Presenting Author Name
Jewel Paskaruk

Presenting Author Category
Undergraduate Student

Research Category
Basic Science

Abstract Title
SIRT3 Deficiency in the Liver Results in Hepatic Steatosis and Elevated Circulating Lipids in Gestational Diabetes

Background
Gestational diabetes mellitus (GDM) is the most common pregnancy complication, affecting around 5-10% of pregnancies at the time of delivery in Canada, with obesity being a major risk factor. Adaptations to pregnancy require a shift from glucose to fat utilization for energy. Fat accumulation in the liver contributes to insulin resistance, which is characteristic of GDM. This project investigates the role of Sirtuin 3 (SIRT3), a mitochondrial protein deacetylase that regulates energy pathways such as fatty acid oxidation during pregnancy.

Objective
SIRT3 deficiency in the liver induces hepatic steatosis and elevated circulating lipids during pregnancy.

Methods
Mice with liver-specific-deletion of SIRT3 (SIRT3-LKO) were generated by crossing Sirt3tm1.1Auw mice from Jackson Labs with albumin-promoter driven cre-recombinase mice. SIRT3-LKO mice and controls were 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 gestational day 18.5. Lipids were histologically visualized in liver using Oil Red O. Serum and liver lipids were measured biochemically.

Results
SIRT3-LKO mice exhibited significant hepatic steatosis during pregnancy, as indicated by a 2-fold increase in Oil Red O positive area of stained liver sections ($p<0.0001$) and a 1.8-fold increase in hepatic triglyceride concentration ($p<0.05$) compared to control mice. Serum triglyceride and free fatty acid concentrations were elevated by 1.4-fold ($p<0.01$) and 2-fold ($p<0.05$), respectively, in the pregnant SIRT3-LKO mice compared to controls.

Conclusion
Our results reveal that loss of SIRT3 in the liver during pregnancy leads to hepatic steatosis and dyslipidemia. These alterations in lipid handling are likely to exacerbate liver insulin resistance and glucose intolerance, which are metabolic hallmarks of GDM. These findings suggest that SIRT3 regulates liver lipid metabolism during pregnancy and could be a therapeutic target.

Authors

Name	Role	Profession
Jewel Paskaruk	Presenting Author	Undergraduate
Khushali Trivedi	Co Author	Graduate
Bo Xiang	Co Author	Technician
Vernon Dolinsky	Co Author	Full Professor