Mentor Abstract #1

Project Title: Determination of bacterial sensitivity to a novel antimicrobial compound (Vetericyn®)

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Abstract:

Infectious Bovine Keratoconjunctivitis (IBK) is commonly encountered in bovine medicine, with infections ranging from mild ocular discharge to permanent blindness. Prevention of IBK through vaccination has been largely unsatisfactory, while treatment of IBK has been limited to injectable antibiotics and anti-inflammatories. Topical antimicrobial medications have limited efficacy or are impractical for daily use.

A novel non-toxic, broad-spectrum antimicrobial ophthalmic wash called Vetericyn® recently became available for animal use which is heavily marketed to bovine producers with claims to kill numerous pathogens, including Moraxella bovis, in a manner similar to an animal’s own immune system. The practical appeal of the product is its safe, non-medicated “natural” approach for prophylactic eye disinfection or ulcer treatment; however, the efficacy of this product has not been validated on the most common veterinary bacterial ocular flora and pathogens. Given the great risk to ocular health that surface infection may pose, a broad-spectrum prophylactic or therapeutic antimicrobial agent that does not facilitate the development of multiple-drug resistant bacteria is of significant value if it truly kills common veterinary ocular pathogens. A substantial improvement to current antibiotic-dependent therapy would benefit large animal veterinary medicine from both a food safety and animal welfare perspective.

The purpose of this study is to evaluate the in vitro effect of Vetericyn® against clinical Moraxella bovis, Moraxella bovoculi and Mycoplasma bovis isolates, to evaluate the in vivo efficacy of the product on the eyes of normal cattle, and to concurrently survey the bovine ocular bacterial population. Our hypothesis is that Vetericyn® will be more effective than treatment with commercial eye wash but less selective than antibiotic agents. We will test Vetericyn® against clinical IBK isolates at the Iowa State University Clinical Microbiology Laboratory and then proceed to test its ability to affect the presence of ocular bioflora resident in normal cattle.
Mentor Abstract #2

Project Title: Environmental induction of multi-drug-resistant *Salmonella* Typhimurium virulence mechanisms

Principle Investigator(s): Shawn Bearson

Collaborating Investigator(s): Brian Brunelle, Brad Bearson, Jennifer Jones

Abstract: (300 words or less)

In the U.S., *Salmonella* is the most common cause of bacterial food-borne illness and is estimated to annually cause 1.2 million cases, 23,000 hospitalizations, 450 deaths, and $2.6 billion in social costs. Many of these *Salmonella* isolates are resistant to one or more classes of antibiotics. According to the National Antimicrobial Resistance Monitoring System (NARMS), 9.1% of the non-typhoidal *Salmonella* isolates in humans were resistant to 3 or more classes of antibiotics. For *Salmonella enterica* serovar Typhimurium isolates, one of the most prevalent causes of foodborne salmonellosis, 27.3% of the isolates were resistant to 3 or more classes of antibiotics, and 20.8% were resistant to 5 or more classes.

Multidrug-resistant (MDR) *Salmonella* is associated with increased morbidity in humans compared to sensitive strains. Possible rationales for these clinical observations in humans are treatment failure, underlying health issues of the patient, or antibiotic-enhancement of *Salmonella* virulence. Studies have demonstrated that sub-inhibitory concentrations of antibiotics can alter global gene expression in bacteria, including cellular processes such as motility, attachment, and invasion. This project will employ bacterial growth studies, cell culture assays and various molecular biology techniques to analyze the response of *Salmonella* during antibiotic exposure under various environmental conditions. The antibiotics to be investigated represent antibiotic resistances detected in MDR *Salmonella* as well as antibiotics used in animal husbandry as growth promotants in feed.

Our goal is to establish the genetic pathways that are involved in altering the virulence of *Salmonella* following antibiotic exposure. As livestock production systems continue to increase in size/complexity and antibiotic usage in feed becomes increasingly controversial, identifying the virulence mechanisms in *Salmonella* that are altered during antibiotic exposure may identify alternative pathogen control methods for future exploration and exploitation.

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Mentor Abstract #3

Efficacy evaluation of canine serum and plasma against protease activity for treatment of keratomalacia

Principle investigator: Dr. Gil Ben-Shlomo

Corneal ulcers are common in dogs and considered to be a serious ocular illness that requires immediate medical attention. If not identified early or if secondary infection occurs, keratomalacia (“melting” corneal ulcer) may develop. Keratomalacia is a rapid degradation of the corneal stroma caused by various proteases acting on the corneal collagen. This condition may lead to a rapid deepening of the ulcer, and even perforation of the eye, and considered as eye and vision threatening condition. The most commonly used anti-proteases are serum and plasma. Despite of their enormous importance and common use, the veterinary literature is lacking information regarding the efficacy of canine serum and plasma against keratomalacia in terms of potency and as a function of time. In addition, there is no information regarding the contamination risk of serum and plasma over time when used for ocular treatment. The goal of the proposed study is to comparatively evaluate the efficacy of canine serum and plasma against protease activity and the risk of contamination.

Fresh serum and plasma will be collected from a healthy dog, determined by physical examination and complete blood work. The fresh blood will be separated into serum and plasma, which will be placed in a sterile dropper bottle as done in clinics and will be kept refrigerated at 4°C. A commercial kit (EnzChek gelatinase/collagenase assay, Molecular Probes Inc, Eugene, Ore) will be used to evaluate the anti-protease activity of serum and plasma at different time points. In addition, the tip of the dropper bottles and their content will be cultured for bacterial growth at the same time points to evaluate potential bacterial contamination. Then, the evaluation will be repeated with serum and plasma kept at room temperature to evaluate the effect of temperature storage on efficacy and contamination risk.

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Mentor Abstract #4

Proposal for 2013 Summer Scholars Project

Project title: Design and Assessment of a Canine Pelvis and Limb Model to Teach the Diagnosis of Coxofemoral Laxity Secondary to Canine Hip Dysplasia

Principle Investigator: Mary Sarah Bergh DVM, MS, DACVS, DACVSMR
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Department of Veterinary Clinical Sciences
Iowa State Lloyd Veterinary Medical Center

Abstract:

Hip dysplasia is a common orthopedic condition in dogs that can lead to debilitating pain and lameness. Canine hip dysplasia (CHD) is characterized as a developmental disease resulting in excessive laxity within the hip, which results in secondary osteoarthritis. Diagnosis can be made on orthopedic examination with the Ortolani maneuver, or on radiographs. Early diagnosis of CHD can allow for treatment options that are not as effective in the adult animal or in later stages of the disease process. Data from one of our previous studies documented that 78% of surveyed recent graduates from the Iowa State University College of Veterinary Medicine were not comfortable in diagnosing canine hip dysplasia and 92% reported that they felt a customized pelvic limb (hip) model would help them learn or be more confident in performing the Ortolani maneuver. We hypothesize that we can create a three-dimensional model to effectively teach veterinary students how to perform the Ortolani maneuver and improve their comfort level and confidence in diagnosing hip laxity associated with CHD. The specific aim of this study is to create a canine pelvis and limb model to mimic a dog with coxofemoral laxity, and to test its efficacy as a learning tool for veterinary students. The Summer Scholar will gain an excellent working knowledge of the canine coxofemoral joint anatomy and hip dysplasia. With the Mentor’s assistance, she/he will design and create the model as well as design and carryout a hypothesis-based research project to evaluate the effectiveness of the model. The end goal of the project is to write and submit a manuscript to the Journal of Veterinary Medical Education, with the Scholar’s assistance. Funding to create the model will be provided by the Mentor.

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Mentor Abstract #5

Impact of Cache Valley, Cholul and Schmallenberg Viruses on Ovine Health in the Midwest

Principle Investigator(s): Bradley Blitvich
Collaborating Investigator(s): Eric Burrough, Annette O’Connor, Paul Plummer

Abstract:

There has been a dramatic increase in the incidence of embryonic and fetal death and stillbirths in pregnant sheep as well as congenital defects such as arthrogryposis and hydranencephaly in lambs in the Midwest in the last few years. The reasons for this increase are not known but two explanations are that these outbreaks were caused by a recently introduced pathogen or an indigenous pathogen with increased virulence. The losses associated with these outbreaks are substantial and therefore it is very important to the local sheep industry that the pathogens responsible for these outbreaks are identified so that appropriate control measures can be implemented. Because the clinical features associated with these outbreaks are consistent with the disease patterns of some orthobunyaviruses, we will test the hypothesis that orthobunyaviruses are the cause of these outbreaks. Three specific aims have been designed to test this hypothesis. In specific aim 1, sheep sera will be tested for antibodies to 10 different orthobunyaviruses. We will test for antibodies to both indigenous orthobunyaviruses (i.e. Cache Valley virus) and exotic orthobunyaviruses (i.e. Schmallenberg and Cholul viruses). This study will be performed using sera obtained from sheep in 22 states (8 from the Midwest, 14 from elsewhere in the USA). In specific aim 2, we will evaluate risk factors for virus exposure. Such information will allow us to identify potential risks as well as protective practices that producers can implement to reduce the likelihood of orthobunyavirus infection. In specific aim 3, tissues from aborted ovine fetuses and dead lambs that exhibited congenital defects will be tested for orthobunyaviruses. Overall, the studies outlined in this grant application will generate data that the U.S. sheep industry can use to improve the health and management practices of sheep in the Midwest and elsewhere in the nation.

