Integrated transcriptome and multi-tissue mineral analyses of healthy stocker cattle fed complexed or inorganic trace mineral supplement

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Introduction

Trace mineral supplementation is common in beef cattle production, however the impact of supplementation on inflammatory signaling and immunity in high-risk cattle remain unclear. We employed high-throughput RNA sequencing and multi-tissue mineral analyses to identify specific genomic mechanisms and spatial mineral trends related to ad libitum mineral supplementation.

Materials and methods

High-risk beef steers (n = 56; ~231 kg) were randomly stratified into one of 3 supplement groups fed over 60 days: 1) sulfate-sourced Cu, Co, Mn and Zn (INR; custom blend), 2) amino acid-complexed Cu, Mn, Co and Zn (AAC; Zinpro Availa© 4), or 3) amino acid-complexed Cu, Mn, Co and Zn (Availa 4) plus trace mineral and vitamin drench (Zinpro ProFusion™) (COMBO). Individuals never diagnosed with clinical disease were included in this study. Serum and liver biopsies (n = 9 INR; n = 6 AAC; n = 10 COMBO) were analyzed for Cu, Co, Mn and Zn concentrations at d0, d28, and d60. RNA samples (n = 4 INR; n = 4 AAC; n = 4 COMBO) from whole blood at d0, d13, d28, d45, and d60 were sequenced (NovaSeq 6000; ~43M reads/sample) and bioinformatically processed through ARS-UCD1.3 reference-guided assembly (HISAT2/Stringtie). Differences and correlations of mineral concentrations were performed with generalized linear mixed-models and Spearman's Rank coefficients, respectively ($P < 0.05$). Differentially expressed genes (DEGs) were identified with glmmSeq and edgeR (FDR < 0.05). Functional enrichment analyses of DEGs were performed with KOBAS-i (FDR < 0.05).

Results

Minimal differences were observed between AAC versus COMBO (n = 2 DEGs) and INR versus COMBO (n = 0 DEGs) across time. The AAC versus INR comparison resulted in 107 DEGs (d13-d60) with the following traits increased in AAC: metabolism of carbohydrates/fat-soluble vitamins, antigen presentation, ATPase activity, B- and T-cell activation. Osteoclast differentiation and neutrophil degranulation were both decreased in AAC, compared to INR. Serum and liver levels of Cu and Co increased overtime in all 3 groups, with liver Cu levels increased in COMBO (487.985 µg/g) versus AAC (392.043 µg/g) at d60 ($P = 0.013$). Serum and liver Cu concentrations (ρ=0.579, $P = 6.59e-08$) and serum and liver Co concentrations (ρ=0.466, $P = 2.80e-05$) were linearly correlated.

Significance

This study identified gene expression differences in high-risk cattle fed either inorganic or amino acid-complexed mineral supplements, centered around adaptive immune-mediated and metabolic mechanisms increased in AAC when compared to INR. Liver and serum concentrations of Cu, Mn, Co and Zn were statistically similar between all 3 groups overtime, with Cu and Co levels within serum and liver samples possessing positive linear correlation. Further trace mineral research identifying differences in cattle requiring treatment for clinical disease is forthcoming.

