



**CUMMINGS SCHOOL  
OF VETERINARY MEDICINE AT TUFTS UNIVERSITY**

**SUMMER RESEARCH  
TRAINING PROGRAM AWARDS  
2016**

**ABSTRACT BOOK**

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## 2016 Summer Research Proposals

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**Awardee:** Pamela Bay V'18

**Mentor:** Dr. Lisa Freeman and Dr. John Rush

**Funding Source:** Berkley Fund

**Title:** Development of an Objective Cardiac Nutritional Risk Index for Dogs with Congestive Heart Failure

**Summary:** Congestive heart failure (CHF) is a progressive disorder that has a high mortality rate, with affected dogs often succumbing to heart failure within 3 months to 1 year after diagnosis. Congestive heart failure is commonly associated with nutritional alterations, with muscle loss (cardiac cachexia) being one of the most problematic nutritional concerns. In humans, cardiac cachexia is an important and independent predictor of mortality, however the effect of cachexia and other nutritional alterations on survival in dogs with CHF has yet to be reported. To assess prognosis in humans with CHF based on their nutritional alterations, several nutritional indices have been developed. These indices use values from patients' body weight, complete blood counts (CBC) and serum biochemistry profiles to objectively assess an individual's level of malnutrition and survivability. No such indices exist in dogs, but a proven nutritional index would be a valuable tool for veterinarians to better assess individual dogs with CHF and to allow for timely nutritional intervention in dogs identified to be at risk for malnutrition. Therefore, the aim of this study is to develop a cardiac nutritional risk index, similar to ones used in humans, to better assess nutritional status and prognosis of dogs with CHF.

The proposed study will use data from ten previous studies conducted in dogs with CHF to develop a cardiac nutritional risk index (CNRI). A variety of data will be statistically evaluated for potential use in the CNRI equation, including data used in human nutritional risk indices (e.g., body weight, albumin), as well as other physical examination findings (e.g., muscle condition score) and data from CBCs (e.g., lymphocyte count, hematocrit) and serum biochemistry profiles (e.g., blood urea nitrogen, glucose, triglycerides) that have been associated with nutritional status and survival in previous veterinary and human studies. These data will be collected from the records of dogs from the ten previous studies on CHF and will be compared to degree of cachexia and survival times to develop a valid CNRI that can be tested in future prospective studies as an endpoint for clinical trials, as well as to provide valuable clinical information for the veterinarian and owner regarding an individual patient's prognosis.

**Awardee:** Alexandra Bemis V'18

**Mentor:** Dr. Chris Pirie

**Title:** Comparative Gonioangiography of Sodium Fluorescein and Indocyanine Green in the Normal Canine Eye

**Funding Source:** NIH

**Summary:** Glaucoma is a common cause of blindness in dogs. It is defined as destruction of retinal nerve fibers that results from an increase in intraocular pressure. This increase in pressure can be caused by a variety of mechanisms that take place at the iridocorneal angle, which is where the outflow pathways for aqueous humor are located. In humans, neovascularization of this region is associated with glaucoma; it is hypothesized that these new vessels could be contributing to this disease process by obstructing the outflow path and trabecular meshwork in the iridocorneal angle. Therefore, the ability to identify neovascularization could allow for early detection of glaucoma and/or assessment of efficacy of treatment for this disease. Angiography is a technique used to visualize vessels and their filling patterns by intravenously injecting a dye. Gonioangiography is the application of this technology specifically to evaluate the iridocorneal angle. The vasculature of the iridocorneal angle has previously been minimally assessed in canines due to cost-prohibitive imaging equipment. However, Pirie and Alario (2013) have successfully used a modified digital single lens reflex (dSLR) camera in conjunction with sodium fluorescein gonioangiography to image this region, but, widespread leakage of the dye from the iridial vessels that occurred with this technique may have concealed vasculature in the region. Indocyanine green is an alternative dye used in human angiography; it is less prone to leakage because it is more highly protein bound than sodium fluorescein. The objective of this study would be to use a dSLR camera adaptor to describe and compare the vasculature and filling patterns of the normal canine iridocorneal angle employing sodium fluorescein and indocyanine green gonioangiography.

**Awardee:** Stephanie Chubb V'18

**Mentor:** Dr. Marieke Rosenbaum

**Title:** Assessing Zoonotic Gastrointestinal Parasitism in Dogs among Unstably Housed and Domiciled Pet Owners in Worcester, Massachusetts

**Funding Source:** NIH

**Summary:** The psychological and social importance of the human-animal bond in unstably housed populations has been documented, though the health status of the pets in these relationships is

unknown. Because unstably housed people often face barriers to regular health care and good health outcomes, it is presumed that their pets face similar hardship. To begin to address this gap in knowledge, we plan to partner with existing Tufts' community outreach initiatives at the soup kitchen and health assessment program in St. John's Church (Worcester), Worcester Housing Authority animal clinics, and a local pet pantry called Kibble Kitchen to reach these pets and their owners.

