NC1192 Station Annual Report (2022)

NC1192, "An integrated approach to the control of bovine respiratory disease"

Chair: Sharif Aly, BVSc, MPVM, PhD
Secretary: Sarah Depenbrock, DVM, MS, DACVIM (LAIM)

School of Veterinary Medicine, UC Davis.

Participating Experiment Stations (Report submitted):

AL	Auburn University
CA	University of California Davis
KS	Kansas State University
MS	Mississippi State University
TX	Texas A&M University - VERO
WA	Washington State University

Participants of Annual Meeting:

Sarah Depenbrock (UCD), Sharif Aly (UCD), Grant Dewell (IA state), George Smith (NIMSS), Terry Lehenbauer (UCD), Kathe Bjork (USDA NIFA), John Richeson (west TX), Paul Morely (TAMU VERO), Mathew Scott (TAMU VERO), Manuel Chamorro (Auburn), Natalia Cernicchiaro (KSU), Chris Chase (SD state), Mike Sanderson (KSU), Betsy Karle (UCD), David Renter (KSU), Florencia Meyer (MS state), Heather Fritz (UCD), Jared Taylor (OK state), R Pereira (UCD), Jodi McGill (IA state) Bob Larson (KSU), Will Crosby (MS state), Sarah Capik (TX), Amelia Woolums (MS state)

Invited talks/presentations: George Smith (Michigan State University, NIMSS representative), Kathe BJORK (USDA NIFA update).

Annual meeting minutes:

Date: August 31st, 2022; 11 AM- 5 PM EST

Meeting format: online via Zoom platform
https://ucdavis.zoom.us/meeting/register/tJMpdu2srzwpHtwCtBEzU_sRAOIj1wMiEjj7

In attendance: Grant Dewell, George Smith, Terry Lehenbauer, Kathe Bjork, John Richeson, Paul Morely, Mathew Scott, Manuel Chamorro, Natalia Cernicchiaro, Chris Chase, Mike Sanderson, Betsy Karle, David Renter, Florencia Meyer, Heather Fritz, Jared Taylor, R Pereira, Jodi McGill, Bob Larson, Will Crosby, Sarah Capik, Amelia Woolums

11:00-11:20

- Sharif introduced the meeting and current leadership; Sharif Aly (SA) is Chair, Sarah Depenbrock (SD) is secretary.

- Group followed with individual introductions and welcoming new members.
- Sharif encouraged new members or those in attendance without official membership to apply for official membership.

11:20-11:40

- NIFA updates provided by Dr. Bjork (KB) the National Program Leader, Animal Health, Division of Animal Systems, USDA-National Institute of Food and Agriculture. Updates from NIFA are appended to the meeting minutes in a separate document provided by Dr. Bjork entitled, "NIFAUpdate-NC-1192-08092022".
- KB comments regarding what makes a good NIFA grant proposal:
    - Proposal must pass administrative review; recommends authors pay attention to the specifics of the RFA down to the details such as page length and other important criteria that would fail administrative review.
    - Get in touch with NPL (national program leader) to the program area of interest (see attached NIFA update for contact list of NPLs) early in development to help guide applications to the appropriate program for best review.
    - Volunteer to be on a NIFA review panel to get acquainted with proposals and what people are looking for etc.
    - Look in RFA for things that fit. For example, if you are a new faculty, try for a seed grant. Look at ways to strengthen grants based on project types.
    - Do note that these grants are highly competitive, but reviewers want the project to be successful, so pay attention to the reviews if resubmitting (ex, sample size, other methodology critiques) and correct or revise the proposal.
- KB comments regarding NIFA grant funding for the BRD conference associated with NC1192.
    - Apply in 2023 for 2024 conference. Look at RFA for a conference grant. Send the letter of intent 195 d (?) (says in RFA) before the intended event. Note that the grant goes up to $50,000, but be efficient with funds, as requests that high are unlikely to be awarded. The grant will be peer reviewed, similarly o a research proposal.
    - Chris Chase adds - more likely to be successful if you provide the program in the proposal, and apply for $10,000 or less.
    - P Morley adds CRWAD also has used NIFA conference grants, and CRWAD is interested in supporting NC1192 meeting in conjunction
- Announcements from George Smith (administrative advisor to N1192): his role is to guide the group formalities and to help the group be successful. Compliments to the group on how far the group has come; good work buying in to the process for highlighting collaborations. Notes that signing up for NC1192 is handled by the local university (not handled centrally by the USDA). The process of signing up is simple and signup is encouraged. Notes that a challenge with most multistate groups is setting meeting dates - he recommends we set the next meeting date at this meeting. Notes that the nature of the reporting and what we are supposed to accomplish is to focus on how we can work together, with less emphasis on individual research accomplishments. For

reporting, focus on collaborations and collaborative efforts, with less emphasis on research findings. Projects will be judged at midterm review and 5-year renewal on **collaborative efforts**. Emphasizes that the purpose of this meeting is collaboration. There is also an award for multistate research; competition for this award requires a strong effort for collaboration and an accomplishment that 'moves the needle' for BRD. George is willing to help the group, if interested contact him.

11:40-2:30 Discussion of experiment station reports

- Order of presentation determined by SA and SD - Participants present based on order their state joined the union. *Please note, more details of each station update are included in the final working group report.*
- Manuel Chamorro (Auburn university, # 22): Collaborated with University of TN - evaluated the effect of three different weaning methods on beef calves related to transport and haptoglobin. Also collaborated with MS state - evaluating effects of intranasal mod live vaccination at weaning.
- Amelia Woolums (MS State #20): Notes active collaborations with Al, CA, KS, SD, TX. With KS and TX, investigating haptoglobin and mod live viral vaccine on feedlot cattle. Also briefly notes investigating parasite effect on feedlot performance. With TX, MS and GA, looking at AMR in stocker cattle given Tulathromycin metaphylaxis or not. Notes that she used Paul Morley's method for quantifying *M. haemolytica* on DNPS from total DNA. Discussed MDR increases with metaphylaxis with Tulathromycin, but metaphylaxis does protect against BRD treatment, and is associated with increased weight gain.
- Matthew Scott (TX, #28): Working with whole blood transcriptomes in dairy calves: how time, development, or vaccination affects host gene expression (inflammation, immune response). Very interested in inflammatory mediator mechanisms and responses. No differentially expressed genes at weaning (there were differences at some earlier time points after time zero.); he suggests inflammatory resolution is probably a part of normal development. Also investigating the effect of vaccination and animal marketing processes on host gene expression and disease rate at arrival to feedlot. Specific gene expression is associated with not contracting disease (ex: collagenase).
- Paul Morley (Tx): Compared swab isolations from NS, DNPS double guarded, and Proctology swab (which reaches both nasal and nasopharyngeal) (Proctology swab: https://www.puritanmedproducts.com/816-c.html Double-head 8" proctology swab (i.e., 2x4" swabs) https://www.puritanmedproducts.com/818.html#skucode=818 Single head 8" proctology swab https://www.puritanmedproducts.com/25-808-pr.html#skucode=25-808%201PR Also Compared rope and water trough samples to individual animal swabs and discussed importance of molecular methods for identification of respiratory pathogens, particularly in rope or trough samples.
- Grant Dewall (IA #29): Notes he does not have a station update to share, but wants to follow up on a previous meeting and organize quarterly webinars for research and technology updates. Plans to start in October, **looking for volunteers.**

- Richard Pereira (CA#31): presented a study on the effect of time, temperature and container type/ transport media on *M. haemolytica* isolation.
- Sarah Depenbrock (CA): Presented a study done in collaboration with John Wenz at WSU investigating AMR in respiratory pathogens and enteric marker bacteria in weaned dairy heifers in CA.
- Betsy Karle (CA): Presented a study on dairy calf group housing using a minimally laborintensive method to modify existing plastic hutches with outdoor pens and assessing health outcomes, behavior and growth in Northern CA.
- Sharif Aly (CA): Presented a related study to Karle on simple modifications to central valley wooden calf hutches to create group housing and likewise assessed association of housing type to health and behavior outcomes.
- Natalia Cernicchiaro (KS #34): Robust update on several publications her station has accomplished this year. Topics included stall side leukocyte measuring device; predictive models for low mortality cohorts; predictors of heart disease death; and others.
- Chris Chase (SD #40): presented several collaborative research updates including topics related to intranasal vaccine, stall side leukocyte count technology updates, and a novel antiviral therapy.

