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CUMMINGS SCHOOL of VETERINARY MEDICINE

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ABSTRACT BOOK

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2014 Summer Research Proposals

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Awardee: Arianne Baker V'17
Mentor: Dr. Claire Sharp

Award Type: Morris Animal Foundation

Research Project: Prospective, Multicenter Evaluation of Blood Transfusion Requirements in Dogs Following Trauma.

Summary Although blood loss is the most common cause of early mortality in dogs and people suffering trauma, and transfusions of blood products are the foundation of treatments for traumatic blood loss, the transfusion requirements and prognosis for dogs sustaining trauma are not well described.^{1,2,3,4} Our goal in this proposed study is to better understand the transfusion requirements of dogs sustaining trauma so as to provide data supporting future interventional clinical trials in veterinary trauma patients aimed at improving outcomes, and guide blood banking blood banking practices in veterinary trauma centers.

Our proposed study will use data from the REDcap database, into which all of the nine provisional veterinary trauma centers are prospectively recording information for all dogs evaluated after a witnessed or suspected traumatic incident starting September 1, 2013 and continuing indefinitely. For the purposes of case enrollment, trauma is defined as any tissue injury that occurs suddenly as a result of an external force, including blunt force injury, penetrating injury, or crushing injury. For our study, we will extract the dog's age, sex, breed, type of trauma (blunt versus penetrating), severity of illness (as determined by the ATT score), blood transfusions requirements, and outcome for each trauma entry. We will evaluate our hypotheses as related to this set of data using standard statistical analyses.

Our proposed study will serve as the first prospective study to look at the transfusion requirements of dogs sustaining trauma and will be one of the first prospective studies using the data obtained from the trauma database established with the veterinary trauma center network. The results of our study will serve to better define the population and prognosis of trauma patients with severe hemorrhage. Given the involvement of the Tufts emergency and critical care medicine faculty in the development of the VetCOT initiative, and Tufts role as a provisional trauma center, studies such as this will be a vital part of advancing our understanding of veterinary trauma epidemiology and ultimately trauma care.

Awardee: Ruby Cheng V'16

Mentor: Dr. Cynthia Webster

Award Type: Merial Scholars Program

Research Project: Effects of Conditioned Media from Canine Umbilical Derived Mesenchymal Stem Cell on Bile Acid Induced Apoptosis in Human Hepatocellular Carcinoma Cells and Rat Hepatocytes

Summary: Cholestasis, the slowing of bile flow, accompanies many acute and chronic hepatopathies. The pathologic progression of cholestatic disorders is fueled by the retention of endogenous cytotoxins including bile acids. Bile acids cause hepatic injury through activation of apoptotic death receptors and intracellular stress signaling. Preliminary data from our lab has described that bile acid induced apoptosis proceeds through a C-Jun-N terminal kinase (JNK) dependent pathway. Currently there are few therapeutic options available to halt the pathologic effect of bile acids. The aim of this investigation is to understand the effect of mesenchymal stem cells (MSCs) on bile acid induced apoptosis in human hepatocellular carcinoma cells and rat hepatocytes respectively. Mesenchymal stem cells (MSCs) are multipotent progenitor cells that are capable of differentiating into many cell types of mesodermal origin. Factors released by MSCs can up-regulate gene transcription and promote post-translational events that induce cell proliferation and repair after cell injury. MSCs can have paracrine effects on normal and malignant hepatocytes; both pro- and anti- apoptotic effects have been described. Our hypothesis is that canine MSC-CM promotes apoptosis in hepatic cancer cells, and inhibits apoptosis in primary hepatocytes after bile acid induced injury. Currently there are no studies looking at the effect of MSC-CM on bile acid induced apoptosis, therefore this study contributes to the body of literature regarding the application of MSCs as a potential therapeutic strategy for cholestasis and hepatopathies.

Studies were conducted in HuH7-Ntcp cells, a human hepatoma cell line that has stably transfected with rat Ntcp, to enable them to take up and respond to bile acids, and primary rat hepatocytes isolated from male Wistar rats by a two-step collagenase perfusion procedure. Canine Wharton's Jelly-derived mesenchymal stem cells were isolated from canine umbilical cord. Pooled samples of canine MSCs were grown to confluence and serum starved for 24 hours. The media was collected and centrifuged sequentially at 300g and 2000g for 10 minutes and the final supernatant collected and frozen. HuH7-Ntcp cells were cultured in either regular serum free media (SFM) or in a 1:1 mixture of regular SFM and MSC-CM for two hours. Some cells were treated with glycocheno-deoxycholate (GCDC, 150 uM for two hours), the major circulating hepatotoxic bile acid in humans. Apoptosis was evaluated morphologically by fluorescent microscopy of Hoechst stained cells, which were identified by the presence of either nuclear fragmentation or chromatin condensation. A total of 500 cells were counted and the results were expressed as percentage of apoptotic cells. Apoptosis was identified biochemically by immunoblotting for the active 17 kD fragment of caspase 3. Equal protein loading was verified by immunoblotting for actin. Similar experimental setup was used in rat hepatocytes.