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Mentor Abstract #6

Project Title: Investigation of CD47 in solid tumors of equids

Principle Investigator(s): Stephanie S. Caston, DVM, Diplomate ACVS - LA

Collaborating Investigator(s): Brett A. Sponseller, DVM, PhD, Diplomate ACVIM; Jesse M. Hostetter, DVM, PhD, Diplomate ACVP

Abstract: (300 words or less)

Equine species (horses, mules, donkeys) are sometimes afflicted with various types of skin tumors. Solid tumors in man have been shown to express a protein (CD47) that helps the tumor avoid destruction by the host defenses. Increased CD47 expression in some tumors correlate with decreased probability of patient survival. Antibodies targeting CD47 have been used in *in vitro, in vivo*, and clinically to inhibit the growth of tumors and to prevent the spread of tumors. We will investigate expression of CD47 in equine solid tumors.

Our hypothesis is that equine solid tumors highly express CD47 and normal, healthy skin does not express CD47. This expression will be compared to a human tumor as a positive control. Specific aims for this work include development of an immunohistochemical assay, and detection of expression of CD47 in skin and tumors. Tumor types collected in this study will include but are not limited to mast cell tumors, melanomas, squamous cell carcinomas, and sarcoids. Future work will include comparison of expression between tumor types and eventual use of antibody treatment in clinical cases. If the marker (CD47) is highly expressed on tumor cells, treatment of the tumor with an antibody to the marker may enable the body’s cells to better recognize and destroy the tumor cells.

During this study, removal and/or biopsy of solid equine tumors and biopsies of normal skin will be performed. These tissue samples will then be used to determine expression of the CD47 marker in solid tumors. Expression of the CD47 marker will be investigated in this study with the use of immunohistochemistry and will be compared to a positive control (human tumor) and to a negative control (normal equine skin). We expect these studies to result in a novel clinical approach to treating solid equine tumors of the integument.

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Mentor Abstract #7

Project Title: Development of an AIDS Vaccine.

Principle Investigator: Dr. Michael Cho

Abstract/Description of Work:

The primary focus of the Cho laboratory is development of a vaccine against human immunodeficiency virus (HIV-1), the virus that causes AIDS. In connection with this research, we characterize biochemical and immunological properties of viral envelope glycoprotein, develop and evaluate novel vaccine vectors, and examine virus-host interactions at various levels. One of the major obstacles in developing an effective vaccine against HIV-1 is the inability to elicit neutralizing antibodies (Nabs) that are broadly reactive against the large number of HIV-1 isolates that exist. The high degree of genetic variation of viral envelope glycoprotein (viz. gp120 and gp41) is the primary reason for the difficulty in inducing broadly reactive Nabs. Extensive glycosylation and complex structure of the protein also contribute. Hence, one of our goals is to better understand the biochemical and immunological properties of gp120/gp41.

Summer scholars will have the opportunity to become involved in various aspects of our lab's protein biochemistry pipeline for HIV vaccine development. The pipeline includes protein design, engineering and expression of recombinant proteins in bacteria or mammalian cell lines, protein and DNA purification, vaccine preparation, immunization of animals (usually rabbits), and subsequent evaluation/isolation of neutralizing antibodies from these immunized animals. The evaluation of immune responses generated by various antigens and vaccine delivery platforms will allow the intern to gain valuable insight into the challenges of modern vaccine design against rapidly evolving pathogenic organisms, especially viruses.

We have recently added PRRS virus expertise to our research group and subsequently plan to apply our HIV-1 vaccine strategies to PRRS vaccine development.

We would prefer students with a strong interest in biology or microbiology with classwork completed in those fields if possible. Biochemistry and classic molecular biology will be employed in the lab, so interest in these areas is also a benefit, but not a required background.

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Project Title: A study to investigate the sedative and analgesic effects of romifidine, an alpha-2 agonist, in cattle following castration.

Principle Investigator: Dr. Hans Coetzee
Collaborating Investigator: Dr. Matt Stock

Abstract:
A growing concern by the consuming public desires pain relief provided to food producing animals. This is especially evident for routine procedures such as castration and dehorning since preemptive analgesia can be provided in advance of the painful stimuli, thereby preventing the sensitization of the nervous system to subsequent stimuli that could amplify pain. Although a presumed painful response has been associated with castration through behavioral, physiological, and neuroendocrine changes, only 1 in 5 veterinarians use analgesia at the time of castration. Methods to detect pain as well as pharmaceutical options for antinociception in cattle need to be further explored. Alpha-2 agonists are commonly employed by cattle veterinarians to provide both sedation and analgesia for procedures. A recent review of the literature investigating behavior, physiology, and neuroendocrine changes following castration with and without analgesia suggested the use of a sedative agent that also provided analgesia such as an alpha-2 agonist would be beneficial to the pain response observed. Additionally, romifidine has been noted by the investigator to provide excellent sedative properties in cattle.

This study will test the hypothesis that romifidine, an alpha-2 agonist currently labeled for horses and dogs, will provide sedative and analgesic effects in cattle. Additionally, these effects will help to mitigate the pain response following castration. Animal-side evaluation following administration of the drug and castration include chute exit speed calculation and infrared thermography. Our group has used these techniques to demonstrate changes associated with painful procedures and response to analgesic intervention. Additionally, plasma samples will be collected at specific times following drug administration to determine drug metabolism in cattle using liquid chromatography-mass spectroscopy methods. These samples will also be used for determining plasma cortisol and substance P concentrations following castration, which allow for a pain response to be evaluated on a physiologic and neuroendocrine level. The results of this study will assist practitioners in potentially providing another sedative / analgesia for use during routine husbandry procedures.

Participation in this project will provide the Summer Scholar with a mix of live animal and laboratory experiences. The student will be given the opportunity to spend time working with cattle gaining hands-on experience in routine husbandry procedures such as castration as well as catheter placement and collection of blood samples. Once the animal phase is completed, the student will assist in the processing and analysis of the samples using cutting-edge analytical equipment. The outcome of this project will be the publication of practitioner-relevant data regarding the clinical use of an alpha-2 agonist, romifidine, in the aid of sedation and pain relief following castration in cattle. Furthermore, participation at a national bovine practitioner meeting where results of the study can be presented will be strongly encouraged and supported.

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Mentor Abstract #9

Project Title: Age related changes in the intestinal microbiome protect neonatal piglets from Clostridium difficile infection

Principle Investigator(s): Dr. Nancy Cornick

Collaborating Investigator(s): Drs. Glenn Songer, Darin Madsen and Greg Phillips

Abstract: Clostridium difficile-associated diarrhea is a significant cause of gastroenteritis in neonatal piglets. While the majority of very young piglets are culture positive for the organism, the population of C. difficile appears to decline over the first 2 months of life. Significant disease in piglets is confined to the neonatal period, generally 2-5 days after birth. Natural microbial succession of the intestinal microbiome occurs as neonatal animals are exposed to the maternal microbiota and to the diversity of microbes present in their environment. We hypothesize that this shift in the intestinal microbiome protects animals from overgrowth of C. difficile and that this protection can be extended to neonatal animals through the use of fecal transfers. The objectives of the project are to determine if: 1) Alteration in the intestinal microbiome due to naturally occurring bacterial succession protects piglets from infection by C. difficile; and 2) Fecal transplants protect piglets from C. difficile challenge. We expect to demonstrate that piglets will become resistant to challenge with C. difficile by about 6 days of age and that neonatal piglets treated with fecal transfers will be protected from disease after a C. difficile challenge. Current practice of treating sows with antimicrobial agents have not been entirely successful and alternative control strategies, such as fecal transplants, have the potential to make a positive impact on the swine industry.

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Mentor Abstract #10

Principle Investigator(s): Dr. Reneé Dewell
Collaborating Investigator(s): Dr. Grant Dewell; Mr. Doug Bear
Abstract: (300 words or less)

As part of the management of compromised cattle, the Beef Quality Assurance (BQA) Feedyard Assessment was developed. This assessment can be located at:
http://www.bqa.org/CMDocs/bqa/Feedyard_Assessment_062209_Blank.pdf

This assessment is designed to target three main areas—Animals, Records and Best Management Practices (BMP), and Facilities and Equipment. Although Iowa enjoys a reputation as a leader in BQA, feedyard assessments have not yet been a focus in this state. The objective of this project is to obtain baselines for BQA welfare parameters in Iowa by conducting BQA Feedyard Assessments throughout Iowa. The student will be trained in properly conducting BQA assessments at feedyards prior to completing assessments independently. The student will also be responsible for inputting data obtained from the assessments. The data will be compiled and basic descriptive statistics will be generated to determine baselines for various parameters measured with the BQA assessment tool. The analyzed data will be used to better describe Iowa feedyards and to provide information for training and extension in welfare areas that may represent challenges to some feedyards. It is expected that participating feedyards will:

- Have a better understanding of their feedyard’s strengths and challenges
- Be able to identify and benchmark key areas of animal care and well-being
- Develop a plan to maintain and support strong points and to strengthen areas where the yard is challenged

The project has great benefit to the Iowa cattle industry because we will help further Iowa feedyard stewardship and welfare by confidently and correctly conducting assessments, providing valuable feedback to participants, and providing useful data regarding important benchmarks and trends among Iowa Feedyards. Dissemination of this data will likely increase consumer confidence in Iowa beef. Students applying for this project should have a strong work ethic, excellent communication skills, be able to work independently, and have substantial cattle experience.

