Project Title: Comparative Hematology in a One Health Approach - Pathophysiology and Prognosis of Inappropriate Metarubricytosis of Humans and Canines

Principle Investigator(s): Dr. Claire Andreasen

Collaborating Investigator(s): pending at NC State; the preliminary work will focus at ISU CVM

Veterinary Scholar Focused Abstract: (300 words or less):
The project will address comparative hematology in a retrospective study of inappropriate metarubricytosis in dogs and determine if the same clinical syndromes and diseases contribute to this occurrence in dogs similar to the diseases and conditions in human beings. Also, cell levels will be examined to see if prognostication factors are correlated in various diseases. Currently, prognostication of metarubricytosis in dogs has been restricted to heatstroke. In dogs, as sometimes occurs in people, inappropriate metarubricytosis has been associated with endotoxemia, sepsis, pancreatitis, and bone marrow injury, especially to the endothelial cells and erythroid marrow islands or effacement/replacement of marrow components. Lead toxicity also can result in inappropriate metarubricytosis in both species. The association of various diseases and conditions resulting in canine inappropriate metarubricytosis is currently antidotal. Outcomes of this project are to review human and canine literature related to inappropriate metarubricytosis; understand the proposed and validated pathogenesis; use laboratory information medical records to identify canine inappropriate metarubricytosis cases; design an analysis of cases to determine the associated syndromes in dogs compared to human beings; and determine if the level of inappropriate metarubricytosis is a prognosticator in specific syndromes. The project will require hypothesis driven experimental design to determine results, computer skills, and the ability to learn statistical analysis.
Project Title: Development of an antibiogram for the ISU LVMC Small Animal Hospital

Principle Investigator(s): Blong, AE

Collaborating Investigator(s): Walton B

Veterinary Scholar Focused Abstract: (300 words or less):

A hospital antibiogram serves as reference tool to determine the antibiotic susceptibility patterns for local bacterial isolates. It is a critical piece of information when deciding empiric antibiotic therapy in critical ill patients for both community and hospital acquired infections. The antibiogram can help determine what types of bacteria are most typically cultured from certain areas (lung vs urine) as well as the most likely susceptibility pattern for those bacteria. The development and use of a hospital antibiogram is recommended by the CDC as part of an antibiotic stewardship program. The ISU LVMC does not currently have an active antibiogram available for use.

The purpose of this project is to 1) develop an antibiogram for clinical use at the LVMC, 2) develop a method of data collection that will allow annual updating of the antibiogram, and 3) development of concise visual aids and dissemination of the information to hospital staff. The project will involve data mining the results of microbiological cultures obtained from patients of the LVMC Small Animal Hospital. The data will then need to be organized into a useful format and analyzed to produce an antibiogram for hospital use. Then, using the antibiogram data, recommendations for antimicrobial selection will also be developed. The information will then developed into visual aids and disseminated to the hospital staff. The project data will need to be presented at least once as a presentation to LVMC hospital clinicians.

The antibiogram and the recommendations developed from it will also allow a subsequent “before and after” study assessing compliance and appropriateness of initial antibiotic selection.
Project Title: Presence, tissue distribution, and concentration of residues associated with administration of barbiturates and other commonly used pharmaceuticals to euthanize livestock

Principal Investigator(s): Stephanie S. Caston

Collaborating Investigator(s): Scott Radke, Renee Dewell, Brett Sponseller

Veterinary Scholar Focused Abstract:

Animals euthanized with barbiturates or that have received other pharmaceuticals and then processed via rendering present an increased negative risk to pet-food safety and wholesomeness, and animals disposed of in other ways may represent a risk for animals that scavenge, or the environment itself. At present, tissue distribution and concentration of barbiturates and other pharmacologic agents such as sedatives, tranquilizers, and disassociatives in deadstock that have been euthanized is not well-defined. Our group proposes to 1) determine the tissue distribution and concentration of barbiturates and commonly used pharmacologic agents administered in livestock species including: equids, swine, and ruminant species 2) Determine the stability of commonly used pharmacologic agents to typical rendering temperatures 3) Assess the stability of barbiturates and commonly used pharmacologic agents that were administered prior to euthanasia in livestock species at temperatures in excess of 50 degrees higher than typical rendering temperatures. Tissue samples have been previously collected and archived. Tissues collected include mesenteric fat, muscle, spleen, kidney, and liver, rib bone, and aqueous or vitreous fluid.

