# Time-course RNA-Seq analysis defines immunological and inflammatory mechanisms influenced by bovine respiratory disease

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## Introduction

Bovine respiratory disease (BRD) remains the leading disease in beef cattle. Host gene expression at facility arrival may indicate BRD risk, however, time-course RNA-Seq could define how BRD development influences immunological and inflammatory responses. Here, we evaluated blood transcriptomes of high-risk beef cattle at 3 timepoints to illustrate BRD-associated host response.

## Materials and methods

Sequenced mRNA from 36 cattle (2015: n = 9; 2017: n = 27) across 3 timepoints (n-samples = 100; days 0, 28, 63) were processed through ARS-UCD1.2 reference-guided assembly (HISAT2/Stringtie2). Cattle were categorized into BRD-severity cohorts (Healthy, n = 14; Treated_1, n = 11; Treated_2+, n = 11) via frequency of antimicrobial treatment. Assessment of time-course gene expression patterns within each BRD cohort were modeled via auto-regressive hidden Markov models (EBSeq-HMM; Posterior probability > 0.5, FDR < 0.01). Linear mixed models (glmmSeq) and post-hoc analyses (edgeR quasi-likelihood) identified differentially expressed genes between and across cohorts over time (FDR<0.10).

## Results

A total of 2,580, 2,216 and 2,381 genes changed significantly across time within Healthy, Treated_1 and Treated_2+ cohorts, respectively. In all 3 cohorts, gene expression related to neutrophil response, cytokine production, and type-I interferon response decreased over time. Production of specialized resolving mediators (SPMs) decreased at d 28, then increased by end-of-study (d 63) across all 3 cohorts. SPM production and alternative complement were differentially expressed between Healthy and Treated_2+ at d 0, but identical between all three cohorts by d 63.

## Significance

At-arrival SPM expression, not directionality, differentiated Healthy and Treated_2+ cattle. Host gene expression appeared most variable at arrival, then stabilized between all 3 BRD cohorts overtime. This study demonstrates host expression patterns best define severe BRD development at facility arrival.