Through this study, we aim to determine the prevalence of zoonotic gastrointestinal parasites in dogs owned by unstably housed individuals via fecal parasite analysis, to qualitatively understand the bond these unstably housed individuals share with their dogs, and to determine how this bond might promote or protect zoonotic parasite transmission via the use of a standardized survey and semi-structured interviews. Specifically, we expect to find high levels of gastrointestinal parasitism in dogs of unstably housed owners compared to published prevalence values in this area, and expect to find numerous pet-owner interactions among unstably housed and domiciled owners that may promote parasite transmission (i.e. sleeping with pet, lack of regular access to sanitation, health and veterinary care). On a larger scale, our data will inform the need for subsidized and sustainable pet care in vulnerable canine populations as a benefit not only to the pet and their owner, but also to the general public. We affirm the One Health belief that pet health is an important contributor to human mental and physical health in the unstably housed population, and aim to highlight this interplay through our research.

**Awardee:** Eric Granato V'19

**Mentor:** Dr. Sandra Ayres

**Title:** Evaluating Anit-Mullerian Hormone Receptor II on Theca Cells of Rattus Norvegicus Ovaries and Anti-Mullerian Hormone in Blood/Serum during the Estrous Cycle

**Funding Source:** USDA

**Summary:** Mismanagement of the global pet population by their human stewards has led to a population crisis with high economic, ecological, and humanitarian costs. The most effective solution currently is sterilization, sterilized individuals will remain in their ecological niche and effectively compete with any non-sterilized insurgents. However, effective sterilization campaigns are limited by monetary cost and scarce human resources. The current best method of sterilization is the surgical removal of the gonads, this approach has major hurdles when applied in middle to low income nations and is even inadequate in the United States. The development of an affordable and stable vaccine, based on targeting AMHR II, would allow Tufts to initiate a new One-Health campaign centered on community involvement and veterinary training. Tufts could send a handful of veterinarians and scientists to a hot spot to test a vaccine and ear tag sterilization campaign. Members of the community could be trained to give our vaccine and tag animals using indigenous knowledge to control pet

populations on a scale greater than we could accomplish top down. A grassroots approach would also overcome cost and skill barriers of previous efforts and have a higher impact.

While these lofty goals represent our long term ambitions they are not without scientific basis. AMHRII is expressed in the granulosa cells of females and sertoli cells of males. These cell types are necessary for oocyte and sperm development and survival. If the support system is destroyed the animal would be rendered sterile. Additionally AMHRII seems to be confined to the gonads, meaning any targeted sterilization would have minimal effects on the rest of the system. The function of theca cells includes androgen and progesterone production. It is possible AMRHII plays a role in the regulation of theca cells and can be manipulated. We have chosen to examine the relationship of AMHRII on the theca cells of rats because the findings should translate to cats and dogs, the carnivores we most want to regulate, as these species are all polyovulatory. If we can show that theca cell AMHRII expression increases in correlation with peaking sex hormones and serum AMH during the estrus cycle it would lend weight to our idea that they play a regulatory role. The previous lack of interest in theca cell's possible regulatory role allows us the unique opportunity to produce novel findings and answer long standing questions. This project will monitor rats through their 4-5 day estrous cycle. At each stage; proestrus, estrus, metestrus, and diestrus the animals will be sacrificed and ovarian tissue as well as blood/serum will be collected for analysis to see if AMHRII and AMH changes with the cycle stage.

**Awardee:** Brittany Grenus V'18

**Mentor:** Dr. Felicia Nutter

**Title:** Evaluation of the Efficacy of Three Different Sampling Sites for the Detection of Elephant Endotheliotropic Herpesvirus (EEHV) in Asian Elephants in Ireland

**Funding Source:** NIH

**Summary:** Elephant Endotheliotropic Herpesvirus (EEHV) causes an acute hemorrhagic syndrome in both Asian and African elephants, and, as such, poses a threat to the conservation of the species. There are several species of the virus, but their prevalence in range countries and zoos is largely unknown. It is also not known why some elephants acquire a fatal hemorrhagic disease, while others only carry a latent form of the infection, but EEHV experts believe that the virus is endemic to elephant populations. The acute, fatal form of the disease primarily affects juvenile elephants. Early detection of viremia in EDTA whole blood samples prior to the development of clinical signs allows for earlier treatment and better survival rates in juvenile elephants. As such, weekly screening of EDTA whole blood samples is considered a tool for the management of captive elephants. It is the goal of this study to (1) examine the prevalence of EEHV shedding in Asian elephants, (2) compare the efficacy of conjunctival swabs, oral swabs, and trunk-wash samples for the detection of EEHV in Asian elephants, and (3) perform weekly screenings of EDTA whole blood samples for the detection of EEHV viremia in Asian elephant calves at the Dublin Zoo in Ireland. It is hypothesized that trunk-wash samples will be the most effective method for the detection of EEHV in Asian elephants. This study will be performed using previously validated

methods for EEHV detection in conjunctival swab, oral swab, trunk-wash, and whole blood sample analyses.