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Mentor Abstract #11

Project Title:
Learning and Memory Assessments in Canines

Principle Investigator(s):
N. Matthew Ellinwood

Collaborating Investigator(s):
None

Abstract: (300 words or less)
Canine models of neurodegenerative diseases are important for developing therapies for humans affected with homologous conditions. For a number of studies it would be useful to have cognitive measures by which to assess functional outcomes of potential therapy.

This project entails the assessment of learning and memory normal dogs and dogs affected with a neurodegenerative lysosomal storage disease known as MPS IIIB. This disorder, also known as Sanfilippo Syndrome type IIIB, is a fatal heparan sulfate storage disorder. Children with this disease succumb to their illness in their mid-teens, and there is currently no therapy. Gene therapy and enzyme replacement therapy are both potential approaches to treat disease. A spontaneous canine model of MPS IIIB exist has been used in the past to assess gene therapy, however studies have only concentrated on biochemical and histopathological outcomes and not functional cognitive outcomes. The goal of this study is to assess learning and memory in normal and affected dogs to develop a cognitive outcome that could be use to assess pre-clinical trials using the canine model. The modality to be used is a learning reversal task involving a T-Maze evaluation mechanism.

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Mentor Abstract #12

Project Title: Comparison of reported prognostic data to actual survival times for soft tissue sarcomas in dogs

Principle Investigator(s): A. Fales-Williams, DVM, Ph.D., Dipl. ACVP
Collaborating Investigator(s): M. Ackermann, J. Hostetter, E. Whitley, M. Yaeger, R. Myers, J. Haynes

Abstract:
Our department wishes to compare the actual prognostic data for specific tumors to the reported prognostic information. For example, a new grading scheme for soft tissue sarcomas groups the tumors into well (I), moderately well (II), and poorly differentiated (III) sarcomas. The latter category is associated with an extremely poor prognosis due to the high likelihood of metastasis and local regrowth, while the first two are associated with varying levels of tumor regrowth. We seek to determine whether this reported data is appropriate for the subset of cases reviewed by the ISU Department of Veterinary Pathology. Using our collection of histopathology cases, a student will collect cases from the last 2-5 years that meet specific criteria for tumor type. The student will be responsible for selecting cases for inclusion by reviewing cases in the ISU CVIS data base. The student will then coordinate the administration and data interpretation of a survey that will be sent to referring DVMs to inquire about survival times and other issues related to patient follow-up. Additional immunohistochemistry staining may be required for post-review of these cases; if so, the student will gain experience in optimizing an IHC marker for future use in our histopathology lab. The successful candidate will have excellent communication skills, the independence to manage and interpret survey results, and the scientific stubbornness to make a new IHC marker work.

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Mentor Abstract #13

Summer Scholar Research Proposal abstract:

Project Title: Establish Reference Interval for Voided Urine Samples in healthy adult Alpacas.

Principle Investigator: Heather A. Flaherty

Collaborating Investigator: Weston Brown

Establishing reference intervals for voided urine samples in healthy adult alpacas is necessary for proper interpretation of biochemistry results. An establishment of reference intervals is often expensive and time consuming. The major steps involved in establishing reference intervals is: Selection criteria, Establishing a reference sample group that includes at least 60 healthy animals, the collection and processing of samples, determining the reference values and reference distribution with established reference intervals. The selection criteria would include voided urine samples from healthy adult alpacas with ages between 1-6 years old. Ideally 120 animals would be sampled, due to possible health issues, outliers (based on data), sample difficulties, a minimum of 60 animals would be used to establish reference intervals.

The voided samples would be used to measure, pH, Blood (hemoglobin/myoglobin), bilirubin, Glucose, Ketones, Protein and Urine specific gravity (refractometer). Sediment exam would be performed on the spun urine to identify crystals, casts, leukocytes, erythrocytes and the presence of bacteria.

The establishment of reference intervals for voided urinary samples in adult alpacas is necessary for proper interpretation of biochemistry values. It would aid in the interpretation of azotemia, increased cholestatic enzymes, muscle damage, electrolyte imbalances, protein loss and renal damage.

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Mentor Abstract #14

Project Title:

NEURONAL DAMAGE IN NEURODEGENERATIVE DISEASES

Principal Investigator:

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Summary:

Neuronal loss is a hallmark of brain neurodegeneration associated with human pathologies such as Parkinson’s, Alzheimer’s and Huntington’s disease. Many neurodegenerative disorders in domestic and farm animals are clinically and morphologically similar to their human counterparts. However, relatively little research work has been done to understand their causative nature by veterinary scientists. Neurodegenerations in domestic animals are generally relatively rare conditions. However they do represent an extremely large spectrum of defects that, as a whole, represent an important group of diseases. Many of these neurodegenerations are very similar to diseases in humans and there is increasing evidence suggesting that in many neurodegenerative disorders, common cascades of molecular events occur despite widely diverging clinical and morphological presentations. This research project aims to identify the molecular mechanisms by which neuronal cell death associated with neurodegenerative disorders occurs. To achieve this, we will use novel molecular/cell biology techniques to determine the role of oxidative damage and mitochondrial dysfunction in neuronal cell death using Parkinson’s disease models as experimental paradigms. This experience will provide veterinary students with a clear insight into the mechanisms associated with neuronal cell death and with the knowledge regarding the use and availability of research tools to characterize these diseases better at the molecular level as future veterinary scientists.
Title: Retinal pathology and neural death associated with the progression of transmissible spongiform encephalopathy.

Investigator: Heather West Greenlee, Biomedical Sciences, Iowa State University College of Veterinary Medicine.

Collaborating Investigator: Justin Greenlee, Virus and Prion Disease Unit, National Animal Disease Center.

Abstract: Accumulation of abnormal protein in nervous tissues is a hallmark of prion diseases. Prion diseases or transmissible spongiform encephalopathies (TSEs e.g. Bovine Spongiform Encephalopathy a.k.a. ‘Mad Cow’) are a group of neurodegenerative conditions that naturally affect both humans and animals. Prion diseases are an excellent model to study neurodegeneration caused by abnormal protein accumulation (such as Alzheimer’s disease and Parkinson’s disease), as they are infectious, with known inoculation times facilitating the study of the earliest disease associated pathology. In mouse models, TSEs have consistent and well-defined incubation periods, making them ideally suited to dissect early events in neuronal death associated with accumulation of protein aggregates. While a great deal is known about the pathology associated with the end-point of TSEs and other neurodegenerative disorders, early pathologic events, and mechanisms to monitor these changes are not well developed. Our prior work has demonstrated changes in retinal function and morphology associated with the progression of prion disease in cattle.

Students on this project will work primarily at the National Animal Disease Center. The project will employ a variety of laboratory and clinical techniques to map changes in retinal morphology and function to landmark events in the central nervous system during the development of TSEs, primarily in mouse models of disease.

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Project Title: Impact of trace mineral nutrition on immune response in receiving cattle

Principle Investigator(s): Stephanie Hansen, Assistant Professor, Beef Feedlot Nutrition

Abstract:

Multiple projects are ongoing in our laboratory focused on the interaction between trace mineral status of beef cattle and health, performance and carcass characteristics of those cattle. The receiving period is particularly stressful for young cattle, when calves are newly weaned and shipped long distances to the feedlot for finishing. The trace mineral status of these cattle is often unknown, and deficiency of trace minerals can have negative impacts on the immune response. Minerals such as zinc and copper play important roles in B cell and neutrophil function. These trace minerals and others also are critical in the inflammatory response. Our aim is to better understand the role of trace minerals in beef cattle immune response, and also what optimal concentrations of trace minerals should be in the diet to achieve a sufficient, but not overzealous, immune response.

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Mentor Abstract #17

Project Title:
Morphometric analysis of spinal cord to aid in early diagnosis of cervical spondylomyelopathy (‘wobbler disease’) in horses

Principle Investigator(s): Dr Nick JEFFERY, Dr Cody ALCOTT
Collaborating Investigator(s): Dr Sina SAFAYI

Abstract:
Cervical spondylomyelopathy (CSM, aka ‘wobbler’ disease) is a common cause of neurologic dysfunction in young horses and, although treatment can be effective, it can be difficult to identify affected animals early in the course of the condition, when treatment is most likely to be efficacious. Veterinarians have a limited ability to detect early cases through physical and neurologic examination alone, because of variability in responses between individual animals and the difficulty in adequately manipulating such large animals.

