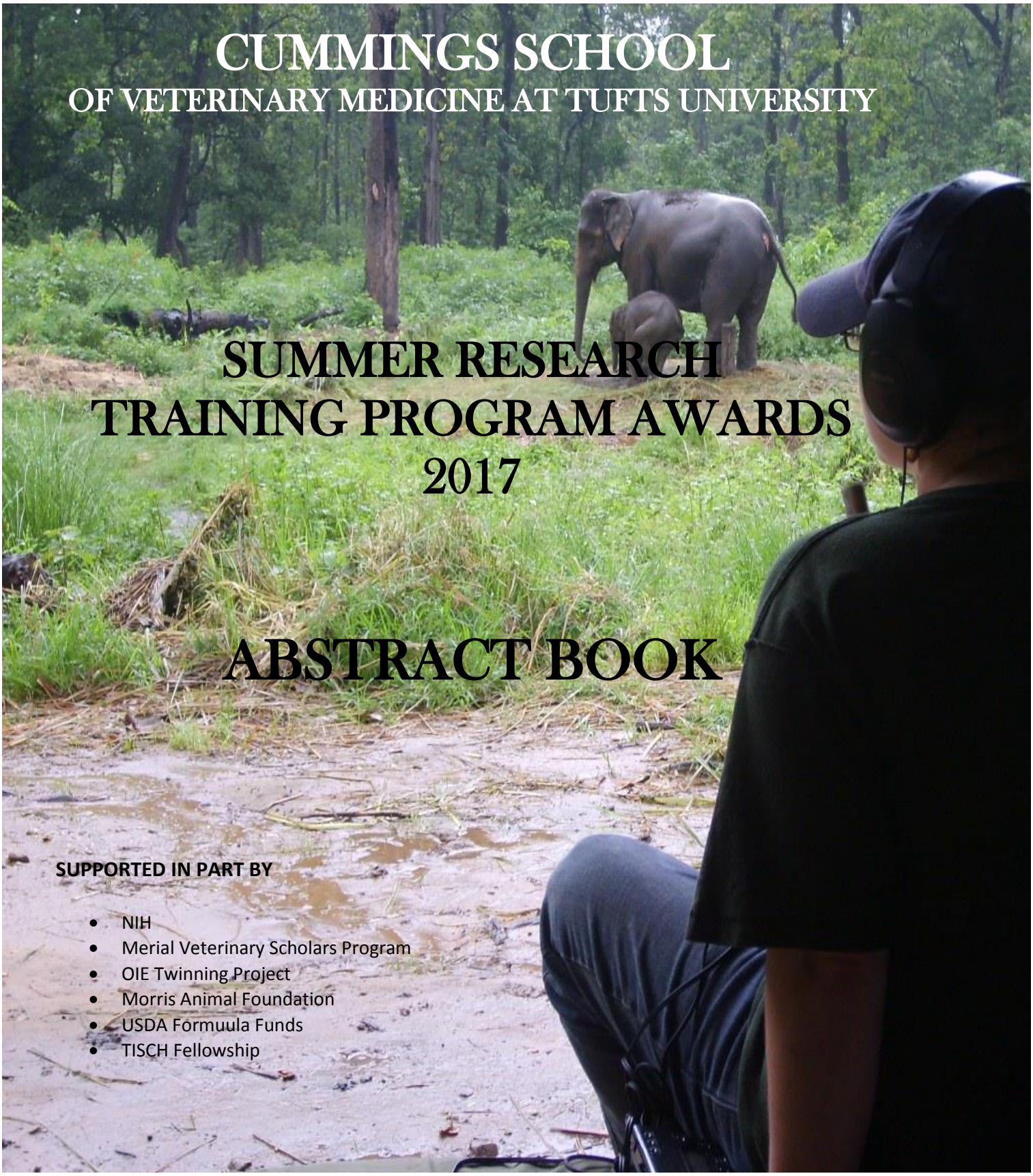

CUMMINGS SCHOOL
OF VETERINARY MEDICINE AT TUFTS UNIVERSITY

SUMMER RESEARCH TRAINING PROGRAM AWARDS 2017

ABSTRACT BOOK

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- NIH
- Merial Veterinary Scholars Program
- OIE Twinning Project
- Morris Animal Foundation
- USDA Formuula Funds
- TISCH Fellowship

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Aw**ardee:** Sarah Adrianowycz V'20

Mentor: Dr. Elizabeth Rozanski

Funding Source: NIH

Title: Characterization of Pyometra Isolates from Clinical Cases

Summary: Study Objectives: To characterize uterine fluid samples from over 60 canine patients that were collected during ovariohysterectomy as definitive therapy for pyometra. Samples will be compared between dogs that received prompt surgery (PS) and those that received delayed surgery (DS), as these differ in the utilization of antibiotics.

Hypothesis: Dogs that have been treated with antibiotics will exhibit a different microbial profile than dogs who were not treated with antibiotics before sampling. We also hypothesize that E. coli is the most commonly identified microbial organism in bitches with pyometra and that dogs treated with antimicrobials for more than 48 hours prior to ovariohysterectomy will more commonly have resistant microbes.

