Abstract Book

SUMMER RESEARCH TRAINING PROGRAM AWARDS 2010

TUFTS UNIVERSITY

CUMMINGS SCHOOL OF VETERINARY MEDICINE

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2010 Summer Research Training Program Awards

Awardee/Mentor	Award Type	Title of Research Project
Alison Allukian V'12 Dr. R. Alders	US Army	Cold Chain Monitoring in Support of Efficacious Newcastle Disease Vaccination Campaigns in Village Chickens in Tanzania.
Laurel Bifano V'12 Dr. S. Shaw	NIH	Determining the Prevalence of Methicillin Resistant Staphylococcus Colonization Amongst Staff at the Cummings School of Veterinary Medicine at Tufts University
Alison Borek V'13 Dr. M.R. Paradis	NIH	Use of a Real Time-PCR Assay to Detect *Salmonella spp.* and Evaluate the Effectiveness of the Isolation Protocols at the Large Animal Hospital at Tufts Cummings School of Veterinary Medicine
Elizabeth Carbone V'13 Dr. S. Shaw	NIH	The Effects of Acepromazine on Platelet Function and its Relationship to Clinically Significant Bleeding
Bronwen Childs V'12 Dr. C. Kirker-Head	US Army	Lower Limb Protection Strategies for the Athletic Horse
Andreas Eleftheriou V'13 Dr. J. Ellis	US Army	Gender Differences in Gram-Negative Bacteria and Antibiotic Susceptibility Differences in Gram-Positive Bacteria in Herring Gulls (*Larus argentatus*)
Ariel Fagen V'13 Dr. N. Dodman	NIH	Calming the Kenneled Canine: The Use of Psychoacoustic Music
Mariah Foose V'13 Dr. R. Alders/Dr. P. Skelly/Dr. E. Gilot	US Army	*Toxoplasma gondii* and the Health of Seropositive Feral Cats (*Felis catus*) in Rural France
Laura Harvey V'12 Dr. M. Pokras	US Army	Clinical Pathology of the Chinese Pangolin: A Conservation Approach
Katie Holmes V'13 Dr. D. Bedenice	NIH	Subcutaneous Pharmacokinetics of Florfenicol in Healthy Adult Alpacas
Thanhthao Huynh V'12 Dr. J. Epstein	US Army	How Significant is Illegal Wildlife Trade's Impact on Transmission of Emerging Zoonotic Disease
Luke Jandreski V'13 Dr. F. Tseng	Morris	Turtle Hatching Success in Relation to Clinical Data and Incubation Methods
Marian Karnas V'13 Dr. E. Byrnes	NIH	Consequences of Adolescent Use of Cannabanoids Expressed in Adult Offspring
Jay Katz V'13 Dr. G. Kaufman	NIH	Establishing Indirect Blood Pressure Values for Asian Elephants (*elephas maximus*) in Nepal

Awardee/Mentor	Award Type	Title of Research Project
Lauren Krone V'13 Dr. J. Lindenmayer	NIH	Feasibility of Adopting and Using Electronic Veterinary Medical Record: A Pilot Study Using Companion Animals as Sentinels for Population and Public Health
Jonathan Kuo V'13 Dr. S. Telford	US Army	A Survey of Avian Malaria Species in Taiwan Using Blood Smears and PCR
Dawn Lenihan V'13 Dr. L. Freeman/ Dr. E. McCobb	NIH	Measuring the Effects of Reading Assistance Dogs on Reading Ability and Attitudes Towards Reading: A Pilot Study
Jennifer Mahon V'12 Dr. E. Rozanski/ Dr. A. de Laforcade/ Dr. M.R. Paradis	Morris	Do Horses with Pituitary Pars Intermedia Dysfunction Exhibit Altered Hemostasis?
Megan McCarthy V'13 *(UNC)* Dr. R. Bridges	Merial	Effects of Vassopressin on Stress Impaired Maternal Behavior in Rats
Heather McFarland V'13 Dr. M. Pokras	US Army	Is There a Link Between Climate Change Hemoparasites, and Respiratory Fungal Infections in Common Loons (*Gavia immer*)?
Lori Newman V'13 Dr. R. Alders	NIH	Prevalence of West Nile, Avian Influenza and Newcastle Disease Viruses in Raptors in Beijin, China During Summer
Jennifer Riley V'13 Dr. M. Pokras	NIH	A Noninvasive Assessment of Adrenal Activity in Malayan Sun Bears (*Helarctos malayanus*) in Relation to Common Stressors of Captivity
Katherine Rodriguez V'12 Dr. A. Karas	NIH	Nest Building Behavior as Indicator of Well-Being in Post-Surgical Mice
Paula Shover V'13 *(UNC)* Dr. R. Boudrieau Dr. M. Kowaleski	Merial	Biomechanical Evaluation and Comparison of Veterinary Orthopedic Plate/Constructs in Cyclic Fatigue Four-Point Bending and Torsion Testing
Samantha Swisher V'12 Dr. S. Ayres	NIH	Comparison of Short and Long Progesterone Priming Protocols in Goats
Jana Thomas V'12 Dr. F. Tseng	NIH	Evaluation and Management of Pain in Injured Red-Tailed Hawk (*Buteo jamaicensis*)
Deborah Thomson V'12 Dr. R. Alders	US Army	Identification of Priority Diseases in Village Chicken Flocks Vaccinated Against Newcastle Disease in Tanzania
Lauren Wedig V'12 Dr. A. Koong/Dr. J. Keating	NIH	Evaluating the Ability of a Novel Group of Compounds, Irestatins to Inhibit Multiple Myeloma Tumor Growth in a Mouse Xexograft Model.