Transcranial magnetic motor evoked potentials (TMMEP), which are muscle responses evoked by a (painless) magnetic stimulation of the brain through the skull, provide an objective measure of spinal cord conduction and so have huge potential as a tool for reliable diagnosis of spinal disease. This technique has been used in horses but its value in diagnosing CSM has not been investigated; furthermore, the spinal cord pathways that carry the impulses have not been defined.

This project will bring together the data from TMMEP recordings with anatomic information from the spinal cords of horses that have died because of CSM. Using routine microscopy plus specialist software, such as Image J and Cellprofiler, the student will develop methods to quantify the damage in the spinal cord of affected animals and use appropriate statistical tests to relate this to changes in conduction through the spinal cord. The project will therefore provide training in preparation of CNS specimens for microscopy, histology and image analysis techniques including quantitative analysis of histologic material and statistical analysis. These techniques will provide excellent tools for students to use in their future careers since they can be applied to a wide range of laboratory investigations and clinical specialties.

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Abstract:
Idiopathic inflammatory bowel disease (IBD) is a common cause of chronic gastrointestinal disease in dogs. Accumulating evidence in human IBD and animal models suggests that imbalances in the composition of the intestinal microbiota contribute to chronic intestinal inflammation. Current treatments for IBD include the administration of nonspecific anti-inflammatory drugs which may confer serious side effects and do not address the underlying basis for disease, namely, altered microbial composition. Modulation of the intestinal microbiota has been suggested as one approach to manage IBD. Probiotics (viable, non-pathogenic bacteria that exert health benefits beyond basic nutrition) offer an attractive, physiologic, and non-toxic alternative to shift the balance from harmful bacteria to protective bacterial species and treat IBD. The aim of the proposed study is to investigate the influence of VSL#3 treatment on the concentrations and spatial distribution of mucosal bacteria using fluorescence in situ hybridization with 16S rRNA targeting probes. We hypothesize that VSL#3 used as an adjunct to standard therapy (i.e., elimination diet and prednisone) will induce a beneficial alteration in the mucosa-associated microbiota leading to remission of gastrointestinal signs in dogs with IBD. There is a need for additional data to provide proof of efficacy in probiotic therapy before these agents can be applied to widespread clinical use. These studies will also provide highly relevant insight into the microbiologic effects of probiotics for treatment of canine IBD.

The student scholar will design, perform molecular studies, and interpret data of FISH performed on archived sections of inflamed intestinal mucosa in IBD dogs pre- versus post- VSL#3 treatment. These studies will be conducted in laboratories at the CVM and on campus (ie, molecular biology for fluoroscopy).

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Project Title:  ImageStream cytometry for the characterization of parasitic nematode eggs

Principle Investigators: Drs. Doug Jones, Terry Engelken, and Matt Brewer

ABSTRACT

Parasite control programs are estimated to reduce the cost of cattle production by approximately $190 per head and similar benefits are observed in other livestock. However, internal parasites are developing resistance to commonly used dewormers. Resistance exists in the United States including in Iowa in a variety of livestock species and represents tremendous health and productivity challenges.

One obstacle obstructing deworming programs is the lack of a method for identifying nematode species and resistant infections with a single laboratory test. Many nematode eggs are similar in appearance thus requiring molecular identification which is not cost effective at the level of the producer. Characterizing resistant populations requires microscopic fecal examination before and after administration of an antiparasitic drug. Such investigation requires handling livestock multiple times which is often not feasible. A single test identifying nematodes and their resistance status would offer both convenience and an economic benefit to producers.

Flow cytometry is a powerful tool for characterizing cells based on size, internal structure, and staining properties. This technology is the basis for the blood analysis equipment currently used by veterinarians. ISU-CVM possesses a sophisticated ImageStream cytometry (ISC) system which combines traditional flow cytometry with image capture and analysis. In this system each cell is photographed and subjected to computer analysis to measure identifying features.

The aim of this project is to use ISC to record the cellular characteristics of nematode eggs and apply this data to identify eggs from fecal specimens. In addition, we will establish baseline data for a single sample resistance assay. The summer scholar will be in charge of collecting specimens from a variety of livestock, flow cytometry assays, and identification of parasites.

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Mentor Abstract #20

Project Title: Effect of Locking Plate Configurations on Strength and Stiffness of Lumbosacral Stabilization Procedures

Principle Investigator(s): Karl H. Kraus

Abstract:

Lumbosacral instabilities are an increasingly common condition in large breed dogs. Both German Shepherds and Belgian Malinois are affected with these conditions, and both are used extensively in the US military at an average cost of $4,000. Many other non-military dogs are affected with lumbosacral instability as well. Recently the SOP Locking plate system is being used for LS stabilization, but its biomechanics in the L-S joint has not been reported. The objective of this study is to quantify the strength and stiffness of different configurations of the SOP locking plate system on stabilization of the Lumbosacral joint in dog cadavers.

Twelve large breed dog cadavers will be used in this study. The spine will be harvested then instrumented with SOP plates with: 1) One left SOP plate, two screws in the pedicle of L-7, two screws in the sacrum, 2) Two SOP plates, two screws in the pedicle of L-7 and sacrum, and 3) Two SOP plates, one screw in the pedicle of L-7, and two screws in the sacrum. The spines will be potted and placed in a four point bending apparatus. Extensometers will be placed dorsally and ventrally between L-7 and S-1 across a 3mm gap to measure displacement. The specimens will be tested in a materials testing frame resulting in measures of gp stiffness, bending moment stiffness, load at failure, and bending moment at failure. Measures will be compared between the three groups using repeated measures AVOVA.

The null hypothesis is that there is no difference between the two groups. It is expected that two plates will be both more stiff and more strong than one plate, but there will be no difference between one and two screws in the pedicle of L-7.

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Mentor Abstract #21

Project Title: Evaluation of diagnostic methods for Anaplasmosis in Nebraska cattle herds.

Principle Investigator(s): Dustin Loy DVM PhD Diplomate, ACVM

Abstract:

Bovine anaplasmosis is a commercially significant disease caused by the rickettsial organism, *Anaplasma marginale*. Anaplasmosis causes clinical disease in cattle including low weight gain, reduced milk production, abortions, and mortality. Older naïve cattle are of greatest risk, where a fatal anemia can be caused by infection. Animals that survive infection can go on to become persistently infected or carrier animals, making diagnosis of chronic infections challenging. Anaplasmosis has been described in nearly every state of the United States, and is thought to be increasing in distribution due to climate change and increasing vector distribution. The disease is transmitted by ticks, with more than 20 species have been documented as vectors throughout the world. The commercial significance is great, with economic impact estimated to be greater than $300 million dollars. Diagnosis of anaplasmosis remains complicated. Acutely ill animals can be diagnosed by observation of inclusion bodies along the margins of erythrocytes. Animals that have recently recovered from disease can be diagnosed by serological testing, using ELISA. However it is often difficult to diagnose animals that have circulating *Anaplasma* organisms at low levels or in cases of acute mortality where hemolysis has made cytology difficult. Specific aims of this research are to evaluate molecular diagnostic methods for Anaplasmosis comparison with serologic and cytologic methods in Nebraska cattle herds. Student scholars will receive a noteworthy experience conducting research in a diagnostic laboratory. Broad outcomes will be fundamentals in clinical microbiology and bacteriology, molecular diagnostics and molecular speciation of organisms.

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Mentor Abstract #22

Project title: Correlation of weight loss, previous ownership and upper respiratory infection in cats at animal shelters

Principal Investigators: Claudia Baldwin (VCS), Laura Andersen (VCS)

Collaborating Investigator: Christy Petersen

Understanding the factors that lead to health or disease within an animal shelter are critical for the survival of an animal in many shelter settings. Previous studies have determined that cats with high levels of stress, as measured by inappetence and weight loss after presentation to an animal shelter significantly increases the risk of upper respiratory infection (Hurley et al). Cage moves have also been associated with increased incidence of upper respiratory infection (Polak et al). Factors that lead to feline stress in animal shelters are likely to be multifactorial, including housing type, stray vs. relinquished, comorbid diseases including parasite burden and vaccination status prior to entering the shelter. For this project we hypothesize that free roaming or stray cats will have less stress upon entry into a shelter than previously owned, relinquished cats. Measurement of weight loss in the month after entry into collaborating shelters, cage moves, health screening for ecto- and intestinal parasites and intake history of ownership and vaccination will allow assessment of how these factors correlate with appearance of upper respiratory infection during shelter confinement in previously owned vs. free-roaming cats.

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Mentor Abstract #23

Surveillance of gastrointestinal parasites in companion animals in Midwest shelters

PI and Co-PIs Claudia Baldwin DVM MS, Christine Petersen DVM PhD, Laura Andersen DVM

Gastrointestinal parasitism is a burden on the feline or canine host and contributes to failure to thrive. There is concern for zoonotic disease and public health as people can be infected by certain gastrointestinal parasites of companion animals. Surveillance of gastrointestinal parasites in shelter animals has been performed in the southern and western United States but not systematically in the Midwest. Climate, environment, availability of mammalian hosts, and use of anti-parasite treatments all have an influence on parasite prevalence. The goal of this study is to conduct surveillance of prevalence and diversity of gastrointestinal parasitic infection within companion animals in Midwest shelters.