2:30-2:45 Break

2:45-4:15 Future multistate research & extension collaborations: planning projects, publications, courses, workshops

- SA led discussion on BRD symposium planning for 2024.
    - Committee for BRD symposium assembled: SA and Grant Dewall as co-chairs; SD, Amelia Woolums, Paul Morley, Manuel Chamorro, Natalia Cernicchiaro, John Richeson, Chris Chase as committee members.
        - 1 committee member should be focused on managing funding and corporate sponsorship.
        - Partial funding through NIFA conference grants available to apply for (in grant proposal, recommended to address welfare, AMR, BRD as a model, other areas of potential large impact)
    - Historically BRD symposium held with AVC; considering this for 2024
        - AVC administrative assistant is Sally O'Brian
        - RACE credits can be setup with AVC
    - Proceedings went into Animal Health Researcher Reviews (AAHR) in previous years; advantage = appear on pub med search
    - Past BRD Symposium website 2019: http://brdsymposium.org/

4:15- 4:30 Future meeting locations

- SA led discussion on future leadership.
    - Outcome:
        - 2023 plan: SD to be Chair, Manuel Chamorro to be secretary
        - 2024: secretary to be Mathew Scott

- Future annual meeting plans
    - Morley advocates strongly for incorporating an NC1192 meeting with CRWAD
    - Group discussed moving annual meeting to CRWAD (January 2023) in Chicago, IL.
    - ; **Vote on NC1192 meeting location change:**
        - Motion to switch to CRWAD Jan 2023: Chris Chase
        - Seconded by Amelia Woolums
        - Vote by attendees 12 Yes 1 No
        - Yes: Paul Morley, Terry Lehenbauer, Amelia Woolums, Chris Chase, Natalia Cernichiaro, Sharif Aly, Sarah Depenbrock, John Richeson, Sarah Capik, Florencia Meyer, Grant Dewell, Matthew Scott.
          No: Will Crosby

4:30-5:00 Consensus statement and wrap up.

Accomplishments, impact and deliverables focused on the NC1192 project's objectives

Six stations sent reports for 2022 activities (list of participating stations are on NIMSS website).

SD working on AL, KSU

I. Accomplishments –

Objective 1: *To elucidate pathways by which host characteristics, pathogen virulence mechanisms, and environmental impacts interact to produce BRD, and to develop strategies to mitigate detrimental factors and enhance protective mechanisms.*

1. (CA) A project entitled, "In vitro evaluation of the effect of transport media, temperature, and time on the recovery of *Mannheimia haemolytica* and *Pasteurella multocida*" promoted dialogue and exchange among collaborators in the University of California Davis Veterinary Medical Teaching Hospital (VMTH; Dr Sharif **Aly** and Dr Terry **Lehenbauer**), California Animal Health & Food Safety (CAHFS; Dr Heather Fritz), and Dr. Richard **Pereira** (Veterinary Medical Teaching Hospital [VMTH] at UC Davis, Davis). This project focuses on the evaluation of the effect of transport media, temperature, and time on the recovery of *Mannheimia haemolytica* and *Pasteurella multocida*.

2. (TX) Evaluation of modified live viral vaccination on host gene expression and serum titer levels of beef calves during the cow-calf phase. The USDA funded study (USDA-NIFA #2019-67015-29845) evaluates the whole blood transcriptomes and serum titer levels of calves free of bovine respiratory disease across multiple time points during the cow-calf phase of production, comparing cattle administered a commercial modified live viral (MLV) vaccine to those that were administered a sham control. The study collaborators at Mississippi State University (Amelia **Woolums**, Brandi Karisch) and Texas A&M University (Matthew **Scott**, Sarah **Capik**). Evaluation of the whole blood transcriptomes over time, regardless of vaccine administration, defined a continual increase in gene expression related to inflammatory resolution, fatty acid metabolism, and cytokine-mediated enhancement of acquired immunity. Evaluation of host expression influenced by vaccination depicted an increase in Th17 and natural killer cell activity and differentiation, increase in heat shock protein and cellular chaperone response, and decrease in complement activity in calves having received a MLV vaccine compared to calves having received a sham control. The study also addresses NC 1192 objectives 2, 3, 4 and 5.

3. (TX) Influence of marketing strategies on the at-arrival host transcriptome of beef cattle during the backgrounding phase is a collaboration between at Mississippi State University (Amelia **Woolums**, Brandi Karisch) and Texas A&M University (Matthew **Scott**, Sarah **Capik**) evaluated the whole blood transcriptomes of newly received cattle at a backgrounding operation, to determine differentially expressed genes and mechanisms between cattle marketed directly (Direct) compared to cattle processed through an auction market system prior to transport (Auction). A distinct difference in differential gene expression patterns was determined between the Auction and Direct groups. The

genes contributing to these patterns encoded for antiviral defense (increased in Auction), cell growth regulation (decreased in Auction), immune activation and complement (increased in Auction), inflammatory mediation (decreased in Auction), and skeletal system development (decreased in Auction). Further evaluation of the at-arrival transcriptomes of Auction cattle eventually requiring clinical treatment for bovine respiratory disease compared to Auction cattle which remained clinically healthy throughout the backgrounding phase demonstrated a decrease in gene expression related platelet activation and collagen biosynthesis in diseased cattle. The study was funded by USDA-NIFA #2019-67015-29845. The study also addresses NC 1192 objectives 2, 3, 4 and 5.

4. (TX) Defining genomic mechanisms and immunological complexes involved in bovine respiratory disease through hematological and gene co-expression network analyses. Collaborators at Mississippi State University (Amelia **Woolums**) and Texas A&M University (Matthew **Scott**) applied system biology and weighted network methodology to identify novel at-arrival hematological patterns and genomic mechanisms which strongly correlate with bovine respiratory disease development and severity. The USDA funded work (USDA-NIFA #2020-67016-31469) provides evidence that genes related to alpha-beta T-cell complexes and Th2-type immunity possessed significant correlation with increased erythrocytes, platelets, and respiratory disease development. Genomic mechanisms involved in mitochondrial metabolism and rRNA maturation possessed significant correlation with increased at-arrival eosinophil concentration, fecal egg count per gram, and weight gain over time. Finally, they identified an interactive hub gene network of 52 proteins which may possess transient function involved in BRD development not previously described in scientific literature. The study also addresses NC 1192 objectives 2, 3, 4 and 5.

5. (TX) Defining genomic mechanisms and immunological complexes involved in bovine respiratory disease through hematological and gene co-expression network analyses was funded by USDA-NIFA #2020-67016-31469. Collaborators at Mississippi State University (Amelia **Woolums**) and Texas A&M University (Matthew **Scott**) applied system biology and weighted network methodology to identify novel at-arrival hematological patterns and genomic mechanisms which strongly correlate with bovine respiratory disease development and severity. The work provides evidence that genes related to alpha-beta T-cell complexes and Th2-type immunity possessed significant correlation with increased erythrocytes, platelets, and respiratory disease development. Genomic mechanisms involved in mitochondrial metabolism and rRNA maturation possessed significant correlation with increased at-arrival eosinophil concentration, fecal egg count per gram, and weight gain over time. Finally, they identified an interactive hub gene network of 52 proteins which may possess transient function involved in BRD development not previously described in scientific literature. The study also addresses NC 1192 objectives 2, 3, 4 and 5.

