Multipopulational transcriptomic analysis of high-risk beef cattle on arrival reveals genes and mechanisms which may predict bovine respiratory disease

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Introduction

Bovine respiratory disease (BRD) continues to impact beef cattle production. RNA-Seq has been employed to investigate host response and gene-by-environment regulatory function in cattle at arrival. Nevertheless, studies have been relatively underpowered, and findings remain disputed. Our objective was to analyze at-arrival blood transcriptomes from beef cattle in 2 populations to identify and corroborate BRD-predictive genes and mechanisms.

Materials and methods

Jugular blood samples were collected from 48 calves across 2 independent populations (n = 24, 2017; n = 24, 2019); each included 12 cattle that were diagnosed with BRD within 14 days of arrival, and 12 never demonstrating clinical BRD. Sequenced reads (NovaSeq 6000; ~50M paired-end reads/sample) were processed through ARS-UCD1.2 reference-guided assembly (HISAT2/Stringtie). Sampled cattle were categorized into disease severity cohorts (healthy, treated_1, treated_2+) via frequency of antimicrobial treatment and mortality. Differentially expressed genes (DEGs) were identified through edgeR glmLRT testing (FDR < 0.05). Dimensional reduction, clustering and receiver operating curve (ROC) analyses were performed within R. Functional analysis of DEGs was performed in WebGestalt, Reactome, and STRING.

Results

One-hundred and thirty-two unique DEGs were identified between the 3 cohorts. DEGs upregulated in treated_1 were involved in neutrophil activation, cellular cornification/keratinization, and antimicrobial peptide activation. DEGs upregulated in treated_2+ were involved in alternative complement activation, leukocyte proinflammatory activity, and increased nitric oxide production. Multivariate ROC curves using various combinations of six DEGs demonstrated excellent performance in classifying severe BRD (AUC > 0.900).

Significance

We identified DEGs in multiple populations which corroborate findings from previous RNA-Seq experiments. These findings identify genes and mechanisms relevant for predicting BRD development and severity.