The student scholar will assist in determination of tissue distribution and concentration of barbiturates and other pharmacologic agents. Tissue samples will be extracted, and following determination of sufficient dryness of a portion of each extract, samples will be analyzed using a combination of gas chromatography with mass spectroscopy (GC/MS) and gas chromatography and nitrogen-phosphorus detector (NPD). If necessary, further characterization can be done using liquid chromatography with orbitrap mass spectroscopy. Results will be reported as either “present” or “not present” for the drug of interest. Samples confirmed to have the drug of interest will undergo quantitative analysis to measure concentration in parts per million (ppm). Data entry and data analysis will also be a component of the work for this project.

An understanding of tissue distribution and concentration of barbiturates and commonly used pharmaceuticals associated with euthanasia will provide important data to renderers and veterinarians and owners that need to humanely euthanize and dispose of equid and food animal species.
Project Title: Evaluation of Acclimation and Low Stress Cattle Handling on Health and Performance of Feedlot Cattle

Principle Investigator(s): Grant Dewell

Collaborating Investigator(s): Suzanne Millman

Veterinary Scholar Focused Abstract: (300 words or less):

Bovine respiratory disease continues to be the major cause of morbidity and mortality in feedlot operations despite the advancement in vaccines and antibiotics. Feedlot calves undergo tremendous stress prior to arrival at the feedlot (weaning, comingling, auction market and transportation) and after arrival (comingling, handling and processing, and diet change). The combination of several of these stressors can impair immunity and lead to increased morbidity and decreased performance. This project will enhance the comprehensive animal welfare research program initiated by our research team. The specific objectives of this project are to: 1) Determine the impact that acclimation and low stress cattle handling have on respiratory morbidity and mortality in feedlot cattle. 2) Measure physiological differences (cortisol, haptaglobbin, MMP9 and Creatine phosphokinase) between acclimated and low stressed handled calves compared to traditionally handled calves. 3) Determine the impact that acclimation and low stress cattle handling have on performance of feedlot cattle. Specifically, 80 pens of cattle (40 freshly weaned bawling calves and 40 comingled auction market calves) will be enrolled in the study. Half of the pens will be acclimated and handled with low stress practices and half of the pens will be traditionally handled. Serum samples will be collected from a random subset of calves at initial processing and at re-implant processing. Respiratory morbidity and mortality will be recorded and performance measures will be recorded at the end of the feeding period.
Project Title: Ex vivo comparison of the bursting strength of surgeon’s knots, compared to the forwarder knot combined with surgeon’s knots for closure of ventral midline celiotomy in horses

Principle Investigator(s): Alex Gillen

Collaborating Investigator(s): Dane Tatarniuk, Stephanie Caston, Kevin Kersh, Tamara Swor

Ventral Scholar Focused Abstract: (300 words or less):

Ventral midline incisions have a relatively high incidence of post-operatively complications, ranging from 7.4-47%. It is therefore important that work is undertaken to reduce the incidence of those complications.

It has previously been demonstrated, both in vitro and ex vivo, that self-locking knots have a higher knot holding capacity and knot security compared to the more commonly used square and surgeons’ knots. Previously work has evaluated the forwarder knot to start and continuous suture line and an Aberdeen knot to end a continuous suture line. However, the majority of ventral midline celiotomies require a large incision, utilizing at least two pieces of suture material to close the incision. The authors hypothesize that, a forwarder knot, placed at either end of a continuous suture line, and joined in the middle of the incision will have a higher bursting strength compared to incisions sutured closed using only surgeon’s knots.

A 30cm ventral midline celiotomy will be created in 12 fresh equine cadavers. Horses will be randomly assigned to celiotomy closure with two suture strands of 2 polyglactin 910 in a simple continuous pattern utilizing either two forwarder knots and one surgeon’s knot (F-S-F; n=6), or only surgeons knots (S-S-S; n=6) knot combination. Prior to closure, a 200L polyurethane inflatable bladder will be placed in the abdomen, then insufflated until failure of the celiotomy closure. Treatment group, celiotomy closure time, bursting strength (mmHg), and failure mode will be compared using the Wilcoxon Rank Sum test.
Project Title: Effect of Intravenous Maropitant on heart rate and blood pressure in critically ill dogs and cats.