Experimental Design: Uterine fluid samples were collected from over 60 canine patients at the Foster Hospital for Small Animals at Tufts University between 2011 and 2016 during ovariohysterectomy for definitive therapy for pyometra. Samples were submitted for bacterial culture at a commercial laboratory (IDEXX). Results of the bacterial culture will be compared between dogs that were treated with antibiotics and dogs that were not treated with antibiotics. Prior antimicrobial therapy will be determined from a comprehensive review of the medical record.

Significance of Proposed Research: The results of this study will provide valuable insight into the pathophysiology of pyometra and the role that veterinarians play when diagnosing and treating this illness.

Awardee: Joe Belgrad V'20

Mentor: Dr. MD Hoque

Title: Newcastle Disease Prevalence in Rural Poultry in Chittagong, Bangladesh

Funding Source: OIE Twinning

Summary: Newcastle disease is endemic amongst poor rural areas in developing countries, largely due to inadequate or absent vaccination. Newcastle disease can have drastic economic effects through reduction in flock size and a decrease in egg-laying capacity. Decreased meat and egg production exacerbates existing nutritional problems in developing countries. With reduced yield, farmers are

unable to support their children while supplying food to others, continuing the cycle of malnutrition in Bangladesh. Currently, data is scarce on Newcastle disease's prevalence in rural areas of Bangladesh. This research aims to provide data on its prevalence, making it easier for policy formulation and enacting of prevention techniques. Constraints of this research are largely time and monetary based. Both these factors will determine how many samples can be taken and analyzed. Future studies could analyze specific areas of high disease prevalence for traffic patterns to determine husbandry practices that are facilitating disease spread.

Awardee: Emily Berman V'19

Mentor: Dr. Mark Pokras

Title: Health Impact of Environmental Toxins in Common Loons (*Gavia immer*)

Funding Source: NIH

Summary: The Common Loon, *Gavia immer*, is a charismatic diving bird whose habitat ranges across the US and North America. Breeding pairs spend the summer nesting, laying, and raising young on freshwater lakes in the northernmost US and across Canada. Common Loons are currently listed as a threatened species in two states (Michigan and New Hampshire), and a species of concern in seven states (Connecticut, Idaho, Massachusetts, Montana, New York, Washington, and Wyoming). Because they are drastically affected by changes in the environment including changes in water levels, water quality, and human activity, loons are a sensitive ecological indicator species. With climate change and an expanding human population, these issues are likely going to continue to threaten loons and other sensitive species.

Mercury levels in the environment are strongly linked to human industrial activity such as burning coal and oil, and changes in growth of aquatic microorganisms may be related to changes in climate patterns and water temperatures/quality. Excess microbial growth can cause release of cyanotoxins, such as BMAA and microcystin, which are known toxins to humans and animals. Understanding how these toxins may impact wild bird populations is vital as weather and temperature patterns continue to change. The mercury levels in fish and birds in Maine are among the highest in North America. Mercury has documented harmful effects in people and animals. There are fewer published data available about the effects of cyanobacteria toxins on birds, and they have not been studied in loons.

Common Loons do not currently have published reference intervals for blood chemistry parameters. As an initial part of this study, I will analyze data from previously processed blood samples using appropriate statistical methods to determine reference ranges for parameters including glucose, electrolytes, and kidney/liver enzymes. I will also develop reference ranges for protein electrophoresis that measures albumin and globulin levels. I will use regression analysis to examine the relationship between blood chemistry values and mercury and cyanotoxin levels. The goal is to publish these results to further understanding of wildlife health.

Awardee: Abby Clayton V'19

Mentor: Dr. Felicia Nutter

Title: Antimicrobial Resistance in Rehabilitated Harbor Seals (*Phoca vitulena*) in British Columbia: A Temporal Assessment

Funding Source: NIH

Summary: Antimicrobial resistance (AMR) is one of the greatest threats to global public health, affecting humans and animals in every country. While AMR is a naturally occurring process in microbial species, it has been accelerated in the past century due to antibiotic use, and misuse, in both humans and animals. As a result, antibiotics are becoming ineffective against these evolved bacteria, making normally treatable infections very difficult, if not impossible to treat. Ultimately, AMR is causing longer hospital stays, higher medical costs, and increased mortality.

Marine mammals are recognized as potential sentinels of ocean and environmental health and can contribute to the understanding of AMR trends and transmission routes. Previous studies have documented the prevalence of AMR bacteria in marine mammals, and most specifically harbor seals (*Phoca vitulina*), in both Pacific and Atlantic waters. There is evidence of increased AMR incidence in the Northwest Atlantic Ocean region, and a study of similar design is needed to compare trends in the North American Pacific coast/Northeast Pacific. To create a more holistic picture, I will use both retrospective and prospective components.

