Impact of preweaning vaccination on host response in healthy calves during the cow-calf phase of production

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Introduction
One of the most important tools used in managing and preventing bovine respiratory disease (BRD) is vaccination. Although numerous licensed products exist for various viral and bacterial BRD pathogens, the impact of vaccinating young calves prior to weaning on host gene expression is unknown. Therefore, our objective is to explore differences in host gene expression in calves that were vaccinated preweaning or not via time-course transcriptomics.

Materials and methods
Calves were vaccinated twice preweaning (median age d107, d183) with a 5-way modified live respiratory vaccine or not. Jugular blood was collected from 12 calves (n = 6 vaccinated; n = 6 unvaccinated) when the median age was 107, 114, 183 and 230 days; no calves were identified as BRD cases prior to weaning. Isolated blood mRNA from each time point was sequenced (NovaSeq 6000; ~35M reads/sample), and reads were processed through ARS-UCD1.2 reference-guided assembly (HISAT2/ Stringtie). Linear mixed models (glmmSeq; FDR < 0.05) and post-hoc analyses (edgeR quasi-likelihood; [FDR < 0.10]) identified differentially expressed genes between and across vaccine groups overtime. Functional enrichment analyses for biological functions are to be performed with KOBAS-i (FDR < 0.05).

Results
Calves, regardless of vaccination, demonstrated an increase in gene expression over time related to specialized proresolving mediator production, lipid metabolism, and stimulation of immunoregulatory T-cells. Vaccination linked to increased gene expression related to natural killer cell activity and helper T-cell, specifically Th17 cell, activity and decreased gene expression involved in complement activity and coagulation.

Conclusions
This is the first study to evaluate mechanisms of vaccination and development in healthy calves through RNA sequencing analysis. We defined mechanisms of immune system development in young beef calves free of BRD. Furthermore, controlled inflammatory responses were induced by viral vaccination. This work characterized host-driven mechanisms involved in BRD prevention.