Methods: Collect fecal samples from dogs (or cats) upon admission to partner shelters. Perform fecal flotation and microscopic fecal examination to identify gastrointestinal parasites. Partner shelters will be asked to fill out a survey regarding their protocols for parasite treatment of animals admitted to their shelter. Specific individuals at each shelter partner, i.e. the shelter director, shelter manager, and veterinarian, will be provided the survey. If possible, a second fecal sample will be collected 1 week after initial sample was collected and re-evaluated for presence and type of parasites.

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Mentor Abstract #24

Project Title: Characterization of cholinergic anthelmintic receptors from nematode parasites expressed in Xenopus oocytes

Principle Investigator(s): Richard J. Martin and Alan P. Robertson

Abstract:
Anthelmintic drugs are very important for animal health in developed countries, and human health in developing countries. They are also an important part of drug development research for pharmaceutical companies. New anthelmintics (e.g. derquantel and monepantel) have been developed that selectively target nematode nicotinic receptors of parasitic nematodes. There is still much to be learnt about the mode of action of these compounds and how to limit and control the development of resistance. Our lab has developed expertise for the study of these anthelmintic drugs. We have recently cloned seven genes (unc-38, unc-63, unc-29, acr-8, unc-74, ric-3 and unc-50) from nematode parasites that when expressed together in Xenopus oocytes allows us examine, electrophysiologically, how the pharmacology of the receptor is affected by molecular changes; we are able to test mechanisms of drug synergism and drug resistance.

The project for the summer scholar will examine the effects of developing and existing anthelmintic drugs on nematode nicotinic receptors expressed in Xenopus oocytes using electrophysiological techniques. There will be a focus on the effects of derquantel, abamectin and their interaction. The scholar will be an active member of the team and will help and run experiments along with graduate students in an NIH supported project. The scholar will be exposed to and receive instruction on modern molecular, expression, receptor pharmacology and parasitology techniques. The results of the experiments are expected to be published.

Suggested reading:

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Mentor Abstract #25

Project Title: Evaluation of analgesics to treat chronic hoof pain in the horse.

Principle Investigator(s): Scott McClure, DVM, PhD, DACVS

Abstract:
The objective of the project is to evaluate mechanisms to treat chronic hoof pain. This will be done using the force plate to measure Peak Vertical Force and Impulse in horses with induced lameness.

Lameness in the horse is the most common problem seen by veterinarians. Lameness is usually the result of pain. In the horse, there have been a number of ways to evaluate pain medications. Most evaluations measure the response to a noxious stimulus such as heat. This does not really provide a good evaluation of therapies for pain causing lameness in the horse. We have developed a reversible mechanism, using a band around the hoof, to induce a persistent lameness of 5 days duration. This model better mimics the receptors and responses seen in real life situations.

Clinically it appears that horses with chronic lameness tend to have decreased response to analgesics. This may be due to “ramp up” effects in the spinal cord or inflammatory cascades that are not invoked in short term studies. We will use this model to evaluate potential analgesics for persistent pain in the horse. We propose to induce a moderate lameness (3/5 American Association of Equine Practitioners scale). The lameness will be evaluated subjectively with a score from the AAEP scale from 0 to 5. It will also be evaluated using a force platform to determine how much weight is being placed on the foot. In a randomized crossover block design, the horse will receive an analgesic when 1 forelimb has the band tightened and when the band is tightened on the opposite forelimb, the horse will not receive an analgesic to serve as a control.

I am happy to discuss the project with potential summer scholars.

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Mentor Abstract #26

2013 SSRP Summer Internship Proposal

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Project Title: Development of promoter assays to investigate the interference of PRRSV with the shared promoter regions of effected genes.

Abstract:

Research objectives include developing new approaches to identify porcine reproductive and respiratory syndrome virus (PRRSV) virulence mechanisms and develop better methods to effectively interrupt PRRSV pathogenesis thus enabling strategies to control PRRSV.

Activities that support the development of the research project: Development of promoter assays to investigate the interference of PRRSV with the shared promoter regions of effected genes – firstly bioinformatically and then in vitro.

Activities that support development of the student’s scientific expertise: hands-on training in various methodologies. Methodology includes a combination of in vitro and in vivo studies using both state-of-the-art and time-proven technologies to investigate the pathogenesis, immunology, and vaccinology of PRRSV; as well as to develop methods to detect virulence mechanisms that contribute to a unique expression of disease in swine. Training includes: wetlab experience in virology and molecular biology techniques, one-on-one learning of biostats, proteomics, and bioinformatics though expert mentors. When new results or discoveries are found, the graduate students will be encouraged to disseminate their findings. This would be done locally through NADC VPRU meetings.

The mentor: Provides technical and administrative supervision. Is responsible for making selections for positions, assigning duties, reviewing work, approving/disapproving leave, and evaluating performance. Our meetings (group and face-to-face) with the students would essentially be focused on the project – to keep track of research progress and to problem solve if an experiment or a model does not work. However, it should be emphasized that the Research Scientist will be readily available to students outside of the scheduled hours to discuss, advise and mentor them on career opportunities and the next stage of their academic/research careers.

It should be noted that the Research Scientist has recent experience collaborating with graduate and undergraduate students of the Iowa State University Bioinformatics and Computational Biology Department on research projects within the university setting.
Mentor Abstract #27

Summer Scholars Program 2013

Investigation into diagnosis, treatment and prevention of “Berzerk Males Syndrome” in camelids

Principle Investigator: Dr. Suzanne Millman, VDPAM
Co-investigators: Dr. Jennifer Schleining, VDPAM, Dr. Amanda Kreuder-Krull, VDPAM

A recent review of the literature indicates a scarcity of peer-review research on camelid behavior and welfare. In particular, evidence-based treatment protocols for correcting unwanted camelid behavior are needed. “Berzerk Male Syndrome” is a term used in the popular press and camelid industry to refer to male llamas and alpacas that display extreme and dangerous aggressive behavior towards humans. The condition is believed to be associated with imprinting when crias are bottle-fed, but has also been reported in dam-reared and in female camelids. Camelids diagnosed with Berzerk Male Syndrome are commonly euthanized, due to concerns for human safety and belief that the behavior cannot be corrected. The objectives of this research project are (1) to conduct a survey of llama and alpaca producers and veterinarians to describe current diagnosis, treatment and prevention of Berzerk Male Syndrome, (2) to identify causal factors associated with camelid aggression (including Berzerk Male Syndrome), and (3) to develop and beta-test a behavior modification protocol for aggressive camelids.

During the Summer Scholar project the student will gain understanding about principles of applied ethology and production of llamas and alpacas. The student will gain skills in animal welfare science, experimental design, statistical analysis, and camelid handling. When feasible, the student will also to assist with other research projects in the Animal Welfare laboratory, involving cattle, poultry and swine. The ideal student will have strong interests in animal welfare and animal behavior. Practical experience handling camelids is desirable, but not a requirement. Some weekend and evening work may be required during experimental trials. The student must have a valid driver’s license.

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Project Title: Swine Serological Responses to *Mycoplasma hyopneumoniae* Surface Proteins

Principle Investigator: Chris Minion, Professor VMPM

Abstract:
Despite efforts by the swine health industry, *Mycoplasma hyopneumoniae* (*Mhyo*) continues to have a significant negative production impact on swine producers. Currently available vaccines consist of bacterins, which help to reduce disease but don’t prevent colonization or pneumonia from occurring. This demonstrates the need for improvement in vaccines. The question, however, is what should the targets be in the vaccine and how should it be administered? The former question will be addressed in this proposal. To determine this, we need a way to quickly assess serological responses to specific *Mhyo* proteins in a quantitative manner. *Mhyo* has been particularly difficult to study because of the variable proteolytic processing that occurs to its major surface proteins resulting in difficult to interpret immunoblot analyses and identification of the targets of antibody responses across a large set of sera and field strains. We propose to employ a protein microarray consisting of purified unprocessed *Mhyo* proteins. Thus, our hypothesis is that we will be able to quantitate antibody responses in a manner similar to microarrays leading to identification of a subset of proteins most frequently recognized during infection. We have antisera from challenged animals that cover incrementally a 118-day period. We also have constructed and sequenced genetic clones of the majority of the surface-located proteins for recombinant expression. Our project will consist of three steps: 1) expression and purification of 45 surface proteins of *Mhyo*; and 2) printing of protein arrays on nitrocellulose; and 3) assessment of antibody responses to these proteins by pigs infected with *Mhyo* either from our challenge study or from clinical samples. We expect to be able to identify the antigens most frequently recognized by *Mhyo*-infected swine and through our set of sera, how quickly pigs respond and for how long (out to 118 days). This information can then be used to produce a multi-component vaccine.

