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## Exogenous porcine somatotropin administered to late-pregnant gilts alters hepatic metabolism of protein and energy in pig foetuses

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### keywords

Foetal growth, Gene expression, Glucose pathway, Fatty acid oxidation, Protein degradation

### Introduction

Physiological maturity is one of the most important factors that influence piglet survival at birth and until weaning. The maturity of the neonate is determined by the degree of tissue development attained during gestation, which is dependent on the availability of maternal nutrients to support foetal growth and on the nutrient uptake per foetus. The somatotropin-IGF axis is the main regulator of growth and metabolism in mammals. Farmer and Langendijk (2019) showed that gilts injected with recombinant porcine somatotropin (pST) during late gestation had greater circulating concentrations of IGF-I and glucose and lower circulating concentrations of urea than controls. These changes in the metabolic status of gilts may modify nutrient availability for the uterine-placenta entities. This study aimed to investigate the effects of pST treatment of gilts during late gestation on gene expression levels in the liver of their foetuses.

### Material and Methods

Yorkshire × Landrace gilts were bred via artificial insemination using pools of semen from Duroc boars. On day 89 of gestation, gilts were separated in two groups: control (CTL, n = 15) or treated (pST, n = 17). Control gilts received daily injections of 1 mL of sterile water, whereas treated gilts received daily injections of 5 mg of pST from days 90 to 109 of gestation. All gilts were killed on 110 + 1 days post-conceptus. In each litter, pairs of foetuses of the same sex (16 females and 14 males in CTL group, 16 females and 18 males in pST group) were selected to represent small (0.89 kg + 0.03 kg) or medium-sized (1.18 kg + 0.03 kg) categories. Foetuses (n = 64) were euthanized, and the liver was immediately excised, weighed, cut and frozen in liquid nitrogen. Total RNA was extracted from the liver and mRNA abundance of genes was assessed by qPCR. Data were analysed by ANOVA with the fixed effects of maternal treatment (T: CTL or pST), class of foetal weight (W: small or medium), sex (S), and their interactions (T × W and T × S).

### Results and Discussion

Average foetal weights were not affected ( $P > 0.10$ ) by treatment, with values of 1.06 kg ± 0.17 kg and 1.14 kg ± 0.16 kg for pST and CTL gilts. As there were no T × W effects on weights and gene expression levels, only the main effects of treatment were described herein. Liver weight (relative to foetal weight) was higher (+8%,  $P = 0.04$ ) in pST than in control foetuses. Several genes participating in glucose metabolism had an altered expression in the liver of foetuses from pST gilts as compared with controls. The expression of glucose transporter SLC2A1 (GLUT1) was greater ( $P < 0.01$ ) in pST foetuses, which may favour glucose uptake by foetal hepatocytes. The mRNA levels of glycogen synthase kinase (GSK3B) and fatty acid synthase (FASN) were lower ( $P < 0.05$ ), whereas expression levels of genes controlling fatty acid oxidation (FABP3 and CPT1A) were greater ( $P < 0.04$ ) in the liver of pST foetuses. This suggests an inhibition of energy-consuming processes (glycogen and lipid biosynthesis) and the activation of energy-producing pathways (mitochondrial oxidation) in the liver of pST foetuses compared with controls. The mRNA levels of alpha1-AMPK (PRKAA1), a cellular energy sensor, tended to be higher ( $P = 0.07$ ), and that of PGC-1 (PPARGC1), a coactivator induced by fasting, were greater ( $P = 0.03$ ) in pST foetuses, suggesting an energy deficit in the liver of those foetuses as compared with controls. The activation of hepatic energy-producing pathways may sustain somatic development of the liver in pST foetuses. Increased expression levels of

genes involved in fatty acid oxidation in the liver of pST foetuses, compared with controls, can also prepare the postnatal burst of mitochondrial biogenesis and the shift towards the reliance on mitochondrial fatty acid oxidation as the major source of ATP production at birth. The liver may also catabolize fatty acids to produce 3-carbon substrates for gluconeogenesis, which has been described as an important adaptive response to supply glucose for other glucose-consuming foetal tissues such as skeletal muscle. There was no treatment-associated difference in expression levels of key genes acting in protein synthesis, but expression levels of genes involved in intracellular degradation of proteins (CTSB and PSMD1) and targeting substrates for ubiquitin-mediated protein degradation (GS3KB) were greater ( $P < 0.05$ ) in the liver of pST foetuses. These changes suggest a higher utilization of protein sources in the liver of pST foetuses, which is consistent with their reduced circulating concentrations of urea compared with controls. There were only few interactions (6 genes) between sex and treatment, with more significant effects in males than in females for the affected genes (data not shown).

### *Conclusion and Implications*

Significant changes related to energy and protein metabolism were observed in the liver of foetuses from pST treated gilts, which may beneficially affect robustness of their neonates as compared with controls.

### *Acknowledgments*

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### *References*

Farmer C and Langendijk P 2019. Exogenous porcine somatotropin stimulates mammary development in late-pregnant gilts. *Journal of Animal Science* 97, 2433-2440.

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