**Awardee:** Alexandria Hicks-Nelson V'18

**Mentor:** Dr. Benjamin Nephew

**Title:** The Impact of Intranasal Hormone Intervention on Lactating Rat Dams Exposed to an Early Life Chronic Social Stress Model of Postpartum Depression and Anxiety

**Funding Source:** NIH

**Summary:** The aim of this project is to investigate the behavioral effects on F2 juveniles and adults following F1 intranasal hormone intervention. At the F1 generation the lactating rat dams were exposed to early life stress, given Dr. Nephew's previous research into a rodent model for postpartum depression and maternal anxiety. The chronic social stress (CSS) model is achieved by antagonizing F0 lactating rat dams with a foreign male for an hour a day for two weeks; the resulting maternal care in the F0 and F1 females can be characterized by sectioning off the cage with a low plastic grid to measure such ethogram entries as nursing, moving the nest, and standing away from offspring. CSS model F0 dams have shown depressed maternal care; depressed maternal care is displayed again in the F1 lactating dams that experienced the CSS model as pups of antagonized F0 dams. F2 offspring have been shown to exhibit behavioral abnormalities associated with the presence of absences of early life stress in their F1 dam's lifetime. However, attempts have not been made to treat the CSS model at the level of the F1 dams and track the generation implications to determine F2 social behavior amelioration, and thus, my project.

My hypothesis is that intranasal administration of oxytocin to F1 lactating dams that were raised by F0 CSS model dams will promote control-like maternal behavior in the F1 females, and their offspring will exhibit control-like social behavior. Oxytocin is a hormone known to play a key role in maternal bond formation and depression. Previous work done by the Nephew lab has shown altered oxytocin gene and receptor expression in CSS models and their offspring, raising the question of its role in the CSS model and transgenerational depressed maternal care. I will investigate the effects of oxytocin by following the CSS model in lactating Sprague-Dawley F0 rat dams, impregnating their F1 progeny, and administering intranasal oxytocin or saline to the F1 generation. Female F1 behavior towards their F2 progeny will be monitored by camera to be later reviewed for ethogram action tally and summation using ODLog. F2 social interaction data will be gathered by recording novel pairs of juveniles and then adults in an open field. Data from the experimental groups' F2 offspring will then be compared, along with a control group, using a one way ANOVA followed by Tukey's HSD for pairwise comparisons if there

is an overall treatment effect. All graphs will be presented as a mean + SEM and the level of statistical significance will be set to  $p \leq .05$ .

**Awardee:** Melissa Icaza V'18

**Mentor:** Dr. Patrick Skelly and Dr. Akram Da'darah

**Title:** Characterization of Schistosome Tegumental Tyrosinase and Effect on Viability and Infectivity

**Funding Source:** NIH

**Summary:** Schistosomiasis is a major world health concern, affecting millions of people and countless animals each year. At the Molecular Helminthology Lab at Tufts Cummings SVM Dr. Skelly studies the integument of schistosome. This tissue is particularly important because it is the main point of contact with host tissues and interaction with the immune system. In this Summer Research Proposal, we will specifically be looking to characterize a tyrosinase homolog, designated as SmTyr which has not yet been studied. We hypothesize that the function of SmTyr is similar to the tyrosinases found in insects, where it is involved in wound healing as a defensive enzyme. This potentially makes it a critically important protein for the schistosome.

The specific aims of this summer research project are to:

1. Characterize the tissue distribution of schistosome tegumental tyrosinase at the following life stages: cercaria, schistosomula, and adult male/female.
2. Determine the importance of schistosome tegumental tyrosinase in the survival and morphology by suppressing the expression of the gene via RNAi

Our hypothesis is that tegumental tyrosinase is essential for schistosome survival. We aim to characterize the protein and test this hypothesis, potentially leading to a new target for schistosome treatment and control. Characterization will be completed via:

1. Live assays to determine the activity of the enzyme at different life stages
2. Real-time PCR using cDNA to determine level of gene expression at life stages
3. Immunohistochemistry to determine enzyme distribution in the organism

We aim to determine the importance of SmTyr to schistosome survival by treating with small interfering RNAs to suppress gene expression and:

1. Monitoring morphology and viability in vitro
2. Infecting mice and later attempting to collect any adult worms

Gene suppression will be monitored via live activity assay and Western blotting. All results will be compared to wild type schistosomes. Early stages of experiments will begin this spring during a self-styled selective.

