

MSc DEFENCE – Tuesday, September 23rd

Student: Jesse Olson

Title: **FOLIC ACID AND VITAMIN B12 IMBALANCE THROUGHOUT DEVELOPMENT AND EARLY LIFE PROGRAMS GLUCOSE TOLERANCE AND ADIPOSITY IN ADULT FEMALE MICE**

Time and Location: 9:00 am Pathology Education Centre

Supervisor: Dr. Angela Devlin

Abstract

Risk for cardiometabolic disease may be programmed or accelerated by prenatal or early postnatal nutritional imbalances. For example, population studies have reported greater adiposity and insulin resistance in children from mothers with high folic acid (FA) intakes and low vitamin B12 (B12) status during pregnancy. In Canada, it has been reported that women of child-bearing age have adequate folate status, but 5% of those women may be vitamin B12 deficient during the early stages of pregnancy. Currently, the mechanisms underlying FA/B12 mediated programming of adiposity and glucose homeostasis are not known.

Objective: To investigate the molecular mechanisms underlying the programming of adiposity and glucose metabolism in adult mice by developmental exposure to maternal FA and B12 imbalance.

Methods: Female C57BL/6J mice were fed one of the following diets during pregnancy and lactation: high folic acid with adequate B12 (HFA+B12), high folic acid deficient in B12 (HFA-B12), or a control diet. At weaning, female offspring mice were fed either a control diet or Western diet for 30 weeks.

Results: At 20 wks post weaning, offspring mice fed the control diet that were from dams fed the HFA-B12 diet had greater glucose intolerance ($P < 0.05$) than offspring from dams fed the control or HFA+B12 diets. This was also observed at 30 wks post weaning and was accompanied by lower beta cell mass. Interestingly, offspring mice from HFA-B12 diet fed dams had greater ($P < 0.05$) islet *Mafa* mRNA expression than offspring from control or HFA+B12 diet fed dams.

Offspring fed the post weaning western diet from females fed the HFA-B12 diet had lower ($P < 0.05$) fasting blood glucose concentrations than offspring from control diet fed dams and lower ($P < 0.05$) fasting insulin concentrations than offspring from control and HFA+B12 diet fed dams. This was accompanied by greater ($P < 0.05$) beta cell mass in offspring from HFA-B12 diet fed dams compared to offspring from dams fed the HFA+B12 diet.

Conclusions: These findings provide evidence that programming of glucose intolerance in adult females by maternal FA/B12 imbalance may involve direct effects on pancreatic beta cells and is influenced by diet during adulthood.