

APPENDIX D
SAES-422
Multistate Research Activity
Accomplishments Report

Project Number: NC1192

Project Title: An integrated approach to control of bovine respiratory diseases (NC-1027)

Period Covered: January 1, 2016 – December 31, 2016

Date of This Report: August 17, 2018

Annual Meeting Date(s): September 13, 2017

Participants of Annual Meeting:

Chase, Christopher (Christopher.Chase@SDSTATE.EDU) – South Dakota State University;
Dewell, Grant (gdewell@iastate.edu) – Iowa State University; Lehenbauer, Terry
(tlehenbauer@vmtrc.ucdavis.edu) – University of California – Davis; Ollivett, Theresa
(ollivett@wisc.edu) – University of Wisconsin – Madison; Palomares, Roberto
(palomnr@uga.edu) – University of Georgia; Woolums, Amelia (amelia.woolums@msstate.edu)
– Mississippi State University; Xiang, Shi-hua (sxiang2@unl.edu) – University of Nebraska – Lincoln

Brief summary of minutes of annual meeting:

Annual meeting was held in conjunction with the AABP's Annual Conference in Omaha, NE. Station reports were delivered from those members in attendance: Wisconsin, Georgia, UC-Davis, Mississippi State, Iowa, and Nebraska-Lincoln.

Ollivett is current secretary and organized the meeting. Vander Ley is president. Discussed the next BRD Symposium which will be held in 2019. Terry Lehenbauer volunteered to chair the organization committee. Chris Chase has been in contact with Bayer who has expressed interest in supporting the BRDS. Logo for BRDS updated (**Woolums**).

Discussed the need for consensus on BRD vaccination strategies and collaboration amongst NC1192, AABP, AVC, and ACVIM. Lehenbauer to bring up collaboration at the AABP Executive Committee meeting later that day.

Accomplishments:

Member activities focus on the project's 5 objectives and are outlined below.

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.

At the University of California – Davis, members are evaluating the association between gram negative non-fermenting bacteria in the upper respiratory tract of dairy calves on the presence of opportunistic bacterial pathogens and clinical respiratory disease.

At the University of Wisconsin – Madison, the Czuprynski laboratory is exploring the ability of bacterial BRD pathogens to attach and form a biofilm, in an effort to gain insights into mechanisms by which these organisms colonize the upper respiratory tract in healthy cattle. We have developed a cell culture method to assess biofilm formation by *M. haemolytica* and *P. multocida* on bovine respiratory epithelial cells. Using fixed primary bovine bronchial epithelial cells, we observed *M. haemolytica* biofilm formation and found it is inhibited by addition of bovine mucin. Prior viral infection of the epithelial cells (BHV-1, BVD, BRSV) had negligible effect on subsequent biofilm formation by *M. haemolytica*. We are exploring interactions among bacterial species (i.e. *M. haemolytica* and *P. multocida*) and find that they mutually antagonize biofilm formation. Inhibition of *M. haemolytica* biofilm formation requires viable *P. multocida* cells, does not occur when *M. haemolytica* and *P. multocida* cells are separated in a transwell chamber, and is not reproduced by *P. multocida* conditioned medium. These findings suggest that *M. haemolytica* and *P. multocida* cells must be in close proximity for inhibition to occur.

In a second line of research in the Czuprynski laboratory, interactions among endothelial cells and neutrophils in response to *Histophilus somni* are being investigated. Prior studies indicated that *H. somni* causes changes in endothelial cells and platelets that contribute to a procoagulant environment. These changes in turn could lead to the thrombus formation commonly seen during *H. somni* infection in vivo. We found that exposure of bovine PMNs to conditioned medium (CM) from *H. somni* infected bovine endothelial cells increased the pro-coagulant activity of PMNs alone, or PMNs co-cultured with endothelial cells. This effect was not likely due to residual lipooligosaccharide (LOS) in the conditioned medium, because the addition of polymixin B or LOS alone had minimal effect. To investigate further the effect of *H. somni* infected endothelial cell conditioned media on PMNs, we examined PMN expression of tissue factor activity. We did so using a bioassay that measures activation of factor X into activated factor Xa. The latter is the product that marks the convergence of the intrinsic and extrinsic

coagulation pathways. Conditioned media from *H. somni* exposed TBBE cells caused an increase in tissue factor activity on bovine PMNs. These data suggest PMNs and endothelial cells can interact together to enhance formation of a fibrin clot.

More recently, the Czuprynski lab found evidence that bovine macrophage derived microparticles contain tissue factor. Bovine monocyte-derived macrophages were incubated with *H. somni* (at a 1:10 ratio) in RPMI with 10% heat inactivated fetal bovine serum. After a 6 hr incubation at 37°C with 5% CO₂, membrane-shed microparticles were isolated from the conditioned media of monocyte-derived macrophages incubated with or without *H. somni*. Microparticles were washed twice with Ca²⁺ and Mg²⁺ free HBSS, and procoagulant activity assessed by a one-step recalcified plasma clotting assay. We observed greater procoagulant activity in microparticles from *H. somni* stimulated macrophages than from unstimulated control macrophages. Microparticle procoagulant activity was inhibited by addition of an anti-tissue factor antibody. These results suggest that bovine monocyte-derived macrophages release microparticles after exposure to *H. somni* cells that might amplify thrombus formation in bovine histophilosis. In addition, the Czuprynski laboratory initiated a new collaborative study with Drs. Ollivett and Suen (UW-Madison) to define the microbiome in the tonsils of cattle.

At Mississippi State, members determined the genetic characterization of multidrug resistant (MDR) *M. haemolytica* (Mh) isolates shed by conventionally managed high risk stocker cattle over 21 days after arrival. In continuation of work described last year, and in collaboration with the Frye and Jackson labs at the USDA ARS US National Poultry Research Center and the McClelland lab at UC Irvine, we characterized antimicrobial (AM) susceptible and also MDR isolates shed by stocker cattle that received AM metaphylaxis with or without subsequent AM therapy for BRD. On d0 only 1 of 50 cattle shed Mh resistant to drugs of 3 or more classes (and for which CLSI breakpoints exist for BRD), while 44/50 shed MDR Mh on d14. One hundred eighteen isolates were characterized by pulsed field gel electrophoresis (PFGE); 38 pulso types were found. Thirty-three isolates were subjected to whole genome sequencing; fourteen known AMR genes were predicted *in silico*. Of the 33 isolates sequenced, 4 were susceptible to enrofloxacin and the remainder were resistant (based on CLSI breakpoint). All 29 resistant isolates had mutations in the *gyrA* and *parC* genes that had been previously associated with quinolone resistance, while the 4 susceptible isolates had wild-type genes. It is not clear how the prevalence of genetically variable isolates with the same AMR genes can increase so quickly; it may be that they were present in all cattle on d0 but at levels too low to detect; alternatively, perhaps different genotypes are rapidly transmitted between cattle, or perhaps genetic resistance determinants are rapidly transmitted between bacteria. We expect to evaluate these possibilities in future research.