Replicating the methods of Wallace, et al (2013.) I will retrospectively analyze the medical records for harbor seals treated at the Vancouver Aquarium Marine Mammal Rescue Centre (MMRC). This study will determine the temporal patterns of AMR bacteria cultured from rehabilitated Pacific harbor seals over the last 10 years in British Columbia, Canada, and compare them to trends observed in Atlantic harbor seals. Prospectively, I will swab harbor seal pups in rehabilitation at the MMRC during the 2017 rescue season (July-October 2017) for culture and antimicrobial susceptibility testing upon admission and release into the wild (two time points sampled per animal.) This will establish current AMR prevalence, as well as determine he associated risk and impact of rehabilitation care on the animals' AMR prevalence upon release back into the environment. There are many possible entry points for antimicrobial resistant bacteria into the marine environment, including freshwater outflow, wastewater treatment runoff, and aquaculture, but that is much larger area of potential research. Rehabilitation facilities, where ill and injured animals are commonly treated with antibiotics and then released back into the wild, could be another potential entry point of AMR pathogens into the environment.

We hypothesize that harbor seals treated at MMRC experienced an increased cumulative ncidence of cultured AMR bacterial over the past 10 years, and that harbor seal pups treated during the 2017 season at MMRC will have an increased prevalence of AMR bacteria when released into the wild as compared to admission.

Awardee: Alison Coates V'19

Mentor: Dr. Allen Rutberg

Title: Public Perceptions of Deer Population Control: Hunting vs. Immunocontraceptives

Funding Source: NIH

Summary: Specific Aims:

1) Determine the public's perception and understanding of two different methods of deer population control—immunocontraception in the town of Hastings-on-Hudson, New York (NY) and hunting in Blue Hills Reservation, Massachusetts (MA).

2) Evaluate the quality of communication between the identified communities and the researchers and policy makers who initiated the population control measures.

3) Recommend possible changes in policy and/or communication style for future efforts to control deer populations. I aim to understand and more accurately describe the relationship between the public and the policy makers.

Methods:

I will conduct this project using quantitative surveys and qualitative focus groups. For my survey, I will have statements regarding population control and general conceptions of animal welfare and ask participants to rank their agreement on a Likert Scale. I plan to use Stata 14.2 for statistical analysis of descriptive statistics and Chi-square tests.

I will also conduct focus groups in the two communities. The purpose of these groups is to identify any themes or concerns within the communities that are not addressed in the survey. The focus group will be recorded per permission of those involved, and will have roughly six people in each focus group.

Significance:

Increased human wildlife interactions can lead to increases in vehicle accidents, infectious disease transmission, property damage, and environmental destruction (Hassell, Begon, Ward, & Fèvre, 2017) (Mass Audubon, 2017). In recent years' populations of many wildlife species have been increasing (Flather, Knowles, & Brady, 2009). In the Northeast, both deer and human populations are high, interaction are severe, and several different methods are being explored to control deer populations.

The purpose of this study is to characterize the relationships between the public and researchers and policy makers regarding deer population control. A clearer understanding of how the public perceives researchers and policy makers and population control measures may aid in shaping successful future policy and communication techniques.

Awardee: Charles Cummings V'19

Mentor: Dr. Marieke Rosenbaum and Dr. John Runstadler

Title: A Survey of Influenza A Prevalence Among Wild Urban Rodents in Boston, MA

Funding Source: Morris Animal Foundation

Summary: Influenza virus is a single-stranded, negative-sense, RNA virus with a segmented genome and envelope in the family Orthomyxoviridae. It kills thousands of people every year and causes billions of dollars in loss of productivity. Influenza infections are not just limited to humans. In 2015, an outbreak of highly pathogenic avian influenza (HPAI) cost the U.S. poultry industry about a billion dollars and cost roughly 50 million birds their lives.

Wild, urban rodents are an understudied but plausible species that may contribute to the epidemiology of influenza in urban environments. Urban rats are numerous, ubiquitous, and have shared environments and frequent contact with humans and wild birds – both established as important hosts for influenza. Murine models are commonly used to study the pathogenesis of influenza, which demonstrates their susceptibility to infection, and the use of guinea pigs is increasing as a model of influenza transmission. Yet few studies have ever looked for influenza specifically amongst wild, free-roaming rodents. Those that have, usually look for it in association with outbreaks of avian influenza in rural settings. These studies have had varying results with some finding strong evidence of influenza infection in wild rodents and others not. This study would be, to the best of the author's knowledge, the first investigating the prevalence of influenza virus amongst urban rodents.

We will determine the prevalence of urban rodents shedding influenza virus. This will be accomplished by performing real time reverse transcriptase-PCR on nasal and oropharyngeal swab samples of rats trapped in Boston by pest-control services and by the City of Boston's inspectional services. We will culture samples from those PCR positive animals in order to determine the strains of influenza viruses in Boston's urban rat population. We will also determine the exposure of urban rats in Boston to influenza virus using lung extract to find antibodies to influenza. Data will be analyzed using R. Both Chi squared tests and independent ttests will be performed. Analyses will include determining whether sex or weight significantly affect infection status.

