

Transcriptomic analysis reveals effects on oxidative phosphorylation and canonical Wnt signaling by form of selenium in the intercaruncular tissue of beef heifers at maternal recognition of pregnancy

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Selenium (Se) is supplemented to the diet of grazing beef cattle in regions where the soils and hence forages are deficient in this mineral. When cattle consume forage, organic forms of Se (OSe) are physiologically available, whereas inorganic Se (ISe) is typically used in commercial vitamin-mineral supplements. We have investigated the effects of supplemental Se as ISe or a 1:1 mixture of ISe:OSe (MIX) and have observed significant effects on the corpus luteum (CL) and endometrium in grazing beef cows and heifers. In comparison to ISe, heifers supplemented with the MIX-form Se have an increase in peripheral concentrations of progesterone (P4) during the early luteal phase of the estrous cycle, at a time when increased P4 has been shown to improve embryonic development. Indeed, we have reported that form of Se affects the abundance of mRNA transcripts encoding IFN τ - and P4-induced proteins in the caruncular (CAR) and intercaruncular (ICAR) tissues of the uterine endometrium at maternal recognition of pregnancy (MRP), and that MIX-form Se increases length of the conceptus. To expand upon previous findings, we used RNA-sequencing herein to investigate transcriptomic changes in the ICAR tissue of the endometrium at MRP. Twenty Angus-cross heifers underwent a 45-day period with no supplemental Se (depletion) followed by a 45-day period with ISe alone (repletion). Heifers were then randomly assigned to treatment of a vitamin-mineral mix containing 35-ppm Se as ISe (n = 10), or 1:1 mixture of ISe:OSe (n = 10, MIX) for 90 days before insemination. Heifers were then killed on d17 of presumed pregnancy. Reproductive tracks and conceptuses were collected and only heifers with a fully intact conceptus were utilized for further analyses (n = 6 per treatment). RNA-sequencing was conducted on total mRNA from ICAR biopsies to explore the transcriptomic effects in response to form of Se. Differences in gene expression were determined using Differential Expression and Pathway Analysis (iDEP.96), and differentially expressed genes (DEG) were subjected to canonical, functional, and network analyses using QIAGEN's Ingenuity Pathway Analysis (IPA). RT-PCR was used to corroborate RNA-sequencing results. At P < 0.05, there were 838 DEGs with 427 transcripts upregulated, and 411 transcripts downregulated in MIX versus ISe heifers. The top canonical pathway upregulated in ICAR tissue of MIX versus ISe heifers was oxidative phosphorylation with upregulated transcripts encoding components of complex I (NADH dehydrogenase), complex III (cytochrome c reductase), and the rate limiting complex IV (cytochrome c oxidase). This suggests an increase in the production of ATP in the ICAR of MIX supplemented heifers compared to ISe. An increase in energy may permit the MIX-form to meet an increase in demand for glucose and nutrients, consistent with the increase in conceptus length previously observed at MRP. Additionally, we observed significant effects on the abundance of transcripts encoding proteins in the canonical Wnt signaling pathway (DKK1, FZD6, LRP6, CTNNB1) in MIX compared to ISe indicating a change in the signal transduction pathway that affects cellular

proliferation and functions during this peri-implantation period. Overall, results to date are consistent with our premise that supplementation with MIX as a 1:1 ratio of ISe and OSe, versus ISe as the industry standard, induces a more favorable physiological response at the establishment of pregnancy in beef cattle consuming forages grown on Se-poor soils.