At the South Dakota State University, members are investigating the effects of bovine herpesvirus 1 on monocyte-derived dendritic cell cytokine production and surface marker expression. Blood was collected from 5-6 month Holstein Friesians and monocytes were isolated from the collected blood. Monocyte-derived dendritic cells were produced from the monocytes. The MDCCs were infected after 7 days with strains of Cooper and LA BHV-1 and time points

were taken. After sample collection, the MDDCs were analyzed using flow cytometry and qPCR. For the qPCR, cytokines produced by MDDC were analyzed. Results for the qPCR were run in the program REST, indicating if the cytokines were up or down-regulated. The Cooper strain significantly down regulated MHC I, MHC II, and CD86 compared to the control. LA down-regulated CD86 compared to the control, however Cooper down-regulated much faster. Cooper significantly down regulated of IL6, IL10, IL12, and IFN-gamma. LA showed significant up-regulation of IFN-alpha and IFN-beta as well as late down-regulation of IFN-gamma. The Cooper strain had much greater negative effect on MDDCs than LA in affecting both surface marker and cytokine expression.

Members from Washington State have evaluated dairy calf samples from populations in California (n=2000) and New Mexico (n=800), and 150 DNA and diagnostic samples from Wisconsin and validated three chromosomal regions (loci) that were associated with bovine respiratory disease (BRD) susceptibility. These loci will be important to consider for genomic selection for improving resistance to BRD.

In a second study from Washington State, weaned beef cattle were challenged with a single BRD pathogen and compared to non-challenged controls to identify gene expression differences across multiple tissues to better understand the disease process and to confirm genes associated with BRD susceptibility. Messenger RNA abundance in healthy lung and lung lesions in lymphoid tissues in the bronchial lymph node, retropharyngeal lymph node, nasopharyngeal lymph node and pharyngeal tonsil were collected at the peak of clinical disease in BRD pathogen challenged beef cattle. Gene expression in these tissues showed coordination of the host's immune response through specific gene networks. Differential gene expression crosstalk among genes identified key regulators of the immune response and could be used as a basis for development of therapies for BRD and for genomic selection.

In a third study coordinated by members at Washington State but held in Colorado, approximately 1000 beef steers were investigated to determine if they had lung lesions at harvest. Data from cattle with lung lesions were compared to pathogen diagnostic data collected prior to harvest to identify loci and pathogens associated with sub-clinical BRD. Clinical BRD results in substantial losses in carcass value whereas subclinical BRD carcasses were not of lesser value. Loci associated with subclinical BRD were different than those associated with clinical BRD. Therefore, genomic selection for clinical BRD may not dramatically reduce the prevalence of subclinical disease. To reduce both subclinical and clinical disease, different loci will need to be selected for.

Objective 2:

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

At UC-Davis, members are working on the development and validation of a clinical scoring system for bovine respiratory disease in post-weaned dairy cattle based on signs easily observed from a distance. A validated clinical scoring system could enhance early detection of bovine respiratory disease and initiate appropriate treatment. Validation results will be compared to a previously published, validated scoring system in preweaned calves with a diagnostic sensitivity of 73%, a screening sensitivity of 47%, and specificity of 87%. Also being developed is a risk assessment tool for the prevention of bovine respiratory disease in preweaned calves on California dairies. This project identified risk factors for BRD on California dairies by directly correlating management practices on dairy farms to prevalence of BRD in the calves subjected to these practices. (2017 AABP Research Summary). New insights learned from this project include risk factors that are positively (lagoon water to flush manure, calf to calf contact in calves > 75 days old, metal type hutches) and negatively (feeding saleable milk, feeding pasteurized milk, extra shade over hutches) associated with BRD.

The Wisconsin Veterinary Diagnostic Laboratory (WVDL) evaluated 1,418 (45.15% decrease) samples for respiratory viruses and *Mycoplasma bovis* (Table 1). The greatest percentage of positive samples were for *Mycoplasma bovis* (29.8%) or bovine respiratory corona virus (19.9%). The bacteriology laboratory evaluated 1918 samples (2.64% decrease) (Table 2). The greatest percentage of positive cultures were for *Pasteurella multocida* (22.1%) or *Mannheimia haemolytica* (13.3%). In August 2016, the WVDL added molecular testing for *Pasteurella multocida*, *Histophilus somni*, *Mannheimia haemolytica* and *Bibersteinia trehalosi*. We have data demonstrating an increase in sensitivity for these pathogens using molecular testing rather than culture alone. This might lead to a change in rates in the year 2017.

Additionally, the WVDL performs susceptibility testing using minimum inhibitor concentrations (Table 3). Notably, we observed significant reduction in susceptibility for *B. trehalosi* to gentamicin (3%) as compared to 2015. Additionally, we observed significant reduction in susceptibility for *P. multocida* to gentamicin (5%), neomycin (3%), and tylosin (3%) as compared to 2015. We observed significant reduction in susceptibility for *M. haemolytica* to clindamycin (2%) and for *H. somni* to chlortetracycline (11%), clindamycin (21%), neomycin (12%), oxytetracycline (5%), penicillin (5%), spectinomycin (8%), sulphadimethoxine (6%), tilmicosin (9%), tulathromycin (15%), and tylosin (9%) as compared to 2015. For *E. coli*, we observed a reduction in susceptibility to florfenicol (6%) and tiamulin (2%), while we observed a

reduction for *Salmonella* species to florfenicol (4%), neomycin (5%), and TMP/Sulfa (7%) as compared to 2015.

Table 1 Real time PCR positive samples for viruses and *Mycoplasma* (1418 submissions to WVDL)

<u>Respiratory Pathogen</u>	<u>No. Positive</u>	<u>% Positive</u>	<u>Change from 2015</u>
Bovine respiratory syncytial virus	98	6.9	Increase of 1.9%
Bovine respiratory corona virus	282	19.9	Increase of 1.7%
Bovine viral diarrhea virus	26	1.8	Increase of 0.6%
Bovine herpes virus 1	32	2.3	Increase of 0.1%
<i>Mycoplasma bovis</i>	423	29.8	Increase of 12.5%

Table 2 Culture positive samples for bacterial BRD pathogens (excluding *Mycoplasma*, 1918 samples at WVDL).

