Lipid conference abstract

Title: Deciphering the role of the placenta in the developmental programming of diabetes and obesity risk

Amanda Nancy Sferruzzi-Perri

Centre for Trophoblast research, Dept Physiology, Development and Neuroscience, University of Cambridge, UK

Introduction: Seminal work using human epidemiological data showed that low birthweight, an indicator of poor nutrition during *in utero* development, increased the risk of the child to develop diseases like obesity, type 2 diabetes, and heart disease in adult life[1]. These findings were supported by work in experimental animals that showed adverse gestational environments, like maternal malnutrition, induce structural and molecular changes in key metabolic organs of the fetus/offspring resulting in an increased risk of the offspring to develop disease[2,3]. Fetal development depends on the placenta, which both transfers nutrients from mother to fetus, and secretes hormones that modulate maternal metabolism to favour fetal nutrient supply[4-6]. However, little is known about the importance of placental endocrine function in maternal physiological adaptations supporting fetal growth and in the long-term metabolic health of the offspring.

Methods: To address this key knowledge gap, we are selectively manipulating the function of endocrine cells in the mouse placenta. This is achieved by genetically altering expression of the imprinted growth gene, *Igf2,* that controls their formation and function[7-9].

Results: Unpublished data from the laboratory has shown that mouse dams with genetically-disrupted placental endocrine function do not become glucose intolerant or insulin resistant in pregnancy, which are important factors for increasing glucose and lipid availability for the developing fetus[10]. These changes are related to perturbed placental hormone expression and reduced fetal glucose supply and growth *in vivo*. Postnatally, the offspring supported by malfunctioning placentas exhibit reduced insulin sensitivity and altered adiposity on a chow and obesogenic diet. Programmed alterations in the metabolic profile of the offspring were related to structural and molecular changes in key organs, like the white adipose tissue.

Conclusions: Using a novel and robust mouse model, our data highlight the important role of placental endocrine function in the developmental programming of obesity and diabetes risk.

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