Awardee: Alison Allukian V'12

Mentor: Dr. R. Alders

Award Type: US Army

Research Project Cold Chain Monitoring in Support of Efficacious Newcastle Disease Vaccination Campaigns in Village Chickens In Tanzania.

Summary: Poultry compromise an integral part of the rural Tanzanian economy. The population of village chickens is estimated at 32.6 million, with over 70% of the rural population keeping chickens. Village poultry is important to rural Tanzanians for nutrition, income, and cultural reasons, and disruption of it could mean major consequences. Considering the dependence on village poultry, their health is very important and thus precautions must be taken to maintain healthy chickens.

New Castle disease is the most important endemic infection in village poultry and is credited as the number one cause in village poultry death in Tanzania. It is a significant veterinary and economical concern because of its extremely high morbidity and mortality rates. Annually, it is estimated that 30-80% of village chickens die from New Disease and with village chickens selling for $2-3 a bird the direct annual cost could range from $19.6 to $ 78.1 million.[2]

Proper measures to prevent infection in village poultry were made possible with the I-2 Newcastle disease vaccine.[1] However, considering the environmental conditions these vaccines are exposed to in Tanzania and the fragility of the live virus to excess heat, cold, or light, it is important that these vaccines are transported properly to ensure that there is no loss of potency to the vaccine to render it ineffective.[3] In order to do this, there must be a functional and validated cold chain for storage and transportation of the vaccine. The purpose of this study is to validate that the cold chain used to deliver thermotolerant New Castle Disease vaccine from the Central Veterinary Laboratory (CVL) in Dar es Salaam to village chickens in Singida District can adequately maintain the potency of the vaccine. I will be measuring the temperature in the refrigerators at the CVL and also en route to the villages with a data logger. This information will be analyzed to ensure that vaccine environment remains between 2-8 degrees Celsius, which would be consistent with the guidelines put forth by both WHO and the manufacturers for maximum vaccine potency.

Awardee: Laurel Bifano V'12

Mentor: Dr. S. Shaw

Award Type: NIH

Research Project: Determining the Prevalence of Methicillin Resistant Staphylococcus Colonization Amongst Staff at the Cummings School of Veterinary Medicine at Tufts University

Summary: Antibiotic resistant strains of bacteria are a common concern in both human and animal medical communities. While many of these infections are nosocomial in origin, carriage and infection with Methicillin Resistant strains of *Staphylococcus* have also been demonstrated in the community. Many domestic animals, including dogs, cats, horses, pigs, and cows can both be infected with and serve as reservoirs for different species of *Staphylococcus*, including *S. aureus* and *S. Intermedius*. Both zoonosis and reverse zoonosis of these species of *Staphylococcus* have been confirmed.

Recently, high rates of Methicillin Resistant *Staphylococcus aureus* (MRSA) have been identified in certain animal populations. This has raised concern that people working with these animals may also be at increased risk for colonization with MRSA strains. A subsequent study conducted at a veterinary conference found a 6.5% carriage rate among 412 attendees, which is well above the 1% risk expected for an average risk community member. This indicates that concern about colonization of veterinary staff is valid.

In this study, we will assess the levels of MRS colonization at a large veterinary teaching hospital. We will obtain nasal swabs from two voluntary study groups: a high animal contact positions group (veterinarians and technicians) from Tufts affiliated animal hospitals and a low animal contact group (administrative staff) on the same campus. The samples will be enriched and cultured and *Staphylococcus* isolates will be identified through standard techniques. Subsequent plating on oxacillin salt agar will assess methicillin sensitivity. We will compare the rate of MRS colonization between the two study groups to determine if high animal contact groups have higher levels of colonization than the low contact controls.

Subsequently, relatedness of MRS strains will be assessed. MRS strains will be speciated with API strips and relatedness will be assessed with 16s-23s ribosomal RNA intergenic space polymorphism technique. We will also sample confirmed MRS infections in hospitalized animals in June and July to determine if they are related to strains sampled from veterinary staff. This will allow us to assess the possibility of zoonosis and reverse zoonosis.