**Awardee:** Jessica Levine V'19

**Mentor:** Dr. Flo Tseng and Dr. Felicia Nutter

**Title:** Fecal and Feather Glucocorticoid Assays in African Penguins (*Spheniscus demersus*)

**Funding Source:** NIH

**Summary:** Molting is a stressful and energetically demanding time for penguins. Drawing blood for routine procedures, even from animals living in zoos and aquaria and accustomed to being handled, can be a stressful event which may affect cortisol levels<sup>1</sup>. Because fecal glucocorticoid assays have already been shown to be accurate indicators of stress levels in the African penguin (*Spheniscus demersus*) and Adelie penguin (*Pygoscelis adeliae*) in relation to weather and human interaction<sup>2,3</sup>, these assays provides a non-invasive method for measuring changes in corticosterone levels during molting and applying it may provide insight into differences in corticosterone levels in normally versus abnormally molting penguins. Another non-invasive method of stress measurement in avian subjects is through feather corticosterone assay<sup>4</sup>. Feather corticosterone measurement could be useful for long-term non-invasive stress hormone measurement, particularly in seasonally molting species such as penguins. In this study, I will develop an assay to measure corticosterone levels in feathers collected from molting penguins. I will establish a second assay to measure fecal glucocorticoid levels in molting penguins. I will use the fecal and feather assays to compare pre-molt, molting, and post-molt corticosterone values in normally and abnormally molting penguins.

**Awardee:** Rachel Madenjian V'18

**Mentor:** Dr. John Mandelman and Dr. Robert Bridges

**Title:** Evaluation of Barotrauma in Cusk Following Recreational Fishing Capture

**Funding Source:** NIH

**Summary:** Relatively little information is known regarding the bottom-dwelling teleost, cusk, a National Marine Fisheries Service species of concern whose population has been declining since the late 1960s. Presently, cusk are often taken and discarded as bycatch in fisheries targeting cod and haddock.<sup>6</sup> As the stock populations for more coveted species like cod continue to diminish, cusk will become a more significant target in the Gulf of Maine recreational rod-and-reel fishery. In order to preserve the population, the impact of recreational fishing on the species must be assessed, so practices in addition to catch and release can be implemented to promote the survival of cusk caught as bycatch.

Cusk suffer barotrauma when hauled up from the seabed due to the rapid reduction in barometric pressure, resulting in the expansion of gas in the swim bladder and other tissues.<sup>7</sup> While external injuries are commonly assessed in species that face barotrauma, internal injuries are often undetected. In spite of the fact that external injuries appear life-threatening, there is evidence that these signs may be partially mitigated by recompression and release of cusk at the ocean floor.<sup>2</sup> Investigators are studying the potential of a release device to return cusk to their habitat following capture in an effort to decrease post-release mortality. Understanding the complete set of barotrauma faced by the species will provide insight about their ability to survive once returned to the seabed. Additionally, characterizing the types of barotrauma experienced by cusk and the factors that influence severity will aid in the development of techniques to mitigate injury and mortality from fishing capture. We would like to characterize the full spectrum of injury induced by barotrauma in cusk. The objectives of this study are to:

- Quantify the prevalence and severity of external and internal barotrauma in cusk;
- Assess the influence of a) depth of capture and b) fish length on the prevalence and severity of barotrauma in cusk.

**Awardee:** Amanda Nee V'18

**Mentor:** Dr. Hellen Amuguni

**Title:** Peste des Petits Ruminants in Karamoja, Uganda: A Gender-Sensitive Qualitative Study of Small Ruminant Management and Resources for Eradication

**Funding Source:** Lawrence Fund

**Summary:** Peste des Petits Ruminants (PPR) is a viral disease of small ruminants spread throughout Asia and Africa that poses a major challenge to sheep and goat health. The virus has the potential to decimate 90% of naïve herds and currently places 80% of the world's small ruminants at risk of infection. In 2015, the FAO and the World Organization for Animal Health (OIE) released a plan to eradicate this virus by 2030 through the example of the successful Rinderpest eradication, hinging upon the cooperation between community based animal health workers and governmental programs.

Karamoja, a culturally independent region of north eastern Uganda practices agro-pastoralism and is home to approximately 2 million sheep and 1.6 million goats (Ministry of Agriculture, 2009). The region's first outbreak of PPR in 2007 spurred a government-led vaccination campaign. Since then, a scarcity of veterinary resources and an emphasis on movement have been identified as challenges hindering the campaign's success.

Gaps in knowledge of seasonal herd movement, community awareness of PPR, and potential agents of change within the social infrastructure are creating challenges for effective community-engaged eradication strategies. Therefore, this study aims to answer the question, which members of Karamojong communities are facilitating seasonal small ruminant husbandry and how does their knowledge of PPR management contribute to endemicity of PPR in Karamoja, Uganda despite government vaccination programs?