Awardee: Rachel Cooper V'17

Mentor: Dr. Gillian Beamer

Award Type: NIH

Research Project: Oxidant Damage in Tuberculosis-Infected Macrophages.

Summary: Pulmonary tuberculosis (TB), the most common form of disease caused by *Mycobacterium tuberculosis* (*M.tb*), is characterized by macrophage and granuloma necrosis resulting in cavitation of lung tissue and transmission of *M.tb* to new hosts. Mechanisms of macrophage death in pulmonary TB are central to disease pathogenesis and to transmission of bacilli. Additionally, there is evidence that oxidants contribute to the disease process in animal models. In pulmonary TB, oxidant production has been linked to neutrophils; these cells produce abundant reactive oxygen species (ROS) and their presence indicates a poor prognosis. However, surprisingly little is known about oxidant damage in *M.tb* infection. Our aim, therefore, is to determine the effects of oxidants on *M.tb*-infected macrophages. Here, we hypothesize that oxidants contribute to macrophage death and inability to control *M.tb* bacilli, in part through the oxidation of lipids, proteins, and nucleic acids.

We will test this hypothesis by exposing *M.tb*-infected macrophages to the model oxidant, hydrogen peroxide (H_2O_2), *in vitro*. Oxidative damage to macrophages will be assessed by the following metrics and corresponding methods: (a) Loss of antioxidant capacity using a standard copper reduction colorimetric assay; (b) Oxidation of lipids, proteins, and DNA by ELISA; (c) Mechanisms of macrophage death by apoptosis or necrosis by ELISA; and d) Control of *M.tb* growth by Colony Forming Unit assay. Results will be graphed and analyzed by ANOVA.

Preliminary data indicate that *M.tb* infection increases the susceptibility of macrophages to oxidant damage, so we expect to see several specific results: H_2O_2 will (a) diminish the antioxidant capacity of macrophages; (b) increase lipid, protein, and DNA oxidation over control levels; (c) promote necrosis over apoptosis; and (d) cause extracellular release of *M.tb* bacilli in association with necrosis.

Awardee: Rebecca Falender V'16

Mentor: Dr. Lois Wetmore

Award Type: NIH

Research Project: Effects of Methadone and Hydromorphone on Peri-anesthetic Gastroesophageal Reflux, Regurgitation, and Vomiting

Summary: In this study, we will measure the incidence of perioperative gastroesophageal reflux (GER) and regurgitation in dogs pre-medicated with morphine prior to undergoing elective stifle surgery for a torn cruciate or luxating patella.

During anesthesia, GER has been shown to occur in 17-27% of cases and, in a smaller number of dogs, is also associated with regurgitation. In a clinical trial conducted last summer, this research group found that 30.77% and 28.57% of dogs refluxed after being administered methadone or hydromorphone respectively as their pre-anesthetic opioid; however, a previous study by Wilson et al found that with the use of morphine, 50-60% of dogs refluxed. While these two studies were conducted with a slightly different protocol and methodology, the results suggest that methadone and hydromorphone may be superior opioids at reducing the incidence of GER and regurgitation. The objective of this study is thus to measure the incidence of GER and regurgitation after preoperative administration of morphine versus methadone or hydromorphone (with or without glycopyrrolate) using our previously used protocol and methodology.

The experiment will be a study of 50 dogs undergoing elective orthopedic surgery at the Foster Hospital for Small Animals. Dogs will be randomly assigned to one of six premedication treatment groups: morphine (1 mg/kg IM) with or without glycopyrrolate (0.01 mg/kg IM), hydromorphone (0.1 mg/kg IM) with or without glycopyrrolate (0.01 mg/kg IM) or methadone (0.3 mg/kg IM) with or without glycopyrrolate (0.01 mg/kg IM). All patients will receive a pre-operative dose of acepromazine appropriate for their age, breed and weight (0.01-0.05 mg/kg IM) with the opioid. The dogs will be induced with propofol (4 mg/kg IM, to effect), and maintained with isoflurane. A sensor tipped catheter will be placed following intubation to measure their esophageal pH during surgery and assess for reflux. The patient will be monitored for regurgitation during their time at the hospital. One month post-surgery, the client will be called to ascertain if any further regurgitation or signs of esophagitis or aspiration pneumonia were observed.

Opioids are a critical part of surgical pain management; however, GER from anesthetic agents may result in post-anesthetic esophagitis, stricture formation, and, in the case of regurgitation, aspiration pneumonia.² Our goal is to identify the preferred pre-anesthetic opioid to minimize the incidence of these side effects for dogs that require anesthesia in the future.