6. (TX) Assessment of immunological and inflammatory mechanisms involved in bovine respiratory disease through time-course transcriptomic analyses (TAMU VLCS M. **Scott** startup funds) funded collaborators at Mississippi State University (Amelia **Woolums**,

Brandi Karisch) and Texas A&M University (Matthew **Scott**) utilized a time-course RNA-Seq approach with whole blood from multiple populations of high-risk beef cattle to define how bovine respiratory disease (BRD) risk and development influence gene expression related to immunological and inflammatory functions over time. They identified 2580, 2216, and 2381 genes changed significantly across time within cattle never treated for BRD (Healthy), treated one time throughout their backgrounding phase (Treated 1), and treated twice or more/died during their backgrounding phase (Treated 2+), respectively. In all three cohorts, gene expression related to neutrophil response, cytokine production, and type-I interferon response decreased over time. Production of specialized resolving mediators (SPMs) decreased by 28 days on feed, then increased by end-of-study (~63 days) across all three cohorts. Genes involved in SPM production and alternative complement were differentially expressed between Healthy and Treated 2+ at arrival, but identical between all three cohorts by end-of-study. The study also addresses NC 1192 objectives 2, 3, 4 and 5.

7. (SD) **South Dakota State** investigators are collaborating with the **National Animal Disease Center** in Ames on mass spectrometry for proteomics analysis of BVDV-infected macrophages. Freshly isolated macrophages were infected with either of 3 strains of BVDV: severe acute ncpBVDV2a 1373 strain, the moderate virulent ncp2a 28508-5 strain, and cpBVDV1b TGAC. The supernatant from these different BVDV infected macrophages was then used to treat neutrophils. The determination of the effect of BVDV infected supernatants of neutrophils oxidative burst activity is in process. ongoing.

Objective 2: *To develop and validate methodologies for accurate BRD diagnosis, objective risk assessment, and surveillance to detect new trends in BRD occurrence.*

1. (AL) Serum Haptoglobin levels before and after transport to backgrounder farm in beef steers weaned by 3 different methods. Serum Haptoglobin is an important acute phase inflammatory marker of cattle. Increased serum levels of Haptoglobin have been described in stressed weaning-age beef calves following transport and in calves undergoing other disease conditions such as bovine respiratory disease (BRD). Researchers from Auburn University (Maggie Justice, Kim Mullenix, Soren Rodning, and Manuel F. **Chamorro**) in collaboration with **The University of Tennessee** (Liesel Schneider) assessed the effects of 3 different weaning methods (Abrupt, Fence-line, and Nose-flap) on the levels of serum Haptoglobin of beef steers from 3 different sources immediately before and 24h and 14 days after transport (6 hours) to a backgrounder farm. The mean serum Haptoglobin levels immediately before transport and 14 days after transport were similar and comparable among steers from different treatment groups; however, the mean serum Haptoglobin levels 24h after transport were significantly increased in Abruptly-weaned steers compared with Fence-line and Nose-flap groups (0.09 mg/mL vs. 0.02 and 0.02, respectively). The mean ADG during the first 15 days of arrival to the backgrounder farm was significantly lower in Abruptly-weaned steers compared with Fence-line and Nose-flap groups (0.4 kg/d vs. 1.1 and 0.8, respectively. Based on preliminary results of this study, abrupt weaning appeared to promote a pro-inflammatory phenotype and reduced performance in beef steers following transport. Reducing pro-inflammatory responses during weaning and transport improves performance of beef calves during the early backgrounding period.

2. (KSU) Blood leukocyte differentials can be useful for understanding changes associated with BRD progression. Collaborative research between industry representatives from **Merck Animal Health** (J. Nickell and J. Hutcheson), and from **Veterinary and Biomedical Research Center** (K. Lechtenberg and C. Cull) and investigators at **KSU** investigated BRD disease progression in 30 Holstein steers challenged with bovine herpesvirus 1 and *Mannheimia haemolytica* using point-of-care and laboratory-based blood leukocyte differentials. Point-of-care leukocyte, lymphocyte, and neutrophil concentrations were significantly associated with the respective cell concentrations obtained from the laboratory-based leukocyte differential. Cell concentrations reported by both assays differed significantly over time, indicating shifts from healthy to viral and bacterial disease states. Lymphocyte concentrations, lymphocyte/neutrophil ratios obtained from both assays, and band neutrophil concentrations from the laboratory-based assay were significantly associated with lung consolidation, enhancing assessments of disease severity. The point-of care leukocyte differential may be a useful alternative to assess BRD progression by improving turnaround time and providing logistical advantages compared to laboratory-based assays (Baruch et al., 2021).

3. (KSU) Collaborative research between an academic partner from another institution (L. Wisnieski; College of Veterinary Medicine, **Lincoln Memorial University**, Harrogate,

TN) and investigators from **KSU** used classification models including logistic regression, decision tree, random forest, discriminant linear, and naïve Bayes to identify risk status of cattle cohorts within the first 45 days of arrival. Accuracy in discriminating BRD risk between models ranged from 10.9% to 79.4%. Sensitivity and specificity ranged from 44.7% to 100%, and 0% to 83.7% respectively. Random forest was most accurate and correctly identified 42 of 47 high risk cohorts (sensitivity: 89.4%). Specificity was 60.6%. Random forest models were accurate when classifying cohorts entering the feedlot as low risk (Rojas et al., 2022). Similarly, random forest models to predict weekly mortality for cattle purchase groups from arrival at the feeding location (Day 1) to Day 42 and cumulative mortality from Day 43 until slaughter were built using records, weather, and transport data available at the time of purchase. The models performed well among purchase groups with low weekly mortality but performed poorly in high mortality purchase groups. Although high mortality purchase groups were not accurately predicted utilizing the models in this study, the models may potentially have utility as a screening tool for very low mortality purchase groups after arrival (Wisnieski et al., 2022).

4. (WA) A USDA-NIFA funded proposal between PD Seabury from **Texas A &M** and Co-PD **Neibergs** was continued to identify pathogen profiles and loci associated with enhanced resistance to BRD in 1000 pre-weaned calves in Ohio. Bacteriology and virology are being used to identify pathogen profiles from mid-nasal and deep pharyngeal swabs and Illumina BovineHD BeadChips will be used for genotyping. Genome-wide association results will be compared with previous results in pre-weaned dairy calves in California and New Mexico. Currently we have about 500 more samples to collect from the dairy. Analysis was also completed on previous samples taken on beef and dairy cattle affected with BRD and the risk of BRD was evaluated by pathogen incidence. This was presented at the annual American Society of Animal Science meeting.