Principal Investigator(s): Bonnie L. Hay Kraus, DVM, DACVS, DACVAA

Collaborating Investigator(s): Dr. Shelly (Ting Ting) Chi, Dr. Rebecca Walton, Dr. April Blong

Veterinary Scholar Focused Abstract: (300 words or less):
Maropitant is a neurokinin-1 antagonist approved for the prevention and treatment of vomiting from a variety of clinical reasons in both dogs and cats. Previous studies conducted at the ISU Lloyd Veterinary Medical Center have also shown that maropitant is effective in preventing vomiting and signs of nausea in dogs when administered subcutaneously (SC) one hour prior to the administration of opioid anesthetic premedication. Currently, all canine and feline anesthetic patients receive maropitant prior to anesthesia and many remain on the drug post-operatively to help with nausea and vomiting which can be a side effect of opioid analgesic drugs. The disadvantages of SC administration are the relatively long onset of action (30-60 minutes) and pain on injection. Recently, intravenous (IV) administration has been added to the maropitant proprietary label after safety and efficacy studies were completed. The advantages include a faster onset of action and potential avoidance of painful injection. Label recommendations for the rate of administration is slowly over 1-2 minutes. A decrease in blood pressure of 10-20mmHg for 5-10 minutes was observed by Boscan et al (2011) after IV administration in healthy anesthetized dogs. Clinically, we have also observed a significant decrease in arterial blood pressure, especially in critically ill patients, some of which have experienced a prolonged negative effect on systemic blood pressure. This study will examine the effects of IV administration of maropitant on heart rate and blood pressure in awake canine and feline patients admitted to the ISU LVMC intensive care unit. The student investigator will be trained to obtain and document vital parameters (heart rate and non-invasive blood pressure) in hospitalized canine and feline patients receiving IV maropitant treatment and will also use a behavioral scale to document negative reaction to IV administration.
Project Title: Evaluating High-Dose Intravenous Vitamin C Pharmacokinetics in Healthy Beagle Dogs

Principal Investigator(s): Margaret Musser, DVM, DACVIM (Oncology), Asst Professor
Chad Johannes, DVM, DACVIM (SAIM, Oncology), Asst Professor

Collaborating Investigator(s): Jonathan Mochel, DVM, MSc, PhD, DECVPT, Assoc Professor

Veterinary Scholar Focused Abstract: (300 words or less):
This project will be the first phase in investigating the potential role of high-dose intravenous (IV) vitamin C as a therapy for dogs with various types of cancer. This will be a pilot pharmacokinetic study in healthy Beagle dogs to obtain preliminary data which will help establish a relevant high-dose protocol (which has not been evaluated or determined); although previous work has been completed from which a safe starting dose can be extrapolated. Future studies in collaboration with the University of Iowa are in the planning stages and will allow us to evaluate the use of high-dose IV vitamin C in combination with radiation therapy and chemotherapy treatments in dogs with naturally occurring cancer (i.e., osteosarcoma). These canine studies may help drive additional human studies at the University of Iowa.
Johne’s disease in beef cattle: improving diagnostic techniques

Project Title:  Johne’s disease in beef cattle: improving diagnostic techniques

Principle Investigator(s): Amanda Kreuder, DVM, PhD, DACVIM (LAIM)

Collaborating Investigator(s):  Adam Krull, DVM, PhD

Veterinary Scholar Focused Abstract: (300 words or less):

