How does preweaning vaccination impact gene expression in cattle that remain healthy or develop BRD later in life?

Hudson McAllister,[1] BS, MS; Sarah Capik,[2] DVM, PhD, DACVPM; Bradly Ramirez,[1] BS; Kelsey Harvey,[3] PhD; Robert Valeris-Chacin,[1] DVM, PhD; Brandi Karisch,[4] PhD; Amelia Woolums,[5] DVM, PhD, DACVIM, DACVM; Matthew Scott,[1] DVM, PhD

[1]Texas A&M University College of Veterinary Medicine
Veterinary Education, Research, and Outreach Program, Canyon, TX 79015
[2]Tumbleweed Veterinary Services, PLLC, Amarillo, TX 79118
[3]Prairie Research Unit, Mississippi State University, Prairie, MS 39756
[4]Department of Animal and Dairy Sciences, Mississippi State University, Mississippi State, MS 39762
[5]Department of Pathobiology and Population Medicine, Mississippi State University, Mississippi State, MS 39762

Introduction

Bovine respiratory disease (BRD) remains a priority topic within livestock research. A leading topic of BRD-related research is vaccination of pre-weaned calves to mitigate the effects of BRD post-weaning. Comparison of gene expression pathways in vaccinated and unvaccinated calves that develop or resist BRD would help clarify factors that may result in benefits following vaccination.

Materials and methods

Eighty-four bull calves were enrolled in a whole-plot, split-plot design to quantify the impact of controlled management tactics on health outcomes and performance. First, each calf was randomly assigned to receive vaccination or not (VAX or NOVAX), then assigned to split plot where half of the cattle were directly shipped to a backgrounding facility or, simultaneously, sent to an auction market/order buyer facility prior to shipment (Direct or Auction). Calves were evaluated at 4 timepoints: T1; vaccination (median age = 107 days); T2, 7 days post-vaccination (median age = 114 days); T3, revaccination and surgical castration (median age = 183 days); T4, weaning (median age = 230 days). Blood samples were taken at each timepoint into Tempus™ RNA blood tubes (Applied Biosystems). At T1, calves were tested via ear notch ELISA for bovine viral diarrhea virus (BVDV) persistent infection and received a multivalent respiratory vaccine (Pyramid® 5, Boehringer Ingelheim Animal Health) subcutaneously (VAX) or given 0.9% saline subcutaneously (NOVAX); there were no BVDV-positive calves. At T3, calves were revaccinated identically as T1 and surgically castrated. All calves received a multivalent clostridial bacterin-toxoid subcutaneously (Covexin® 8, Merck Animal Health) at T3. Groups (VAX and NOVAX) were maintained with no direct contact. In the 45-day backgrounding phase, cattle were examined daily by trained caretakers for signs of BRD and treated based on a standard protocol. Cattle were defined as BRD (treated for BRD during backgrounding) or NO BRD (not treated for BRD during backgrounding). Isolated mRNA from each time point was sequenced (NovaSeq 6000; ~35M reads/sample) and reads were processed through ARS-UCD1.2 reference-guided assembly (HISAT2/StringTie2). Following normalization, edgeR and glmmSeq were used to identify DEGs (FDR < 0.05), then were analyzed for functional enrichment of gene ontology terms, Reactome pathways, and KEGG pathways via KOBAS-i (FDR < 0.05). The identity and number of DEG at each time point between VAX and NOVAX cattle, and between BRD and NO BRD cattle, were described.

Results

At T2, there were multiple DEGs between VAX and NOVAX (n = 26) and BRD vs. NO BRD (n = 12). At T3, there were multiple DEGs between VAX and NOVAX (n = 47) and BRD vs. NO BRD (n = 10). At T4, there were multiple DEGs between VAX and NOVAX (n = 32) and BRD vs. NO BRD (n = 51). Overtime, VAX cattle had increased gene expression related to cellular response to stress, neutrophil degranulation, and antigen processing and presentation compared to NOVAX cattle. Cattle diagnosed with BRD later in the backgrounding phase had increased gene expression for pathways related to oxygenation, cellular metabolism, and cytokine signaling compared to cattle which would go on to remain healthy during backgrounding. Time was evaluated by comparing timepoints and blocking for the effects of VAX and BRD, resulting in 10,397 DEGs across all timepoints. These DEGs enriched for pathways related to the innate and adaptive immune system and interleukin signaling.

Significance

This project evaluates the relationship between respiratory vaccination in the early life of beef cattle and long-term health outcomes through state-of-the-art molecular approaches. This first-of-its-kind study identified immune and metabolic genomic mechanisms that may influence health and performance outcomes of cattle in similar production systems. These findings provide a foundation for future research in developing disease-predictive assays and targeted management approaches in commercial beef cattle operations.

