

## **Periconceptional and early preimplantational undernutrition alters gene expression of metabolic and gluconeogenic regulating factors in the liver**

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**Introduction:** Maternal undernutrition during gestation can result in insulin resistance and glucose intolerance, leading to the development of type-2 diabetes. The effect of maternal undernutrition during the periconceptional period, however, has not been widely investigated. The metabolic master switch, AMP-Activated Protein Kinase (AMPK) and the master integrator of external signals, peroxisome proliferator-activated receptor  $\gamma$  co-activator 1 $\alpha$  (PGC-1 $\alpha$ ) play critical roles in liver metabolism. More importantly, the capacity of the liver for gluconeogenesis which is regulated by phosphoenolpyruvate carboxykinase, PEPCK, is critical in maintaining glucose homeostasis.

**Hypothesis:** We hypothesise that periconceptional (PCUN) and early preimplantational (PIUN) undernutrition will result in a decrease in gene expression of the metabolic regulators, AMPK and PGC-1 $\alpha$ , as well as an increase in the gluconeogenic regulator, PEPCK in the fetal liver in late gestation.

**Methods:** Control ewes were fed 100% metabolisable energy (ME) from -45d to 6d after conception. Ewes in the PCUN group were fed 70% ME from -45d to 6d and ewes in the PIUN group were fed 70% ME from conception to 6d postconception. Liver samples were collected at 136-138d gestation. The mRNA expression of AMPK- $\alpha$ 1, AMPK- $\alpha$ 2, PGC-1 $\alpha$  and the mitochondrial and cytosolic forms of PEPCK (PEPCK-M, PEPCK-C) were analysed using Real Time-PCR.  $p < 0.05$  was considered statistically significant.

**Results:** Hepatic mRNA expression of AMPK- $\alpha$ 1 was decreased in the PIUN singleton compared to the control and PCUN groups. There was no difference, however, in the expression of AMPK- $\alpha$ 2. The expression of PGC-1 $\alpha$  and the cytosolic form of PEPCK was decreased in the PIUN and PCUN groups compared to the control group, with no difference in the expression of the mitochondrial form of PEPCK.

**Conclusion:** Periconceptional and early preimplantational undernutrition may result in a dysregulation of hepatic energy metabolism and a decrease in gluconeogenesis. The decrease in AMPK- $\alpha$ 1 mRNA expression in the PIUN group may be due to a mismatch between the oocyte and the early embryo's energy status.