Johne’s disease, a chronic diarrheal disease of ruminants, has historically been considered an economically important disease of dairy cattle with little impact on U.S beef herds. Evaluation of Iowa State Veterinary Diagnostic Laboratory submissions shows a substantial increase in Johne’s positive animals from Iowa cow-calf operations over the past several years. Johne’s is a devastating disease that has no treatment or cure, is difficult to diagnose, and once present on a farm may be challenging to eradicate. The current recommendations for whole herd testing to eradicate Johne’s disease from beef herds are extrapolated from data in dairy herds; however, no studies have been done to validate these testing strategies in beef cattle. Thus, there is a critical need to improve whole herd testing strategies for beef operations as well as to continue to develop new testing modalities to improve the accuracy of detection of Johne’s infected animals (including beef and dairy cattle as well as sheep and goats) prior to shedding. To address this need, the summer scholar will assist in research directly comparing the use of currently available tests (fecal PCR and blood ELISA) as well as a novel method of disease detection using volatile organic compounds (VOCs) in the feces to identify infected animals. The summer scholar will be responsible first for analyzing diagnostic laboratory data regarding Johne’s submissions to determine trends and collect data for analysis. The scholar will then be responsible for performing ELISA testing of paired serum and fecal samples to determine the best test to use for diagnosis of subclinical infections in beef cattle. Finally, the scholar will assist with development of a new diagnostic test using VOCs which we hope will be able to identify Johne’s infected animals earlier in the disease process.
Project Title: Whole genome sequencing to evaluate antimicrobial resistance in Salmonella from three different food producing species (poultry, cattle, and swine)

Principle Investigator(s): Adam Krull, DVM, PhD

Collaborating Investigator(s):
Orhan Sahin, DVM, PhD, DACVM
Amanda Kreuder, DVM, PhD, DACVIM (LAIM)

Veterinary Scholar Focused Abstract: (300 words or less):

Salmonella is one of the most costly diseases to producers in many areas of food production in the United States, both from a food safety as well as an animal health standpoint. Monitoring of antimicrobial resistance acquisition in Salmonella isolated from animal food sources is also of utmost concern to ensure that appropriate treatments are available for human cases. The most common method to evaluate an organism's susceptibility to an antibiotic utilizes 2-fold dilutions of the antibiotic to determine the minimum amount of antibiotic needed to inhibit growth of the organism. The lowest dilution of antibiotic required to inhibit growth is known as the MIC or minimum inhibitory concentration. While this provides useful clinical information, it does not provide information on the genetic elements responsible for the resistance profile, nor does it allow for tracing of the relatedness of isolates or spread of resistance genes. The use of whole genome sequencing of bacterial organisms allows us to study the genetic resistance patterns present and compare them to the phenotypic resistance seen on MICs while being able to more accurately trace the origin of the bacteria and development of resistance. For this project, the summer scholar will be responsible for analysis and comparison of whole genome sequencing data of three separate serotypes of Salmonella from three different source species: Salmonella enteriditis (poultry), Salmonella Dublin (cattle) and Salmonella I 4,5,12; i- (swine). The student will also be responsible for antimicrobial resistance testing of these isolates in the lab and will gain valuable experience in advanced methods in microbiology during this project such as MLST typing and PCR.
Project Title: Comparison of circulating Vitamin D in Captive Black Rhinoceros in North America

Principle Investigator(s): June Olds, DVM

Collaborating Investigator(s): Jesse Goff, DVM PhD

Veterinary Scholar Focused Abstract: (300 words or less):

Hypothesis/Objectives:
North American captive black rhinoceros circulating Vitamin D levels will be influenced by husbandry conditions such as outdoor access, latitude, season, diet, and supplementation.

Abstract: Published “normal” reference values (RV) for circulating 25-hydroxy-vitamin D$_3$ (25OHD) for the critically endangered black rhinoceros (“BR” - *Diceros bicornis* spp.) [55 ng/ml +/- 34.2 ng/ml] reflect data from a small sample size (n=28) of free-living BR in Zimbabwe. Few results for 25OHD have been published for captive BR. Vitamin D is essential to calcium homeostasis, but also serves important roles in immune function. Research in humans is focused on the autocrine function of Vitamin D and suggests the importance of preventing *subclinical* vitamin D deficiency because of increased risks for developing multiple diseases. The objectives of this study are: 1) Determine seasonal variations and husbandry influence of circulating 25OHD in captive North American BR, and 2) to create a method-comparison for a commercial Vitamin D ELISA test kit for future use in South Africa to assess vitamin D levels in free-ranging BR. Ultimately, this information may provide guidance for appropriate captive rhinoceros management.