<u>Bacterial Pathogen</u>	<u>No. Positive</u>	<u>% Positive</u>	<u>Change from 2015</u>
<i>Histophilus somni</i>	149	7.8	Increase of 2.1%
<i>Pasteurella multocida</i>	424	22.1	Decrease of 2.2%
<i>Mannheimia haemolytica</i>	255	13.3	Decrease of 0.4%
<i>Bibersteinia trehalosi</i>	47	2.5	Increase of 0.5%
<i>Salmonella</i> species	102	5.3	Increase of 0.2%
<i>Gallibacterium anatis</i>	16	0.8	Decrease of 0.2%
<i>Trueperella pyogenes</i>	149	7.8	Increase of 2.4%
<i>Escherichia coli</i>	251	13.1	Increase of 5.2%

Table 3 Percent susceptibility of a microorganisms to the antimicrobials listed using the Clinical Laboratory Standards Institute (CLSI) breakpoints for minimum inhibitor concentrations at WVDL. The table below represents data from all samples and was not exclusive to respiratory samples. Therefore, many *E. coli* and *Salmonella* species were isolated from feces or other sample types.

Antimicrobial	Microorganisms					
	<i>P. multocida</i>	<i>M. haemolytica</i>	<i>H. somni</i>	<i>E. coli</i>	<i>Salmonella spp</i>	<i>B. trehalosi</i>
Ampicillin	100%	90%	99%	46%	64%	68%
Ceftiofur	100%	100%	98%	61%	NI	NI
Chlortetracycline	92%	92%	89%	25%	59%	41%
Clindamycin	0%	1%	45%	0%	0%	0%
Danofloxacin	100%	100%	NI	NI	NI	NI
Enrofloxacin	93%	86%	88%	64%	NI	NI
Florfenicol	96%	95%	94%	10%	43%	83%
Gentamicin	85%	95%	NI	86%	99%	93%
Neomycin	39%	78%	17%	67%	82%	80%
Oxytetracycline	60%	73%	55%	23%	59%	20%
Penicillin	95%	70%	79%	0%	0%	0%
Spectinomycin	76%	88%	74%	4%	0%	2%
Sulphadimethoxine	48%	69%	43%	38%	42%	68%
Tiamulin	51%	92%	95%	0%	0%	71%
Tilmicosin	70%	85%	80%	0%	0%	78%
TMP/Sulfa	0%	99%	NI	65%	88%	NI
Tulathromycin	89%	92%	76%	NI	NI	NI
Tylosin (Tartrate/Base)	2%	0%	74%	NI	NI	NI

TMP/Sulfa- trimethoprim/sulfamethoxazole

At SDSU, the infectious agents associated with bovine respiratory disease complex were monitored by bacterial culture, virus isolation, and fluorescent antibody techniques. Bacterial agents isolated from bovine pneumonic lungs, tracheal swabs, and nasal swabs are as follows (July 1, 2016-June 30, 2017): *M. haemolytica*, n = 238; *P. multocida*, n = 258; *H. somni*, n = 146; *B. trehalosi*, n = 25. Viral agents from bovine pneumonic lungs are as follows (July 1, 2016-June 30, 2017). This data was not available yet at the time of the writing the report isolations: BVDV, n = 3; BHV-1, n = 9; BHV-4 (DN-599), n = 20. ELISA ear notch BVDV tests were conducted on 7287 samples and there were 62 positives (0.85%). PCR tests were done for BVDV, BHV-1, BCV, BRSV and Mycoplasma. Pooled ear notch was done on 1371 submissions with 82 positive samples, 5.9% case positive. BVDV PCR was also done on nasal swabs, tissue, whole blood/serum /milk samples (704 submissions 20 positives, 2.8% positive). BHV-1 PCR was also done on nasal swabs, tissue, whole blood/serum (352 submissions 16 positive, 4.5%). BCV PCR was also done on nasal swabs and tissue (340 submissions 67

positive, 19.7%). BRSV PCR was also done on nasal swabs and tissue (340 submissions 58 positive 17.1%). Mycoplasma bovis PCR positive samples had 98 with 57 positive, 58.2%). Sequencing of reproductive isolates of BHV-1 indicate that they are almost exclusively vaccine strains.

At the University of Georgia, members are investigating an expanded set of phenotyping measures that include direct in vivo measure of circulating T cell phenotypes and cell activation markers that could help to define the immune responses to BRD agents (BVDV and BHV-1) across the timeline of acute infection to provide new tools for study of immune products in the pathogenesis of BRD component infections.

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

Member from UW-Madison, have performed three studies pertaining to Objective #3. The first study investigated the impact of antibiotic treatment in calves suffering from clinical and subclinical lung lesions, as well as those with upper respiratory infection (normal lungs, but look sick). The goal is to optimize antibiotic usage on dairies by determining which calves best respond to antibiotic therapy and limiting antibiotic usage to those animals. Results from this study were presented at AABP 2017 in Omaha, NE.

The second UW study investigated several factors, including the impact of separating sick calves within the group pen, the role of serotonin in the BRD process, and performance changes and feeding behaviors and attitudes associated with the BRD subtypes (subclinical pneumonia, clinical pneumonia, and upper respiratory disease). Preliminary results demonstrate that calves with clinical pneumonia were more likely to have a higher attitude score compared to calves with upper respiratory tract infection or subclinical pneumonia. These early results were presented at the 50th Congress of the International Society for Applied Ethology on July 12, 2016 in Edinburgh, Scotland.

The third UW study investigated the impact of ampicillin treatment on lung lesions and upper respiratory microbiome in preweaned dairy calves affected with acute, severe pneumonia after experimental challenge with *Pasteurella multocida*. Data collection was completed in August 2017. Project contributes to the MS program of Dr. Chelsea Holschbach (MS program, UW Dairy Science) and Dr. Sarah Raabis (PhD program, UW SVM). Results will be presented in part at ACVIM 2018 and AABP 2018.

Member from Mississippi State, have performed three studies pertaining to Objective #3. The first study evaluated the effect of on-arrival vaccination and deworming on stocker cattle health and growth performance. In research described the past 2 years, we found that high risk stocker cattle vaccinated with modified-live 5-way viral and multivalent clostridial vaccines at arrival had significantly higher BRD morbidity and mortality than cattle not vaccinated, although measurement of serum neutralizing titers to BHV-1 and BVDV1 in vaccinated cattle indicated that they did mount a humoral immune response following vaccination. In order to determine whether these findings are consistent across groups of stocker cattle, we repeated this study in spring 2017, and plan to repeat it again, for 3 trials total, in spring 2018. Analysis of the results of the 2017 trial are ongoing.

The second MS study evaluated the immune response in stocker cattle vaccinated intranasal 12 hours after transport. It is common for producers who purchase stocker cattle to vaccinate them on arrival, but it is not clear whether the stress of transportation has an impact on immunity. In the summer of 2017 we conducted a study to assess the impact of a 9-hour episode of transportation on the immune response to intranasal vaccination with a modified live BHV-1/BRSV/PI3V vaccine and SC MLV BVDV vaccine. Three groups of 25 cattle received either 1) transportation for 6 hours, 2 hours rest, then transportation for 3 hours, followed by vaccination 12 hours later; 2) transportation but no vaccination; or 3) no transportation but vaccination. We will measure SN antibody titers to BHV-1 and BRSV, concentrations of IgA directed against BHV-1 and BRSV in nasal secretions, and concentrations of interferon alpha, beta, and gamma in nasal sections, from samples collected at multiple time points over 21 days after vaccination, to determine whether transportation has an impact on immune responses to IN vaccination.