Awardee: Alison Borek V'13

Mentor: Dr. M.R. Paradis

Award Type: NIH

Research Project: Use of a Real Time-PCR Assay to Detect *Salmonella spp.* and Evaluate the Effectiveness of the Isolation Protocols at the Large Animal Hospital at Tufts Cummings School of Veterinary Medicine

Summary: Salmonellosis is a potentially fatal disease among horses and humans. Nosocomial outbreaks of the disease have occurred at veterinary teaching hospitals (VTHs) throughout the country. In order to prevent the spread of this disease, it is important to isolate infected horses promptly and to implement stringent cleaning and disinfection protocols. This study will focus on evaluating the current biosecurity protocols at Tufts Cummings School of Veterinary Medicine (TCSVM), Hospital for Large Animals (HLA) by analyzing the environmental contamination with *Salmonella* spp. from hospitalized horses. We will utilize a real-time PCR assay for the detection of *Salmonella* organisms, which provides reliable results more quickly than standard culture methods. Horses that are at-risk for *Salmonella* infections will be tested for the presence of *Salmonella* organisms via real time-PCR. Concurrently, environmental samples will be taken from specified locations around the stall of a potentially infected horse and tested for the presence of *Salmonella* organisms via real time-PCR. In addition, we will evaluate the optimal time of incubation in enrichment broth before performing the real time-PCR.

Awardee: Elizabeth Carbone V'13

Mentor: Dr. S. Shaw

Award Type: NIH

Research Project: The Effects of Acepromazine on Platelet Function and its Relationship to Clinically Significant Bleeding

Summary: Acepromazine is an effective pre-anesthetic sedative commonly used in canine patients. There is equivocal evidence that it inhibits hemostasis by affecting platelet function.

We propose to evaluate platelet count and function in healthy canine clinical patients sedated either with acepromazine or an alternative before elective surgery. To do this, we will collect blood samples from the control and experimental groups before sedation, after sedation, and at the end of surgery.

We will assess platelet function using a multiplate impedance aggregometer, a machine that records electrical resistance in a blood sample as platelets aggregate. We will then correlate the data to subjective bleeding scores provided by the surgeons operating on the subjects in order to assess possible clinical relevance to hemostasis.

We hypothesize that acepromazine will significantly reduce platelet count and aggregation, but that the surgeons will not notice impaired hemostasis in acepromazine-sedated subjects. Although a similar study was conducted in 1992, our study is distinguished in its use of the most recently validated methods and protocols, and its evaluation of clinical patients.

If our hypothesis can be demonstrated in healthy subjects, further research could then be conducted to assess the risk of acepromazine use in patients at increased risk of bleeding.

Awardee: Bronwen Childs V'12

Mentor: Dr. C. Kirker-Head

Award Type: US Army

Research Project: Lower Limb Protection Strategies for the Athletic Horse

Summary: Horses are large cursorial (running) mammals, weighing 450-500 kg (990-1100 lbs). They are capable of rapid acceleration and attaining upper speeds of 22 m/s (44 mph). Horses' large body mass and characteristically slender limbs leave them prone to overuse injuries, especially during high-speed activities like racing. Injuries predominate about the metacarpo-phalangeal (fetlock) joint, including stress fractures and tendonitis, which can progress to catastrophic injury if loading is continued. Similar repetitive stress injuries are seen in humans working at the extremes of physiological ability, including athletes and military recruits.

The incidence of equine lower limb injury is unacceptably high. Further, injuries of this type in horses often have catastrophic consequences for the animal's overall health. Reducing the injury rate has long been a goal; previous approaches have included alteration of ground surface, modification of training techniques, use of drugs and nutraceuticals, and easing of training and competition schedules. Others have attempted to positively impact lower limb biomechanics by limiting extremes of motion. Several types of external support systems (boots, bandages, etc) have been assessed but data has been inconclusive.[a-f] Further, none of the materials tested to date appear able to provide sufficient support to the limb during weight-bearing unless they are so bulky or stiff as to limit motion during the rest of the stride.

The goal of the proposed research is to test leg-wear that utilizes novel materials (smart-fabrics) to provide a dynamic response to limb loading forces in such a way as to attenuate or completely eliminate fetlock hyperextension while allowing for normal motion. The first objective is to better characterize the movements and motions of the lower limb joints during the maximum loading phase at a gallop using a modified XROMM and/or high-speed camera system. Then, building off of a prototype model previously developed by the TCSVM research group, we will use a surrogate limb and materials testing device to identify the optimal orientation and quantity of smart-fabric fibers to prohibit fetlock hyperextension.