Materials & Methods: Fresh or banked frozen serum samples are being solicited from North American (N.A.) AZA-accredited zoos housing captive BR. The student will create a brief questionnaire to request information about the health status and husbandry of the animals sampled, including housing, diet fed at the time of sample collection, and supplements provided. Serum samples from N.A. rhino will be processed in a commercial U.S. laboratory using High Pressure Liquid Chromatograph paired with a triple quadropole mass spectrometer (HPLC/MS/MS), then method comparison created for commercial ELISA 25OHD test kits. Phase 1 of this project will focus on the captive population questionnaire and the identification of a reliable test for use in the field in South Africa (Phase 2).
Project Title: Determination of biomechanical variables of the foot in normal reticulated giraffes

Principle Investigator(s):

Jennifer A. Schleining, DVM, MS, DACVS-LA; Veterinary Diagnostic and Production Animal Medicine

Collaborating Investigator(s):

June Olds, DVM; Veterinary Clinical Sciences and Blank Park Zoo
Drew Gall, DVM; Blank Park Zoo

Veterinary Scholar Focused Abstract: (300 words or less):

Lameness in ungulate species is a common condition with the majority of pathology originating in the foot. While biomechanical variables such as identification of the major weight bearing claw, distribution of weight, and certain gait characteristics have been identified in domestic bovine species, these same variables have not been identified in giraffes. A recent year-long treatment regimen for lameness in a giraffe originating from a displaced second phalanx fracture at the Blank Park Zoo provides the impetus for this proposed project. Using a pressure walkway system (Tekscan Walkway™) giraffes at the Blank Park Zoo in Des Moines and Henry Doorly Zoo in Omaha, Nebraska will have measurements determined during multiple sessions in which data will be collected from normal footfalls as the animal walks across the walkway. Measurements include Pressure characteristics, Center of Pressure, Force, and stride length. Results of the study will be used to identify the main weight bearing claw in giraffes in zoo environments, gait characteristics, center of pressure, and other pressure characteristics that will help direct appropriate treatments for lameness in giraffes in the future.
Project Title: Development of a novel in vivo model of conjunctivitis in the dog

Principle Investigator: Dr. Lionel Sebbag

Collaborating Investigators: Dr. Rachel Allbaugh, Dr. Jonathan Mochel

Veterinary Scholar Focused Abstract:

Conjunctivitis, or inflammation of the conjunctiva, is a common disease in dogs that has several etiologies, including dry eye (keratoconjunctivitis sicca), allergies (allergic conjunctivitis), viral infection (canine herpesvirus-1), corneal ulceration or foreign bodies. Conjunctivitis is also common in humans, a condition known as ‘pink eye’. If left untreated, conjunctivitis can cause pain, ocular discharge, and secondary bacterial infection of the ocular surface. Also, conjunctivitis can negatively affect the tear film dynamics (production, drainage) as the tear ducts become ‘clogged’ by the surrounding swollen conjunctiva. However, little is known about the impact of conjunctivitis on the ocular surface.

A deeper understanding about conjunctivitis and its associated detrimental effects would enable clinicians to better diagnose, treat and monitor ocular surface diseases. This is best achieved by developing a ‘model’ of conjunctivitis, in which the disease can be induced in a reproducible manner. Since the conjunctival tissue (but not the cornea) is rich in histamine receptors, we hypothesize that the use of topical histamine eye drops will induce a reproducible, dose-dependent, and reversible conjunctivitis in dogs.

Preliminary data obtained in one dog are promising – indeed, a single drop histamine eye drop induced conjunctivitis within 10 minutes, which was moderate or severe when 10 mg/mL or 100 mg/mL concentration was used, respectively.

The aim of the study is to develop and optimize this in vivo model of conjunctivitis in the dog. An escalating scale of histamine concentrations will be used, and dogs will undergo an ophthalmic examination at pre-determined times. Several criteria of the modified Hackett-McDonald score (degree of conjunctival hyperemia, chemosis, and discharge) will be used to determine a ‘clinical score’ for each dog at each time following histamine administration. The severity and duration of the conjunctivitis will be assessed with and without the use of anti-histamine drop during the recovery period.
Project Title: Effect of dietary butyrate and/or prebiotics on modulating the mucosal immune system of the intestinal tract of commercial turkeys

Principle Investigator(s): Matthew J. Sylte, USDA-ARS-NADC

Collaborating Investigator(s): Torey Looft, USDA-ARS-NADC

Veterinary Scholar Focused Abstract: (300 words or less):