The specific aims of this project are three-fold: 1) to determine the degree of small ruminant herd contact and mixing with regards to seasonal management in Karamoja, Uganda 2) to clearly define roles in small ruminant husbandry within the members of the Karamojong communities 3) to assess the knowledge and perception of PPR within Karamojong communities.

This cohort study will be qualitative in nature, utilizing key informant groups in 21 villages of both Kotido and Moroto districts of Karamoja. Separate cluster samples of men and women will be engaged in focus groups consisting of translator-facilitated semi-structured interviews, participatory mapping, seasonal calendars, and ranking exercises. The data generated by these participatory epidemiological exercises will be assessed via the analytical program, Stata®. Quantifiable measurements will be analyzed for agreement using Kendall's agreement coefficient (W) to assess gender-biased recall within a village, between villages in a district, and between a northern and southern district of Karamoja, Uganda.

The primary goal of this study is identify key persons engaged in small ruminant husbandry, localize hotspots of seasonal inter-herd contact for targeted management alterations and vaccination campaigns, and characterize PPR interpretation amongst a diverse region for intervening organizations such as the Ugandan Ministry of Agriculture to implement efficacious eradication schemes.

**Awardee:** Chrystal Nguyen V'18

**Mentor:** Dr. Andrew Hoffman

**Title:** Effects of Wharton's Jelly Mesenchymal Stem Cells on Neuron Ischemic Reperfusion Damage

**Funding Source:** Merial Scholars

**Summary:** Patients who undergo strokes and seizures suffer from neuronal cell damage. This leaves them cognitively impaired from the cell damage caused from the loss of blood flow to the brain, but interestingly, the majority of the damage occurs when blood flow returns to the brain. This is called ischemic reperfusion. Wharton's Jelly mesenchymal cells, or WJ-MSCs, are stem cells derived from Wharton's Jelly in umbilical cords. They secrete exosomes, nanovesicles that contain anti-inflammatory and neuroprotective miRNA. When they are hypoxically preconditioned, the WJ-MSCs release more exosomes.

A potential treatment to strokes and seizures is utilizing the miRNA from the exosomes to decrease the amount of cell death. The miRNA, in the exosomes, because of their healing properties, decrease cell damage when transplanted into neuronal tissue.

Hypoxic preconditioning can increase the amount of exosomes produced by WJ-MSCs, which in turn increase the amount of miRNA produced. We can simulate ischemic reperfusion on neurons and culture them with these miRNA at various stages. After each trial, we can determine the effectiveness of the exosomal miRNA based on decreased neuronal cell death.

**Awardee:** Shad Orechovesky V'18

**Mentor:** Dr. Diane Schmidt

**Title:** Hotspot Analysis of Asymptomatic Dengue Carriers and Circulation of Dengue in Vector Species in São Paulo State, Brazil

**Funding Source:** NIH

**Summary:** Dengue fever is one of the WHO's neglected tropical diseases with roughly 100 million symptomatic cases per year and \$2.1 billion in economic costs in the Americas alone. Current efforts to control the disease rely on broad vector eradication campaigns that have not significantly slowed the increase in disease incidence. The state of São Paulo, Brazil is the most populace in South America and holds the highest number of dengue cases in the Americas. Controlling dengue in São Paulo would have a profound effect, both in terms of economic benefits and human welfare. Dengue virus has four serotypes (DENV 1-4) and, while long-term immunity is conferred, it is only for the specific infective serotype. This has hampered control efforts as more than one serotype can be in an area resulting in patients with multiple infections of dengue fever over time. If the serotypes in circulation were known, actions could be taken to protect the portion of the population most susceptible to that serotype and decrease its prevalence in the region. In order to know which serotypes are circulating in the region, we propose to run qRT-PCR on asymptomatic household members of dengue-positive hospital patients in São Paulo state. Additionally, mosquitoes collected from the areas surrounding the households of the above patients will also be tested for dengue virus. Finally, ArcGIS will be used to correlate the location of dengue serotypes in asymptomatic humans and the mosquitoes. We expect there will be a statistical correlation between the two.

**Awardee:** Samantha Sangster V'18

**Mentor:** Dr. Maureen Murray

**Title:** Comparison of Post-Release Movements and Survival of Rehabilitated and Wild Harbor Seal (*Phoca vitulina*) Pups

