Abstract #9 (0346_0513_000014)

GESTATIONAL DIABETES RESULTS FROM HEPATIC STEATOSIS IN ADIPONECTIN DEFICIENT MICE

Brittany Gruber, Children's Hospital Research Institute of Manitoba, University of Manitoba; **Bo Xiang**, Children's Hospital Research Institute of Manitoba, University of Manitoba; **Laura Cole**, Children's Hospital Research Institute of Manitoba, University of Manitoba; **Vernon Dolinsky**, Children's Hospital Research Institute of Manitoba, University of Manitoba; **Grant Hatch**, Children's Hospital Research Institute of Manitoba, University of Manitoba; **Christine Doucette**, Children's Hospital Research Institute of Manitoba, University of Manitoba

Background:
Obesity and hepatic steatosis [VD1] are risk factors for gestational diabetes mellitus (GDM), a common complication of pregnancy. Adiponectin is a fat derived hormone that improves hepatic steatosis, insulin sensitivity. Low levels of circulating adiponectin are associated with GDM development.

Objective:
We hypothesize that adiponectin deficiency causes fatty liver during pregnancy, contributing to the development of GDM.

Methods:
We compared pregnant (3rd trimester) adiponectin knockout (KO) (strain B6;129-*Adipoq*^{tm1Chan}/J) and wild-type mice, and assessed parameters of hepatic lipid metabolism. Impact of adiponectin supplementation was measured by administering adenovirus mediated full length adiponectin at the end of the second trimester and comparing to GFP-control.

Results:
In the third trimester, fasting pregnant adiponectin KO are hyperglycemic on a low-fat diet (9.2mmol/L vs. 7.7mmol/L in controls, $p<0.05$); and are glucose intolerant and have elevated gluconeogenesis (determined by pyruvate tolerance test) relative to wild-type. Pregnant adiponectin KO mice develop hepatic steatosis, and a 3-fold elevation in hepatic triglycerides ($p<0.05$) relative to wild-type. Gestational weight gain and food consumption were similar in KO and wild-type mice. Adenoviral-mediated adiponectin supplementation to pregnant adiponectin KO mice improved glucose tolerance, prevented fasting hyperglycemia, and attenuated fatty liver development.

Conclusion:
Adiponectin deficiency increased hepatic lipid accumulation during the period of pregnancy associated with increased fat utilization. Consequently, adiponectin deficiency contributed to glucose intolerance, dysregulated gluconeogenesis and hyperglycemia characteristic of GDM. Adiponectin supplementation rescued the metabolic defects of adiponectin deficiency during pregnancy.