Awardee: Tess Gannaway V'16

Mentor: Dr. Jennifer Steele

Award Type: NIH

Research Project: The Effects of Food Sharing, Gender, and Awareness on *Opisthorchis viverrini* Infection in Khon Kaen, Thailand

Summary: Across the world food-borne parasitic infections are acknowledged as both a serious and an emergent threat. In Southeast Asia, particularly in Northeast Thailand, *Opisthorchis viverrini* has been identified as the most common and problematic of all food-borne pathogens. The human liver fluke is contracted through the consumption of raw fish and can lead to cholangiocarcinoma, a disease that is often fatal [2]. Although national levels of infection have fallen since intervention strategies were employed in the 1980's, a particular area of Thailand, Khon Kaen, still shows the highest incidence of *O.*

viverrini in the world [2]. It is clear to researchers in Khon Kaen that traditional intervention strategies based only on disease pathology are insufficient to reduce incidence in Khon Kaen. Instead researchers like those working at the Lawa Project have started to examine the complex social and cultural risk factors associated with the consumption of raw fish. My goal is to examine the effects of food sharing and gender related risk factors on the incidence of *O. viverrini* infection in the Lawa Lakes region of Khon Kaen, Thailand as well as to explore whether or not awareness of the parasite contributes to villagers' decisions to consume raw fish. These aims will be achieved using questionnaires designed with help from public health officials in Khon Kaen. I will accompany these same officials who are fluent in the local dialect to administer the questionnaires and collect data for analysis.

Awardee: Andrew Gestrich V'17

Mentor: Dr. Deborah Kochevar, Dr. Mark Pokras and Dr. Tomas Martin-Jimenez

Award Type: NIH

Research Project: Compound Specific Scalability: A Novel Approach to First-in-Species Dosing

Summary: Allometric scaling and related techniques remain in wide use despite the continued development and availability of advanced *in silico* modeling systems. Given that a number of factors (i.e. age, sex, lactation status, disease) may influence the pharmacokinetic (PK) parameters for a given animal, value remains to be garnered from the improvement of mathematical PK models that allow veterinary practitioners to make quality estimations when complete information may not be found in the primary literature.

This project aims to improve upon two of the most basic and widely used systems for prediction of PK parameters and dose for novel species/drug combinations: allometric scaling and species-species constants. Allometric scaling, despite widespread use, uses body weight (BW) as an independent variable, which inadvertently adds a level of additional variability to the analysis. An additional complication is found in multispecies allometric graphs, which allow outlier species at either end of the graph to more dramatically affect the slope of the graph, while mid-BW species will have more influence over the line's intercept (Riviere, in press). Species-species constants have the advantage that they are empirically derived and avoid the inclusion of body weight, but when used in isolation they may leave the analysis vulnerable to anomalies in either the model species or target species.

This project presents a form of multi-species analysis that relies upon inverse variation weighting. Inverse variation weighting is based upon the coefficient of variation for each species-species constant and allows for a multi-species approach where the degree of influence that each species-species

constant has on the result is dependent upon the past predictability (defined here as an inverse of the variability) of the relationship between the llama and each model species. The llama is used as a model species for the analysis due to its sustained growth in popularity in the US, the size of the PK data set available for the species, and anecdotal reports that camelid PK parameters have been difficult to predict through the classic approaches.

Species-species constants are generated between llama versus cow, horse, sheep, goat, pig, and rabbit based on a literature review. PK data is included in the analysis only for healthy, adult animals; models of disease or inflammation are excluded; and a variety of assays that are reasonably expected to differentiate parent compound from active metabolites are allowed. Classic dual logarithmic plots (the allometric scaling approach) are also presented for comparison. The inverse variation model is shown to outperform both species-species constants and multi-species allometric plots in the accuracy of PK predictions for the llama.

Awardee: Heather Houser V'17

Mentor: Dr. Melissa Mazan

Award Type: NIH

Research Project: Parasite Load and Clinical Health Indicators in Exotic, Native and Cross-bred Cattle in Nyagatare District, Rwanda

Summary: Blood-borne and gastrointestinal parasites are a major challenge to livestock productivity in Sub-Saharan Africa (Mattioli 2000). Thumbi et al. identified theileriosis, haemonchosis, and heartwater disease as the top three causes of disease-induced death (60%) in calves less than one year old in Busia, Kenya (2013). Exotic cattle are genetically more susceptible to these parasites, but are also capable of much higher milk production than Rwanda's native Ankole cattle. The government of Rwanda is therefore pursuing a policy of importing and cross breeding cattle for increased health and increased productivity. There is a critical need to evaluate the parasite load and clinical health of cross-bred cattle compared to native and exotic breeds. Operating out of the University of Rwanda Veterinary Ambulatory Clinic, we will use fecal and blood samples to determine average parasite load across breeds, and will measure packed cell volume, total protein, and body condition score to determine clinical health across breeds. We expect to see a lower parasite burden and higher body condition score (BCS), packed cell volume (PCV), and total protein (TP) in native cattle breeds; a higher parasite burden and lower BCS, PCV, and TP in exotic breeds; and an intermediate parasite burden and intermediate BCS, PCV, and TP in cross breeds.