5. (CA) NC1192 collaborators **Depenbrock** and **Aly** from the University of California Davis station collaborated with Wenz from **Washing State University** on a project entitled, “Prevalence of in-vitro phenotypic and genotypic antibiotic resistance in respiratory bacterial isolates from weaned dairy heifers in California with and without respiratory disease and the association with farm level management variables and enteric bacterial minimum inhibitory concentrations". Data analysis related to health records and genomic analyses are ongoing, however significant accomplishments in the surveillance portion of the study have been completed as described below. Antimicrobial drug (AMD) use for bovine respiratory disease (BRD) continues to be concerning for development of antimicrobial resistance (AMR) in respiratory and enteric bacteria of cattle. The scope and impact of AMR in California’s weaned dairy heifer population has not previously been described. This study aimed to provide data regarding AMR in respiratory isolates, and identify relationships between respiratory and enteric AMD susceptibility, in weaned dairy heifers. Antimicrobial resistance, including multidrug resistance, in respiratory isolates appears to be widespread in weaned dairy heifers; this

finding has not previously been reported and raises concern for the future efficacy of AMD used to treat respiratory diseases in weaned dairy heifers. The most prevalent AMR phenotype, using applicable CLSI breakpoints, in the respiratory isolates studied was against tetracycline. Additionally, more than 50% of *P. multocida* isolates were resistant to each of 7 AMD commonly used to treat BRD (florfenicol, gamithromycin, tildipirosin, tilmicosin, danofloxacin, enrofloxacin and tetracycline). Multidrug resistance to tetracycline in addition to other AMD was common in this study; out of 25 different patterns of AMR or MDR, 20 patterns include tetracycline resistance. Enteric bacterial MIC were consistently high for tetracycline; greater than 50% of both *E. coli* and *Enterococcus* spp. isolates had MIC at the highest concentration of tetracycline tested. If the USDA NARMS breakpoint of 4μg/mL is applied, 82 and 63 % of *E. coli* and *Enterococcus* spp. isolates, respectively, would be considered resistant. The *E. coli* isolates in the study population also demonstrated AMR (according to USDA NARMS breakpoints) to gentamicin, ampicillin, trimethoprim sulfamethoxazole and sulfadimethoxine in 2, 17, 25 and 78 % of samples, respectively. The *Enterococcus* spp. isolates in the study population also demonstrated AMR (according to USDA NARMS breakpoints) to tylosin in 26% of samples. Classification of resistance in respiratory isolates to the macrolide AMD gamithromycin and tulathromycin was associated with higher MICs in matched enteric samples from the same calves at the same time points for the same macrolide antibiotics. (Depenbrock et al 2021)

Objective 3: *To develop and validate management practices and responsibly applied therapeutic and preventative interventions, such as vaccines, antimicrobials, and immunomodulators, to minimize the impact of BRD on cattle, producers, and society.*

1. (MS) Quantification of the impacts of pre-weaning vaccination and post-weaning commingling on BRD morbidity and mortality during postweaning backgrounding. In a USDA NIFA funded project, and collaboration between MS (Brandi **Karisch**, Kelsey Harvey, Jane Parish, Amelia **Woolums)** and KS (Brad **White**, Bob **Larson)**, and collaborators at Texas A&M (Sarah **Capik**, Matt **Scott)**, we are determining the impacts of preweaning vaccination and postweaning commingling through an auction market on BRD morbidity and mortality in weaned beef calves during the postweaning backgrounding period. Calves born in one of the cow-calf herds in the Mississippi Ag and Forestry Experiment Station (MAFES) are randomly allocated to groups to be vaccinated against respiratory viruses or not preweaning; calves in each of vaccinated or not-vaccinated treatment groups will be randomly allocated to travel through an auction market and order buyer facility, or not, after weaning. Cattle will then all be transferred to TX for backgrounding. While vaccination and commingling are widely recognized risk factors for BRD, little properly-controlled research has been published to allow objective quantification of the degree of effects of these factors. In 2021 we completed the first of 3 trials and the second of 3 planned trials is underway.

2. (TX) Metaphylaxis for respiratory disease in high-risk stocker cattle: impacts on *Mannheimia haemolytica*, the microbiome and the resistome. Bovine respiratory disease

(BRD) is the leading cause of morbidity and mortality in beef cattle, and mass antimicrobial administration (metaphylaxis) is the most effective prevention. Metaphylaxis can also be life-saving in other livestock and humans, but the practice may be compromised by spread of multidrug resistant (MDR) pathogens. MDR isolates of the BRD pathogen *Mannheimia haemo*lytica can be found in 90% of some cattle 14 days after metaphylaxis. The mechanisms leading to MDR after metaphylaxis are unknown, but rapid transfer of mobile genetic elements (MGE) encoding antimicrobial resistance (AMR) is likely. The study is a USDA NIFA funded collaboration between TX (**Capik, Morley**) and MSU (**Woolums, Karisch)** we are using a randomized field trial assessing treated and untreated conventionally managed cattle, we are 1) comparing prevalence of nasopharyngeal (NP) MDR *M. haemolytica* isolates, AMR genes, and MGE, using culture, susceptibility testing, and whole genome sequencing; 2) comparing NP metagenomes, using 16S amplicon sequencing; 3) comparing the NP resistome, using target-enriched sequencing of AMR and MGE gene sequences; and 4) using target-enriched sequencing to compare absolute abundance of *M. haemolytica* and sequences specific to other BRD pathogens. This approach will provide never before reported description of the ecology of respiratory AMR in cattle receiving metaphylaxis, revealing targets for mitigating AMR.

- In 2021 we completed the fourth of 4 trials required for this research. We collected nasopharyngeal swabs on day 70 from calves in the third of 4 planned trials, and we completed the fourth planned trial, and collected nasopharyngeal swabs from the 84 enrolled cattle at arrival (day 0), day 21, and day 70. ‘
- Importantly, the antimicrobial susceptibility profiles for all *M. haemolytica* isolates from all 4 trials have been determined.
- For all trials together, the BRD morbidity rate at day 21 was 20%; for META cattle across all trials the day 21 BRD morbidity rate was 12% and for NO META cattle it was 28%. For all trials together, the BRD morbidity rate at day 70 was 22%; for META cattle the day 70 BRD morbidity rate was 14% and for NO META cattle the day 70 BRD morbidity rate was 30%
- Regarding *Mannheimia haemolytica* isolation from the cattle: in trial 3, at day 70, *M. haemolytica* isolation from nasopharyngeal swabs for META and NO META cattle was 21% and 13%. For trial 4 cattle, the *M. haemolytica* isolation rate for META and NO META cattle on day 0, 21, and 40 was, respectively, 45% and 41%, 41% and 52%, and 15% and 10%.
- Regarding antimicrobial resistance in *M. haemolytica* isolated from META and NO META cattle at d 0, 21, and 70: when multidrug resistance (MDR) was defined as resistance to antimicrobials in 3 or more classes, the percent of *M. haemolytica* isolated that were MDR on day 0 for META and NO META cattle was 21% and 27%. The percent of isolates that were MDR on day 21 was 69% for META cattle, and 9% for NO META cattle (P = 0.0002). For META and NO META cattle that required additional antimicrobials after arrival (META-TX and NO META-TX), the percent of *M. haemolytica* isolates that were MDR was 100% for META-TX cattle and 53% for NO META-TX cattle.

- The odds of treatment for BRD was 3 times greater for NO META than META cattle (P = 0.0002). However, the proportion of *M. haemolytica* isolated from cattle that received metaphylaxis that were MDR was significantly higher than the proportion of MDR *M. haemolytica* isolates from NO META cattle (P = 0.0002).
- We have also completed isolation of DNA from nasopharyngeal swabs of all cattle in all 4 trials in preparation to begin metagenomic sequencing. We have completed development of the novel targeted pulldown assay to allow identification and sequencing of *M. haemolytica* genomes in total DNA isolated from bovine nasopharyngeal swabs.

3. (AL) Effect of vaccination of young beef calves with an intranasal modified-live virus (MLV) BRSV vaccine within 6 hours of birth on clinical protection against experimental challenge with BRSV at 3.5 months of age. BRSV vaccines are commonly administered to young calves between 3 and 30 days of life; however, maternal antibodies interfere with vaccine responses. Vaccination of young calves with a MLV BRSV vaccine shortly after birth could avoid interference by maternally derived immunity and result in better priming of immune responses before complete absorption of passive antibodies from colostrum. Researchers from Auburn University (Manuel F. **Chamorro**, David Martinez, Thomas Passler, Laura Huber, and Paul H. Walz) in collaboration with Mississippi State University (Amelia **Woolums**) assessed the effect of vaccination of beef calves under 6 hours of age with an IN MLV BRSV on clinical protection against experimental BRSV challenge at 3.5 months of age. Respiratory signs were not observed before challenge. After challenge, respiratory scores were similar between groups. On the challenge day, >40% of calves in each group were febrile and 8% of each group had positive nasal BRSV RT-PCR results. Serum and nasal secretion BRSV-specific antibody titers were similar and consistent with BRSV exposure before challenge in both groups. All calves tested positive for BRSV in nasal secretion samples after challenge and the duration of shedding was similar. Conclusions: Vaccine-virus or natural BRSV exposure occurred before challenge. Based on these results, it appears that vaccination at birth does not offer advantages on immune priming or clinical protection for beef calves in BRSV-endemic cow-calf herds. Results from this study will be presented as a scientific abstract at the 2022 World Buiatrics Congress in Madrid, Spain on Sept 26th, 2022.