Awardee: Andreas Eleftheriou V'13

Mentor: Dr. J. Ellis

Award Type: US Army

Research Project: Gender Differences in Gram-Negative Bacteria and Antibiotic Susceptibility Differences in Gram-Positive Bacteria in Herring Gulls (*Larus argentatus*)

Summary: Antibiotic resistance (AR) has become an important global public health concern. Wild birds are considered to be carriers of bacteria pathogenic to humans and are thought to be an important reservoir of AR bacteria. Particularly gulls may be important reservoirs of AR bacteria since they forage at settings where they may obtain AR bacteria. Gulls often interact with humans, which creates a public health concern. Little is known about the prevalence of antibiotic resistant Gram-positive bacteria in gulls. In poultry litter, over 85% of the bacteria identified were Gram-positive. Such a large group of bacteria could be an important reservoir of AR. Additionally; there is very little data on gender differences in carriage of AR bacteria in wild birds. Females may be at a higher risk of acquiring AR bacteria than are males during copulation. Gender differences may also result from competition over food resources. Such differences could have a significant impact since one gender may have a greater role in AR dissemination than the other. We aim to describe the type and prevalence of AR in Gram-positive bacteria in Herring Gulls (*Larus argentatus*) and to determine any gender differences in the type and prevalence of AR- Gram-negative bacteria. We will collect female samples from Herring gulls on Appledore Island. In the laboratory, each sample will be mixed and placed into a cryovial with glycerol in 1X PBS before transport to Tufts University. In order to describe the type and prevalence of AR in Gram-positive bacteria we will use Sensititre microdilution plates for Gram-positives to assess antibiotic susceptibility of the community of Gram-positive bacteria per sample. Aliquots from samples will be serially diluted before susceptibility testing on Phenylethyl alcohol agar to provide enrichment media for Gram-positive bacteria. We will use PCR and 16s rRNA sequencing to identify a subset of Gram-positive colonies. We will conduct a multivariate analysis in order to compare Gram-positive bacteria susceptibility profiles. In order to determine potential gender differences in carriage of AR Gram-negative bacteria we will use samples collected in summer 2009 and samples we will collect in 2010. We will conduct serial dilutions on MacConkey agar without antibiotics and with either tetracycline, ceftazidime or ciprofloxacin. PCR and 16S rRNA sequencing will be used to identify a subset of AR Gram—negative isolates and ANOVAs will be used for each antibiotic to compare prevalence of AR Gram-negative bacteria between males and females.

Awardee: Ariel Fagan V'13

Mentor: Dr. N. Dodman

Award Type: NIH

Research Project: Calming the Kenneled Canine: The Use of Psychoacoustic Music

Summary: The use of music in mood alteration and behavior modification has been thoroughly examined in humans (e.g., Evans 2002; Gebhart & Georgi 2007; Menon & Levitin 2005; Watkins 1997) and researchers are beginning to explore its effectiveness on animals as well (Wells 2004; Wells, Coleman & Challis 2006; Wells 2009). Stress alleviation is of particular importance in shelter environment where adoptions are more successful when animals exhibit calm, quiet yet sociable behavior (Wells & Hepper 1992). Previous studies have supported the effectiveness of classical music and psychoacoustically arranged music in calming shelter dogs (Wells, Graham & Hepper 2002; Wagner, Spector & Leeds 2004; Makeig & Makeig 2007). However, no research to date has explored the efficacy of different types of music on stress levels using a purely objective measurement tool; all studies have relied on subjective questionnaires. This study will measure physiological response to three music selections (and a control) through pre-exposure and post-exposure salivary cortisol levels (Beerda, et al, 1996) and heart rate monitoring (von Borell, et al. 2007). In addition, activity levels will be measured during music exposure via an objective count of the number of times the dog paces across lines on the floor of its run (Endo & Shiraki 2000; Yirmiya, et al. 2001).

Awardee: Mariah Foose V'13

Mentor: Dr. R. Alders, Dr. P. Skelly and Dr. E. Gilot

Award Type: US Army

Research Project: *Toxoplasma gondii* and the Health of Seropositive Feral Cats (*Felis catus*) in Rural France

Summary: *Toxoplasma gondii* is a protozoan parasite with the domestic cat (*Felis catus*) as its only definitive host. It is the causative agent of Toxoplasmosis, which may bring about pathology in the immunocompromised, congenital infection, or abortion. Extensive research has been performed concerning seropositivity to *T. gondii* in cats and effects of the infection on intermediate hosts, but an association between seropositivity and the general health of cats has not been given the same consideration.

The proposed study would evaluate the hypothesis that an association exists between the seropositivity status of feral cats for *T. gondii*, shedding of oocysts in feces, and poor health. This question will be

investigated by assessing the health of the cats in a feral colony in Boult-aux-bois, Ardennes, France and determining their Toxoplasma seropositivity status in order to compare seropositive and seronegative individuals. Blood samples will be obtained to measure hematological parameters, including blood count, hemoglobin, and hematocrit, and biological parameters, including albumin, urea, and creatine. A modified agglutination test (MAT) for anti-*T. gondii* IgG antibodies will also be conducted. Fecal samples will be collected to measure oocyst levels by real-time polymerase chain reaction. Comparisons of mean, frequency, and variance, simple and complex linear models, a mixed logistic regression model, and a mixed descriptive factorial analysis will be used to analyze the data. It is hypothesized that seropositive cats will have more abnormal physiological parameter measurements, consistent with poor health, and shed greater numbers of oocysts when compared with seronegative cats.

