

## **C1 - Beck**

Project Title: Identification of the apicomplexan target of triazine antiprotozoals and mechanism of drug-resistant coccidiosis

Principal Investigator(s): Dr. Josh Beck

Collaborating Investigator(s):

### **Abstract:**

Coccidiosis is an intestinal infection caused by coccidian parasites of apicomplexan phylum that results in major losses in domestic livestock production as well as disease in companion animals and humans. Triazines are an important class of anticoccidial drugs widely used to control coccidiosis but resistance to these compounds threatens to undermine their effectiveness. Judicious management of triazine use to curb resistance and development of improved compounds is limited by the lack of known mechanisms of action or parasite resistance for these drugs. Apicomplexa is a large group of protozoa of veterinary and medical importance which also includes the human malaria parasite *Plasmodium falciparum*. Interestingly, triazines are effective against a broad range of apicomplexans, including *P. falciparum* and we hypothesize that the target(s) of these compounds is conserved among these related parasites. Here, we propose to exploit the tractability of *P. falciparum* as a model apicomplexan to identify these conserved targets and/or mechanisms of resistance. In aim 1 (year 1), we will use an established approach for in vitro evolution of resistance to triazines by culturing *P. falciparum* with sublethal drug concentrations followed by whole genome sequencing to identify resistance-conferring mutations, revealing candidate triazine targets. In aim 2 (year 2), we will determine the biological function of these candidates using reverse genetic approaches in *P. falciparum* and evaluate target orthologs in relevant coccidian species to verify their importance for triazine resistance in the species that cause coccidiosis in production animals. Collectively, this work will reveal targets and/or mechanisms of resistance for an importance class of anticoccidials. This project is consistent with the 2023 ILHAC research priorities to address Coccidiosis in Poultry, Sheep and Goats as well as and the IVMA priority to address the threat of antiparasitic resistance for all species.

## **C2- Engelken**

Project Title: Evaluating the effect of surface treatment with a commercial sodium bisulfate powder (ParlorPal®) on the development of digital dermatitis lesions and calf performance in a bedded pack feedlot facility.

Principal Investigator(s): Dr. Terry Engelken

Collaborating Investigator(s): Dr. Amanda Kreuder, Dr. Enoch Meira, Dr. Rachel Friedrich

Digital Dermatitis (DD) has become a leading cause of lameness in Iowa feedlots. DD results from a combination of pen conditions, environmental contamination, and a poorly understood series of interactions between multiple families of bacteria. This disease causes painful lesions on the heels of affected cattle that decreases animal performance, increases production costs (labor and materials), and represents an important animal welfare concern for feedlot producers and their veterinarians. Since traditional antibiotic therapy is ineffective, control measures for DD typically center around the strategic use of footbaths containing 5-10% copper sulfate or formaldehyde. These solutions can be quite irritating to both the cattle and feedlot personnel and in some cases represent an environmental hazard. We hypothesize that the strategic treatment of the bedding pack and pen floor with a commercially available drying agent will decrease the moisture content and pH of the manure, reduce ammonia production, and reduce the bacterial load in the bedding pack in the pen. With cooperation from a local feedlot and the manufacturer of the drying agent, we will utilize 10 pens (5 treated; 5 control) with 180 head per pen, to determine the feasibility of using this product as an intervention tool against DD. Changes in animal performance (total gain and average daily gain), DD lesion incidence and severity, and the number of footbath treatments will be compared between pens. The expected changes in the pen environment should result in improved foot health, fewer animals affected with DD lesions, and a reduction in the need for footbath use. This in turn should improve animal performance, decrease production costs, and enhance animal welfare.

### **C3- Gorden**

Project Title: Pilot study to validate a hand-held luminometer with indicator organism tests to enumerate bacteria in whole milk to be fed to dairy calves

Principal Investigator(s): Dr. Patrick Gorden

Collaborating Investigator(s): Dr. Cody Sacquitne

Abstract:

According to the USDA National Animal Health Monitoring System Dairy 2014 study, morbidity and mortality associated diarrheal diseases continues to be one of the most common calf health challenges dairy producers experience and is the most common reason why antibiotics are used in pre-weaned calves. Bacterial contamination of colostrum, milk and milk replacer solution is a common, but often unrecognized cause of failure of passive transfer and/or neonatal calf diarrhea. On-farm investigation of diarrheal outbreaks in which elevated bacteria is a differential currently require the collection of milk samples to be later submitted to a microbiology laboratory, which has substantial time lag and cost. Adenosine triphosphate (ATP) bioluminescence (luminometry) is a common tool for performing comprehensive evaluation of feeding and housing equipment cleanliness on dairy farms. One manufacturer of bioluminescence equipment markets an indicator organism test system to monitor total bacteria, total coliform bacteria, and total Ecoli in milk that will provide same day bacterial count results. In this proposal, we describe a two-year project to validate the use a luminometry system to quantitate bacterial counts in milk (year one) and colostrum (year two) to be fed to calves. Our hypothesis of this work is that the use of improved rapid diagnostic tests to quantify bacterial counts in milk and colostrum will improve overall calf health on dairy farms. We plan to collect 300 whole milk samples to complete the validation of a luminometry system to estimate total bacteria, coliform, and Ecoli and compare these results to laboratory based total bacteria counts and total coliform counts as the gold standard. The results of this work will allow for rapid bacterial enumeration, potentially on-farm. In the end, this should help reduce morbidity on dairy farms.