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Mentor Abstract #29

Project Title: Retrospective Analysis of Perioperative Mortality in the Surgical Correction of Canine Portovascular Anomalies

Principle Investigator(s): Jo Ann Morrison and Krysta Deitz

Abstract:
Portovascular anomalies (PVAs) are common congenital lesions of the portal circulation in canines. These aberrant vessels divert portal blood from the hepatic vasculature directly to the systemic circulation. Thus, portal blood has reduced hepatocyte contact and hepatic dysfunction results. It is well documented that certain breeds are over-represented (Yorkshire terrier, Maltese, Miniature Schnauzer among others). Portovascular anomalies are named for the vessels that are involved. The most common congenital PVA is a single, extrahepatic portocaval shunt, where a single vessel diverts blood from the portal vein directly into the caudal vena cava. The clinical manifestations of congenital PVAs are extremely varied, from clinically insignificant to profound hepatic encephalopathy and death. The recommended treatment for PVAs is surgical correction with the goal of surgery to provide gradual and complete occlusion of the shunting vessel and restore normal hepatic perfusion and function. Current surgical recommendations are to pursue shunt ligation by either ameroid constrictor placement or cellophane banding. Unfortunately, perioperative mortality remains unacceptably high. Few risk factors for perioperative mortality have been widely identified or accepted. The goal of this study is to retrospectively (via electronic medical record (EMR) search) analyze the cases of congenital PVAs that have undergone attempted surgical correction in our hospital. An initial EMR search using the key words portosystemic shunt identified 84 surgical reports in a 10 year period. Two populations of dogs will be identified, those that survived the perioperative period and were discharged from the hospital, and those that did not. These two populations will be compared and factors that significantly differed between the groups will be identified. If possible, a scoring system may be developed that may be utilized prospectively in future clinical cases.

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Mentor Abstract #30

Project Title: Development and Validation of Detection Methods for non-O157 Shiga toxin-producing *Escherichia coli*

Principle Investigator(s): Rodney A. Moxley

Abstract: This project will be held in the laboratory of Dr. Rodney Moxley, School of Veterinary Medicine and Biomedical Sciences at the University of Nebraska-Lincoln during the Summer 2013 semester. The research will be conducted as part of a Coordinated Agricultural Project (CAP) grant from the USDA-National Institute for Food and Agriculture (NIFA). The overall CAP grant is focused on understanding and controlling Shiga toxin-producing *Escherichia coli* (STEC) throughout the beef system. This internship will help support Objective 1 of the STEC CAP project, which involves development and validation of detection methods for STEC. The objectives of the internship are: 1) to learn how to conduct cultural- and molecular (DNA)-based detection methods, and to understand the scientific basis associated with them; and 2) to conduct a research project to be assigned, which will implement some or all of these methods. The methods to be addressed include: aseptic technique and preparation of nutrient and selective bacterial culture media for STEC; preparation of bacterial culture plates through manual and automated methods; culture, isolation and characterization of STEC; STEC quantification by manual serial dilution and plating, and also operation of a spiral plater; operation of a computerized colony counter; isolation and purification of DNA; standard PCR; and quantitative real-time PCR. The student also will be expected to present data in progress at weekly laboratory meetings in attendance with graduate students and other laboratory staff.

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Mentor Abstract #31

**Project Title:** Impact of Poultry Practices on Emergence of Plasmid-Bearing *E. coli*

**Principle Investigator:** Lisa K. Nolan

**Collaborating Investigators:** Catherine M. Logue and Ganwu Li

Abstract: Although *Escherichia coli* on retail poultry and in poultry litter are expected to reflect fecal flora, *they do not*. Instead, the *E. coli* in these locations contain plasmids contributing to abilities to kill chickens and cause human disease. Such plasmids may harbor multidrug resistance (MDR)-encoding islands or co-transfer with large R plasmids, conferring MDR, to other bacteria during conjugation. Though the mere presence of such plasmid-bearing *E. coli* (PBEC) on meat is alarming, the fact that they are emergent is even more so. We contend that retail poultry and poultry environments, contaminated with PBEC, are reservoirs of virulence and resistance plasmids important in human urinary tract infections (UTI) and meningitis. Also, we hypothesize that these plasmids confer a selective advantage for survival on their host bacteria since PBEC are emergent despite energetic analyses predicting their loss from populations over time. Thus, it seems likely that modern poultry production practices, including use of antimicrobial agents to reduce microbial load on poultry and in their environment, actually favor selection of PBEC having enhanced capacity to cause disease and resist therapy.

Our overall goal is to understand the impact of poultry production and processing practices on the ecology of PBEC so that we can design interventions to ameliorate their detrimental impact on human and animal health. Here, we will test the hypothesis that current ‘on-farm’ and ‘in-plant’ production practices favor selection of PBEC. Our supporting aims will be to 1) understand the ecology of PBEC on chicken farms; 2) understand the ecology of PBEC on carcasses at processing; 3) understand the ecology of PBEC spread into the environment; and 4) examine the role of various agents on the selection of PBEC. The data collected will be used to develop ‘best practices’ to reduce PBEC contamination on retail poultry and in poultry environments.

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Project Title: Influence of Topical Otic Medications on Ear Cytology

Principle Investigator(s): James O. Noxon, DVM

Collaborating Investigator(s): Diana Miller, DVM

Cytology is one of the key diagnostic tools used in veterinary otology. Unfortunately, by the time cytology is performed, many patients have already received one or more topically-administered otic medications. These topical formulations generally include an antibacterial agent, and anti-yeast agent, and a glucocorticoid in an ointment or propylene glycol base. Clinically, we often see crystalline materials that we assume are residue of these previously-applied topical medications; however, this has not been confirmed with any studies. In this project, we will use normal, healthy, privately owned dogs (students, staff, and faculty) and instill various otic medications following label instructions (generally for 5-7 days). We will perform otic cytology at days 0 (prior to instilling medication), day 5 or 7 (the final day of treatment), at day 7 or 9 (2 days post therapy) and one week after therapy was concluded. Investigators will not have knowledge of the specific product utilized when evaluating the samples. At the conclusion of the study, we will attempt to quantify the amount of residue found at each sample and the nature of the residue and correlate with the specific commercial product used.

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Mentor Abstract #33

Project Title: Efficacy of Over-the-Counter Wipes For Management of Malassezia Dermatitis in Dogs

Principle Investigator(s): James O. Noxon, DVM

Collaborating Investigator(s): Diana Miller, DVM

*Malassezia pachydermatis* infections are very common secondary infections in dermatology. They are known to be flare factors for dogs with allergic skin disease and cause intense pruritus, manifested by frequent or non-stop licking, biting, chewing and rubbing at the feet, muzzle, axillary and inguinal regions. Strategies to control infections include the use of systemic anti-yeast medications, and topical therapy with shampoo, sprays, and wipes that contain active ingredients with anti-yeast activity. Commercial wipes are very helpful to manage difficult to reach areas, such as facial folds, lip folds, and the ventral interdigital spaces. However, many clients switch, generally without veterinary recommendations, to the use of over-the-counter wipes available for feminine hygienic or infant cleaning purposes. These commercial human products often contain ingredients that are considered anti-fungal. This project will investigate two aspects of the use of over-the-counter wipes in veterinary dermatology> Phase 1 will be an in vitro component to determine if the wipes do have anti-yeast activity. Phase 2 will be a blinded clinical trial in patients presented to the ISU dermatology service with yeast infections of the skin.

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Mentor Abstract #34

Computed Tomography (CT) as an Early Screening Tool for the Detection of Mycobacterial Lesions in Red-necked Wallabies (*Macropus rufogriseus*)

Primary Investigator: June E. Olds, DVM, Veterinary Clinical Sciences  
Co-Investigator: Kristina Miles, DVM, M.S. – Veterinary Clinical Sciences

Abstract

Four adult Red-necked Wallabies (*Macropus rufogriseus*) within a collection of 24 adults in the Blank Park Zoo have been identified with granulomas or abscesses containing acid-fast organisms since May 2012. All animals were diagnosed late in the course of disease, with lesions greater than 6 cm detected by radiography or palpation. *Mycobacterium avium, Subspecies hominissuis* was identified by mycobacterial culture and genotyping by NVSL. *Mycobacterium avium Subspecies hominissuis* is ubiquitous in the environment and is commonly isolated from non-tuberculous infections in humans and swine. Antemortem diagnostic tools for the detection of mycobacterial infections in macropods are largely unavailable. Frequently, the clinical signs of non-tuberculous mycobacteriosis are not evident until late in the course of the disease and may be non-specific. Intradermal tuberculin testing produces inconsistent results and is therefore of limited diagnostic value. Radiography is useful for localizing the site of infection in cases where osteomyelitis or calcified lymph nodes are present.

Mycobacteria have been associated with pulmonary, hepatic, splenic, and spinal abscess, lymphadenopathy, and spinal osteomyelitis in Red-necked wallabies. Affected wallabies identified within BPZ have been diagnosed with mediastinal or mesenteric lymphadenopathy and/or pulmonary abscess. In humans, radiography appears to be one of the most sensitive methods for diagnosing tuberculosis.