Seropositivity for *T. gondii* is relatively high in rural France, estimated at over 50% for both human and feline populations, making this area an ideal setting for a study of this nature. Analyzing the feral cat population in Boult-aux-bois will have broader application to cat populations in other areas and advance veterinary knowledge concerning the effects of Toxoplasmosis on domestic cats.

Awardee: Laura Harvey V'12

Mentor: Dr. Mark Pokras

Award Type: US Army

Research Project: Clinical Pathology of the Chinese Pongolin: A Conservation Approach

Summary: The purpose of this study is to develop reference hematology parameters for the endangered Chinese pangolin, *Manis pentadactyla*. Blood samples will be drawn from both wild and captive *M. pentadactyla,* and evaluated for complete blood counts (CBC) and serum chemistries. My hypotheses are:

- There will be no significant variation between the blood samples from the wild *M. pentadactyla* and the captive population of *M. pentadactyla.*
- There will be no significant variation between the blood samples from male and female *M. pentadactyla*.
- There will be no significant variation between CBC's calculated manually and those obtained from the use of the Hemavet 950 analyzer.

In addition, I will characterize and quantify any hemoparasites found while conducting the differential white blood cell counts.

Wild pangolins will be captured in southern Taiwan, and transported to the Pingtung Rescue Center for Endangered Wild Animals at the National Pingtung University of Taiwan. Blood will be collected from the ventral tail vein after the pangolin has been anesthetized with isoflurane. CBC's, manual and automated, and serum chemistries will be run on the samples. Blood samples will also be collected from captive pangolins at the Pingtung Rescue Center and the Taipei Zoo using a similar protocol.

The Chinese pangolin has recently been reclassified as an endangered species by the IUCN. The species is threatened by intensive poaching which supplies bush meat and traditional Chinese medicine. At present, there is a lack of published physiological data, which makes assessing the overall health of injured pangolins difficult. Establishment of reference hematological values for wild and captive pangolins will aid veterinarians and wildlife managers in making the best possible conservation decisions. Due to the endangered status of the Chinese pangolin, the survival of individuals is imperative to the maintenance of the species' genetic pool.

Awardee: Katie Holmes V'13

Mentor: Dr. D. Bedenice

Award Type: NIH

Research Project: Subcutaneous Pharmacokinetics of Florfenicol in Healthy Adult Alpacas

Summary: **Objective:** The goal of this study is to determine the pharmacokinetics of florfenicol following single and repeated subcutaneous injections in healthy adult alpacas. Additional aims include the identification of potential side effects of florfenicol on hematological and clinical parameters following long term use.

Animals: Six healthy, client-owned, adult male or non-pregnant female alpacas.

Procedures: Six alpacas will participate in a three-part study. Single dosages (20 mg/kg and 40 mg/kg) will be administered subcutaneously in a blinded, randomized, cross-over design to animal groups A and B. Following a 14 day washout period, each group will receive the alternative dose. Following an additional 14 day washout period, all alpacas will receive a subcutaneous injection of 40 mg/kg every other day for 14 days. Anticoagulated blood samples will be obtained at designated time points following drug administration. The plasma will be separated and evaluated using High Performance Liquid Chromatography. All procedures will be performed following written consent and IACUC approval.

Clinical Relevance: Alpacas significantly contribute to the non-food producing livestock population in the United States and represent a high percentage of patients in large-animal private practice as well as critical care and surgical caseload in referral hospitals. Many conditions affecting alpacas require prolonged antibiotic therapy. These infections are potentially polymicrobial and necessitate use of safe but widely distributed, broad spectrum antimicrobials. Florfenicol is a broad-spectrum antibiotic with wide body tissue penetration. Many bacterial isolates are sensitive to this drug at relatively low concentrations. Florfenicol has been studied in a variety of large animal species but its pharmacokinetics in alpacas have not been evaluated to date. Florfenicol is currently used empirically for the treatment of systemic infections in alpacas, based on dosage extrapolation from data of other species. The pharmacokinetics of florfenicol need to be evaluated specifically in alpacas to ensure safety and bioavailability for clinical use in this species.

Awardee: Thanhthao Huynh V'12

Mentor: Dr. J. Epstein

Award Type: US Army

Research Project: How Significant is Illegal Wildlife Trade's Impact on Transmission of Emerging Zoonotic Diseases?

