

## Global gene expression in the endometrium of primiparous dairy cows during the early-luteal phase of the estrous cycle

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The uterine endometrium plays a central role in early conceptus-maternal communication for the establishment and maintenance of pregnancy. Primiparous Holstein dairy cows were used in a randomized block design to evaluate gene expression changes in the endometrium during the early-luteal phase of the estrous cycle induced by two different feeding strategies: total mixed ration (TMR) vs. pasture + TMR applied during early lactation. In particular, during the first 65 days of lactation, cows were fed either [i] TMR *ad libitum* (17 kgDM/d offered; 70% forage, 30% concentrate; **T1**) or [ii] grazing of alfalfa (*Medicago sativa*; 6-h am grazing in 3-d strips; pasture allowance=20 kgDM/d) plus TMR (70% of *ad libitum* TMR; 12 kgDM/d offered; **T2**). At  $45 \pm 1$  d, cows were synchronized and at d 7 of the estrous cycle (d 0 = estrous) endometrial biopsies were obtained. A total of 10 endometrium samples (5 cows per treatment) were analyzed using RNA sequencing. Sequence reads were mapped to the bovine reference genome (bosTau7) using Tophat and the resulting alignments were used to reconstruct transcript models using Cufflinks. Gene expression differences were tested using edgeR package. From the 14,753 genes detected in the transcriptome, 102 genes were differentially expressed (FDR = 0.10; fold change  $\geq 2$ ) between T1 vs. T2. Specifically, 20 genes were significantly upregulated in T1 while 82 genes were upregulated in T2. Many of these genes are involved in biological processes such as regulating enzymatic activity (e.g. phospholamban, secretoglobin family 1A member 1), protein binding (e.g. caveolin 3, alpha-2-HS-glycoprotein) and immune response (e.g. immunoglobulin heavy constant epsilon, major histocompatibility complex class II DQ beta, myelin protein P0-like). Functional enrichment analysis, using both Gene Ontology and KEGG databases, revealed significant terms associated with cell and tissue development, cell adhesion, endopeptidases, calcium ion transport, calcium signaling, tryptophan metabolism, among others, with most of the genes being upregulated in T2 compared to T1. Overall, this study characterized genes and pathways expressed in the endometrium of dairy cows at day 7 of the estrous cycle, and evidenced a differential endometrial environment according with a nutritional management during early lactation in which most of the genes differentially expressed were upregulated in grazing cows.

Key words: dairy cows, nutrition, transcriptome