Awardee: Nida Intarapanich V'16

Mentor: Dr. Emily McCobb, Dr. Elizabeth Rozanski , Dr. Rachel Touroo and Dr. Robert Reisman

Award Type: NIH

Research Project: Characterization and Comparison of Injuries CAUSED by Spontaneous vs. Illegal Organized Dog Fighting

Summary: Dogfighting is a vicious blood sport involving physical abuse, neglect, and illegal gambling. It is a felony in all 50 states and is often associated with organized crime, racketeering, drugs, firearms, and other forms of violence.

Many dogfighters attempt to treat their animals' injuries by themselves, rather than seeking veterinary care, presumably in order to avoid detection. If dogfighters visit a veterinarian, they often provide a variety of explanations for their dog's injuries. A frequent claim is that the fight was spontaneous and accidental—usually a dominance or territorial dispute. However, we hypothesize that spontaneous fights between dogs with no fighting background will result in a different pattern of injury when compared to organized dog fights involving dogs that are specifically bred, trained, and conditioned to fight.

This retrospective case-control study will compare cases of known spontaneous dog fights involving two medium-sized, same-sex dogs with cases of known illegal dogfighting. Cases of spontaneous fights will be selected from the Foster Hospital for Small Animals at Tufts. Organized dogfighting cases will be drawn from American Society for the Prevention of Cruelty to Animals (ASPCA) records of dogs seized in connection with dogfighting law enforcement raids.

Patient signalment and injuries will be recorded in a standard fashion from medical records. Variables will be compared between spontaneous and organized dogfighting in order to identify possible associations. Additionally, exploratory factor analysis will be used to identify patterns in the location of wounds for each group of dogs.

To our knowledge, this would be the first study to compare spontaneous and organized dogfighting injuries. Establishing evidence-based patterns of injury will help clinicians identify victims of dogfighting and aid in the prosecution of this crime.

Awardee: Rachel Jania V'16

Mentor: Dr. Alison Robbins

Award Type: USDA

Research Project: Determining Suitable Breeding and Upland Habitat of Eastern Spadefoot Toads (*Scaphiopus holbrookii*) in Massachusetts for Reintroduction and Habitat Modification Efforts

Summary: Goals - To help in finding areas in Massachusetts that would be suitable for eastern spadefoot toad reintroduction and related habitat modification efforts.

Objectives - To better understand the range of habitat types that eastern spadefoot toads can occupy in Massachusetts, especially in biotypes other than barrier beaches, specifically: 1) soil types occupied by the species and 2) vegetation and land cover assemblages occupied by the species.

Research Questions - The following are to be applied to 1km diameter circles centered on the breeding pool location (if known) or reported location of eastern spadefoot toads in Massachusetts. We are particularly interested in all non-barrier beach occurrences (*e.g. occurrences in locations other than Cape Cod National Seashore, Sandy Neck, Plum Island, and Crane's Beach.*)

- What soil types predominate within 1km of each occurrence? (List the soil types.)
- What are the drainage classes of the dominant soils? (Are they all "excessively drained"? See the following URL for some basic terminology: <http://nesoil.com/muds/explain.html - drainage>)
- Are all occurrences within areas dominated by glacial fluvial (outwash) deposits?
- What is the range and maximum value for elevation above sea level for all the occurrences?
- What is the percentage of the following basic land cover types within 1km of each occurrence: forested, field and other open vegetation, bare soil, urban (all types of impervious substrates and structures)? (We will need to discuss how to combine the existing land cover categories.)
- What general vegetation types predominate in the 1km circles? (This will likely require visits to each site, which we may or may not be able to do this summer.)

Awardee: Daniel Kelleher V' 17

Mentor: Dr. Stephano Pizzirani

Award Type: NIH

Research Project: Investigation on the Expression of Collagen Type 1 Alpha-2 Chain in Normal Canine Anterior Uvea

Summary Anterior uveitis is common in the dog and the most common form of uveitis in humans. Most of the clinical cases in both species are classified as idiopathic and remain without an etiological diagnosis; autoimmune mechanisms are often considered responsible. An experimental model of autoimmune anterior uveitis (EAAU) has been created in Lewis rats using a melanin associated antigen (MAA) from lysates of bovine iris and ciliary body. A specific peptide, 37 amino acids long (22kD of molecular weight) has recently been isolated in rat and bovine iris and ciliary body and proven to be the autoantigen responsible for inducing the experimental disease. The peptide belongs to a well conserved protein in different species, specifically Type 1 collagen alpha 2 chain (COL1A2). To date, no information is available about the presence of COL1A2 in the iridal stroma of dogs. The only research on the presence of the COL1A2 in dogs has been conducted in relation to osteogenesis imperfecta, a skeletal disease caused by mutations to the COL1A1 and COL1A2 genes.

Other than in bovine and rats, type 1 collagen has been reported in human iris stroma. We hypothesize that COL1A2 is a skeletal protein of the iris stroma and that the 37 amino acid COL1A2 sequence is present in the iris and ciliary body in normal canine eyes.

The primary objective of this study is to investigate the presence of COL1A2 in the anterior uvea in normal dogs using Western Blot (WB) and immunohistochemistry (IHC). The possible discovery of COL1A2 antigen in canine anterior uvea will open new horizons to the understanding of the pathophysiology of idiopathic uveitis.