Summary: The wildlife population provides a significant reservoir for emerging zoonotic diseases, some of which threaten human public health. With an escalating trend in wildlife trade, the likelihood of disease transmission rises in correlation with the introduction of wild animals and animal products into new environments where there is increased opportunity for inter-species transmission. The increased demand for bushmeat globally may also represent an increase in risk of zoonotic disease emergence through hunting and consumption of raw bushmeat. The illegal wildlife trade further augments the risks associated with wildlife mobility. In the last decade, the United States is reported to invest an estimated $2.8 billion into the legal wildlife trade, importing 20% of the products from international venues. Assessments for illegal wildlife trade are currently unreliable; however, it can be assumed that it parallels (and possibly exceeds) that of legal trade. With the United States involved in the import of a large quantity of wildlife materials, it is important to evaluate the types of pathogens introduced into the country via these hosts and to correlate the health risks and potential relationship to current emerging infectious diseases. We aim to investigate the diversity of viral and bacterial pathogens in various species which are imported into the US through collaboration with the U.S. Fish and Wildlife Service (USFWS) in New York and the National Wildlife Health Center (NWHC) in Madison Wisconsin. We will collect biological samples from and perform a health check (e.g. physical exam) on exotic animals which have been confiscated by the USFWS in New York. We also have access to tissue samples from primates that have been illegally imported through the bushmeat trade. Samples collected will be screened for zoonotic and novel pathogens using molecular techniques including PCR and quantitative real time PCR (at the NWHC), and microarrays through collaboration with the Center for infection and Immunity at Columbia University in New York.

Awardee: Luke Jandreski V'13

Mentor: Dr. Flo Tseng

Award Type: Morris Animal Foundation

Research Project: Turtle Hatching Success in Relation to Clinical Data and Incubation Methods

Summary: This project will attempt to identify relationships between maternal case data for turtles admitted to the wildlife clinic and the hatch rate of their eggs. To accomplish these objectives, any incoming injured turtles will have their cloacal temperature, hydration status, injury type and severity of injury recorded. These factors will be analyzed to determine if there is a correlation with rate of

successful egg hatching. The hypotheses to be tested are: The rate of egg hatching will be negatively correlated with severity of injury on admission and with increased cloacal temperature and dehydration status of the female turtle on admission. The rate of egg hatching will be higher in eggs that are naturally laid or artificially induced from live turtles and lower in eggs that are harvested from dead or euthanized turtles.

A protocol for incubating the eggs will also be created, testing two popular market substrates for reptile hatching; vermiculite and HatchRite. This will be done to determine which substrate leads to a higher rate of hatching success in collected eggs. Such data can be used to help current rehabilitators with a working protocol for incubation, and to help strengthen the populations of native turtles by increasing hatch rates among rehabilitated turtle eggs. When eggs are laid, induced or collected (post mortem), each clutch will be split into two even groups, and randomly divided between the two incubator types (Vermiculite or HatchRite substrate). The incubators will be monitored for humidity and temperature to keep the variables in an optimal range (26-28C, 80-90% humidity). Once data on substrate type and hatching success are collected, the data will be analyzed to demonstrate whether any significant correlations exist and whether these differ from species to species. The hypothesis is that there will be a higher rate of hatching success using the HatchRite substrate due to its continuous source of moisture when compared to vermiculite substrate.

Awardee: Marian Karnas V'13

Mentor: Dr. E. Byrnes

Award Type: NIH

Research Project: Consequences of Adolescent Use of Cannabanoids Expressed in Adult Offspring

Summary: Drug abuse and its consequences in the community have always been a major concern of society. The most widely abused, illicit recreational drug is marijuana and the number of abusers increases yearly. Of particular concern is the rising number of adolescents who experiment with this drug with no thought of the effect it may have on themselves or their offspring in later years.

Other drugs, such as morphine, have been shown to have effects on the offspring of adolescent users even when use had been stopped before pregnancy. The receptors for morphine and for cannabaniods are very closely linked and therefore lead to the hypothesis that cannabaniod use during adolescence may have a more a lasting effect than currently believed. It may even have an effect on the offspring of users years later. Cannabaniod use may increase sensitivity to both morphine and to cannabaniods, decrease motivation, and increase anxiety in the user and in her offspring.

This experiment will use a rat model identical to the model used for other similar drug exposure experiments. These rats will be exposed to cannabaniods during adolescent development and then exposure will cease when maturity is reached. The rats will then be bred and a conditioned place preference (CPP) test will be performed on the resulting offspring. This test has been used on humans to test the rewarding effects of drugs and to reliably predict drug abuse.

This experiment will either confirm or disprove this hypothesis and help adolescents to make more informed decisions regarding drugs like marijuana that may affect the rest of their lives and the lives of everyone around them.

Awardee: Jay Katz V'13

Mentor: Dr. G. Kaufman

Award Type: NIH

Research Project: Establishing Indirect Blood Pressure Values for Asian Elephant (*Elephas maxiums*) in Nepal

Summary: To date, there is insufficient experimental data for blood pressure in non-sedated Asian elephants (*Elephas maximus*). Only 2 studies have been performed to determine normal base-line blood pressure (BP) values for elephants and of the 19 animals used, only eight were Asian elephants. None of these eight were measured using indirect blood pressure techniques. This project aims to measure and establish normal blood pressure values for Asian elephants *in-situ* using indirect blood pressure measurement techniques and a sample size of at least 25 elephants. The establishment of *in-situ* values will guide the use of indirect blood pressure techniques in clinical and research applications with non-sedated Asian elephants, and will enhance the ability of veterinarians to care for this endangered species.