Awardee: Adrian Dannis V'20

Mentor: Dr. Elizabeth Byrnes

Title: The Effect of Previous Opiate Exposure on the Adolescent and Adult Microbiome

Funding Source: NIH

Summary: Opioids have been used for centuries to effectively control severe pain (Sobczak, Sałaga, Storr, & Fichna, 2014). Currently, opioid use is at an all-time high in the United States; between increased legal prescriptions and rising consumption of illegal drugs, opioid abuse has been coined "America's 50-state epidemic" (Bosman, 2017). The use of opioids is often accompanied by multiple side effects, including off-target effects on the gastrointestinal and immune systems. Despite the long history of opioid use to combat pain, the full extent of opioid side effects are still not completely understood (Wang & Roy, 2016).

It has become increasingly evident that the microbiome is involved in the regulation of various aspects of metabolism (Wang & Roy, 2016). Of particular relevance to this proposal, researchers have demonstrated that opioid use directly induces dysbiosis in the microbiome (Banerjee et al., 2016). Additional studies have shown of an adolescent microbiome is distinct and thus the effects of opioids on the microbiome cannot be assumed to be similar to that of an adult (Agans et al., 2011). Considering the increasing prevalence of teen opioid use, it is critical to fully assess the effect of opioids specifically on the unique adolescent microbiome. This project will examine the effect of opioid exposure on the microbiome of adolescent and adult female Sprague-dawley rats. Animals will be exposed to either a morphine or saline vehicle for 10 days and the drug will be subsequently withdrawn. Fecal samples will be collected 6 weeks after the last injection from both opioid exposed and saline control groups of both ages. Using fecal bacterial DNA, the microbiomes of all four populations will be characterized by bacterial species and quantified. The composition of the opioid-treated and untreated microbiomes can then be compared within each age group. Additionally, a glucose tolerance test will be conducted at the time of fecal collection to assess glucose homeostasis, an established marker of microbiome diversity. Ultimately, this study will provide novel data regarding the potentially long-lasting effects of previous opiate use on the microbiome in the adult versus the adolescent.

Awardee: Mary Davis V'19

Mentor: Dr. Melissa Mazan

Title: The Effect of Time Since Last Vaccination of Equine Herpes Virus-1 Titer Level in Horses

Funding Source: Merial Scholars Foundation

Summary: An estimated 2.7 million horses compete at shows annually across the United States. Due to the high risk of disease spread at horse shows, many organizations require vaccination for Equine Herpes Virus-1 (EHV-1) within a certain time period of the show, usually in accordance with the guidelines presented by the American Association of Equine Practitioners (AAEP). According to the AAEP, horses that move locations frequently, as is the case with competing, should be revaccinated for EHV-1 every six months.

A study using 55 mares, ages 2 through 7 years old has shown that antibody titers for EHV-1 increase in the first two months, and decrease to levels before booster at about four months. Although the sample size was ample for an equine study, the sample population was not representative of the equine population as a whole. The purpose of this study is to determine if the titer response over time is repeatable, and to determine if there is a difference in titer response when comparing age, breed, and sex of the horse.

The study will use approximately 200 horses of varying age, breed, and sex. Blood will be collected and sent to Cornell's Animal Health Diagnostic Center for testing using the EHV-1 (Rhinopneumonitis) serum neutralizing test. Horses will be sorted into groups based on the amount of time since last vaccination; three, six, and 12 or more months. Once the titer levels are received from Cornell, data analysis will be run. Correlations between amount of time and antibody titer will be determined, if any, as well as between sex and titer, age and titer, and breed and titer.

Awardee: Ezra Frager V'20

Mentor: Dr. George Church and Dr. Patrick Skelly

Title: Synthesis of Elephant Endotheliotropic Herpes Virus Using Oligonucleotide Assembly in Yeast

Funding Source: NIH

Summary: One of the greatest threats to Asian elephants in captivity and the wild is the *Proboscivirus* Elephant Endotheliotropic Herpes Virus (EEHV). It causes rapid-onset of acute hemorrhagic disease that is often fatal.[3,4] For a species that is already endangered,[5] it is critical that the scientific community do what they can to help wild populations recover and preserve captive populations so that we may one day restore them to the wild. Being a keystone species and engineers of their environment,[5] the extinction of their species would have significant impact on their native ecosystems. If a method of curing EEHV is developed this will help elephant conservation efforts and may have human applications as well. Currently treatment involves early detection, supportive care, and human anti-herpesviral medication that has not yet been proven to help.[3] EEHV so far has been resistant to culture and has not been able to be studied closely enough to create useful therapies.[3] No group has been able to culture this virus in a laboratory setting to facilitate potential vaccine/treatment development. Samples of EEHV obtained from infected elephants have fragmented genomes. Here, we aim to chemically synthesize the virus *de novo* and use this to infect elephant cells in culture. In this way, we aim to establish a culture system for the virus with the long-term aim of developing anti-EEHV therapeutics.