The food and drug administration guidance 209 and 213 have phased out growth promotion and disease prevention claims by medically important antibiotics in food producing animals, leaving veterinarians with fewer options to treat disease and maintain a healthy and safe food supply. Given these limitations on use of medically important antibiotics in food producing animals, efficacious alternatives to antibiotics are needed to maintain health in commercial turkeys. For example, the inclusion of prebiotics in feed may impact the integrity of the animal’s intestinal epithelial barrier function and improve host immunity. Recently, anaerobic bacteria in the colon of rodents, producing the short chain fatty acid butyrate, affected the development peripheral regulatory T cells (pTreg) in the intestinal lamina propria, which function to promote immunological tolerance towards the intestinal microbiota. Microbial-derived butyrate also enhances intestinal barrier function, which promotes animal health. It is unclear whether butyrate-producing bacteria in the cecum of commercial turkeys affect the development of pTregs. The addition of dietary prebiotics, such as xylooligosaccharide (XOS), may impact the amount of butyrate produced by the intestinal microbiota. Recently, in-feed XOS promoted the growth of Bifidobacteria, which promoted butyrate production by other intestinal bacteria. The goal of this study is to feed commercial turkeys an encapsulated form of butyrate (that delivers its content to the cecum of pouls), or prebiotics (e.g., XOS or other), and test whether the treatment affects the development of pTregs in the cecal lamina propria, as well as evaluating barrier function and expression of anti-microbial peptides (e.g., β-defensins) and cytokines. The work for this project will provide the opportunity to perform RNA extractions, real-time RT-PCR, isolation of cells from the intestinal lamina propria and subsequent data analysis. It will also include microscopic evaluation of intestinal tissues, paired with immunohistochemistry, staining for different cellular populations.
Title:
Ex-vivo biomechanical comparison of articular compression and stiffness of three differing lag screw repair configurations for complete, sagittal plane fractures of the equine proximal phalanx

Co-Summer Scholar Faculty Advisors
Dr. Dane M. Tatarniuk, DVM, MS, DACVS-LA (Equine Surgery)
Dr. Kevin D. Kersh, DVM, DACVS-LA (Equine Surgery)

Project Co-Investigators:
Dr. Karl H. Kraus, DVM, MS, DACVS (Small Animal Surgery)
Elyse R. Durket, DVM (Resident, Equine Surgery)

Veterinary Scholar Focused Abstract:

Stress fractures are common injuries in racehorses. In the equine proximal phalanx bone, a common configuration is a sagittal plane fracture. Fractures are repaired using lag screws, and various screw configurations exist:

1. Placement of a single 4.5mm bone screw halfway between the dorsal and palmar surface and immediately distal to the articular surface
2. Placement of a single 5.5mm bone screw in the same location as option 1
3. Placement of two 4.5mm bone screws in the same transverse plane, with one screw near the dorsal surface and the other near the palmar/plantar surface.

Currently, a lack of knowledge exists regarding which repair provides superior articular compression and stability at the fracture gap.

Thirty proximal phalangeal (P1) bones from mature thoroughbreds will be biomechanically tested. Specimens will undergo CT to ensure they are normal. A model of a sagittal plane fracture will be created using a band saw. Proximal phalangeal bones will be randomly assigned to three repair configuration groups (10 per group):
(1) single 4.5 mm  (2) single 5.5 mm  (3) two parallel 4.5 mm screws

Phase 1 – Pressure sensitive film will be inserted in the fracture gap to measure compressive pressure (mpa), compressive force (N), and area of compression (cm²) along the articular surface using digital software.

Phase 2 – Bones will be biomechanically tested to determine construct stiffness. Extensometers will be placed along the fracture gap. Bones will be fixated and load applied.
in shear using a materials testing machine. Applied load and displacement will allow calculation of construct stiffness.