For this study, indirect blood pressure measurements will be taken on captive working elephants in Nepal. These values will then be compared with the ongoing research of Dr. Kirk Suedmeyer of the Kansas City zoo – who is establishing indirect blood pressure parameters for Asian and African elephants in the United States. I hypothesize that the blood pressure of Asian elephants living in North America will be the same as those living in their natural habitats in Nepal.

Awardee: Lauren Michelle Krone V'13

Mentor: Dr. J. Lindenmayer

Award Type: NIH

Research Project: Feasibility of Adopting and Using Electronic Veterinary Medical Record: A Pilot Study Using Companion Animals as Sentinels for Population and Public Health

Summary: Animals are recognized as sentinels for infectious diseases and environmental toxins that threaten human and animal health. The National Center for Foreign Animal and Zoonotic Disease Defense (FAZD) reports that 75% of emerging, infectious diseases are zoonotic. Of these diseases,

current research has recognized animals as sentinels for Lyme disease[1], West Nile Virus, Foot and Mouth disease and Rift Valley Fever. Similarly, studies of household and environmental toxin exposures, including that of asbestos and pesticides, implicate that companion animal exposure to such toxins mirrors that of their human counterparts.

Population and public health will benefit from the surveillance of sentinel companion animal health. To date, efforts to establish surveillance systems among animal populations have been directed towards wildlife (RESPOND)[2] and domestic livestock (USDA). However, companion animals share the environment most closely with human owners. At present there exist a few networks of veterinary practices, including Banfield the Pet Hospital and VCA, whose use of an electronic veterinary medical record (EVMR) may serve surveillance purposes. These have been used to identify health threats to animals[1] and human populations. Consequently, these EVMRs are restrictive as most veterinary practices do not desire affiliation with Banfield the Pet Hospital and VCA networks.

Veterinary practices not in the Banfield and VCA networks either continue to use paper records or electronic veterinary medical records created primarily for billing purposes. Very few of these practices use an EVMR that is based on patient encounters. Thus, there is a need to establish the proportion of Massachusetts practices that use any kind of electronic record, the reasons for their use (billing, encounters), and the interest in networking among multiple practices to establish and monitor population-based indicators of health and disease among companion animal populations.

Awardee: Jonathan Kuo V'13

Mentor: Dr. S. Telford

Award Type: US Army

Research Project: A Survey of Avian Malaria Species in Taiwan Using Blood Smears and PCR

Summary: Although human malaria in Taiwan has been well documented and controlled, knowledge of the distribution and organisms involved with avian malaria is limited. Only two extensive studies on the distribution of avian malaria have been conducted in the past 35 years. Due to economic development and the continuous import and export of animals, the distribution and diversity of malaria has likely changed since the last study.

Identification of malaria parasites is also important for conservation efforts due to the relative susceptibility of endemic avian species to introduced strains of malaria. From an economic standpoint, malaria strains from wild birds may infect domestic species, negatively impacting areas such as the poultry industry. It is thought that introduction of new strains of malaria into the Hawaiian ecosystem played a role in the extinction of at least nine species of birds.

In addition, blood smears, while effective, are traditionally one of the only ways to screen for malaria. However, they are insensitive to latent malaria infections. A molecular method would avoid this problem as they can identify parasites regardless of life cycle stage. Implementing a molecular PCR

screening process run in conjunction with a blood smear would thus enhance the accuracy of the screening process.

The primary objective of my project is to catalogue the different species of avian malaria in Taiwan. My secondary objective is to implement a screening process for malaria using PCR. Blood samples will be collected from birds brought to the wildlife centers around Taiwan and from birds trapped in the field. Blood smear assays will then be used to screen the samples for malaria, at which time a tentative diagnosis can be made. Basic CBC and chemistry tests will also be run on all samples to provide baseline data on the birds. PCR assays can then be performed to screen and identify parasites via amplification of the cytochrome b gene.

Awardee: Dawn Lenihan V'13

Mentor: Dr. L. Freeman and Dr. E. McCobb

Award Type: NIH

Research Project: Measuring the Effects of Reading Assistance Dogs on Reading Ability and Attitudes Towards Reading: A Pilot Study

Summary: Reading ability has a positive impact on all areas of academic learning. Unfortunately, inadequate reading programs and a lack of motivation to read has led to a large number of children who struggle with reading. Reading Education Assistance Dogs (READ) is a reading program that uses therapy animals to increase a child's desire and ability to read. However, no data exists to demonstrate the effectiveness of such programs. Demonstrating the effectiveness of the READ program would justify spending more time and effort on their implementation, ultimately reaching more struggling readers.