Awardee: Sanna Gough V'20

Mentor: Dr. Sawkat Anwer, Dr. MD Rahman and Dr. MD Hoque

Title: Prevalence of Subclinical Mastitis in Bangladesh

Funding Source: OIE Twinning

Summary: Due to a milk shortage, dairy cattle farming is essential to the Bangladesh economy. However, recent shifts toward cross breed cow use and intensive farming practices have increased the incidence of mastitis in Bangladesh dairy farms [9, 11, 14, 16]. This infection decreases farm profitability and is painful to the cow [4, 6, 15]. Currently there are no standardized treatment protocols for mastitis in Bangladesh. This leads to uncontrolled antibiotic treatment. The antibiotics are often over-used or under-dosed, resulting in antimicrobial resistance [3,10]. The Chittagnong Veterinary and Animal Sciences University (CVASU) aims to curb antimicrobial resistance and increase dairy farm profitability by developing an udder health control program (UHCP). The goal of my study is to assist in this process by quantifying the prevalence of mastitis and its causal agents in Bangladesh. California Mastitis Tests (CMT) and bacteriological cultures will be conducted on milk samples taken from 300 lactating cows in the Chittagong area. The resulting data will serve as a baseline for UHCP development.

Awardee: Delaney Honeyford V'19

Mentor: Dr. Kevin Lindell

Title: A Survey of Coxiella burnetii Prevalence in Small Ruminant Operations in Southern New England

Funding Source: NIH

Summary: Coxiella burnetii, the causative agent of Q fever in humans, can infect a variety of animals, with ruminants acting as the primary reservoir. Infection can result in reproductive health problems in small ruminants, or animals can be asymptomatic. This is problematic because small ruminants are the major source of human Q fever outbreaks, through environmental contamination or consumption of unpasteurized dairy products. To date, there is no data available on C. burnetii prevalence in small ruminants in New England.

The proposed research is a cross-sectional study to evaluate the seroprevalence and milk shedding of C. burnetii in small ruminants on operations in southern New England (Massachusetts, Connecticut, and Rhode Island). This project has three specific aims: (1) to determine the seroprevalence of C. burnetii in small ruminants on operations in southern New England, (2) to determine how well seroprevalence is associated with positive milk samples, and (3) to assess which management practice and farm

characteristics are associated with prevalence. This will be accomplished by collecting blood and milk samples from ewes and does on operations in southern New England and testing them for C. burnetii via ELISA and PCR, respectively. A standardized self-administered questionnaire about different farm and management characteristics will be administered to producers. The information gathered from the survey will be analyzed with sample results to determine farm risk factors associated with C. burnetii positive status.

In addition to elucidating the seroprevalence and degree of milk shedding of C. burnetii, this study will provide new information about risk factors associated with C. burnetii that are unique to small ruminants producers in southern New England. These results can be used to design and implement methods to limit transmission of the bacteria, and thus reduce prevalence. A reduction in prevalence would benefit animal and human health, as well as reduce economic losses for producers.

Awardee: Deanna Ineson V'20

Mentor: Dr. Elizabeth Rozanski

Title: Serum histamine and Tryptase Levels in Dogs Presenting with Anaphylaxis: An Emergency Department Study

Funding Source: Merial Scholars

Summary: Study Objectives: To investigate differences in serum levels of histamine and tryptase in three groups of dogs, including healthy dogs, dogs with life threatening allergic reactions (anaphylaxis) or local urticaria, and dogs with mast cell tumors.

Hypothesis: We hypothesize that dogs with allergic reactions and dogs with mast cell tumors will have elevated levels of serum histamine and tryptase compared to healthy dogs.

Experimental Design: This study will investigate the differences in serum histamine and tryptase levels between healthy dogs, dogs with mast cell tumors, and dogs showing signs of local and/or systemic anaphylaxis. Serum samples from subjects will be frozen for batch analysis using a validated commercial ELISA.

Purpose: The goal of this study is to establish if a common emergency condition, namely local and systemic anaphylaxis, is associated with systemic increased histamine and tryptase.

Awardee: Jessica Levine V'19

Mentor: Dr. Flo Tseng

Title: Comprehensive Assessment of Health and Survival Rates of Injured or Ill African Penguins (*Spheniscus demersus*) Admitted to a Rehabilitation Center in South Africa