Awardee: Katherine Leonard V'16

Mentor: Dr. Michael Kowaleski

Award Type: Merit

Research Project: Short Term Outcome of Total Hip Replacement in Juvenile Dogs

Summary: Total Hip Replacement (THR) is a procedure used to treat a number of coxofemoral disorders including canine hip dysplasia, an extremely common orthopedic problem in the canine population. Healing times and complication rates have been reported for this surgery in general. However, previous studies have included dogs of all ages and therefore the data on outcome and complications in juvenile dogs is lacking. The objective of this retrospective study is to assess the short-term outcome of total hip replacement surgery in dogs up to 14 months of age.

Medical records from the Foster Hospital for Small Animals and the Veterinary Teaching Hospital at the University of Florida will be searched. Patients who underwent THR at 14 months of age or younger will be included in the study. Information on signalment, clinical exam findings, radiographic findings and complication rate will be gathered based on follow-up physical examinations and radiographic examinations. This information will then be compared to historical data for THR.

Awardee: Caitlyn Little V'17

Mentor: Dr. Felicia Nutter and Dr. Julie Ellis

Award Type: NIH

Research Project: Eastern Wild Turkey (*Melagris gallopavo silvestris*) Health Status, Population Ecology, and Potential Health Implications of Interactions with Livestock on the Cummings Campus

Summary: The campus for the Cummings School of Veterinary Medicine at Tufts University is located on 594 acres of land in central Massachusetts. Of this area, approximately 200 acres consists of farmland with surrounding wooded areas and wetlands. Hunting on this campus is prohibited, and as such the area has become a refuge for local wildlife. The eastern wild turkey (*Melagris gallopavo silvestris*) is one species that has taken advantage of this resource, with a visible turkey population using the campus. This research project will develop baseline normal blood values, morphometrics and body condition, and examine the prevalence of lymphoproliferative disease virus (LPDV) and avian pox, pathogens of importance to wild turkey populations. Additionally, fecal samples will be used to evaluate the exchange of potential pathogens between the turkey population and the livestock on campus. Very little research has been done regarding these topics in the United States and the Cummings Campus provides a unique environment in which to collect baseline data that will be the basis for a proposed larger longitudinal study.

We hypothesize that wild turkeys on campus host bacterial pathogens that could be transmitted to livestock on the farm. Turkeys have been observed foraging in food troughs and in livestock grazing areas and there is concern that fecal contamination of feed and forage could be a cause of illness in livestock. We also hypothesize antibiotics used to maintain healthy livestock will be reflected in the patterns of antibiotic resistance in bacteria in the turkey gastrointestinal tracts. Finally, we hypothesize that avian poxvirus and lymphoproliferative disease virus (LPDV) will be present in the wild turkey population on the Cummings Campus.

Awardee: Alexa Ortiz V'17

Mentor: Dr. Allen Rutberg

Award Type: NIH

Research Project: Second Year Immunocontraceptive Effects of PZP Vaccine on Jarita Mesa wild Horse Population

Summary: The Porcine Zona Pellucida (PZP) immunocontraceptive vaccine has been studied on wild horses for over 20 years. The challenge of implementing this vaccine in wild horse territory management strategies has been to develop a vaccine that is cost-effective, has a long efficacy, and can be delivered to the horses with minimal stress. This research project will be determining the second year effects of the PZP vaccine on the foaling rate of the wild horse population located on the Jarita Mesa Wild Horse Territory in New Mexico. The single injection vaccine was emulsified with Freund's Modified Adjuvant and contained booster time-release pellets. The injections were given by remote darting, with the horses rounded up by a bait trap. This research is the first of its kind having all these variables together, if proven successful this method will be the least invasive, most cost-effective, and most efficacious vaccine discovered to date. The primary objectives of this study are to assess the effects of the vaccine on fertility through foal counts and to compare body condition, mare interchange rate and behavior in the treated and untreated mares. General population numbers and demographics will also be determined for this territory to aid supervisors in management decisions. The timing of vaccine administration will be analyzed to determine if this variable had any effects on the foaling rate of the treated mares. This research will be completed by observing the wild horses at water access points on the mesa during the dry season. All horses will be documented for approximate age (foal, yearling, adult), gender, markings, location of observation, and time of observation. Foal status of the treated and untreated mares will be determined based on affiliative behavior, such as nursing, resting, or proximity during fast paced movement like running. All data will be put into the Wild Horse Identification Management System and from there total population numbers can be determined, along with foaling rate, mare interchange rate, and the effects of immunization timing on the foaling rate. If this vaccine is effective for a second year, with minimal health and social behavior effects, it could become a major management tool used by the BLM and USFS to control the wild horse populations¹. This vaccine, delivered in the context of bait-trapping, would reduce the need for helicopter round-ups, and the confinement of additional horses in long-term holding facilities, and decrease the amount of stressful human interaction faced by the horses in association with hand injections¹. Currently there are over 45,000 horses in captivity; every horse not entering long-term holding would save the government around \$16,000². Therefore, this research could impact management practices on every wild horse territory while saving money and reducing conflict among different land-use groups to ensure a sustainable ecosystem for all interests.

