ABSTRACTS

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AMPK REGULATES EXTRAVILLOUS TROPHOBLAST INVASION

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The placenta is involved in the transport and exchange of gases, nutrients, and waste products at the mother-fetus interface. During the early stages of pregnancy, trophoblasts, the primary stem cell lineage in the placenta, play a crucial role in embryo implantation and in spiral artery remodeling. Improper progression of these initial stages can lead to various adverse effects for both mother and fetus. At a cellular level, AMP-activated protein kinase (AMPK) contributes not only to the maintenance of cellular homeostasis, but also possibly to the regulation of cell invasion, an important step in spiral artery remodeling.

It is proposed that AMPK regulates extravillous trophoblast cell invasion.

Using a transwell invasion assay, we determined that Metformin and 5-Aminoimidazole-4-carboxamide ribonucleotide (AICAR) – an AMPK activator – increase trophoblast invasion. Conversely, Compound C, an AMPK inhibitor, decreases the cells' ability to invade over a 32 hour period. Manipulation of AMPK expression via siRNA technology reduced trophoblast invasion across all of the pharmacological treatments. Altered expression of genes linked to trophoblast cell invasion, such as TIMP-1 .TIMP-2, MMP-2 and MMP-9 were also observed.

AMPK was shown to play a role in altered trophoblast invasion through various invasion markers. Future steps include evaluating integrin expression, involved in cellular movement, to further elucidae this relationship.

MATERNAL HIGH-FAT DIET ALTERS MATERNAL AND FETAL GLUCONEOGENESIS AT E14.5 IN THE LIVER.

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Maternal obesity is associated with increased risk of offspring metabolic dysfunction in adulthood. Lipotoxicity, a metabolic syndrome, has been linked with gluconeogenic changes in clinical and animal studies. The impact of maternal obesity on fetal gluconeogenesis at embryonic day (E)14.5, is unknown. We hypothesize that a maternal high fat diet (HFD) will result in increased fetal liver gluconeogenesis.

Four-week-old C57BL/6 genetically-standardized laboratory mice were fed a control standard purified diet (CON; 17% kcal fat) (n=7) or HFD (60% kcal fat) (n=9) for 6 weeks prior to mating with control fed C57BL/6 males. They were maintained on this diet throughout gestation. Observation of a vaginal plug confirmed pregnancy and designated E0.5. Dams were sacrificed at E14.5, and maternal and fetal livers were collected. Transcript levels of key liver gluconeogenic enzymes were investigated by RT-qPCR.

High-fat females weighed more than controls at the time of mating and throughout gestation. At E14.5, maternal blood glucose and circulating insulin and leptin were elevated in high-fat dams. mRNA of maternal cytosolic phosphoenolpyruvate carboxykinase (PEPCK-C), a key enzyme in the gluconeogenic pathway, was significantly reduced ($p<0.0001$) in livers of high-fat dams. Maternal hepatic nuclear factor 4 alpha (HNF4α) mRNA, a known transcription activator of PEPCK, was decreased ($p=0.0004$), along with mRNA of the upstream insulin receptor substrate 2 (IRS2) ($p=0.0018$) in high-fat livers. Fetal PEPCK-C ($p=0.0068$) and pyruvate carboxylase ($p=0.0003$) mRNA levels were also decreased in the high-fat livers.

Maternal HFD is associated with downregulated mRNA transcript levels of major gluconeogenic enzymes in the maternal and fetal liver at E14.5. This does not support the hypothesis, and is likely due to an overabundance of triglycerides and altered maternal-fetal glucose gradient. The altered gluconeogenic profile in maternal and fetal liver at E14.5 may underlie the increased risk for offspring metabolic dysfunction later in life. Future research should investigate lipid metabolism and the expression of gluconeogenic factors.

Newsgeek. *Baby in the Womb.* 2017. Available from: https://www.thenewsgeeks.com/wp-content/uploads/2017/06/baby-in-the-womb-1024x500-e1502005407940.jpg [Accessed: 12th February 2018]