4. (AL) Effect of intranasal modified-live virus vaccination in weaning-age beef calves simultaneously challenged with BoHV-1 and BRSV shortly after weaning. About 60.6% of beef calves from cow-calf operations in the United States do not receive any vaccine before weaning. This is concerning for southeastern cow-calf operations where smaller producers market their naïve calves through local sale or auction barns and repeated exposure to respiratory pathogens may occur before arrival to feedlots or backgrounder operations. There is inconsistency on the benefits of vaccination at arrival or delayed vaccination. Researchers from Auburn University (Manuel F. **Chamorro**, David Martinez, Thomas Passler, Shollie Falkenberg, Laura Huber, and Paul H. Walz) in collaboration with Mississippi State University (Amelia **Woolums**) assessed the effect of vaccination of beef steers with a combination vaccine protocol at branding and weaning

(MLV SC/MLV IN) or a single dose of an IN MLV vaccine at weaning on clinical protection against simultaneous experimental challenge with IBR and BRSV. Results from this study are preliminary. Clinical scores and performance outcomes (individual BW and ADG) following challenge were similar between treatment groups. Additional results are pending.

5. (KSU) Collaborative research between **KSU** investigators and industry representatives from Innovative **Livestock Services** (B. Depenbusch) used data from several US feedyards from 2017 to 2020, and found that the probability of a non-infectious heart disease death increased with additional BRD treatments and was modified by placement weight, arrival quarter, and sex. Similarly, days on feed when heart deaths occurred during the feeding period, sex, year and quarter of arrival, and potential effects of cohort demographics related to heart disease death timing were associated with non-infectious heart deaths. Days on feed at death tended to decrease as arrival weight increased; however, this effect was modified by year and quarter of arrival. Steers that died of a heart disease died later (113 d ± 6.28 d) compared to heifers (101 d ± 6.44 d) (Johnson et al., 2022).

6. (KSU) Collaborative research between **KSU** investigators and industry representatives from **Merck Animal Health** (J. Nickell and J. Hutcheson), and **Innovative Livestock Services** (B. Depenbusch) evaluated impacts of different metaphylaxis programs, conventional control approaches and targeted prediction technologies for control of bovine respiratory disease (BRD) on health, beef production, antimicrobial use and economic related outcomes in commercial feedlot calves with different BRD risk status. Pull-and-treat programs resulted in less antimicrobial use than metaphylaxis, significantly more cattle became morbid and died, and less total beef production occurred when metaphylaxis was not used. Targeted prediction technologies, provided promising results in terms of reducing the number of BRD antimicrobial treatments (Horton et al., 2021 and 2022; Nickell et al., 2022).
7. (TX) Impact of management decisions during the cow-calf, backgrounding, and feedlot phases of beef production on BRD morbidity and mortality risks was funded by USDA (AFRI; 2022) and is in its year 2 of 3 years of live animal data collection. The study led by **S.F. Capik**, **R.L. Larson**, **B.J. White**, D.E. Amrine, **A.R. Woolums**, J. Parish, **B.B. Karisch** will 1) examine the effect of vaccination twice during preweaning on preweaning performance and BRD morbidity and mortality during backgrounding; 2) quantify the impact of marketing decisions on BRD morbidity, mortality, and performance by comparing weaned beef calves sent directly to a backgrounding operation or sent via an auction market and order buyer; and 3) evaluate associations between pen and yard level management factors and health outcomes during the feedlot phase of production. The objectives of the study are to quantify the impact of vaccination twice during preweaning on performance and BRD morbidity and mortality during the subsequent backgrounding phase; determine the impact of exposure to animals from multiple sources on BRD morbidity, mortality, and performance by comparing weaned

beef calves sent directly to a backgrounding operation to calves sent via an auction market and order buyer; determine associations between pen and yard level management factors and health outcomes during the feedlot phase of production. The study also addresses NC 1192 objectives 1 and 4.

8. (TX) Metaphylaxis for respiratory disease in high-risk stocker cattle: impacts on *M. haemolytica*, the microbiome, and the resistome is a USDA NIFA AFRI project in its live animal data collection phase led by Sarah **Kapik** and collaborators **A.R. Woolums**, **B.B. Karisch**, W.B. Epperson, J.R. Blanton, J.G. Frye, C.R. Jackson, **P.S. Morley**, K.E. Belk, **S.F. Capik.** The project determines the factors that most importantly contribute to expansion of MDR in BRD to help veterinarians and cattle producers use evidence-based practices to maintain cattle health and preserve AM efficacy, which is necessary to support the sustainability of U.S. cattle production. Following metaphylaxis, high rates of MDR in *M. haemolytica*, the bacteria most commonly isolated from lungs of cattle with acute BRD, have been found. Long-acting macrolides and other classes of AM are valuable tools for the control and treatment of BRD, but the MDR seen in *M. haemolytica*, *Pasteurella multocida*, and other bacterial respiratory pathogens threatens our ability to keep cattle healthy. The MDR in BRD pathogens is likely driven by transfer of mobile genetic elements (MGE), such as plasmids or integrative conjugative elements (ICE), between bacterial genera. Assessment of the bacterial metagenome of the bovine respiratory tract reveals numerous other taxa that may harbor MGE and contribute to the ecology of resistance. Scientists have emphasized the importance of "background bacteria", members of the microbiome that are not known to be pathogenic, as being critical reservoirs for AMR genes that can be transferred to pathogens. However, there is still much that is not known about the role of the larger, entire microbiome as it relates to AMR in cattle given AM to control or treat BRD. This proposed research has important foundational relevance, as it will provide novel information about the true expanse of the resistome in cattle given metaphylaxis. The objectives of the project are to compare the prevalence of AMR genes and MGE in MDR *M. haemolytica* isolated from nasopharyngeal swabs (NPS) of cattle given tulathromycin META or not, and/or other AM treatment; and describe genomes or genetic elements of known bacterial BRD pathogens in the nasopharyngeal metagenome of cattle given META or not, and/or other AM treatment.

9. (SD) **South Dakota State** collaborators conducted intranasal vaccines trials to measure mucosal responses in collaboration with **MS, IA**, and **NADC**. Improved mucosal measurements. Conducted a dairy cow transition response to intranasal vaccines with MS. Demonstrated higher levels of IFN following administration vs control animals.