The third MS study assessed pharmacokinetics of tulathromycin after administration by dart gun. To facilitate efficient treatment and minimize stress related to gathering cattle following daily assessment of cattle for BRD, many producers use remote delivery devices (dart guns) to administer antimicrobials. However, little research has tested the plasma concentrations of drug following administration of common antimicrobials by dart gun. In ongoing research, we are assessing the plasma concentrations of tulathromycin in cattle following administration by CO₂-powered dart gun, pump dart gun, or needle injection, in a 3-way crossover study.

Member from SDSU have performed two studies pertaining to Objective #3. A prebiotic essential oil (EO) mixture was studied for its effect on animal health. The study objective was to determine the optimal feeding rate of EO when added to a milk replacer (MR) compared with feeding a control or a yeast cell wall additive (YCW). One hundred Holstein calves from a commercial dairy farm were blocked by birth date and randomly assigned to 1 of 5 treatments. Treatments were a control (CON), a 24:20% CP:fat (as-fed basis) MR (24:20 MR) without EO; EO mixed into the 24:20 MR at a rate of 1.25 g/feeding (EO-0.5), EO mixed into the 24:20 MR at a rate of 2.5 g/feeding (EO-1.0), or EO mixed into the 24:20 MR at a rate of 3.75 g/feeding (EO-1.5); or 24:20 MR with YCW mixed in at a rate of 2 g/calf at each feeding. The 24:20 MR was fed in a bucket 2 times/d at a rate of 0.27 kg/calf daily for 14 d, which was increased to 0.40

kg/calf at 2 times/d until d 35 and then reduced to 1 time/d at d 36 to facilitate weaning at d 42. All data were analyzed using PROC MIXED as a completely random design. Calves fed EO-0.5 demonstrated greater ($P < 0.05$) ADG (0.65, 0.71, 0.64, 0.64, and 0.63 kg/d for the CON, EO-0.5, EO-1.0, EO-1.5, and YCW, respectively) through d 56 compared with calves fed EO-1.0 and YCW and tended ($P < 0.10$) to have greater ADG than calves fed the CON and EO-1.5. Total BW gains were greater ($P < 0.05$) for calves fed EO-0.5 compared with calves fed EO-1.0 and YCW, with calves fed the CON and EO-1.5 being intermediate and similar. Body length and wither height gains were greater ($P < 0.05$) for calves fed EO-0.5 compared with calves fed the other treatments. Hip width gains were similar ($P < 0.10$) among treatments. Hip height gains were increased ($P < 0.05$) for calves fed EO-0.5 compared with calves fed the CON, EO-1.0, EO-1.5, and YCW. These results demonstrate that supplementing EO-0.5 (1.25 g/calf daily) in a 24:20 MR may be the optimal feeding rate to enhance growth rates compared with feeding a 24:20 MR and a 24:20 MR containing YCW or other inclusion rates of EO.

In a second study, SDSU members evaluated the protective immune response to different antigens included in vaccines, determining the best timing for vaccination and understanding the impact of the age of calf on vaccination. This study measured the serum antibodies present against four viruses common in BRDC following vaccination: bovine viral diarrhea virus 1 and 2 (BVDV1 and BVDV2), bovine respiratory syncytial virus (BRSV), and bovine herpesvirus (BHV1). The serum antibody titers were determined for more than 1600 calves at 3-week intervals starting at time of first vaccination. Dam age (years), time of weaning (initial vaccination or booster vaccination), and age of calf within year-season (days within Year-Season) classification all were found to have a significant effect on measured traits such as initial titer score and overall response score. Increased initial titer score was indicative of circulating maternal antibody levels, and was negatively correlated with each response trait (initial, booster, and overall response). Calves given their initial vaccination at weaning had higher antibody titers to BVDV1 and BVDV2, but calves given their initial vaccination before weaning had higher antibody titers to BRSV and BHV-1. A circulating antibody titer score was determined for each virus (titer score 0.38 for BVDV1, 1.5 for BVDV2, 3.88 for BRSV, 1.5 for BHV1) at which individuals would not positively respond to initial vaccination if they had a greater titer score but would positively respond if below this score. This information can be used to improve vaccination protocols to allow for a greater response rate of individuals and better protection.

At UC-Davis, sodium iodide was evaluated as a preventive strategy for respiratory disease in pre-weaned dairy calves (Data analysis is being completed.) Active excretion of iodine on respiratory mucosal surfaces in pre-weaned dairy calves were achieved via oral administration of 20mg/kg NaI. Treated calves had slightly worse respiratory scores and thoracic ultrasound scores and slightly more treatment events for pneumonia from enrollment until weaning.

Members from Iowa State University performed a bio-marker pilot study to identify metabolic biomarkers in serum and nasal secretions and identified 4-5 unique biomarkers that may assist in diagnosing respiratory disease in cattle. Research continues on this multiyear project to investigate impact of acclimation of newly received feedlot cattle on health, performance, stress

and behavior. Preliminary results show some improvement in morbidity and mortality, average daily gain, and cortisol levels over time. Acclimated calves have altered behavior compared to control calves.

Objective 4:

To determine how attributes of cattle production systems including epidemiologic, societal, and economic forces contribute to BRD, and to develop ways to catalyze change in those systems to reduce the occurrence of BRD and improve cattle health, welfare, and productivity.

Member from UC-Davis have performed three studies pertaining to Objective #4. The first study involved a survey of management practices related to bovine respiratory disease in preweaned calves on California dairies. The size, scale, and management practices of California dairies may differ compared with those for dairy herds elsewhere in the United States. This project provided a cross-sectional description of current dairy demographics and management practices in California that may influence the incidence of BRD in preweaned dairy calves. (Manuscript published in *Journal of Dairy Science*.)

In a second UC-Davis study, epidemiology of bovine respiratory disease in preweaned calves on California dairies was investigated. This project described and characterized by season the occurrence, diagnosis, and treatment of bovine respiratory disease (BRD) in preweaned calves on California dairies. Additionally, this project identified management practices that were associated with either higher rates of BRD or decreased risk of BRD for preweaned calves. (Manuscript in preparation.)

Lastly, at UC-Davis, the effect of macroenvironment and microenvironment temperature and humidity on the risk of respiratory disease in pre-weaned dairy calves during summer months was investigated (Manuscript in preparation.) In this study, compared to the macroenvironment at the calf raising area, maximum daily temperatures measured inside a calf hutch had a stronger association with BRD suggesting that hutch systems may have a distinct microenvironment. Also, daily maximum humidity was a significant predictor of BRD with a greater magnitude in the micro compared to the macroenvironment.