**Funding Source:** NIH

**Summary:** The goal of this study is to utilize satellite-tracking data to compare the post-release movements and survival rates of rehabilitated harbor seal pups to those of wild harbor seal pups in order to ascertain the efficacy of current rehabilitation and release protocols at the Vancouver Aquarium. Harbor seal pups are one of the most commonly stranded marine mammal species in North America and considerable rehabilitation and release efforts are expended on them every year. In this

study transmission durations, cumulative distances traveled, average daily distances, average rates of travel, and geographic distribution patterns will be assessed in an effort to determine whether rehabilitated seals behave like their wild counterparts. The few studies that have been conducted on the post-release movements and behaviors of rehabilitated harbor seals suggest that successful integration of rehabbed pups into the wild may be heavily dependent on local population and habitat specific factors. Though studies conducted in England and California have found that rehabbed and wild seal pups appear to behave similarly, Gaydos and Vilchis (2012) found that the movement and distribution of rehabilitated harbor seal pups were remarkably different from those of wild pups in San Juan County, Washington. According to harbor seal population censuses, the coastal waters of northern Washington and southern British Columbia may be the most densely populated in the world. The Marine Mammal Rescue Centre (MMRC) at the Vancouver Aquarium in British Columbia rescues and rehabilitates stranded harbor seal pups from the same densely populated area. This study will use MMRC Argos Satellite Tracking data from rehabilitated harbor seal pups and compare their movements and survival to those of the wild cohorts in San Juan County, WA in the Gaydos and Vilchis (2012) study.

This study will in effect replicate the study of Gaydos and Vilchis (2012) with a different sample of rehabilitated harbor seals. Such replication is necessary to determine whether the movements and survival of rehabilitated harbor seals do differ significantly from wild seals in northern Washington and southern British Columbia. Furthermore, consistent findings between this study and the Gaydos and Vilchis (2012) study would indicate that rehabilitation programs and release protocols would need to be reevaluated in both San Juan County, WA and Vancouver, BC in order to release rehabilitated harbor seals that can successfully integrate into the wild, survive, and reproduce.

**Awardee:** Giles Siddons V'18

**Mentor:** Dr. Patrick Skelly

**Title:** Do Schistosomes Inhibit the Activity of Human Thrombin?

**Funding Source:** NIH

**Summary:** Schistosomes are parasitic flukes that can live in the blood of their human hosts for years. Being large (~1 cm long, ~1 mm diameter) foreign bodies in direct contact with host blood, these parasites are expected to trigger the coagulation cascade and produce local thrombi, (clots), but this is not seen. It has been suggested that schistosomes are capable of inhibiting the activity of human thrombin, an essential enzyme in the clotting cascade. Specifically, it has been reported that a schistosome protein - Sm22.6 - found on the worm surface (tegument) is a potent thrombin inhibitor.

However, this inhibition has only been shown through in vitro studies using high concentrations of recombinant Sm22.6 protein.

Our hypothesis is that intact parasites disrupt thrombin activity, and that the tegument protein Sm22.6 contributes to this disruption. To test this we will first perform kinetic measurements of thrombin activity on a synthetic substrate in the presence or absence of normal schistosomes. If a significant effect is observed, we will proceed using established RNAi techniques to suppress expression of the Sm22.6 gene in parasites, and repeat thrombin kinetic measurements using the Sm22.6-suppressed worms. Comparing thrombin activity in the presence of Sm22.6-suppressed worms vs. untreated worms will reveal the extent to which the Sm22.6 protein plays a role in thrombin inhibition by live, intact parasites.

**Awardee:** Kenneth Siu V'18

**Mentor:** Dr. Jeffrey Mariner

**Title:** An Epidemiological Assessment of Peste des Petits Ruminants (PPR) and Evaluation of PPR Vaccine Program Effectiveness in Karamoja, Uganda

**Funding Source:** NIH

**Summary:** Peste des Petits Ruminants (PPR) is a respiratory disease of small ruminants that causes significant herd morbidity and mortality in naïve populations. PPR negatively affects the livelihoods of communities that depend on small ruminants for nutritional and economic security. They are easily slaughtered or sold to meet pressing needs and serve important function in social relationships through dowry, loans and gifts. PPR has been validated as a problem for low income small ruminant farmers which has led to the implementation of government organized vaccination programs. However, vaccination programs in areas such as Karamoja, Uganda have so far failed to achieve the recommended level of herd immunity and as a result, PPR remains endemic in the region.

Using cross-sectional, mixed methodology, the proposed study will contribute to our understanding of the epidemiology of PPR in Karamoja, Uganda. This will be accomplished by determining the seroprevalence of PPR in small ruminants in the area, and by administering a questionnaire to key informants regarding herd characteristics, PPR knowledge, and the vaccination program. Blood samples will be collected from about 400 goats/sheep belonging to Karamojong villagers and will be assessed utilizing a validated, ELISA-based test for PPR antibodies. Questionnaires will cover vaccination status, basic demographic information, perceived effectiveness of the vaccination program, perceived prevalence of PPR in the area and knowledge of PPR epidemiology. The geographic distribution of PPR vaccination status and seroprevalence of PPR will be directly compared utilizing ArcGIS.