10. (SD) **South Dakota State** collaborators developed a dual challenge model in collaboration with **SD, OK, ONTARIO;** BVDV with M. haemolytica- in a vaccine comparison study with **OK** and **NADC**. The dual challenge model was successful, as

indicated by the BVD PCR results, lung lesion development and microscopic attributes of lung lesions. colostrum-fed dairy X beef calves were vaccinated at ~30 days of age with either a placebo (CON), an adjuvanted parenteral vaccine containing modified live BVDV type 1 and type 2, bovine herpesvirus 1 (BHV-1), bovine parainfluenza virus (PI3) and bovine respiratory syncytial virus (BRSV) and *M. hemolytica* toxoid (Pyramid® 5 + Presponse® P5P) or intranasal temperature-sensitive (TS) BHV-1-BRSV-PI3 (Inforce® 3) along with a parenteral vaccine containing modified live BVDV type 1 and type 2 and *M. hemolytica* toxoid (One Shot® BVD)(IOB). The calves were challenged ~150 days post vaccination with BVDV 1b and then 7 days later with *M. hemolytica*. The calves were than euthanized 6 days after the *M. hemolytica* challenge. Clinical signs following BVDV infection were similar in all groups. There was increased rectal temperatures in the IOB on day 7 post BVDV infection. Following *M. haemolytica* infection, temperatures in the CON and IOB groups were significantly elevated. The Pyramid® PVP5 vaccinated animals had no leukopenia following BVDV infection while the CON and the IOB groups had similar levels of leukopenia. BVDV type 1 and 2 serum titers increased following the vaccination with P5P while the BVDV type 1 and 2 serum titers waned in the CON and the IOB groups. The BVD PCR results for buffy coats and nasal swabs indicated higher levels of virus present in CON and IOB versus P5P. Gamma interferon response was higher in animals vaccinated with P5P than CON and IOB groups signifying greater immune memory. P5P had the lowest percent pneumonic tissue (1.6%) among the treatment groups owing to a preponderance of fibrocollagenous matrix expanding interlobular septa and impeding lesion advancement. Lesion development was significantly higher in the IOB vaccinates (3.7%) and not surprisingly was greatest in the CON group (5.3%). Coagulative parenchymal necrosis and necrotic inflammatory cells, the so-called "oat cells" were visualized in microscopic pulmonary lesions across vaccinate groups, inferring *M. haemolytica* underlies parenchymal lung disease although the degree of necrosis and presence of oat cells differed between the vaccinates and was far less in the Pyramid vaccinates owing to lesion reparation and healing

11. (SD) **South Dakota State** collaborators conducted *in vitro* alternative anti-viral therapies with botanicals in collaboration with SD, **MS** and **TX**. Madin-Darby Bovine Kidney (MDBK) cells, Bovine Turbinate (BT) cells, and Human Rectal Tumor-18 (HRT-18)cells were used as in vitro culture systems for BVDV, BRSV and BCV, respectively. Cytotoxicity was established using serial dilutions of oleandrin or PBI-05204. Noncytotoxic concentrations of each drug were used either prior to or at 12 h and 24h following virus exposure to corresponding viruses. Infectious virus titers were determined following each treatment. Both oleandrin as well as PBI-05204 demonstrated strong antiviral activity against BVDV, BRSV, and BCV, in a dose-dependent manner, when added prior to or following infection of host cells. Determination of viral loads by PCR demonstrated a concentration dependent decline in virus replication. Importantly, the relative ability of virus produced from treated cultures to infect new host cells was reduced by as much as 10,000-fold at non-cytotoxic concentrations of oleandrin or PBI-05204. The research demonstrated the potency of oleandrin and PBI-05204 to inhibit infectivity of three important enveloped bovine viruses in vitro. These data showing non-

toxic concentrations of oleandrin inhibiting infectivity of three bovine viruses support further investigation of in vivo antiviral efficacy.

12. (SD) **South Dakota State** collaborators had an NFIA Grant with OK "Does Selection of Beef Cattle for Growth and Carcass Traits Impact Post-Weaning Immunological Phenotype and Robustness Traits?"

Objective 4: *To determine how attributes of cattle production systems including epidemiologic, societal, and economic forces contribute to BRD, and to develop ways to promote changes in those systems to reduce the occurrence of BRD and improve cattle health, welfare, productivity and antimicrobial stewardship.*

1. (KSU) Collaborative research between **KSU** investigators and industry representatives from **Veterinary Research & Consulting Services LLC** (M. Theurer) evaluated risk factors associated with morbidity in the middle and late portions of the feeding phase. Researchers found that quarter of arrival was associated with cohort-level BRD morbidity; specifically, cattle arriving in the second quarter were more likely to be middle or late BRD compared to cattle arriving in the other quarters (Smith et al., 2022).

2. (CA) Collaborators **Aly** and **Karle** from UC Davis and UC ANR designed two trials that investigate the effects of simplified group housing of preweaned dairy calves on bovine respiratory disease under two different management conditions. The block randomized trials occurred in Northern California's less intensive management using communal plastic housing system (3 calf), and Southern California's intensive management using wooden hutches which are characteristically three-unit individual hutches with the two middle dividers removed to create a group hutch. Compared to individual on either location, group housed calves had higher cumulative incidence of BRD compared to individually housed calves, although the difference was statistically significant only in S. CA. In N. CA group plastic hutch calves had a cumulative BRD incidence of 76.2% compared to in 71.4% in calves raised in individual plastic hutches. In S. CA group housed calves had a cumulative BRD incidence of 67% compared to 48% in individually housed calves (P 0.04). Investigators: Sharif **Aly**, Terry **Lehenbauer**, Essam Abdelfattah, Martin Breen from UC Davis and Betsy **Karle** from UC Agriculture and Natural Resources Division.

3. (TX) Evaluating the impact of whole life health history on lung lesions and slaughter data in beef calves is a study led by Sarah **Capik** (startup funds) in collaboration with **A.R. Woolums**, K. Harvey, **B.B. Karisch**, Ty Lawrence, **M.A. Scott.** The study will explore associations with prior health events, antimicrobial treatments, and lifelong performance data with lung lesions and slaughter characteristics. The cattle are a part of the USDA funded project "Impact of management decisions…" and will provide the opportunity for unique additional data collection with minimal additional input of resources. This project is reminiscent of the ranch to rail project that was discontinued, but on a smaller scale and with a greater amount of detail to the health data. The study also addresses NC 1192 objectives 1 and 3.

Objective 5: *To promote dialogue and exchange among scientists, veterinarians, allied industry professionals and cattle producers to advance BRD research initiatives, to implement outreach, to disseminate research results, and to facilitate the translation of research findings to practical field applications*.

- The results of collaborative research with investigators from **KSU** have been presented in local, regional and international conferences, including the World Buiatrics Congress, The Conference of Research Workers in Animal Diseases and Phi Zeta Day at the College of Veterinary Medicine, at Kansas State University.

- Participants from **WA** administered three lectures on genomic selection and BRD to undergraduate students.

- **SD** contributed to an International collaboration with University of Sao Paulo on BRD symposium with WI and MS.

- **SD** station members developed a 2-day preconference seminar on bovine vaccinations with OH, MO and MS.

- **SD** station members published a book on Bovine immunology with MI, MS, and OH.

Objective 6: *To assess the economic impact of BRD across different sectors of cattle industry.*

II. Impact

Objective 1:

