

Longitudinal study on the influence of vaccination, marketing and BRD outcomes on gene expression in beef cattle

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Introduction

Bovine respiratory disease (BRD) is a multifactorial disease complex resulting from the interaction of various pathologic, immune-mediated and management-driven factors. Specifically, management decisions around vaccination against viral components of BRD, marketing through commercial sale systems, and long-haul shipping of cattle modulate the bovine immune system and susceptibility to disease. Therefore, we investigated these factors and their influence on immunomodulation via RNA sequencing methodology.

Materials and methods

To investigate the role that vaccination and marketing systems play in BRD susceptibility, jugular whole blood was collected from 73 bull calves enrolled in a whole-plot, split-plot time-course study. Thirty-three calves were randomly selected to receive a modified live virus vaccine (Pyramid[®] 5; VAC), while 40 did not (NOVAC). Forty calves were transported directly from cow-calf to backgrounding (DIR), while 33 spent time in an auction setting for 3 days prior to transport (AUC). Blood was collected at 6 timepoints: immediately prior to vaccination or not (T1; ~107d), 7 days-post vaccination (T2; ~114d), and immediately prior to booster or not (T3; ~183d), at weaning prior to marketing (T4; ~230d), backgrounding facility arrival (T5; ~234d), and end of backgrounding (T6; ~279d). Throughout the study, cattle were monitored daily for signs of clinical BRD; no signs of BRD were identified at T1-T4. RNA was extracted and sequenced (150 bp; ~35 million reads/sample), and bioinformatically processed with a HISAT2/StringTie2 pipeline. Gene expression was evaluated for differences associated with vaccination, marketing enrollment, and BRD development via edgeR and glmmSeq at T4-T6 (FDR<0.05). Functional enrichment analyses were performed in g:Profiler and KOBAS-i (FDR < 0.05).

Results

At the fourth timepoint, 3, 4 and 18 DEGs were identified for marketing strategy, vaccination and BRD during backgrounding, respectively. Genes involved in later BRD development enriched for oxygenation and lipid metabolism (decreased in BRD), as well as cellular scavenging and leukocyte migration (increased in BRD). At the fifth timepoint, 834, 56 and 364 DEGs were identified for marketing strategy, vaccination and BRD during backgrounding, respectively. Genes involved in vaccination enriched for extracellular matrix organization and neutrophil degranulation, antimicrobial peptides, interleukin

signaling and scavenging by class A receptors (all increased in NOVAC). Genes involved in marketing enriched for neutrophil degranulation, interleukin signaling, type I and II interferon signaling, cellular response to stress, and cornified envelope formation and keratinization (all increased in AUC). Genes involved in BRD enriched for cytokine signaling, interferon signaling, interleukin signaling, neutrophil degranulation and phagocytosis (all increased in BRD). At the sixth timepoint, 135, 17, and 3 DEGs were identified for marketing strategy, vaccination, and BRD during backgrounding, respectively. Genes involved in marketing enriched for cell tight junction formation, cornified envelope formation and keratinization, and interleukin signaling (all increased in AUC).

Significance

These findings improve our understand of the roles that vaccination and marketing play in cattle health and immune function. Additionally, the differentially expressed genes associated with BRD may be utilized as predictors of future BRD diagnosis and outcome in backgrounding systems. Future directions consist of evaluating the interactions of vaccination, marketing and BRD outcome on gene expression with changes in the nasopharyngeal microbial community, to better understand the dynamic nature of BRD in context of management schemes.