#### **C4- Kreuder**

Project Title: Phenotypic and genotypic evaluation of normal and pathogenic flora of the upper and lower respiratory tract of goats pre- and post-pneumonia diagnosis

Principal Investigator(s): Dr. Amanda Kreuder

Collaborating Investigator(s): Dr. Ron Griffith

Abstract:

In this project, the summer scholar will participate in a large clinical trial related to antimicrobial use and antimicrobial resistance in goats and will be part of a team of 6-8 students responsible for completion of the animal portion of the study in association with several faculty and graduate students. As part of this larger clinical efficacy study for treatment of respiratory disease in goats, the summer scholar will be responsible for screening goats on arrival via nasopharyngeal swabs and in the lower respiratory tract at the time of necropsy for the presence of bacterial pathogens in the Pasteurellaceae family. Identified pathogens will have antimicrobial susceptibility testing performed to evaluate the carriage of antimicrobial resistance. Additional samples will be utilized for metagenomic analysis of the upper and lower respiratory flora as time and funding permits. The student will gain valuable experience directly working with goats to perform physical exams, diagnostic sampling, routine treatments and vaccinations, and necropsies as part of the large clinical efficacy study. Additional experience culturing diagnostic samples, performing antimicrobial susceptibility testing, and extracting DNA in a bacteriology lab will also be gained during this work.

## **C5- Mavangira**

Project Title: Utilizing 3D Organoid Technology to Model Bovine Mastitis In vitro

Principal Investigator(s): Dr. Vengai Mavangira

Collaborating Investigator(s): Dr. Karin Allenspach-Jorn, Dr. Jonathan P. Mochel

### **Abstract:**

Bovine coliform mastitis is a major contributor to production losses to the dairy industry by decreasing milk production, early removal of cows from the herd, and deaths from systemic illness. Decades of research have failed to improve effectiveness of current therapies because of lack of appropriate in vitro approaches to explore the mechanisms of coliform mastitis. The current in vitro approach consists of using 2-dimensional (2D) bovine cell cultures and immortalized murine cell lines, which have significant drawbacks and lack direct translational relevance to natural coliform mastitis. Therefore, there is a critical need for better in vitro modeling platforms which more closely mimic natural disease. The advent of organoid technology presents an exciting opportunity to better model coliform mastitis in vitro with the potential for advanced development of practical and effective treatments for clinical mastitis.

## **C6- Opriessnig**

Project Title: Timed infection with porcine respiratory coronavirus infection (PRCV) will decrease the severity of PRRSV-induced respiratory disease

Principal Investigator(s): Dr. Tanja Opriessnig

Collaborating Investigator(s): Dr. Patrick Halbur, Dr. Jianqiang Zhang

Porcine reproductive and respiratory syndrome virus (PRRSV) continues to cause major economic losses in swine worldwide. In 2020 a novel, particularly pathogenic PRRSV cluster was identified in the US (designated as 1-4-4 L1C variant) and is now widespread and associated with high morbidity and mortality in growing pigs. Appropriate control of one pathogen often requires control of coinfections due to interactions and up or downregulation of components of the immune system. It has been shown that PRRSV can be upregulated by many other viruses and bacteria. A virus that does not receive a lot of attention is porcine respiratory coronavirus (PRCV) which was discovered in 1986 in the US. This virus has been largely ignored by diagnosticians and swine veterinarians despite PRCV causing lesions in the upper and lower respiratory tract. We recently successfully isolated a variant PRCV from pigs and confirmed its pathogenicity. When we infected pigs with influenza A virus (IAV) 5 days after PRCV infection, clinical flu signs (cough) in these pigs were significantly decreased compared to single IAV infected pigs while their antibody responses increased. The widespread decline of some ubiquitous pathogens including PRCV could have reduced the pig's overall immunity towards other pathogens such as PRRSV. We hypothesize that PRCV, given several days prior to PRRSV infection will decrease PRRSV virulence and shedding due to a more rapid innate and cellular immune response triggered by the PRCV. To test our hypothesis, 32 pigs will be randomly assigned to one of 4 groups: Group 1: PRCV + PRRSV 5 days later; Group 2: Negative control; Group 3: PRRSV control; and Group 4 PRCV control. At 15 days post initial infection, lungs will be collected, and gross and microscopic lesions will be assessed. Antibody responses and viral shedding will be tested and compared among pigs.