It is hypothesized that CT will be a more sensitive early screening tool for the identification of occult clinical non-tuberculous mycobacteriosis in Red-necked wallabies. Additional findings will include the normal CT anatomy of wallabies, the prevalence non-tuberculous mycobacterial infection, and prevalence of wallaby retrovirus in the evaluated animals.

Terminology and Abbreviations used:

- BPZ: Blank Park Zoo
- ISU: Iowa State University
- LVMC: Lloyd Veterinary Medical Center, Iowa State University College of Veterinary Medicine
- NVSL: National Veterinary Services Laboratory, USDA-APHIS, Ames, IA
- VDL: Veterinary Diagnostic Laboratory, Iowa State University College of Veterinary Medicine
- CBC: Complete Blood Count
- CT: Computed Tomography
- ADDL: Animal Disease Diagnostic Laboratory, Purdue University
- AAZV: American Association of Zoo Veterinarians
- PDS: Patient Score of Disease

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Mentor Abstract #35

**Project Title:** Anatomical Protection after Traumatic Brain Injury.

**Principle Investigator(s):** Diana Peterson

**Abstract:**
Within the last 10 years, exposure to blast pressure waves from explosives has become the primary cause of injury to our military personnel. Of major concern are military personnel exposed to mild blast pressure waves. These individuals may have normal motor functions, however months after the exposure several symptoms appear (e.g., post-traumatic stress disorder, attention deficit disorder, depression, emotional problems, as well as auditory issues such as tinnitus, inability to focus on sounds in a noisy environment, etc...). To examine these issues, we have developed a rodent model for blast exposure. The purpose of this proposal is to: 1) characterize blast-induced damage to GABAergic circuitry within the amygdala, and 2) identify how GABAergic manipulation—via alcohol—has protective and/or detrimental effects on blast recovery. Preliminary data indicate that blast-exposure causes more damage to GABAergic neurons than non-GABAergic neurons in the amygdala. Subsequent behavioral studies indicate that alcohol administration has protective effects on motor, depression and tinnitus formation after blast-exposure. The experiments outlined in this proposal will identify whether these behavioral changes are directly linked to a protective effect of alcohol on neuronal structures post blast-injury.

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Project Title:

Principle Investigator(s): **Gregory Phillips, Ph.D.**

Collaborating Investigator(s): **Michael J. Wannemuehler, Ph.D.**

Abstract: Recent experimental evidence reveals that the bacterial communities (microbiota) that comprise the mammalian gastrointestinal (GI) tract can have a profound influence on the health of the host. Diseases ranging from colorectal malignancies to inflammatory bowel diseases (IBD) have been linked to an abnormal microbiota (dysbiosis). Diseases associated with dysbiosis represent a significant burden on the health care industry, including mortality, lost productivity, and health care costs that exceed $6 billion annually. Despite the importance of bacteria to the wellbeing of humans and animals alike, how the microbiota influences health and disease is still not well understood. To better understand how specific microorganisms interact with the host, we are using a combination of transposon mutagenesis and next-generation DNA sequencing to identify genes important for colonization of the GI tract. Initially, we will target specific strains of *Escherichia coli* associated with IBD, as well as healthy individuals. Mutants that fail to survive in the host will be identified by the loss of specific sequence “signatures” following oral inoculation of mice. This effort requires techniques of molecular biology, bacterial genetics and computational analysis of the results. Identification and characterization of genes important for survival in the host GI tract will lead to new insights into how bacteria interact with the host as well as other members of the microbiota.

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Project Title: **Metagenomics Approaches to Characterize Mastitis**

Principle Investigator(s): **Gregory Phillips, Ph.D.**

Collaborating Investigator(s): **Paul Plummer, DVM, Ph.D., DACVIM(LA)**

Abstract: Mastitis is a major disease of dairy cattle and goats that costs the industry millions of dollars each year. Even sub-clinical disease can significantly impact animal health and milk quality. While multiple bacterial species have been identified as causative agents of mastitis, it is not clear how the bacterial community (microbiota) of the mammary gland serves to protect against disease. Without this fundamental knowledge, we are likely missing novel and more effective means of detecting and treating mastitis. Consequently, our *central hypothesis* is that progression of mastitis causes significant changes to the microbiota that comprise the mammary gland. To test this, we are using next-generation DNA sequencing to profile the microbiota in milk, without the need to culture bacteria. By comparing the microbiota from dairy cows with that of goats, we will further be able to determine if differences in somatic cell counts of the host correlate with composition of the microbiota. Our results should lead to a better understanding of how bacterial pathogens cause disease, and to more effective intervention strategies through identification of the most resilient members of the microbiota. These studies should contribute to novel approaches to prevent mastitis.

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Mentor Abstract #38

**Project Title:** Dose and time response studies on the neurotoxicity of carbonyl sulfide in mice.

**Principle Investigator(s):** Wilson Rumbeiha

**Collaborating Investigator(s):** Vellareddy Anantharam, Arthi Kanthasamy, Elizabeth Whitley

**Abstract:**
Carbonyl sulfide is classified by the EPA as a high priority Clean Air Act hazardous chemical. It is produced as a by-product of coal hydrogenation and gasification and in cigarette smoke. In industry, it is used as an intermediate in the production of thiocarbamate pesticides and herbicides. It is estimated that it is emitted in the environment at the rate of 9500 tons per year. Neurodegenerative diseases are increasing in the U.S population. Although the environment is thought to play a major role in the pathogenesis of these diseases, environmental toxicants which trigger these diseases are not well known. Carbonyl sulfide is a neurotoxicant, but little is known about its mechanism(s) of neurotoxicity. The long-term objective in our laboratory is to study the neurotoxic mechanisms of this environmental pollutant and to characterize the pathological lesions using the mouse model. Our hypothesis is that carbonyl sulfide causes dose and time dependent neurotoxic lesions in the mouse brain. The objective of the summer research project is to conduct a series of experiments to determine dose-response and time-response effects of carbonyl sulfide using the C57 black mouse model. End-points to be evaluated include neurobehavioral tests such as the rotarod, open field tests, elevated plus test, and histopathological assessment of lesions in the brain. Results of these experiments will be used to select suitable doses to be used in future studies to understand the molecular neuropathogenesis of carbonyl sulfide toxicity.

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Project Title: Developing a pig model of cyanotoxin intoxication

Principle Investigator(s): Wilson Rumbeiha

Collaborating Investigator(s): Steve Ensley, Paula Imerman, Elizabeth Whitley

Abstract:
Cyanobacteria harmful algal blooms (CyanoHABs) produce cyanotoxins which poison people, all terrestrial animals including food producing animals, birds and fish world-wide. In Iowa, cyanoHABs commonly produce microcystins, nodularins, anatoxins, and endotoxin. Because of climate change, and coupled with human activities, cyanoHABs have become more frequent both in prevalence and severity in the U.S.A and around the world. In addition, strains of CyanoHABs which were only present in tropical regions of the world have recently emerged in Iowa and other Midwest states, among them the highly toxic cylindrospermopsin. Cylindrospermopsin is on the EPA candidate contaminants list, meaning it has been identified as an important toxin warranting further research. Cylindrospermopsin is a hepatotoxic, nephrotoxic, and reproductive toxin that may also be carcinogenic. Cyanotoxins are not only present in water, but are likely transferred through the food chain as well. There is a great need for an animal model to study the acute and chronic effects of cyanotoxin intoxication in people and livestock. The pig is widely used as a model to study the effects of toxicants in humans because the physiology of its organs closely resembles that of humans. The purpose of the summer research project is to develop an acute model of cylindrospermopsin intoxication in humans using the pig as a model. An acute dose- and time-response study of cylindrospermopsin intoxication in pigs will be conducted. Pigs will be orally dosed with cylindrospermopsin. Results will be used to select an ideal dose for future experiments to further characterize the toxicity and the toxicokinetics of this toxin; and the toxic interaction among other cyanotoxins which are co-produced during the bloom, including endotoxin. This data is needed for health risk assessment of cylindrospermopsin intoxication in humans and pigs.

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Mentor Abstract #40

Project Title: Antimicrobial Efficacy of a Solution Containing Citrate Ion and Isopropyl Alcohol as a Preoperative Preparation in Cattle Under Field Conditions

Principle Investigator(s): Jennifer A. Schleining, DVM, MS, DACVS-LA

Collaborating Investigator(s): Paul Plummer, DVM, PhD, DACVIM(LA); Chong Wang, PhD

Abstract:
The reduction of surgical wound infection is highly dependent on preoperative skin preparation techniques. In large animal species, this is limited to either an iodophor- or chlorhexidine-based preparation in combination with alcohol. The vast majority of published studies occur within a controlled hospital environment and may not be applicable to an ambulatory setting. The proposed study evaluates a novel preoperative skin preparation solution in cattle against the traditional preoperative preparation methods. Briefly, the paralumbar fossa of 100 mature Holstein cows will be randomly assigned to undergo preoperative surgical preparation with a novel surgical antiseptic and alcohol. The opposite paralumbar fossa will be randomly assigned to either a povidone iodine group or a chlorhexidine gluconate group. Microbial samples will be obtained prior to surgical site preparation and at 10 minutes, 6 hours, and 24 hours post-site preparation. Colony forming units will be determined from the microbial sampling plates following 48 hours of incubation. When experimental conditions are compared, it is hypothesized that the citrate ion/alcohol preparation will perform equally or better than the povidone-iodine/alcohol and chlorhexidine preparations as evidenced by reduction in colony forming units and residual activity at the site of the simulated incision.