Awardee: Simone Palladino V'16

Mentor: Dr. Michele Keyerleber, Dr. Kristine Burgess and Dr. King

Award Type: Merial Scholars Program

Research Project: Comparison of Abdominal Ultrasound and Computed Tomography in Dogs with Apocrine Gland Adenocarcinoma of the Anal Sac

Summary Identifying metastasis of canine apocrine gland adenocarcinoma of the anal sac (AGAAS) is a critical part of treatment planning for this disease and may be an important prognostic factor for long-term survival. Apocrine gland adenocarcinoma in the dog is considered to be both locally invasive and

highly metastatic, with metastasis to the regional lymph nodes (LN) being most common¹. Abdominal ultrasound (AUS) is often used to evaluate local lymph nodes in dogs with AGAAS. However, a prior study has shown that magnetic resonance imaging (MRI) is a more sensitive technique than AUS in identifying lymphadenopathy in these dogs, with AUS failing to detect 67% of lymphadenopathy identified on MRI². The role of computed tomography, the imaging modality of choice for radiotherapy planning, has not been evaluated in AGAAS associated lymphadenopathy. The lower cost, shorter anesthesia time, and increased availability of CT may make this a better imaging choice than MRI.

The purpose of this retrospective study will be to compare the efficacy of AUS and CT in detecting lymphadenopathy in the iliosacral lymphocenter in dogs with AGAAS. Dogs treated at TCSVM and Tufts VETS will be included if they had a histopathologic or cytologic diagnosis of AGAAS and underwent both AUS and CT within 4 weeks of each other. AUS and CT images for all patients will be evaluated for lymphadenopathy by a board-certified veterinary radiologist. We hypothesize that CT will be a more accurate technique than AUS for correctly identifying the presence and extent lymphadenopathy and should be considered in any patient with AGAAS to aid in subsequent therapeutic planning.

Awardee: Brenna Rose Pugliese V'17

Mentor: Dr. Carl Kirker-Head

Award Type: NIH

Research Project: Novel Supportive Legwear for Preventing Fetlock Joint Over-Extension in the Fatigued

Summary: Horses, though capable of excelling in extreme performance activities, are prone to injury of the distal limb. Specifically, the “flexor apparatus,” the tendons and ligaments that support the lower leg, can be damaged irreparably. Repetitive motion injuries characterized by accumulated microdamage are a common cause of flexor apparatus (FA) tendinopathy and desmopathy. Recovery from these injuries is often slow and sub-optimal, even under the best circumstances.

Tendon and ligament healing is influenced by mechanical factors, however, and it has been shown that early mobilization following injury benefits healing by decreasing adhesion formation and elevating protein synthesis at the repair site. The healing response might, therefore, be manipulated to the patient’s advantage by applying physiotherapy in a manner that optimizes the repair environment.

These investigators propose that horses with FA injury may benefit from application of rehabilitative legwear designed to prevent over-extension of the metacarpophalangeal joint (MCPJ). As a consequence, FA stress-strain may be attenuated. This should effectively provide: 1) Protection from activity-associated re-injury of the healing tissues; 2) diminution of the inflammatory response in the early post-injury period; and 3) optimization of the local mechanical environment for healing. The legwear may, therefore, have value in rehabilitation programs designed for horses recovering from FA

tendinopathy and/or desmopathy.

This study will serve as proof of concept testing to validate the use of such legwear for horses rehabilitating from FA injury. Fit, ease of use, and wearability of the device will be determined in the early stages of testing using a standardized exercise protocol. Subsequently, the investigators will use a treadmill-based exercise regimen coupled with high-speed videography to evaluate the ability of novel supportive legwear to reduce MCPJ extension. Simultaneously, the ability of the legwear to redirect weight-bearing forces from the FA to the dorsal cannon and pastern bones will be documented. Treadmill testing will be performed with the boot in the “active” state, to attenuate MCPJ motion, as well as in the “inactive” state, which permits physiologic range of motion. Statistical analysis of the MCPJ motion data will allow characterization of the relationship between application of the legwear, MCPJ kinematics, and FA load redirection.

Awardee: Cara Sammons V'16

Mentor: Dr. Sandra Ayres

Award Type: USDA Formula Funds

Research Project: Prevalence of Losses Due to Caprine Mucopolysaccharidosis IIID, and Investigation of the Relationship between Milk Production and the MPSIIID Mutant Allele

Summary: Caprine Mucopolysaccharidosis Type IIID is a recessive genetic disease affecting Nubian dairy goats. Affected animals have two copies of the mutated gene, and this disease leads ultimately to organ failure, progressive dementia and death. Previous research indicates that 25% of the Nubian goat population may be carrying the mutated gene, and limited genetic resources and line breeding may be increasing this percentage.