Funding Source: NIH

Summary: The African penguin (*Spheniscus demersus*) is the only species of penguin native to Africa, living in several colonies off the southern coast of South Africa near Cape Town. The population has declined rapidly over the past 10 years and was upgraded to endangered status on the IUCN Red List of Threatened Species in 2010. Much of the species decline can be attributed to some degree of human involvement. In addition to man-made contributions to the decline of the African penguin, these birds are also susceptible to parasites as well as bacterial, viral, and fungal diseases. The South African Foundation for the Conservation of Coastal Birds (SANCCOB) is the primary facility for the veterinary care, rehabilitation and release of injured or ill African penguins. Health assessment of all the penguins admitted to SANCCOB is important for population health monitoring because it can identify any new or pre-existing health problems affecting the colonies. Using the penguins under veterinary care as sentinels for their colony-mates is a non-invasive way to monitor colony health without disturbing the natural environment and behavior of the colonies through field sampling. In this study, I will assist with health assessment of penguins brought to SANCCOB for rehabilitation by helping the veterinarians perform physical exams and routine blood draws. I will be evaluating body condition through weight and body measurements, interpreting PCV and total protein, and evaluating blood smears and fecal floats. I will assist with necropsies and postmortem sampling to look for pathology that may not be obvious on physical exam, such as aspergillosis or airsacculitis, and determine cause of death based on results from necropsy, histopathology, CBC/biochemistry analysis, bacteriology and virology. Using data from the penguins admitted to SANCCOB during June to August 2017 as well as data from veterinary records of penguins admitted from January 2015 through June 2017, I will assess whether any correlation exists between the initial health status of an African penguin at the time of admission to SANCCOB and success of the rehabilitation and release process.

Awardee: Darby McDermott V'19

Mentor: Dr. Marieke Rosenbaum

Title: Optimizing a Non-Invasive Oral Sampling Technique for Wild-Caught Semi-Captive Ateles, Saimiris, and Lagothrix Species in Peru

Funding Source: NIH

Summary: Bidirectional zoonotic disease transmission between nonhuman primates (NHPs) and people poses a public health risk in Peru. Screening for these diseases in NHPs are not consistently done, due to the inherent risks involved with anesthesia and the equipment and animal handling expertise required in invasive sampling methods. This study seeks to optimize a non-invasive oral sampling technique to enable people to test NHPs for zoonotic pathogens shed through the oral cavity. This will be done through a combination of field work and lab work. Semi-captive NHPs at Taricaya Rescue Center in Puerto Maldonado, Peru, will be used to determine preference for various attractants, ropes, and methods of rope delivery in order to gain adequate saliva samples from these animals. The utility of these saliva samples will be determined by testing for mammalian Cytochrome-B using conventional PCR at The Center for Technological, Biomedical and Environmental Research at La Universidad Nacional Mayor de San Marcos in Lima, Peru. Using a chi-square test and multivariate logistic regression, data will be analyzed to determine whether certain combinations of attractant, rope type, and delivery method increases the odds of getting a saliva sample from NHPs, and whether time spent chewing on rope, volume of saliva samples, and contact with NHPs cheek pouches affects detection of cytochrome B in samples. These findings will help to inform future researchers on how to obtain oral samples from semi-captive NHPs without the use of anesthesia, and may also be useful for screening wild NHPs for zoonotic diseases.

Awardee: Alyssa McDonagh V'19

Mentor: Dr. Marieke Rosenbaum

Title: Urban Backyard Poultry Flocks in Boston: Evaluating *Salmonella* Prevalence and Assessing Antimicrobial Resistance

Funding Source: NIH

Summary: Background/significance: Through the increasing popularity of backyard poultry flocks, more people now have close contact with poultry and poultry coops. This has caused an increase in poultry-associated salmonellosis. However, to date, there have been very limited studies assessing prevalence of *Salmonella* in backyard flocks despite the known public health risk this zoonotic bacterium poses. Backyard flocks also provide us with a unique opportunity to study antimicrobial resistance since flocks are exposed to the external environment, humans, and various animals. Understanding resistance in this

context is important because resistance encoding genes can be passed to people, causing infections that are more threatening to human health. This study will reveal new information on both prevalence and resistance that is applicable to a significant portion of the Massachusetts population, as we estimate that 10,252 Boston households own or plan to own chickens in the future.

Specific aims**:** This study is unique in focusing on backyard poultry and the public health threats that come with urban flock ownership. Our specific aims are twofold. 1) To assess the prevalence of *Salmonella* in backyard flocks and to compare the prevalence to published prevalence reports in commercial poultry flocks. 2) To determine phenotypic antimicrobial resistance profiles for *Salmonella spp.* isolated from backyard flocks. Data obtained from this study will contribute to our understanding of the role backyard poultry may play in human *Salmonella* exposure.

Methods: This is a cross-sectional study occurring in conjunction with The CLUC Study (Chickens Living in Urban Coops). Up to 50 flocks will be included. Composite fecal material, cloacal swabs, and dust samples from each flock will be tested for *Salmonella* using established laboratory methods for isolating *Salmonella*. Discovered isolates will then undergo antimicrobial resistance testing to determine the susceptibility of *Salmonella* to various antimicrobials. Flock and household characteristics will be collected via a standardized survey. Flock-level *Salmonella* status will be stratified by household and flock characteristics, and resistance profiles will be quantified and presented descriptively.

Awardee: Victoria Mello V'19

Mentor: Dr. Gillian Beamer

Title: Establishing Serum Biomarkers as Correlates of Pulmonary Tuberculosis.