Member from UGA, have performed four studies pertaining to Objective #4. The first study evaluated the immune response to subcutaneous and intranasal vaccination in young beef calves. The objective of this study was to compare the serum neutralizing (SN) titers to BHV-1 and BRSV, and mucosal BHV-1-specific IgG and IgA in nasal secretions following administration of intranasal (IN) or subcutaneous (SC) modified-live virus (MLV) booster 60 days after priming calves with IN vaccine between 1-3 weeks of age. A significant decrease in SNA titers to BVDV-1 and -2, BHV1, BRSV and PI3V was observed during the 4-month experimental period,

which was similar for both groups. Moreover, booster vaccination 60 days after priming (by either IN or SC route) did not induce a significant increase in SNA titers against BHV1, BRSV and PI3V in beef calves that received a primary IN MLV vaccine in the face of MA. Significant differences were not observed in SNA titers to BVDV-1 and -2, BHV-1, and PI3V between groups on any time point of the experimental period. Calves in the MLV-SC group had higher ($P=0.03$) SNA titer to BRSV 42 days after the booster vaccination compared to calves in the IN-MLV group. A sustained and gradual increase in BHV1-specific IgA titers in nasal secretions was observed in both (IN and SC) groups after both priming and booster vaccinations. On day 14 after booster vaccination, the BHV1-specific IgA concentration in nasal secretions tended to be higher ($P=0.13$) in the IN-MLV group compared to the SC-MLV group. In conclusion, both routes of booster vaccination stimulated similar systemic and mucosal antibody response in beef calves intranasally prime vaccinated during the first three weeks of life. A cytokine gene expression analysis is being added to this study as a reference of the cell mediated immunity after vaccination. We are in the phase of PCR analysis and manuscript preparation.

In a second UGA study, the effect of injectable trace minerals on the onset of protection from bovine viral diarrhea virus (BVDV) acute infection induced by a MLV vaccine in newly received stressed beef calves was evaluated. The field stage and some of the laboratory analysis for this project have been completed. Administration of ITM at the time of vaccination appeared to mitigate the decrease in CD4 and CD8 T cells and platelets count and reduce their activation in calves challenged with BVDV five days after immunization. We are still performing some laboratory analysis on the immune response and protection after vaccination.

In a third UGA study, the effect of administration of injectable trace minerals on the systemic and mucosal immune responses induced by intranasal MLV vaccination in young dairy calves was investigated. In this study, there was a notable decay in SNA titers in both groups during the experimental period. Significant differences were not observed in SNA titers against BHV-1, BRSV, and PI3V between groups. However, ITM calves tended to have higher SNA titers to BRSV on days 14 and 28 than control calves. There was a significant increase in the levels of BHV-1 specific IgA concentration in both groups on days 14 ($P<0.05$) and 21 ($P<0.0001$) compared to day 0. Further, no significance differences in BHV-1 specific Ig A between groups were observed over the first 21 days after vaccination. Incidence of BRDC was greater ($P=0.03$) in the control group (13.3%; 4/30), compared to ITM (0/30). In conclusion, the use of ITM concurrently with IN MLV vaccination in young dairy calves tended to enhance the antibody production against BRSV diminishing its decay rate, and reduced the incidence of BRDC, which may be associated with enhanced circulating protective antibody and possibly cell mediated immunity. These results were presented in the Conference of Research Workers in Animal Diseases (CRWAD) Chicago IL, Dec 2017. Additionally, we will be performing a cytokine gene expression analysis as a reference for the cell mediated immunity after vaccination.

In a fourth UGA study, the effect of administration of injectable trace minerals at the time of vaccination on the systemic and mucosal immune response and protection against BVDV-2 and BHV-1 infection in dairy calves that were primed with IN vaccine at the second week of age was

assessed. The field stage of this project was done between August and December 2017. Further, a flow cytometric analysis of immunological markers (CD4, CD8, WC1, CD25) was performed after vaccination and challenge with BVDV and BHV1. Finally, 31 animals were euthanized and histopathological studies are pending. Currently, we are performing the laboratory analysis for determination of BHV-1 specific Ig A antibodies and SNA titers against BHV-1, BRSV, and PI3V.

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.

At UW-Madison, Ollivett Curriculum – Annual week-long clinical rotation for 6-8 1-2nd year veterinary students (by lottery) on thoracic ultrasonography in dairy calves. Day 1 is didactic learning and gross wetlab, then 3 days of on-farm ultrasonography and data collection, and day 5 is collated and interpreting data. Also, all dairy interested 4th year students enrolled in Advanced Skills in Dairy Cattle Production Medicine rotation are trained on thoracic ultrasonography. Students participating in Large Animal Internal Medicine rotations are exposed to the US technique and scoring system when appropriate cases are hospitalized. Additionally, in conjunction with Drs. Sebastien Buczinski, Sam Barringer, and Liz Cox, Ollivett teaches a 2 day preconference seminar on calf disease investigation with a large focus on thoracic ultrasonography at AABP. 2017 will be the 2nd year of the seminar.

At Mississippi State and in collaboration with Merck Animal Health, researchers at MS have organized an annual 2-day conference for veterinarians engaged in stocker cattle practice for the past 3 years. Topics presented have included update on VFD, new developments in diagnosis of BRD, inflammatory responses in stocker cattle, influenza D infection in BRD, and update on antimicrobial resistance in stocker cattle.

Members at SDSU have begun planning for the 2019 BRD symposium to be held in August 2019. SDSU provided BRSV isolates to CA and MS and BHV-1 isolates to OK and GA.

Members from UGA studied different management strategies to improve the immune response and protection elicited by MLV vaccines against bovine respiratory viruses. We also obtained information regarding the measurement of circulating T cell phenotype during acute BVDV and BHV-1 infections to assess differential CMI responses between vaccinated and naive calves as a tool to evaluate management practices relative to vaccination. During the development of this

research we established collaborative relationships with a research institutions in Argentina, (CONICET-INTA) through the USA Fulbright Scholar program.

Continuing program with faculty at University of Sao Paulo (USP) in the area of neonatal immune development and protection against BRD (and other) pathogens under funding from FAPESP, and collaborative studies on the impact of intranasal vaccine (EnForce) in dairy cattle relative to parturition (US and Australia) [Development of nasal secretion biomarkers].