The participating student scholar will gain valuable skills in:
- Study design & execution
- Principles of fracture physics / biomechanics
- Principles of lag screw insertion and basic orthopedic principles
- Data analysis and basic statistics
- Preparation of manuscript for peer-review journal submission as first author
- Exposure to equine orthopedics and sports medicine

Further questions about this project are welcome:
Dr. Dane Tatarniuk (dtatar@iastate.edu) & Dr. Kevin Kersh (kkersh@iastate.edu)

Footnote:
a. Topaq Software (Sensor Products Inc., East Hanover NJ
b. Electrodynamic Material Testing System 800LE3, Shakopee, MN

References:
Project Title: Investigation of a universal influenza vaccine for swine and poultry

Principle Investigator(s): David Verhoeven

Collaborating Investigator(s): Brett Sponseller

Veterinary Scholar Focused Abstract: (300 words or less):

Influenza remains a serious threat to swine and poultry due to: (1) vast number of continuously circulating influenza strains within and between herds or from wild birds to broilers/layers, (2) viral shift/drift that occur within the hosts, and (3) difficulty in designing universal vaccines without induction of vaccine-associated enhanced respiratory disease (VAERD)\(^1,2\) in swine or the ability to differentiate between natural infection and vaccine in poultry. Furthermore, while swine influenza vaccines can limit/prevent morbidity or mortality, they generally fail to prevent infection\(^3\). H3N2 viruses are especially difficult to control through current swine vaccines which is further confounded by maternal antibodies in piglets\(^5\). We have recently discovered that vaccinating two different mammal species (mice and horses) with equine H3N8 (live attenuated) led to the broadest nAbs profile to date (within strains: H1N1, H3N2 including H3N2v2, and H5N1 with further binding to H7, H9, and H13 HAs) and protected from multiple H1N1 and H3N2 influenza challenges. Moreover, the vast majority of vaccinated animals had protective HAI (HA inhibition) titers across the viral strains, exhibited similar microneutralization titers, and hybridomas derived from vaccinated animals had protective HAI titers to H1N1 and H3N2 viruses. If this vaccine should work in swine, it could represent a significant advancement toward the long sought universal influenza vaccine. The underlying principle behind this proposal is to explore the host response to our candidate influenza vaccine and determine the correlates of protection, ways to bolster any afforded protection in swine and poultry. However, more qualifying work in protection efficacy, VAERD in swine if any, vaccine delivery, and correlates of protection need to be done in both species. The skills the study will learn are molecular biology techniques for vaccine manufacture, vaccination strategies in both species, and immunoassays to qualify the protective immune responses before and after viral challenge.
Project Title: Mechanisms of systemic hypertension in healthy dogs receiving anti-inflammatory doses of oral glucocorticoids

Principle Investigator(s): Jessica Ward, DVM, DACVIM (Cardiology)

Collaborating Investigator(s): Jonathan Mochel, DVM, MSc, PhD, DECVPT; Wendy Ware, DVM, MSc, DACVIM (Cardiology)

Veterinary Scholar Focused Abstract (300 words or less):
Glucocorticoids (GCs) have a wide variety of clinical applications in veterinary medicine, but their use in patients with heart disease is limited by concern for precipitating congestive heart failure (CHF). One mechanism by which GCs could worsen heart disease is vasoconstriction causing increased afterload. A pilot study by our research group recently found that anti-inflammatory doses of prednisone given to clinically healthy dogs caused a significant increase in systolic blood pressure within 7 days. The objective of this prospective clinical trial is to investigate the underlying mechanism by which exogenous GCs increase blood pressure. Study subjects will be healthy laboratory Beagles. Dogs will receive 5-day courses of prednisone at various doses (0.5, 1.0, 2.0, and 4.0 mg/kg/day). Data will be collected before (day 0) and after (day 5) each prednisone course, and will include noninvasive blood pressure, CBC, chemistry panel, and measures of endogenous neurohormonal systems (plasma renin activity, fractional excretion of sodium and potassium, NT-proBNP, plasma endothelin, etc). Data will be analyzed to detect changes in parameters related to prednisone administration and dose. We hypothesize that short courses of oral prednisone will increase blood pressure in a dose-dependent manner by activating the renin-angiotensin-aldosterone system (RAAS). In addition to exposure to the process of clinical research, this Summer Scholar will gain a significant amount of hands-on experience performing basic clinical skills in dogs (physical examinations, Doppler blood pressure measurement, venipuncture, and urine collection).
Project Title: Effect of Immune Modulators on Digital Dermatitis in Sheep Model

Principle Investigator(s): Dr. Jennifer Wilson-Welder, NADC-ARS-USDA

Collaborating Investigator(s): Dr. Jarlath Nally, Dr. David Alt and Dr. Paul Plummer

Veterinary Scholar Focused Abstract: (300 words or less):