This study will measure the prevalence of the G6S mutation causing Caprine MPSIIID in Nubian goats in Maine, New Hampshire, Massachusetts, Vermont, and Connecticut, examine the actual losses of animals due to MPSIIID, attempt to determine if there is a relationship between milk productivity and the MPSIIID allele, and develop a breeding plan to manage the gene. Blood samples will be collected from approximately 400 sexually mature animals in seventeen herds in the northeast states and sent to Michigan State University for PCR testing to determine the status of each animal as heterozygous (carrier), homozygous dominant (normal), or homozygous recessive (affected). Participating herds have been asked to retain hair follicle samples from any animals that die during the study period of January through September of 2014. Follicles will also be submitted to MSU for PCR testing to determine if the G6S allele contributed to the death of the animal.

Anecdotal reports suggest that animals with the mutated gene may produce more milk, but no data exists to support this relationship. Approximately 175 animals to be included in this study have been involved with the Dairy Herd Improvement Recording program and production records will be available for cross reference. Annual and daily milk production between carrier, affected, and normal groups will be compared, looking for any significant difference.

This study is important to the dairy goat industry because it will provide information about the prevalence of the gene in the New England Nubian population and determine productivity losses, as well as add to the body of information related to the presentation of the disease. This project will raise awareness of the G6S mutation, the clinical signs associated with it, and present an educational opportunity for breeders and veterinarians.

Awardee: Sirrika Samuels V'16

Mentor: Dr. Dominik Faissler

Award Type: NIH

Research Project: Outcome and Complications in Canine Cervical Disk Extrusions (Hansen Type I) Treated Either with a Ventral Slot Procedure or a Cervical Hemilaminectomy

Summary: Cervical intervertebral disk disease (IVDD) is a common problem in a neurological practice, with disk extrusions (Hansen type I) being the most common presentation. The ventral slot procedure is a frequently used technique to relieve spinal cord compression in dogs with an extruded nucleus pulposus. An alternative procedure for surgical spinal cord compression is a cervical hemilaminectomy.

The purpose of this study is to compare post-surgical complications, short and long-term post-operative neurological outcome in dogs with cervical intervertebral disk extrusions (Hansen type I) treated either with a ventral slot procedures or cervical hemilaminectomy. Our hypothesis is that both procedures produce the same incidence of post-surgical complications and similar neurological short-term improvements. The major difference will be a significantly higher occurrence of IVDD in the adjacent disk space in dogs treated with a ventral slot procedure.

In a retrospective manner, data will be collected from the FIRST, PACS and neurosurgery databases of the Foster Small Animal Hospital at Tufts University. We will also include information from referring veterinarians and dog owners to determine complications, short (1 month) and long-term (>24 months) outcomes of these surgeries. Complications will be staged with a modified Spine Adverse Events Severity System (SAVES) to better compare the two treatment groups. Criteria of inclusion includes neurological deficits referring to the spinal cord segment C1-T2, the presence of an extradural spinal cord compression and the confirmation of a disk extrusion at the time of surgery.

Such a comparison of two procedures to correct cervical intervertebral disk disease has never been published so far. The results of this study could influence procedural decision making in the future, since

preliminary results indicate a significantly higher recurrence of disk extrusions in the adjacent disk space in dogs after a ventral slot procedure compared to patients undergoing cervical hemilaminectomy.

Awardee: Meera Sriram V'16

Mentor: Dr. Kevin Lindell

Award Type: NIH

Research Project: *Coxiella burnetii* in Bulk Tank Milk and Raw Milk Consumption in Southern New England

Summary: Given the increasing rates of raw milk consumption in United States today, this two-part study aims to assess the herd-level prevalence of *Coxiella burnetii*, the infectious agent of Q fever, as a function of raw milk sale status in dairy operations. The first part of the study will investigate whether *Coxiella burnetii* prevalence significantly differs in dairies legally authorized to sell raw milk compared to dairies only authorized to sell milk intended for pasteurization. This will be assessed with bulk tank milk (BTM) sampling and PCR analysis, which provides a consistent and reliable “snapshot” of herd prevalence.

The second part of the study aims to characterize management practices as independent factors, to help assess the association between raw milk sale status and *Coxiella burnetii* prevalence, while controlling for potential confounding and effect modification. Using a confidential questionnaire, we will survey basic information, management practices in a dairy operation, and if applicable, raw milk sales and consumption habits. This will help determine the possible source of *C. burnetii* on dairy operations and how management practices promote or decrease potential transmission through raw milk.

The results will help reevaluate the public health concerns surrounding raw milk consumption, in the context of *Coxiella burnetii* prevalence, which is not regularly assessed in dairy herd populations; the prevalence study also aims to reassess the potential endemic nature of *Coxiella burnetii*, particularly in southern New England. This can inform and aid dairy management to improve practices for cow health and biosecurity.