Impact:

- Discovery of biofilm formation and antagonism by respiratory pathogens
- Increased understanding of *H. somnus*, *M. haemolytica*, *P. multocida*, BHV-1 pathophysiology
- Diagnostic laboratories found molecular methods for detecting respiratory pathogens to be more sensitive than traditional culture
- Clinical and ultrasonographic scores were developed and validated for dairy calf BRD
- Risk assessment tool for preventing and managing BRD is under development
- Effect of calf-hood lung consolidation on first lactation milk production was determined
- Short term benefits were detected after treating subclinical pneumonia
- Antimicrobial resistance was investigated to minimize shedding of resistant bacteria
- Detection of new biomarkers and genomic markers for BRD
- Implementation of acclimation will improve overall welfare of cattle, decrease antibiotic use, and make beef production more sustainable
- Trace mineral supplementation with intranasal vaccination reduced incidence of BRD
- Growth in preweaned dairy calves can be enhanced by feeding prebiotic essential oil
- Assessing administration of antibiotics via dart gun will inform producers and veterinarians of efficacy and help determine withdrawal times to ensure food safety
- Understanding transportation effects on immune response will help producers determine the best practice for vaccinating newly purchased animals
- Booster vaccination with either intranasal or subcutaneous injection stimulated similar systemic and mucosal antibody responses in beef calves primed with intranasal vaccination during the first three weeks of life
- New knowledge was generated regarding the dynamics of CD4+, CD8+, CD25+, and gamma-delta lymphocytes that circulate after exposure to BVDV-2 and BHV-1
- The interaction between transferred maternal humoral immunity and the developing microbiome in neonatal calves is evolving
- Outreach efforts have provided veterinarians and producers with tools to enhance early detection and management of beef and dairy calves with BRD

Journal Publications:

Aly SS, Love WJ, Williams DR, Lehenbauer TW, Van Eenennaam A, Drake C, Kass PH, Farver TB. 2014. Agreement between bovine respiratory disease scoring systems for pre-weaned dairy calves. *Anim Health Res Rev*, 15(2): 148-50.

Behling-Kelly E, Rivera-Rivas J, Czuprynski CJ. 2016. Interactions of *Histophilus somni* with Host Cells. *Curr. Topics Microbiol. Immunol.* 396:71-87.

Behling-Kelly E, Rivera-Rivas J, Czuprynski CJ. 2016. Interactions of *Histophilus somni* with Host Cells. *Curr. Topics Microbiol. Immunol.* 396:71-87.

Behura, S.K., P.C. Tizioto, J. Woo Kim, N.V. Grupioni, C.M. Seabury, R.D. Schnabel, L.J. Gershwin, A.L. Van Eenennaam, R. Toaff-Rosenstein, H.L. Neibergs, L.C. Regitano, the Bovine Respiratory Disease Complex Coordinated Agricultural Project Research Team, J.F. Taylor. 2017. Tissue tropism in host transcriptional response to members of the bovine respiratory disease complex. *Scientific Reports*. 7:17938 doi:10.1038/s41598-017-18205-0

Bittar, JHJ, Hurley, DJ, Woolums, AR, Barber, CE, Moliere, F, Havenga, LJ, Norton, NA, Palomares, RA. 2018. Effects of injectable trace minerals on the immune response to *Mannheimia haemolytica* and *Pasteurella multocida* following vaccination of dairy calves with a commercial attenuated-live bacterin vaccine *Professional Animal Scientist*. (PAS-17-01695-in press – Feb 18).

Boukahil I, Czuprynski CJ. 2016. *Mannheimia haemolytica* biofilm formation on bovine respiratory epithelial cells. *Vet Microbiol.* 197:129-136. doi: 10.1016/j.vetmic.2016.11.012.

Cortese VS, Woolums AR, Hurley DJ, Berghaus R, Bernard J, Short TH. Comparison of interferon and bovine herpesvirus-1-specific IgA levels in nasal secretions of dairy cattle administered an intranasal modified live viral vaccine prior to calving or on the day of calving. *Vet Immunol Immunopathol* 2017, 187:35-41.

Doyle D, Credille B, Lehenbauer T, Berghaus R, Aly S, Champagne J, Blanchard P, Crossley B, Berghaus L, Cochran S, Woolums A. Agreement among four sampling methods to identify respiratory pathogens in dairy calves with acute bovine respiratory disease (BRD). *J Vet Intern Med* 2017, 31:954-959.

Chase, C., Fulton, R.W., O'Toole, D., Gillette, B., Daly, R.F., Perry, G., Clement, T., 2017. Bovine herpesvirus 1 modified live virus vaccines for cattle reproduction: Balancing protection with undesired effects. *Vet Micro* 206:69-77. doi:10.1016/j.vetmic.2017.03.016

Chase CCL. 2017. Enteric Immunity: Happy Gut, Healthy Animal. *Vet Clin Food Anim*, in press.

Chase, CCL. 2017. Vaccinology. In *Blackwell's Five-Minute Veterinary Consult: Ruminant* 2nd edition, ed. Chase, Lutz, McKenzie & Tibary. Wiley-Blackwell, Ames, IA, in press.

Chase, CCL, Lutz K, McKenzie E, & Tibary A. 2017. *Blackwell's Five-Minute Veterinary Consult: Ruminant* 2nd edition. Wiley-Blackwell, Ames, IA, in press.

Cortese, VS, Woolums, AR, Hurley, DJ, Berghaus, R, Bernard, JK, Short, TH. 2017. Comparison of interferon and bovine herpesvirus-1 specific IgA levels in nasal secretions of dairy cattle administered intranasal modified live vaccine prior to calving or on the day of calving. *Vet Immunol Immunopathol* 187:35-41.

Costa JF, Novo SM, Baccili CC, Sobreira NM, Hurley DJ, Gomes V. 2017, Innate immune response in neonate Holstein heifer calves fed fresh or frozen colostrum. *Res Vet Sci*;115:54-60. doi: 10.1016/j.rvsc.2017.01.008.

Doyle D, Credille B, Lehenbauer TW, Berghaus R, Aly SS, Champagne J, Blanchard P, Crossley B, Berghaus L, Cochran S, Woolums A. Agreement Among 4 Sampling Methods to Identify Respiratory Pathogens in Dairy Calves with Acute Bovine Respiratory Disease. *Vet Intern Med*. 2017 31(3):954-959.

Froehlich KA, Abdelsalam KW, Chase C, Koppien-Fox J, Casper DP. 2017. Evaluation of essential oils and prebiotics for newborn dairy calves. *J Anim Sci* 95(8):3772-3782. doi:10.2527/jas.2017.1601.

Kiser, J.N., T.E. Lawrence, M. Neupane, C.M. Seabury, J.F. Taylor, J. E. Womack, the Bovine Respiratory Disease Complex Coordinated Agricultural Project Research Team, H.L. Neibergs. 2017. Rapid Communications: Subclinical bovine respiratory disease – loci and pathogens associated with lung lesions in feedlot cattle. *Journal Animal Science*. 95(3):1080-1091. DOI:10.2527/jas.2016.1152

Lehenbauer TW. Control of BRD in large dairy calf populations. 2014. *Anim Health Res Rev*, 15(2): 184-5.