Increased effectiveness of vaccination programs relies on community knowledge and participation. This study will determine if different perceptions exist between the Karamojong communities and the Ugandan veterinary services that may influence the effectiveness of the PPR vaccination program. Questionnaires provided to the key informants in the villages will also be administered to regional Government Veterinary Officers. Questionnaire data will be compared between the two groups utilizing the kappa statistic for interrater reliability. Identifying PPR knowledge gaps and discrepancies between these two stakeholder groups is the first step towards improving vaccination delivery systems and ultimately eradicating PPR in this region. Finally, questionnaires and serological samples will be used to calculate the basic reproduction number, an informative measure of viral transmissibility in local populations that can be used to set herd immunity targets for eradication.

**Awardee:** Laura Sloan V'19

**Mentor:** Dr. Felicia Nutter, Dr. Patrick Skelly and Dr. Sivapong Sungpradit

**Title:** Gastrointestinal Parasites in Sympatric Wild and Domestic Ungulates and Use of DNA Barcoding to Detect Potential Pathogen Sharing at the Wildlife-Livestock Interface in Salakpra Wildlife Sanctuary Thailand

**Funding Source:** USDA

**Summary:** Gastrointestinal (GI) parasite infection causes a number of significant health effects in humans and animals. Most parasites can infect many species. Stunted growth, malnutrition, anemia, changes in organ morphology, and other deficiencies in micronutrients have been linked to parasite infection in humans. Parasite infection also places a strain on production animal yield. Infested domestic livestock suffer from a lower wool and milk production, decreases in bone mineralization, and have been identified to have protein deficiencies post mortem. This project focuses on gastrointestinal parasites in the Salakpra Wildlife Sanctuary (WS), Kanchanaburi Province, Thailand. This is the oldest wildlife sanctuary in Thailand and is home to many native wildlife species, as well as illegal domestic animals and human settlements. While most ecological studies in Salakpra WS have focused on human conflicts with wildlife, none has yet investigated the potential impact this species overlap has on GI parasite infection. This project will document the prevalence of taxa of GI parasites in four ungulate species present within Salakpra WS: Eld's deer (*Rucervus eldii*), banteng (*Bos javanicus*), Asian elephant (*Elephas maximus*), and domestic cattle (*Bos indicus*). Eld's deer, banteng, and Asian elephants are all listed as endangered on IUCN's Red List of Endangered Species. Ten fecal samples from each species will be collected. From each sample, two fecal egg counts will be completed, ova identified, and a portion of the feces will be cultured to permit third-stage larvae to develop. DNA will be extracted from these larvae, PCR performed, and amplified DNA will be sequenced. Sequence comparisons should reveal the identity of the specific taxa present. This sequenced data along with fecal egg counts will provide

information on parasite prevalence, richness, abundance, and aggregation amongst species. Of particular interest is the degree of overlap in the GI parasite populations among the four species under study here.

**Awardee:** Casey Smallwood V'18

**Mentor:** Dr. Dominik Faissler

**Title:** Idiopathic facial paralysis with concurrent head tilt in dogs: a retrospective study

**Funding Source:** NIH

**Summary:** Isolated neuropathies of the head are a common presentation in neurology practice. Disorders such as facial nerve paralysis and trigeminal neuropathy are frequent reasons for presentation. The purpose of this project is to study a novel clinical syndrome that includes facial nerve paralysis *AND* a corresponding head tilt. Dogs presenting with this form of polyneuropathy of the head also show vestibular ataxia and nystagmus. An idiopathic polyneuropathy of the head will be suspected based on a ruling out of other disorders such as otitis media-interna, inner ear tumor, cholesteatoma or other structural brain disease.

Our goal is to retrospectively collect clinical cases of dogs that presented with facial nerve paralysis *and* a corresponding head tilt. With these cases, we hope to gain more information about this idiopathic and pre-existing condition as well as the variation of the clinical presentation, time for resolution, completeness of recovery, and the likelihood for a relapse.

This study will enroll dogs being treated at the Foster Small Animal Hospital at The Cummings School by the neurology service. Criteria for inclusion will be neurological signs referring to dysfunction of the cranial nerves, specifically uni- or bilateral facial nerve paralysis *and* a head tilt to one side. Dogs included will have a complete medical history and follow up, CBC and chemistry profile, chest radiographs, a complete MRI study of head and brain, a CSF analysis and complete testing to evaluate concurrent disorders. The follow-up time should be at least one year.

Despite seen in a neurological practice, this syndrome has not been reported so far. This study performed at The Cummings School of Veterinary Medicine at Tufts University could close the gap. Information gained from a case series about variation of the clinical presentation, concurrent or underlying disorders, outcome and prognosis would be essential for a better management of dogs affected by this condition. Therefore, this study is expected to produce clinically relevant and useful information.