Funding Source: NIH

Summary: *Specific Aim & Hypothesis:* Our primary aim is to identify serum biomarkers (single and in combination) that are strong correlates of pulmonary tuberculosis (TB), to act as surrogate indicators of granuloma necrosis and lung damage and ultimately guide translational studies in humans. We hypothesize that lung levels of neutrophil chemokines and new potential biomarkers (e.g. VEGF, Factor VIII) will be strongly and positively correlated with serum levels in Diversity Outbred (DO) mice infected with *Mycobacterium tuberculosis*.

*Experimental Design/Methods***:** We will test this hypothesis using lung and serum samples previously collected from DO mice that were infected with *M. tuberculosis*. ELISAs will be used to quantify biomarkers in lung and serum samples which will be analyzed statistically to determine correlation with disease indicators (i.e. weight loss) and with each other. Granuloma necrosis will be quantified by annotating digitally scanned histology slides to quantify necrosis.

Significance: Lung tissue, granuloma and cellular necrosis with neutrophil influx are hallmarks of pulmonary tuberculosis (TB) in susceptible humans infected with the deadly pathogen *Mycobacterium tuberculosis*. These same features are observed in the lungs of susceptible *M. tuberculosis*-infected Diversity Outbred (DO) mice, a genetically heterogeneous mouse model of human tuberculosis (TB). Previous results show that pulmonary TB in DO mice is strongly and significantly correlated with lung neutrophil chemokines (CXCL1, CXCL2, CXCL5), and preliminary evidence suggest that neutrophil chemokines may be serum biomarkers that correlate with active lung disease [9]. However, additional research is needed to confirm these findings and to identify new biomarkers in circulation that are correlates of active pulmonary TB.

Awardee: Alexandra Nemeth V'19

Mentor: Dr. Benjamin Nephew

Title: Determining the Value of the Inhalant Particulate Matter Environmental Model of Autism Spectrum Disorders

Funding Source: NIH

Summary: We want to determine whether the inhalant particulate matter (PM) environmental model of ASD can be used as an accurate animal model in future ASD studies. Our specific aim is to determine the effects of PM pollution on inflammation, neuroanatomy, and autism-like behavior in male rat offspring. We propose to have the following two groups: (1) no pollution (Control) and (2) airborne particulate matter (PM) pollution exposure (Stress). We expect that the stress group will exhibit impaired cognition and social behavior, increased anxiety and repetitive behaviors, increased peripheral inflammatory factors, and altered neuroanatomy in the MRI and DTI scans. It is expected that the imaging data will reveal differences in both neuroanatomical volumes and structural connectivity (white matter track morphology), which will strongly suggest changes in functional neural connectivity that can be explored in future studies. This result would support that PM exposures represent environmental stressors involved in ASD etiology through immune-mediated effects on the brain, and would establish the value of the PM environmental model of ASD for use in future studies.

Awardee: Theresa Rooney V'19

Mentor: Dr. Felicia Nutter

Title: Determining the prevalence of *C. burnetii* antibodies in dromedary camels and *C. burnetii* DNA in ticks collected from the same dromedaries in Laikipia County, Kenya

Funding Source: NIH

Summary: This project will investigate whether there is an association between husbandry practices and demographic features of dromedary camels and seroprevalence of Coxiella burnetii (C. burnetiii) in Laikipia County, Kenya. It will also elucidate whether there is an association between dromedary that have antibodies to C. burnetii and dromedary camels that carry ticks that test positive for C. burnetii.

The following specific aims will be addressed: Specific Aim 1: To determine the seroprevalance of C. burnetii in dromedary camels from three ranches in Laikipia County, Kenya that have different husbandry regimes and varying herd demographics.

Specific Aim 2: To determine the prevalence of C. burnetii in ticks that are collected from dromedary Camels in Laikipia County, Kenya.

Specific Aim 3: To determine whether there is an association between dromedary camels seropositive for C. burnetii and those that carry ticks that test positive for C. burnetii.

Thus far, C. burnetii has been identified in both camels and ticks in Kenya. This study will investigate the prevalence of C. burnetii in blood samples and ticks collected from dromedary camels in Laikipia County specifically. This study will also determine whether demographic variables are risk factors for camels contracting C. burnetii. I am partnering with contacts at the Saint Loius Zoo and the Smithsonian Institute, who have conducted previous research on dromedaries in Laikpia County. The knowledge divulged from this study will contribute to the epidemiological understanding of the bacteria and the role that ticks may play in transmitting C. burnetii to camels.

Camels will be tested from three herds in Laikipia County with whom our collaborators have working relationships: Mpala Research Center & Science Foundation, Loisaba, and Suiyan ranches, which each have roughly 130 camels in their herds. To achieve statistical significance, 286 camels will be sampled for this study over the course of three weeks. I will take 8 mL blood samples from the camels' jugular veins, which will be transported to the International Livestock Research Institute in Nairobi. I will analyze the serosamples at ILRI over the course of three weeks using CHE-KIT Q fever ELISA assay by IDEXX. Ticks will be collected from the same camels and transported to a collaborating laboratory in the Netherlands for molecular diagnostics using qPCR to determine the prevalence of C. burnetii DNA.