- (AL) Development of vaccination strategies for cow-calf operations to reduce disease caused by BRSV infection in young calves.
- (WA) Further the understanding of the etiology of BRD and the role that specific pathogens play in BRD in beef feedlot animals and in dairy calves. Provide additional genomic tools for selection of animals resistant/resilient to BRD
- (CA) The manuscript entitled, "In vitro evaluation of the effect of transport media, temperature, and time on the recovery of *Mannheimia haemolytica* and *Pasteurella multocida*" generates practical data on potential factors that could result in a lower recovery of bacteria from deep nasopharyngeal samples; these data are directly relevant to researchers, veterinarians, and producers.
- (TX) Research projects led by Matthew **Scott** and collaborators define host gene expression patterns and genomic mechanisms involved in BRD risk and development. Utilizing cutting-edge next generation sequencing techniques, these findings distinguish potential predictive biomarkers of BRD development and severity, and capture genomic mechanisms indicative of cattle which remain healthy in high-risk settings. Specifically, evaluation of modified live viral

vaccination on host gene expression and serum titer levels of beef calves during the cow-calf phase is the first study to transcriptomically evaluate how host immunity and inflammatory mechanisms are influenced by both time (i.e., development) and MLV vaccines commonly used to control BRD. Our findings indicate mechanisms of immunocompetency in calves never clinically diagnosed with BRD, regardless of vaccine administration, and gene expression related to MLV-induced inflammatory responses involving natural killer cells and Th17 cell promotion. The second study on the influence of marketing strategies on the at-arrival host transcriptome of beef cattle during the backgrounding phase is the first to transcriptomically evaluate how marketing systems influence host gene expression at arrival of post-weaned beef cattle, and the overall association with clinical bovine respiratory disease development. These identified gene expression patterns and differences in at-arrival mechanisms found in blood better our understanding of respiratory disease development and risk as influenced by marketing system strategies. The third study on the genomic mechanisms and immunological complexes involved in bovine respiratory disease through hematological and gene co-expression network analyses allowed for better understanding of gene expression and cellular hematological activity in cattle at arrival, and the discovery of molecules and biological complexes that may predict BRD before the onset of clinical signs. The fourth study which assess the immunological and inflammatory mechanisms involved in bovine respiratory disease through time-course transcriptomic analyses illustrates that host gene expression in high-risk beef cattle is most variable at facility arrival, but stabilizes and appears more alike over time, regardless of BRD treatment; these may be defining mechanisms of compensatory growth in high-risk cattle. Furthermore, this study supports the idea that host gene expression patterns are best defined for BRD development and severity at facility arrival.

- (TX) Research projects led by Sarah **Capik** on the Impact of management decisions during the cow-calf, backgrounding, and feedlot phases of beef production on BRD morbidity and mortality risks will explore the impact of preweaning and marketing management decisions on inflammatory mediators and whether they are predictive of health outcomes or performance during backgrounding. This project will provide novel information regarding common preweaning and marketing management decisions. Available data and the expertise of our team will also allow us to innovatively assess the effects of feedlot management factors on BRD risk. Our over-arching goal is identifying management interventions that reduce BRD incidence and thus decrease the need for therapeutic or preventative antimicrobials. Our goals and this project are directly related to the Animal Health and Disease program area priority of disease prevention and/or control via more effective management approaches. The project on the impact of whole life health history on lung lesions and slaughter data in beef calves provides the opportunity for unique additional data collection with minimal additional input of resources. The project on the metaphylaxis for respiratory disease in high-risk stocker cattle will provide novel information about the true expanse of the resistome in cattle given metaphylaxis.

- (SD) MLV CP vaccines may impair neutrophil migration reinforcing the importance of delaying vaccinate around times of stress. Indirect effect of BVDV-infected macrophage supernatant on neutrophil function.

Objective 2:

- (KSU)Chute-side technologies for BRD detection such as the use of a point-of care leukocyte differential may be a more useful and practical alternative to assess BRD progression than laboratory-based assays. Similarly, we increased our knowledge on risk factors for BRD morbidity; specifically, arrival quarter was associated with the timing of BRD morbidity.
- (CA) The cross-sectional study reported by Depenbrock et al 2021 reports the proportion of resistance (lack of susceptibility) in the respiratory bacterial isolates *P. multocida, M. haemolytica*, and *H. somni* in weaned dairy heifers in California. Additionally, this study reports the MIC distribution for enteric indicator bacteria *E. coli* and *Enterococcus* to the same panel of AMD. The proportions of AMR observed in this study suggest widespread lack of susceptibility (>50% of isolates tested) of *P. multocida* and *M. haemolytica* to many AMD commonly used for treatment or control of BRD including: tildipirosin, tilmicosin, danofloxacin, enrofloxacin and tetracycline. Most (>50%) *P. multocida* isolates were also classified as not susceptible to florfenicol and gamithromycin. Multidrug resistance was common in respiratory isolates, making up 76% (110/145), 70% (83/119), and 30% (29/97) of *P. multocida, M. haemolytica* and *H. somni* isolates respectively. The frequent classification of AMR and MDR in respiratory isolates from a cross-sectional sample of weaned heifers suggests a potentially serious problem of AMR in respiratory pathogens of this population of animals and warrants further investigation and improved BRD prevention in this population.

Objective 3:

- (KSU) we learned that the probability of non-infectious heart disease deaths increased with additional BRD treatments and was modified by placement weight, arrival quarter, sex and days on feed. Moreover, when evaluating models for prediction of BRD morbidity and mortality, random forest models performed better for classifying cohorts entering the feedlot as low BRD risk as well as to predict low mortality purchase groups after arrival.
- (MS) Research on the impact of preweaning vaccination and post-weaning commingling on BRD will provide objective data regarding the relative impacts of preweaning vaccination and postweaning auction market exposure on BRD incidence. Such data are surprisingly rare. This information will support the development of models that identify the most cost-effective management strategies to prevent BRD.
- (MS) The research on metaphylaxis in high-risk cattle has provided new information regarding the impact of such an approach on AMR. Importantly, the administration of long-acting macrolide metaphylaxis at arrival was associated with decreased BRD morbidity. However, it is also associated with significant increase in the proportion of *M. haemolytica* isolated from cattle receiving metaphylaxis that are MDR, compared to control cattle not receiving metaphylaxis. These finding could indicate that cattle that receive metaphylaxis and then require subsequent treatment will not respond to antimicrobials, due to MDR. However, future research will be needed to test this hypothesis, as the number of cattle that required treatment for BRD following metaphylaxis was too low to identify such an effect in this study.
- (SD) Several important vaccine findings 1) the development of a protective IgA immune mucosal response with a mucosal vaccines; 2) established a controlled study that demonstrated IFN levels are increased in transition cows at freshening with IN vaccines 3) demonstrated dual BRD challenge model with BVDV and *M. hemolytica* and 4) additional pathological assessment of BRD lesions from the dual model.

Objective 4:

- (CA) Calf group housing is associated with numerous welfare and positive production outcomes however may be associated with greater respiratory disease transmission. Our group housing trials further our understanding of the drawbacks and benefits of group housing with respect to BRD incidence, welfare indicators and production (growth) parameters in calves. the studies show the increase in bovine respiratory disease risk in group housed calves along with the improved social metrics that are positive indicators for calf welfare. Our findings show that no calf housing system is perfect and that there are options and trade-offs for producers to consider when deciding between different calf raising systems. The impact that may have on antimicrobial treatments and hence resistance is the subject of a follow-up study.

Objective 5:

- (WA) Education efforts in 2022 aimed at educating students on the importance of BRD in beef and dairy production; the role of genetics on predisposition to disease; and use of genomic selection to reduce infectious disease
- (SD) Participating in BRD symposium with University of Sao Paulo- SD, WI and MS. Developed a 2-day preconference seminar on bovine vaccinations with OH, MO and MS. Published book on Bovine immunology with MI, MS, and OH

III. Publications/deliverables-

Peer-reviewed scientific publications:

Martinez DA, **Chamorro MF**, Passler T, Huber L, Walz PH, Silvis S, Raithel G, Thoresen M, Stockler R, **Woolums AR**. The titers, duration, and residual clinical protection of passively-transferred nasal and serum antibodies are similar among beef calves that nursed colostrum from vaccinated or unvaccinated dams and were experimentally challenged with bovine respiratory syncytial virus (BRSV) at 3 months of age. *Am J Vet Res* 2022.

Smith K, Amrine DE, Larson RL, Theurer ME, **White BJ**. Determining relevant risk factors associated with middle-day and late-day bovine respiratory disease morbidity in cohorts of cattle. *Applied Anim Sci*. 2022.

Smith K, Amrine DE, Larson RL, Theurer ME, Szaz JI**, White BJ**. Determining risk factors associated with mid- and late-feeding stage bovine respiratory morbidity and mortality based on individual animal treatments. *Applied Anim Sci*. 2022.