**Awardee:** Ruairi White V'18

**Mentor:** Dr. Marieke Rosenbaum and Dr. Jean Mukherjee

**Title:** A Survey of the Prevalence and Antimicrobial Resistance of *Staphylococcus aureus* in the Wild Urban Rodents of Boston, MA

**Funding Source:** NIH

**Summary:** *Staphylococcus aureus* is a ubiquitous bacteria carried by a multitude of species, including humans and rodents. These bacteria represent a public health concern, as over time they have accumulated resistance to a broad array of antimicrobials. Recently the United States has seen an increase in the prevalence of Community Associated (CA) Methicillin-Resistant *S. aureus* (CA-MRSA). Urban rodents are well-established reservoirs for zoonotic infections and may play a role in spreading antimicrobial-resistant *S. aureus*.

The proposed project is a cross-sectional study to evaluate the prevalence and antimicrobial sensitivity of *S. aureus* carried by wild urban rodents in the city of Boston, MA. The project has three specific aims: (a) to determine the prevalence of antibiotic-resistant *S. aureus* in wild rodents trapped by pest-control services in the city of Boston, MA, (b) to evaluate the proportion of MRSA-positive rodents (as determined by oronasal swab, culture, and PCR) that are shedding the bacteria in their feces, and (c) to assess whether *S. aureus* carrying the *mecC* gene is present in wild rodents in the City of Boston, MA. This will be accomplished by necropsying rodent cadavers provided by a Boston pest control company. Bacteria will be isolated using common microbiological protocols, tested for antimicrobial sensitivity, and molecularly analyzed for the presence of the *mecA* and *mecC* genes.

In addition to elucidating the prevalence and characteristics of *S. aureus* in urban rodents in Boston, this study will also help forge a partnership between Tufts University, Boston University, and Ecologic Entomology LLC pest control services. This partnership may yield future public health studies of rodents and insects in the Greater Boston area and help shape public policy regarding rodent control.

**Awardee:** Emma Winstead V'19

**Mentor:** Dr. Felicia Nutter and Dr. Flo Tseng

**Title:** Investigating Peripheral Immune Function in Abnormally Molting Penguins at Mystic Aquarium

**Funding Source:** NIH

**Summary:** African penguins (*Spheniscus demersus*) are important marine sentinels, and are listed as endangered and show rapidly declining wild populations due to a wide variety of environmental, health and human threats<sup>1</sup>. One of the newest threats to emerge is a little-understood feather loss disorder, first seen in wild African penguin chicks. In captivity, Mystic Aquarium has also reported feather and molting abnormalities in their adult African penguin population, but there is a lack of documentation of this disorder, and a lack of research into whether the wild and captive feather disorders could be related.

Molting has been associated with reduced immunocompetence in other avian species, and this compromised immune function could be an important puzzle piece in understanding the extent and impact of feather loss disorder and abnormal molts. As such, this project aims to (1) document the abnormal molting observed in captive African penguins at Mystic Aquarium, (2) validate mitogen-induced lymphocyte proliferation assays previously used in other avian species to African penguins, and (3) compare T-lymphocyte proliferation in four cohorts of penguins at Mystic aquarium; non-molting penguins with a history of abnormal molt, molting-penguins affected by abnormal molt, unaffected non-molting penguins, and unaffected molting penguins.

We hypothesize that abnormally molting penguins and the healthy molting penguins will show reduced immune function compared to the non-molting, healthy samples. Given the extended duration of abnormal molt, we further hypothesize the abnormally molting penguins will show a decreased immune response compared to the healthy molting group. The methods will follow those established by Finkelstein, et al., combined with the instructions from a commercial BrdU colorimetric ELISA kit.

**Awardee:** Makoto Yamamoto V'19

**Mentor:** Dr. Jeffrey Mariner

**Title:** Role of Cats as Reservoir Hosts in the Disease Transmission of *Opisthorchis Viverrini* in Khon Kaen Providence, Thailand

**Funding Source:** NIH

**Summary:** Foodborne parasites are serious problems especially in Thailand where a lot of people are suffering from an infection caused by a parasitic trematode called *Opisthorchis viverrini*. The infection is contracted when people consume undercooked fish, and it is highly associated with lethal bile duct cancer called cholangiocarcinoma (CCA). Although control measures have been taken for the past 50 years, the prevalence level remains high in northeastern Khon Kaen Province. This is partially due to the lack of attention to cultural and ecological aspects of disease transmission, where major control measures included treatment of the parasite via drug administration and health education on "safe cooking". It is currently hypothesized that the persistent prevalence of *O. viverrini* is partially sustained by the existence of reservoir hosts. Among these hosts, cats are identified as the most important species with a much higher prevalence than dogs. The goals of this project are to investigate how these cats are being exposed to *O. viverrini* and how extensive is the knowledge of the villagers about the roles cats play in disease transmission. These goals will be achieved through collection of quantitative and qualitative data including presence of parasite in cats, movement tracking by GPS collar, and data from surveys and observations. Surveys and observational data will be collected with the help of personnel affiliated with Khon Kaen University Faculty of Veterinary Medicine (hosted by Dr. Sirikachorn Tangkawattana). I will accompany these personnel that are fluent in the local dialect to collect data for analysis