Awardee: Stacey Tanguy V'16

Mentor: Dr. Hellen Amuguni

Award Type: NIH

Research Project: Prevalence of *Mycobacterium bovis* Infections in Cattle of the Eastern Providence of Rwanda

Summary: *Mycobacterium bovis* is a zoonotic agent known to cause tuberculosis in a wide variety of animals including cattle, small ruminants, humans and wildlife. While *M. bovis* has been nearly eliminated from livestock in developed countries, it remains a significant problem in developing countries such as Rwanda, where the population relies heavily on livestock. In the Eastern Province of Rwanda, the potential for *M. bovis* transmission is compounded by the wildlife of Akagera National Park, which may serve as a reservoir for this agent. Despite the threat posed by this agent, no screening or control measures currently exist; therefore the prevalence of *M. bovis* infection in cattle is unknown and its impact on the Rwandan people and economy cannot be properly determined.

In order to establish the prevalence of infection, a blood-based interferon-gamma assay will be used to detect the presence of *M. bovis* in individual cattle found in the Eastern Province. The principal goal of this project is to provide baseline statistical evidence for the presence of *Mycobacterium bovis* in cattle that will aid in future control or vaccination strategies.

Additionally, for each cattle sampled, a survey of the owner will be conducted in order to gather information associated with risk factors and transmission. For cattle, variables will include age, breed, body condition score (assessed by the veterinary team), tuberculosis vaccination status, clinical signs of disease, milk production, frequency of contact with wildlife, and frequency of contact with other livestock. Data pertaining to the household and individual household members will include tuberculosis and HIV status, habits involving meat and milk consumption, and proximity of cattle-human living arrangements. Presence or absence of *M. bovis* infection will be compared to categorical variables using chi-squared analyses and continuous variables using two-sample t-tests. Further, educational materials will be distributed throughout communities to increase awareness of zoonotic tuberculosis and educate individuals on methods to limit transmission of this disease.

Awardee: Kelsey Turley V'17

Mentor: Dr. Claire Sharp

Award Type: Merit

Research Project: Evaluating the Complex Genetic Basis of Gastric Dilation and Volvulus (GDV) in German Shepherd Dogs

Summary: Gastric dilatation and volvulus (GDV) is a common condition in large and giant breed dogs with an unacceptably high morbidity and mortality rate. The German Shepherd dog (GSD) is the most common breed of dog seen with GDV in our hospital, accounting for ~ 20% of all cases. Due to the importance of GDV, several large previous studies have investigated risk factors for the development of GDV. It is known that there is no single cause for GDV, rather its occurrence is multifactorial, with both genetic and environmental factors contributing. We propose to further investigate the genetic component of this risk, as part of a larger study tackling GDV pathogenesis from a systems biology

approach. We will start our investigations by establishing the GDV disease phenotype in 500 GSDs that have already been genotyped by The Broad genomics Institute. Phenotypic classification will require contacting dog owners to determine if their dog has had GDV. This analysis will allow us to establish a group of cases (dogs with GDV) and controls (dogs that did not develop GDV) to use in a genome wide association study (GWAS). We hypothesize that we will be able to explain a substantial proportion of GDV risk with single nucleotide polymorphisms (SNPs) identified in a GWAS. Additionally, since the majority of dogs whose DNA is banked at the Broad Institute are AKC registered dogs, their pedigree is known, and thus the heritability of the disease can be traced. It is our hope that by identifying the predisposing genetic polymorphisms and their associated inheritance patterns we will ultimately be able to provide breeders with information to facilitate targeted breeding and prevent this devastating disease from occurring.

Awardee: Christine Yee V'17

Mentor: Dr. Julie Jameson and Dr. Christopher Schonhoff

Award Type: NIH

Research Project: Using a Murine Model of Obesity to Elucidate the Im Obesity on the Skin of Offspring

Summary: This pilot study will investigate the skin environment of juvenile aged mice born from obese mothers to determine if maternal obesity increases the risk factors for childhood barrier tissue dysfunction. Obesity is associated with chronic low-grade systemic inflammation and this inflammation is exacerbated during pregnancy. This affects the in utero environment in which the fetus develops. The fetus is induced into a state of increased inflammation and if the condition becomes systemic and chronic, there may be long-term consequences throughout child and adulthood. The presence of the pro-inflammatory factor, TNF- α has been shown in adult obesity to impact barrier tissue function in the skin, leading to chronic non-healing wounds and infections. Maternally influenced chronic inflammation may similarly increase TNF- α production and the likelihood of skin dysfunction in offspring.

This study will measure inflammation in the skin environment by quantifying the number of macrophages present in the dermal tissue of juvenile-aged, obesity-influenced pups. The macrophages will also be examined for production of the pro-inflammatory factor, TNH- α . Dermal tissue preparations will be analyzed using flow cytometry and immunofluorescence microscopy with specific staining for CD11b, CD11c, and intracellular TNF- α to identify pro-inflammatory macrophages. *We hypothesize that more pro-inflammatory macrophages will be present in the skin of pups born from obese mothers than non-obese mothers.*

Signs of inflammation in their dermal environment would indicate a long term effect of fetal development in a chronic inflammatory condition and a predisposition to chronic skin wounds and infections. It is important to understand the consequences of gravid obesity as well as the physiological mechanism because then preventative measures can be taken or treatments can be developed to reduce the risk factors and the rate of incidence.