Louie AP, Rowe JD, Love WJ, Lehenbauer TW, Aly SS. Effect of macroenvironment and microenvironment temperature and humidity on the risk of respiratory disease in pre-weaned dairy calves during summer months. (Manuscript in preparation.)

Love WJ, Lehenbauer TW, Kass PH, Van Eenennaam AL, Aly SS. 2014. Development of a novel clinical scoring system for on-farm diagnosis of bovine respiratory disease in pre-weaned dairy calves. *PeerJ*, 2(238): 1-25.

Love WJ, Lehenbauer TW, Karle BM, Hulbert LE, Anderson RJ, Van Eenennaam AL, Farver TB, Aly SS. 2016. Survey of management practices related to bovine respiratory disease in preweaned calves on California dairies. *J Dairy Sci*, 99(2): 1483-94.

Love WJ, Lehenbauer TW, Van Eenennaam AL, Drake CM, Kass PH, Farver TB, Aly SS. Sensitivity and specificity of on-farm scoring systems and nasal culture to detect bovine respiratory disease complex in pre-weaned dairy calves. 2016. *J Vet Diagn Invest*, 28(2): 119-28.

Luo J, Ferguson L, Smith DR, Woolums AR, Epperson WB, Wan XF. Serological evidence for high prevalence of influenza D viruses in cattle, Nebraska, United States, 2003-2004. *Virology* 2017; 501:88-91.

Nickell JS, Keil DJ, Settje TL, Lechtenberg KF, Singu VK, Woolums AR. Efficacy and safety of Zelnate®, a novel DNA immunostimulant, in cattle. *Bov Pract* 2016.

Novo, SMF, Franca dos Reis Costa, J, Costa Baccili, C, Sobreira, NM, Silva, BT, de Oliverira, PL, Hurley, DJ, Gomes, V. 2017. Effect of maternal cells transferred with colostrum on the health in neonatal calves. *Research in Veterinary Science* 112:97-104; 2017 Jan 27; 112:97-104. doi: 10.1016/j.rvsc.2017.01.025.

Novo, S, Franca dos Reis, J, Costa Baccili, C, Sobreira, N, Maia, M, Leite, S, Hurley, DJ, Gomes, V. 2017. Differential immune development in neonatal Holstein heifer calves fed fresh or frozen colostrum. *Pesquisa Veterinaria Brasileira (Brazilian Journal of Veterinary Research)* accepted with minor revision PVB-5038 (in English)

Palomares RA, Hurley DJ, Bittar JH, Saliki JT, Woolums AR, Moliere F, Havenga LJ, Norton NA, Clifton SJ, Sigmund AB, Barber CE, Berger ML, Clark MJ, Fratto MA. Effects of injectable trace minerals on humoral and cell-mediated immune responses to Bovine viral diarrhea virus, Bovine herpes virus 1 and Bovine respiratory syncytial virus following administration of a modified-live virus vaccine in dairy calves. *Vet Immunol Immunopathol* 2016; 178:88-98.

Snyder E, Credille B, Berghaus R, Giguère S. Prevalence of multi drug antimicrobial resistance in isolated from high-risk stocker cattle at arrival and two weeks after processing. *J Anim Sci*. 2017 95(3):1124-1131.

Stephenson MK, Palomares RA, White BJ, Engelken TJ, Brock KV. Prevalence of bovine viral diarrhea virus (BVDV) persistently infected calves in auction markets from the southeastern United States; association between body weight and BVDV-positive diagnosis *The Professional Animal Scientist* 33:426–431.

Van Eenennaam A, Neibergs H, Seabury C, Taylor J, Wang Z, Scraggs E, Schnabel RD, Decker J, Wojtowicz A, Aly S, Davis J, Blanchard P, Crossley B, Rossitto P, Lehenbauer T, Hagevoort R, Chavez E, Neibergs JS, Womack JE. 2014. Results of the BRD CAP project: progress toward identifying genetic markers associated with BRD susceptibility. *Anim Health Res Rev*, 15(2): 157-60.

Woolums AR, Berghaus RD, Smith DR, Daly RF, Stokka GL, White BJ, Avra T, Daniel AT, Jenerette M. A case-control study to determine herd-level risk factors for nursing calf bovine respiratory disease (BRD) on cow-calf operations. *J Am Vet Med Assoc* 2017; accepted.

Scientific presentations:

Bittar JHJ, Palomares RA and Woolums AR. Updates on trace minerals for use in cattle: a research-based summary. *DairyFax* – Oct-Dec 2017 – 9-14

Cramer M. C. and T. L. Olivett. 2016. Associations between a behavioral attitude score and health events in group-housed, preweaned dairy calves. 50th Congress of the International Society for Applied Ethology 12-15th July, 2016, Edinburgh, United Kingdom. (*Poster*)

Chase C, Braun L, Clement T, Daly R, Burcham G, O'Toole D. Are All Bovine Herpesvirus-1 Reproductive Disease Events Vaccine-Induced? 488th annual conference of the American Association of Bovine Practitioners, Charlotte NC, September 15-17, 2016.

Chase, C. Immunopathogenesis in BRD leading to lung lesions and mortality. 3rd Bayer Innate Immunity Global Advisory Meeting, Kansas City, MO, September 20-21, 2016.

Chase C. Being a Scientist and an Entrepreneur- You Can Do it. Student Symposium, Faculty of Veterinary Medicine, Cairo University, Giza, Egypt, November 27, 2016.

Chase C. Microbiome and Immunity: It is More than a Gut Feeling. Faculty of Veterinary Medicine, Suez Canal University, Ismailia, Egypt, November 28, 2016.

Chase C. Keynote Lecture-Function of immune system and how to stimulate it (video conference). Simposio Internacional Leite Integral: Biossegutidade em Fazendas Leiteiras, Curitiba, Brazil, March 30, 2017.

Chase C. Vaccines and vaccination in the dairy herd (video conference). Simposio Internacional Leite Integral: Biossegutidade em Fazendas Leiteiras, Curitiba, Brazil, March 30, 2017.

Chase C. Recognizing and treating adverse effects of vaccines in animals. South Dakota One Health Working Group Seminar: Vaccine-Preventable Diseases of People and Animals, Sioux Falls, SD, April 26, 2017.

Chase C. What's in animal vaccines? Accidental injections and needle sticks: How harmful are they to people. South Dakota One Health Working Group Seminar: Vaccines-Preventable Diseases of People and Animals, Sioux Falls, SD, April 26, 2017.

Chase C. The three levels of immunity in the animal: A case of a good defense preventing too much offense (and damage). 2017 Animal Nutrition Conference of Canada, Quebec City QBC, Canada, May 10, 2017.

Dewell G. 2017. Acclimation of feedlot cattle. ISU Feedlot Short Course, Ames, IA

Gomes, V et al., Vertical transfer of bacteria from dams to neonate calves through colostrum and transition milk ingestion Influence the development of the intestinal microbiome, immunity and incidence of diarrhea. São Paulo Research Foundation (FAPESP-2016/16748-2 2017-2019).