Digital dermatitis is most common in dairy cattle as they enter the milking herd. There is well studied immunosuppression that occurs in the first 100 days of lactation that may be a key element in the development of digital dermatitis. It is hypothesized that the host’s immune system (innate immunity) plays a key role in the development and perpetuation of digital dermatitis lesions. By altering innate immunity with immune-suppressors or immune-enhancers, we can elucidate the role of innate immunity in lesion formation. Additionally, adaptive immunity can be gained through prior exposure to disease or through vaccination. In these studies the parameters measured will include lesion formation, systemic immune response (antibody and CMI) and local immune responses (skin biopsy, post-mortem). Immunosuppression will achieved by administration of dexamethasone. Dexamethasone is well documented for its use as immunosuppressant in cattle to mimic early lactation immunosuppression. Immunostimulation will be provided by dosing with Imrestor, a bovine GCSF product that is commercially available for use in controlling dairy cattle mastitis in the US. White blood cell counts will be monitored by weekly checks. To determine if vaccination can alter immune response and lesion development, animals will be immunized with a mixture of killed lesion material, or killed cultured bacteria derived from DD lesions including but not limited to: Treponema, Fusobacterium, Bacteroides, Porphyromonas, Prevotella, Streptococcus, and Mycoplasma. No vaccine or immune modulation groups will be used as controls. All animals will be scarified, wrapped and inoculated with digital dermatitis lesion homogenate (as described in recent publication: Wilson-Welder et al. Vet Pathol 2017 DOI: 10.1177/0300985817736572). Wraps will be checked twice weekly by scientific staff for integrity and every two weeks feet evaluated for lesion formation. We anticipate observable differences in lesion formation in 4-6 weeks.
Project Title: The role of obesity and age of neutering on development of recessed vulva

Principle Investigator(s): Eric Zellner, DVM, DACVS-SA and Jean-Sebastien Palerme, DVM, DACVIM

Collaborating Investigator(s):

Veterinary Scholar Focused Abstract: (300 words or less): Though recessed, or hooded, vulvas have been associated with an increased risk of urinary tract infections and perivulvular dermatitis in dogs, the overall prevalence of this condition and its association with other factors such as obesity and age of spay has not been reported. We hypothesize that (1) obesity and early age of spay is associated with increased severity of recessed vulvas in female dogs and that, (2) though the prevalence of affected animals is high, urinary clinical signs are scarce in this population. In this project, we will aim to determine the overall prevalence of recessed vulvas in canine patients of the Lloyd Veterinary Medical Center. In addition, severity of this condition will be scored in each dog according to a standardized grading scheme and additional information such as age of spay, body condition score and the presence or absence of lower urinary signs will be collected to determine possible correlations.
Project Title: Novel strategies to control gut dysbiosis and \textit{C. difficile} infection

Principle Investigator(s): Dr. Shankumar Mooyottu

Veterinary Scholar Focused Abstract: (300 words or less):

\textit{Clostridium difficile} (CD) is a spore-forming, strictly anaerobic bacterium that causes a toxin-mediated enteric disease in humans and animals. CD infection has been associated with the use of antibiotics that results in disruption in normal enteric microflora (gut-dysbiosis), subsequent pathogen colonization and severe toxin-mediated colitis. Despite the fact that a majority of the currently used antibiotics can predispose CD infection by disrupting the normal gut flora, antibiotics are still used as the primary line of treatment against infection. Moreover, the Centers for Disease Control and Prevention recently listed CD as one among the three urgent threats in their report on emerging pathogens with antibiotic resistance. Since the toxins are the major virulence factors for CD infection, a search for an alternative, non-antibiotic therapeutic agents, which can reduce CD virulence without causing gut-dysbiosis opens a new research area.

My research focuses on natural anti-virulence molecules that prevent gut-dysbiosis and reduce CD virulence. My research project involves screening and testing various small molecules for their effects on CD toxin production, cytotoxicity, toxin gene expression, sporulation and spore germination using anaerobic bacteriologic and molecular techniques. In addition, we are also investigating the effects of these molecules on the growth and physiology of CD and beneficial gut bacteria using microbiologic and molecular techniques. The results from this research could help the medical and scientific community to develop and validate novel non-antibiotic strategies to control CD infection in humans and animals.