Effects of undernutrition and the presence of an embryo upon endometrium transcriptome in sheep

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The effects of undernutrition and the presence of conceptus on the endometrium transcriptome at Day 14 of the oestrous cycle or pregnancy were investigated. Adult Rasa Aragonesa ewes were allocated to one of two nutritional treatment groups: control (*n*=21; fed to maintenance requirements) and undernourished (*n*=25; fed at 0.5-fold of daily requirements for maintenance). Thirteen control ewes and 18 undernourished ewes were mated to intact rams to establish a pregnant and cyclic group in each nutritional group. Sheep uterus transcriptome profiles were evaluated using an ovine oligonucleotide microarray (Agilent Technol.) containing >10.000 unique elements. Microarray data were analyzed with a mixed model using Proc MIXED (SAS Inst., Cary, NC). Functional analysis of microarray data was performed using the Dynamic Impact Approach (DIA). The DIA analysis of KEGG pathways revealed that metabolic pathways such as `Citrate Cycle´ and metabolism of Cofactors and vitamins such as 'CoA biosynthesis' were up-regulated in control pregnant compared with control cyclic ewes. However, these pathways were not altered between undernourished pregnant and undernourished cyclic ewes. Compared to the cyclic state, pregnancy in control ewes was associated with an up-regulation of lipid metabolism, which was evident by the increase in the expression of genes involved in the pathways related to biosynthesis of unsaturated fatty acids and steroid hormones, as well as the PPAR signaling pathway. None of these pathways were differentially expressed between undernourished pregnant or undernourished cyclic ewes. `Pentose and Glucuronate interconversions´ were up-regulated in control pregnant ewes respect cyclic ewes, probably due to their involvement in the up-regulation of Glycosaminoglycan and Glycosphingolipid biosynthesis relevant for uterine remodeling in pregnancy. Few pathways were differentially expressed between undernourished pregnant and control ewes. However, alterations in immune system pathways were consistent: comparing pregnant and cyclic ewes regardless the nutritional treatment revealed that `RIG-I and Toll like receptors´ and `Chemokine´ signaling pathways were similar. The integrated interpretation of the results suggested that pregnant control animals experienced an activation of metabolic functions in order to satisfy the energy requirements for pregnancy. Nevertheless, when animals were

undernourished, the metabolism in pregnant animals was down-regulated in order to re-prioritize metabolic functions to maintain homeostasis. Alterations of pathways related to immune function, which are essential during maternal recognition of pregnancy, were maintained in both control and undernourished ewes. The present study supports the idea that patterns of endometrial gene expression differ as a function of pregnancy status and plane of nutrition.