Johnson BT, **White BJ**, Amrine DE, Larson RL. Association of feedlot disease treatments on the probability of heart disease syndrome in U.S. feedlot cattle. *Bovine Practitioner*. 2022.

Rojas HA, **White BJ**, Amrine DE, Larson RL. Predicting bovine respiratory disease risk in feedlot cattle in the first 45 days post arrival. *Pathogens*. 2022. 11, 442: 1-14. https//doi.org/10.3390/pathogens11040442.

Wisnieski L, Amrine DE, **Renter DG**. Predictive models for weekly cattle mortality after arrival at a feeding location using records, weather, and transport data at time of purchase. *Pathogens*. 2022: 11(4):473.

Baruch J, **Cernicchiaro N**, Cull CA, Lechtenberg KF, Nickell JS, **Renter DG**. Assessment of bovine respiratory disease progression in calves challenged with bovine herpesvirus 1 and *Mannheimia haemolytica* using point-of-care and laboratory-based blood leukocyte differential assays. *Transl An Sci*. 2021: 5(4):txab200.

Scott MA, Woolums AR, Swiderski CE, Thompson AC, Perkins AD, Nanduri B, **Karisch** BB, Epperson WB. Use of nCounter mRNA profiling to identify at-arrival gene expression patterns

for predicting bovine respiratory disease in beef cattle. BMC Vet Res. 2022. Feb 23;18(1):77. doi: 10.1186/s12917-022-03178-8.

Scott MA, Woolums AR, Swiderski CE, Perkins AD, Nanduri B, Smith DR, **Karisch BB,** Epperson WB, Blanton JR Jr. Multipopulational transcriptome analysis of post-weaned beef cattle at arrival further validates candidate biomarkers for predicting clinical bovine respiratory disease. Sci Rep. 2021. Dec 13;11(1):23877. doi: 10.1038/s41598-021-03355-z.

Scott MA, **Woolums AR,** Swiderski CE, Perkins AD, Nanduri B. Genes and regulatory mechanisms associated with experimentally-induced bovine respiratory disease identified using supervised machine learning methodology. Sci Rep. 2021. Nov 25;11(1): 22916. doi:10.1038/s41598-021-02343-7.

J.N. Kiser, **H.L. Neibergs**. 2021. Identifying loci associated with bovine corona virus in dairy and beef cattle. Frontiers in Veterinary Science - Veterinary Infectious Diseases. https://doi.org/10.3389/fvets.2021.679074

Depenbrock S., **Aly S**., Wenz J., Williams D., ElAshmawy W., Clothier K., Fritz H., McArthur G., Heller M., Chigerwe M.. In-vitro antibiotic resistance phenotypes of respiratory and enteric bacterial isolates from weaned dairy heifers in California. PLoS One. 2021 https://doi.org/10.1371/journal.pone.0260292

Manuscript submitted to Journal of Dairy Science: "In vitro evaluation of the effect of transport media, temperature, and time on the recovery of *Mannheimia haemolytica* and *Pasteurella multocida"*. Authors/co-authors: **Richard Pereira** (corresponding author; UC Davis, PHR, VMTH), Adriana Garzon (Ph.D. student in Pereira Lab), Alejandro Hoyos-Jaramillo (Post-doc in Pereira lab), Stephanie Hustad (Veterinary summer student involved in project in the Pereira Lab), Barbara Byrne (UC Davis, VMTH), Heather Fritz (CAHFS), Terry Lehenbauer (UC Davis, PHR, VMTRC), **Sharif Aly** (UC Davis, PHR, VMTRC).

Chase CCL. 2022. Acceptable Young Calf Vaccination Strategies- What, When and How? *Vet Clin North Am Food Animal Pract* 38, 17–37.

Newman, R.A., **Chase**, C.C.L., Matos, J.R., Abdelsalam, K., Buterbaugh, R., Holland, S.V., Abdelaal, H., **Woolums**, A., Sastry, K.J., 2022. Efficacy of oleandrin and PBI-05204 against bovine viruses of importance to commercial cattle health. *Antivir Chem Chemoth* 30, 20402066221103960. https://doi.org/10.1177/20402066221103960.

Scientific Abstracts/presentations:

1. Martinez DA, **Chamorro MF**, Passler T, Huber L, Silvis S, Raithel G, Thoresen M, Stockler R, Walz PH, **Woolums AR**. Role of Nasal BRSV-IgG1 Titers on Clinical Protection of Calves Against Experimental Challenge with BRSV**.** In proceedings: 2022 ACVIM Forum, Austin, TX June 20-25, 2022. Pp:1

Nickell JS, Hutcheson JP, **Renter DG**, Amrine DA. Reduction in BRD antimicrobial treatments in a US feedlot-based multi-site study using conventional BRD control approach vs. targeted prediction technology. 31st World Buiatrics Congress, September 4-8, 2022, Madrid, Spain.

Horton L, Dewsbury D, Depenbusch B, **Renter DG**. An evaluation of metaphylaxis for bovine respiratory disease in medium-risk feedlot calves and outcomes impacting antimicrobial use. Phi-Zeta research day, March 1, 2022, Kansas State University, Manhattan, Kansas, USA.

Horton L, **Renter DG**, Depenbusch B, Pendell D. Description of feedlot animals culled for slaughter, revenue received, and associations with reported U.S. beef market prices. Conference of Research Workers in Animal Diseases (CRWAD), December 3-7, 2021, Chicago, Illinois, USA.

Crosby WB, R Richeson JT, Loy JD, Gow SP, Seo KS, **Capik SF**, **Woolums AR, Morley PS**. Comparison of sampling and diagnostic techniques for recovery of *Mannheimia haemolytica* from feedlot cattle. Conference for Research Workers in Animal Disease (CRWAD). Chicago IL. December 5-7, 2021.

Scott MA, **Woolums AR**, Swiderski CE, Perkins A, Nanduri B, Smith DR, **Karisch BB**, Epperson WB, Blanton JR. Blood biomarker discovery in high-risk stocker cattle at-arrival: differentiating respiratory health and disease. Conference for Research Workers in Animal Disease (CRWAD). Chicago IL. December 5-7, 2021.

Scott MA, **Woolums AR**, Swiderski CE, Thompson AC, Perkins AD, Nanduri B, **Karisch BB**, Goehl DR. Digital mRNA profiling of high-risk beef cattle at arrival substantiates markers of bovine respiratory disease. Conference for Research Workers in Animal Disease (CRWAD). Chicago IL. December 5-7, 2021.

Pinnell LJ, Doster E, Clawson ML, Loy JD, Wolfe C, **Woolums AR**, **Morley PS**. Strain-level shifts in *Mannheimia haemolytica* taxonomy and function via target-enriched metagenomics. Conference for Research Workers in Animal Disease (CRWAD). Chicago IL. December 5-7, 2021.

Crosby WB, Richeson JT, Loy JD, Gow SP, Seo KS, **Capik SF**, Padilla N, **Woolums AR, Morley PS**. Comparison of sampling methods and diagnostic techniques for recovery of *Mannheimia haemolytica* from feedlot cattle. Conference of the American Association of Bovine Practitioners (AABP). Salt Lake City, UT. October 7-9, 2021.

Scott MA, **Woolums AR**, Swiderski CE, Perkins A, Nanduri B, Smith DR, **Karisch** BB, Epperson WB. Multipopulational transcriptomic analysis of high-risk beef cattle on arrival reveals genes and mechanisms which may predict bovine respiratory disease. Conference of the American Association of Bovine Practitioners (AABP). Salt Lake City, UT. October 7-9, 2021.

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Other activities:
WA station

1. Three lectures on BRD host genomics to undergraduate students in:

ANIM SCI 474	Beef Production
ANIM SCI 472	Dairy Production
VET CLIN 361	Agricultural Animal Health