat sucrose diet (45% kcal fat) for 6-weeks before pregnancy and throughout the 3-week mouse pregnancy to induce GDM. Pregnant mice were sacrificed at embryonic day 18.5 and liver and gonadal white adipose tissue (GWAT) depots were collected for histological visualization of lipids using hematoxylin and eosin and Oil Red O.

Results

SIRT3-LKO mice exhibited hepatic steatosis compared to controls during pregnancy ($p < 0.0001$), assessed by quantifying Oil Red O positive area of liver sections. The diameter and number of adipocytes per GWAT section showed adipocyte expansion in SIRT3-LKO mice compared to controls during pregnancy ($p < 0.0001$) (Two-way ANOVA).

Conclusion

Our results show that deficiency of SIRT3 in the liver leads to hepatic steatosis and adipocyte expansion, independent of diet during pregnancy. This may contribute to insulin resistance observed in GDM. Better understanding the role of SIRT3 in the development of GDM could lead to new therapeutics.

Do you have a table/figure to upload?

No

Authors

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