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Project Title: Mass Euthanasia of Cattle and Application of Oxytet to foot lesions and the possibility of residue in the milk

Principle Investigator(s): Dr. J. K. Shearer

Collaborating Investigator(s): Dr. Paul Plummer and Leslie Shearer

Abstract:

**Euthanasia Project**
APHIS has the responsibility and authority to control and eradicate catastrophic diseases in the livestock industries. Traditional approaches to cattle depopulation may not address the speed and urgency of an animal health emergency on large cattle farms while ensuring humane euthanasia of the animals. Therefore, a rapid, portable and humane depopulation system must be developed to address this need. This project will utilize a prototype pneumatic captive bolt device with air-channel pithing to determine the most efficient and effective ways to humanely euthanize dairy and beef cattle during mass depopulation. This knowledge and ability will be fundamental to carrying out APHIS programs during livestock emergencies on large farms.

**Oxytet project-Goals and Objectives**
The overall goal of this study is to determine what the most common approaches to treatment of claw lesions are amongst trimmers and veterinarians. Secondly, we propose to determine what, if any, beneficial or detrimental effects there may be with the application of topical treatments (tetracyclines and copper sulfate); specifically on: pain within the immediate post application period, effect on the corium within 24 hours following topical treatment or no topical treatment, effects on long-term recovery including clinical appearance and re-epithelialization of the corium at 21-30 days post-treatment, and finally, evidence of detectable residue (tetracyclines).

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Mentor Abstract #42

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Summer scholars (veterinary students) selected through CVM/NIH internship program would learn one or more of the following techniques:

1. Tissue culture experiments
2. Transgenic animal (mouse) breeding, genotyping and phenotyping
3. Isolation and processing of RNA from pathological samples (human and animal samples)
4. Design and perform PCR experiments to amplify alternatively spliced transcripts
5. Run agarose and polyacrylamide gel electrophoresis
6. Perform gene silencing experiments
7. Perform cloning and expression experiments
8. Perform protein isolation and purification
9. Perform immunological tests
10. Write and present scientific report

For more information about a specific research project, please contact:

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Project Title: Metabolic adaptations of *Staphylococcus aureus* to intermediate antibiotic resistance

Principle Investigator(s): Greg A. Somerville, Ph.D. (UNL)

Collaborating Investigator(s): Robert Powers, Ph.D. (UNL)

Abstract:

*Staphylococcus aureus* pose major health risks and cause significant economic hardships to livestock producers, food industries, and veterinary medicine. Bacterial antibiotic resistance is a major problem for veterinarians and physicians that can lead to treatment failures. As new antibiotics are brought to market, bacteria adapt their metabolism and physiology to permit growth in the presence of intermediate concentrations of those antibiotics. We are using NMR metabolomics to identify these metabolic adaptations and determine the feasibility of reversing these adaptations to inhibit bacterial intermediate resistance. If we are successful, then this will extend the usable life of new antibiotics.

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Project Title: *Disease modification in epilepsy*

**Principle Investigator(s):** Dr. T. Thippeswamy

**Collaborating Investigator(s):** Need to discuss with Dr. A.G Kanthasamy's Group

**Abstract:**
Currently available antiepileptic drugs (AEDs) prevent seizures but do not suppress the neurobiological changes that occur after the first seizure. Studies from our laboratory have shown that neuron-glial miscommunication, following status epilepticus (SE), triggers neurodegenerative changes. Therefore the main objective of the research project is to target both neurons and glial cells, at an early stage, to prevent neurobiological changes that occur prior to the disease onset. Convulsive seizures observed during SE precipitate excitotoxicity that is mediated by glutamate receptors linked to the activation of postsynaptic density protein 95 (PSD95) and neuronal nitric oxide synthase (nNOS). This in turn activates glial cells (gliosis—both proliferation and hypertrophy) to produce chemokines, cytokines and inducible NOS (iNOS), all of which contribute to the subsequent neuropathology. Our pilot experiments in a mouse model of epilepsy demonstrated suppression of gliosis, aberrant sprouting (hallmarks of epileptogenesis) and reduction in the number of abnormal EEG events following a combined treatment with an anticonvulsant (diazepam) and an experimental neuro- and/or glio- protectant [an nNOS inhibitor, Nω-propyl-L-arginine (L-NPA); PSD95 blocking peptide (PSD95BP) and/or an iNOS inhibitor, 1400W]. We are currently investigating the effects of single and combination treatment with an AED, PSD95BP and 1400W in a mouse model of epilepsy to identify those proteins and cell types, which may be a novel therapeutic targets or biomarkers of epileptogenesis.

**Under this project, Summer Scholars will have several opportunities to work on control and epileptic mouse brain using one or more of the following techniques:**

i) immunohistochemistry  
ii) Western blot or ELISA  
iii) Video (behavioural) data analysis  
iv) EEG data analysis from control and epileptic mice implanted with EEG electrodes (a telemetry device). Depending on individual’s interest, skills and capabilities, samples from intervention experiments may be given for further analysis.

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Project Title: Characterization of a Novel SCID Pig

Principal Investigator(s): Christopher K Tuggle

Collaborating Investigator(s): N. M. Ellinwood, J. Dekkers, J. Cunnick

Abstract:

At Iowa State, we have discovered a serendipitous mutation causing Severe Combined Immuno-Deficient (SCID) that segregates in a line of pigs selected for feed efficiency. This is the first naturally occurring SCID mutation in pigs, which we have determined is a Mendelian recessive mutation. We have shown homozygous affected piglets are missing both B and T cells, yet can be kept alive by maintaining the piglets on the nursing sow for up to 5+ weeks. We have also succeeded in allogenic bone marrow transplants and currently have three surviving homozygous SCID pigs > 6 months of age. This novel model can now be exploited in several ways. We are collaborating with both biomedical and veterinary scientists to characterize the differences in the innate and adaptive arms of the immune system, as well as the response to bacteria and viruses, between SCID and normal pigs. We are especially interested in determining the dependency of innate cells such as macrophage and NK cells on signals from adaptive immune cells that are absent in the SCID pig. We have developed assays for porcine NK cell function and are collaborating with NADC personnel to assay alveolar macrophage function prior to and during an influenza challenge. Participating in this project would provide a summer intern the opportunity to perform a number of cellular and molecular assays as this unique model is characterized.

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Mentor Abstract #46

**Project Title:** Evaluation of replication, immunogenicity and protection efficacy of EAV-PRRSV chimeric viruses expressing GP5 and/or M ectodomains of PRRSV in pigs

**Principle Investigator(s):** Dr. Jianqiang Zhang

**Collaborating Investigator(s):** Drs. Phillip Gauger and Udeni Balasuriya

**Abstract:**
Porcine reproductive and respiratory syndrome (PRRS) is the most economically important disease affecting the swine industry with an estimated cost of $664 million annually in US breeding and growing pigs. The current commercial MLV PRRS virus (PRRSV) vaccines have several deficiencies including virus shedding, incomplete cross-protection, inability to serologically distinguish infected from vaccinated pigs, and potential reversion to virulence. It remains uncertain which arteriviral proteins are used for attachment to host cells or determinants of cellular tropism. It is also unclear if GP5 alone, the GP5/M heterodimer, or other minor structural proteins (e.g. GP2, GP3 and GP4) are required to induce protective immunity against PRRSV. We recently developed an infectious cDNA clone of the MLV vaccine strain of equine arteritis virus (EAV), the prototype virus in the family *Arteriviridae* which includes PRRSV. We further generated three viable EAV-PRRSV chimeric viruses (EAVrMLVB-PRRSVGP5ecto, EAVrMLVB-PRRSVMecto, and EAVrMLVB-PRRSVGP5&Mecto) by replacing the N-terminal ectodomains of GP5 and/or M proteins of EAV with the corresponding regions of a North American PRRSV type 2 strain. Evaluating the replication kinetics and immune response of these EAV-PRRSV chimeras in pigs would help us understand viral proteins determining cellular tropism and viral proteins inducing neutralizing antibody. In addition, the EAV-PRRSV chimeric viruses can be potential vaccine candidates that may provide a new platform for the prevention and control of PRRSV in swine. The specific objectives of this project are 1) to determine if the EAV-PRRSV chimeric viruses expressing the PRRSV GP5 and/or M ectodomains have the ability to infect and replicate in pigs; 2) to determine if these EAV-PRRSV chimeric viruses expressing the PRRSV GP5 and/or M ectodomains induce PRRSV-specific antibodies (neutralizing and non-neutralizing) in immunized pigs; 3) to determine if immunization with these EAV-PRRSV chimeric viruses can provide protection against subsequent challenge with homologous PRRSV.

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