Awardee: Alison Smith V'19

Mentor: Dr. Annie Wayne

Title: A Retrospective Study Describing the Usage Patterns of Meropenem and Imipenem at Tertiary Veterinary Care Hospitals

Funding Source: NIH

Summary: Antibiotic resistance is a growing problem in both human and veterinary medicine. Certain antibiotics such as carbapenems are reserved for a "last resort" in difficult infections, and are categorized as critically important in human medicine by the World Health Organization. Imipenem and meropenem are two carbapenems in this category, and while they are not licensed for veterinary use, they are prescribed by veterinarians as extra-label drugs.

In human medicine, these two antibiotics are used primarily to treat multidrug resistant E. coli and Salmonella, as well as other life-threatening infections, which have the potential to originate from non-human sources. Some veterinary hospitals have reported policies for the use of these drugs, but the majority do not. There are currently minimal data on prescribing patterns and guidance on the use of these drugs in small animal veterinary hospitals.

As critically important drugs in human medicine, it is important that imipenem and meropenem be prescribed with great care in veterinary medicine. The Foster Hospital for Small Animals utilizes both of these drugs, but it is unknown to what extent and for which types of cases. Therefore, by mining Stringsoft and IDEXX's Vet Connect Portal, I aim to determine the relative use of meropenem and imipenem in cases of infection seen from June 2016 to June 2017, determine if the infection was cultured, and if treatment was de-escalated post-culture. Through a systematic literature search, I also aim to evaluate the current literature for best practices regarding these antibiotics in both human and veterinary patients, and to evaluate if the Foster Hospital uses prescribing practices in accordance to the literature. Finally, I aim to determine the use of imipenem and meropenem at other tertiary care small animal facilities via online survey.

This research will provide knowledge necessary to understand veterinary medicine's potential contribution to antibiotic resistance to carbapenems. It will be useful to use this baseline data to determine the Foster Hospital's need for formal guidelines for the use of imipenem and meropenem in order to limit resistance to last resort antibiotics.

Awardee: Natalie Smith V'20

Mentor: Dr. Claire Fellman

Title: Developing and Optimizing a Whole Blood Lymphocyte Proliferation Assay for Pharmacodynamic Monitoring of Immunosuppression in Dogs

Funding Source: NIH

Summary: Immune-mediated diseases occur commonly in dogs and often have a high mortality rate even with treatment. Therapy for these conditions involves the use of immunosuppressive drugs; however, there is not currently a clinically-available method to measure the effects of immunosuppressive therapy on patients' immune systems. The blood drug concentrations typically used in therapeutic drug monitoring do not necessarily correlate with clinical outcome, so treatment decisions regarding the use of these drugs are often made empirically based on clinical response. There is a need for clinically-available assays that evaluate actual lymphocyte function in response to these therapies to better inform individual treatment decisions.

This project will develop and optimize a whole blood lymphocyte proliferation assay that can be used to monitor immunosuppression in patients being treated for immune-mediated diseases. The assay will be used to measure the effects of three commonly used immunosuppressive agents, cyclosporine, dexamethasone, and mycophenolate mofetil, on T lymphocyte proliferation in vitro. Additionally, the effects of storing samples before measuring lymphocyte proliferation will be investigated, since the ability to store samples would improve the assay's clinical utility.

We will use flow cytometry to measure T lymphocyte proliferation in drug-exposed samples. Whole blood samples from healthy dogs will be treated with varying concentrations of cyclosporine, dexamethasone, and mycophenolate mofetil, then stained with carboxyfluorescein succinimidyl ester (CFSE), a fluorescent dye used to track cell proliferation. The samples will be stimulated to proliferate using concanavalin A, then labeled with a phycoerythrin (PE)-coupled antibody against the canine T lymphocyte surface marker CD3. The viability marker 7-aminoactinomycin D (7-AAD) will be used to exclude any non-viable cells. Live, proliferating T lymphocytes will be identified based on their forward scatter and side scatter properties, and their CFSE, PE-CD3, and 7-AAD fluorescent signals. The percentage of proliferating T lymphocytes in untreated and drug-treated samples, and under different sample storage conditions, will be compared.

We hypothesize that there will be a decrease in T lymphocyte proliferation in whole blood samples treated with any one of the three immunosuppressive drugs, and that the greatest decrease in proliferation will be seen in samples treated with mycophenolate mofetil. Additionally, we hypothesize that storage greater than 48 hours will reduce the proliferation of both untreated and drug-treated lymphocytes, thus reducing the sensitivity of the assay. Once developed, this whole blood lymphocyte proliferation assay will provide a means to objectively assess immunosuppression in dogs being treated for a variety of immune-mediated diseases as a part of routine patient monitoring in the clinical setting. This will allow treatment decisions regarding the use of these immunosuppressive agents to be better individualized to each patient, improving clinical outcome.