Transcriptomic profiling of BRD-attributed mortality in stocker cattle identifies active inflammatory and antiviral pathways at arrival

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Introduction

Diagnosis and management of bovine respiratory disease (BRD), the most significant disease complex in post-weaned beef cattle, relies predominantly upon nonspecific clinical signs. Research is necessary to discern the underlying biological processes associated with BRD acquisition and severity. We hypothesize that at-arrival whole blood transcriptomes of stocker cattle will distinguish host immunologic responses that influence BRD severity, defined by BRD-attributed mortality.

Materials and Methods

Whole blood samples were obtained at arrival from 6 beef cattle that developed BRD within 28 days of facility arrival. Animals were categorized into 2 cohorts based on BRD-attributed mortality; (n=3 ALIVE; n=3 DEAD). Sequenced reads (80M/sample; PE 150-bp) were aligned to the ARS-UCD1.2 bovine assembly and processed in a HISAT2/Stringtie/edgeR/DESeq2 pipeline for differentially expressed genes (DEGs). DEGs were evaluated for relevance to BRD with WebGestalt, STRING, Reactome, and GLAD4U.

Results

114 unique DEGs (FDR<0.10) were identified at arrival between ALIVE and DEAD; 46 DEGs used for downstream analysis were shared between edgeR and DESeq2. Biological processes and pathways enriched in DEAD were related to type-I interferon production and antiviral defense. Genes increased in both cohorts possessed functional associations with TLR4 and IL6. Disease phenotyping indicated viral-induced diseases in DEAD.

Significance

These results demonstrate at-arrival enrichment of type I interferon and antiviral mechanisms segregate with poor BRD outcomes. These discoveries present targets for future development to predict BRD mortality. Further investigation to determine if genes associated with increased TLR4 and IL6 activity at arrival are early indicators of fatal BRD are warranted.