Hoyos Jaramillo, A, Bittar, JH, Hamrick, B, Stanley, S, Gutierrez, A, Miller, K, Wall, S, Norton, N, Ferreira, F, Urdaneta, J, Rodriguez, A, Hurley, DJ, Palomares, RA. Effect of injectable trace minerals, given at the time of vaccination, on the systemic and mucosal immune response to BHV-1, BRSV and PI3 following Intranasal modified live vaccine in dairy calves. 98th Annual Meeting of the Conference of Research Workers in Animal Disease and BVDV Symposium, 3-6 December 2017, Chicago, IL.

McGuirk S., T. Ollivett; S. Raabis, M. Cook, J. Sand, J. Rieman and K. Rottenberg. Effect of anti-IL-10 antibodies on health and performance of preweaned dairy calves: a dose-response study. Proceedings of the AABP Annual Conference. Research Summaries. Sept 16-19, 2016. Charlotte, NC.

Meyer N, Dewell G, Szasz J, Bryant T, McMurphy C. 2017. Critically Evaluating Alternative Cattle Handling Techniques. American Association of Bovine Practitioners, Omaha, NE.

Palomares RA. Effect of Trace Minerals on the Immune Response following Vaccination against Bovine Respiratory Disease. Alabama Veterinary Medical Association. Columbiana AL. Feb, 2017.

Palomares R.A. Trace Minerals (Zn, Cu, Se, And Mn) and immune response and protection against respiratory disease in cattle. Academy of Veterinary Consultants. Denver CO November 2017

Woolums AR, Berghaus R, Smith DR, Daly R, Stokka G, White B, Terrell A, Avra T, Jenerette M. A case-control study of herd-level risk factors for nursing calf bovine respiratory disease (BRD) on cow-calf operations. Proceedings AABP, Columbia SC, September 2016.

Woolums AR, Berghaus R, Smith DR, Daly R, Stokka G, White B, Terrell A, Avra T, Jenerette M. A case-control study of herd-level risk factors for nursing calf bovine respiratory disease (BRD) on cow-calf operations. Academy of Veterinary Consultants Summer Meeting, Denver CO, August 2016.

Outreach presentations:

Introduction to Genomic Testing. Minnesota Dairy Health Conference, Minneapolis, Minnesota.

Genomics of Health and Fertility Traits in Dairy Cattle. Minnesota Dairy Health Conference, Minneapolis, Minnesota.

Whole Genome Sequencing in Cattle to Facilitate Identification of Loci and Putative Causal Variants Associated with Complex Traits. Illumina workshop “Expanding the Genomics Toolkit: From Genotyping to *de novo* Assembly”, Washington State University, Pullman, Washington.

Agrigenomics 2.0 - Advanced Analysis to Accelerate Discovery. Golden Helix webinar.

Genetic Approaches to Reduce Bovine Respiratory Disease in Cattle. 2016. Oklahoma Center for Respiratory and Infectious Diseases, Stillwater, Oklahoma.

Risk Factors for BRD in Preweaning Beef Calves; Use and Abuse of Vaccines to Control Bovine Respiratory Disease; Immunity and Health in Stocker Cattle; Immunity in the Calf: Review and Update. AVMA Annual Convention. Indianapolis IN. July 24, 2017. (4 hours)

Update on Diagnostic Approaches to Respiratory Diseases in Cattle. Panel presentation and discussion with S. McGuirk and S. Buczinski. ACVIM Forum. National Harbor MD. June 10, 2017. (2 hours)

Vaccinating Neonatal Calves; Update on Transition Cow Immunology and Vaccination Programs. Minnesota Dairy Health Pre-Conference and Conference. Minneapolis MN. April 11 – 13, 2017 (2 hours)

Immunity in the Young Calf: What We Know, and What We Don't Know; Keys to Effective Vaccination of Calves. Academy of Dairy Veterinary Consultants Annual Meeting. Boise ID, April 8-9, 2017. (2 hours)

How Does the Immune System Do It? (Inflammation and Innate Immunity); How Does the Immune System Keep it Going? (Adaptive and Mucosal Immunity); and Review of Immune

Stimulants to Support Bovine Health. Illinois State Veterinary Medical Association Annual Convention. Lombard IL. November 5, 2016. (3 hours)

Theses:

Elizabeth Binversie, MS 2017, Thesis title- Using visual observations and thoracic ultrasonography to evaluate treatment success in preweaned dairy calves affected by respiratory disease

Neelu Thakur, MS 2017, Thesis title- Understanding the effect of BVDV on innate immune response of neutrophils

Collaborations, Fund leveraging:

Participating scientists at Georgia: Roberto Palomares, David Hurley, Lee Jones, Brent Credille, Jerry Saliki. Collaborative research involving USP, past studies in collaboration with University of Ghent, and our team in Georgia.

Participating scientists at Mississippi: Amelia Woolums, David R. Smith, Bill Epperson, Brandi Karisch, John Blanton, Robert Wills, Daniel Rivera, Jane Parish

Collaborating scientists at University of Georgia: Ray Kaplan, Steeve Giguère, Brent Credille, Roberto Palomares, David Hurley

Collaborating scientists at USDA ARS: Jonathan Frye, Charlene Jackson

Collaborating scientist at UC Irvine: Michael McClelland

Collaborating scientist at Virginia Tech: Tom Inzana

Collaborating stations (past year): GA, VA

At UW-Madison, the Czuprynski laboratory initiated a new collaborative study with Drs. Ollivett and Suen (UW-Madison) to define the microbiome in the tonsils of cattle and the above studies

involved prior or new collaborative interactions with investigators at Washington State (Srikumaran), Oklahoma State (Confer), and NADC (Briggs).

Palomares RA (PI). Effect of administration of injectable trace minerals on the systemic and mucosal immune responses induced by intranasal modified-live virus vaccination in young dairy calves. Multimin USA, Ft. Collins, CO. 2017. \$ 38,750 (funded as a contract)

Palomares RA (PI). Effect of administration of injectable trace minerals at the time of vaccination on the systemic and mucosal immune response and protection against BVDV and BHV-1 infection in dairy calves that were primed with IN vaccine at the second week of age. Multimin USA Ft. Collins, CO. 2017. \$157,250 (funded as a donation).

United States Department of State, Bureau of Educational and Cultural Affairs. Fulbright Scholar Program. Financial support for Dr. Erika Gonzalez Altamiranda (INTA-Conicet Argentina). Fulbright Scholar at University of Georgia under Dr. Palomares supervision

Credille, BC, Hurley, DJ. Immune Responses to Vaccination in High-Risk Stocker Calves; GA COMMODITY COMM FOR BEEF 1/17-12/17, \$36,000