Therefore, the purpose of this pilot study is to develop and implement a 6-week READ summer program and further to assess the feasibility and effectiveness of the program. A reading program that does not use therapy animals will be run as a control. A Curriculum Based Measurement (CBM) for reading and an Elementary Reading Attitude Survey (ERAS) will be administered to both groups at the beginning and end of the program to detect any improvements in reading ability and changes in attitude toward reading respectively.

We hypothesize that the group participating in the READ program with the therapy dogs will have a greater improvement in attitude toward reading than the control group with no dogs. We also expect the group in the READ program to have a greater increase in reading ability over the 6-week period than the control group. Data generated from this pilot study will be used to determine the feasibility of this program, and to develop preliminary data with which future studies can be designed.

Awardee: Jennifer Mahon V'12

Mentor: Dr. E. Rozanski, Dr. A. Delaforcade and Dr. M.R. Paradis

Award Type: Morris Animal Foundation

Research Project: Do Horses with Pituitary Pars Intermedia Dysfunction Exhibit Altered Hemostasis?

Summary: Pituitary pars intermedia dysfunction (PPID) is a common disease in horses, resulting in high circulating levels of pro-opiomelanocortin (POMC) intermediates, especially alpha MSH and ACTH. It is speculated that the cause of pituitary adenoma formation is neurodegeneration due to oxidative damage. With neurodegeneration comes a loss of dopamine, which inhibits growth of the pars intermedia and secretion of POMC intermediates. Signs of PPID include hirsutism, polyurea and polydypsia. The most common complication of PPID is laminitis.

PPID is similar to hyperadrenocorticism (HAC) in dogs and humans, however, the pars distalis, not the pars intermedia, is the site of adenoma formation in these species. Because of this, dogs and humans with HAC have high circulation ACTH and not all POMC intermediates as horses do. Dogs and humans with hyperadrenocorticism (HAC) experience hemostatic alterations that are indicative of hypercoagulability. Though the exact mechanism for this is currently unknown, hypercoagulability in dogs with HAC is attributed to increases in procoagulant factors II, V, VII, IX, X, XII, and fibrinogen and decreases in antithrombin III (AT III) levels. It is currently unknown if horses with PPID exhibit hypercoagulability.

Thromboelastography (TEG) is the newest modality for evaluating hypercoagulable states in animals. The hallmarks of hypercoagulability on the TEG are a short r time, an increased angle and an elevated MA. Normal values for the TEG in horses have been established. In addition to the TEG, examining prothrombin time/activated partial thromboplastin time (PT/aPTT), fibrinogen and AT III levels allow for a more complete hemostatic profile to be established in patients that are predisposed to coagulopathies.

The goals of this study are to evaluate hemostatic parameters in untreated horses with PPID to observe if they exhibit hypercoagulability. To do this, we will be measuring TEGs, PT/aPTT, fibrinogen, AT III and ACTH values in horses with PPID that are currently untreated. Furthermore, we will seek to correlate hemostatic parameters with overall health of the horse, and with incidence of laminitis.

Awardee: Megan McCarthy V'13/ The University of North Carolina

Mentor: Dr. R. Bridges

Award Type: Merial Veterinary Scholars

Research Project: Effects of Vasopressin on Stress Impaired Maternal Behavior in Rats

Summary: The proposed study will investigate the impact of arginine vasopressin (AVP) on maternal care, maternal aggression, and physical growth of dam and offspring in rats exposed to chronic social stress. It is hypothesized that exogenous AVP will prevent or attenuate the negative effects of chronic social stress by decreasing maternal aggression and increasing maternal care.

This project would consist of treating 3 different groups of lactating dams: one with a low dose of AVP, one with a high dose, and one with a saline control. An untreated control group will also be included. Maternal care and aggression behaviors upon exposure to the social stress of an unfamiliar male intruder will be assessed.

This study seeks to contribute to the development of an effective model of stress-impaired maternal behavior by further examining the role of AVP in modulating maternal care and aggression in stressed individuals. Such a model would offer a framework with which to investigate novel treatments of disrupted maternal behavior, including disorders like maternal depression and anxiety.

Awardee: Heather McFarland V'13

Mentor: Dr. M. Pokras

Award Type: US Army

Research Project: Is There A Link Between Climate Change Hemoparasites, and Respiratory Fungal Infections in Common Loons (*Gavia Immer*)?

Summary: It has been proposed that climate change will result in an increase in vector borne hemoparasite and fungal respiratory infections. Because we have a 20-year record of these diseases in common loons (*Gavia immer*) in New England this species may serve as a good model to measure these changes. This study will investigate if the climate has been changing at lakes where loons breed and if there has been an increase in hemoparasites and fungal respiratory disease over the last 20 years.

Aspergillus spp. is an opportunistic fungus that has been implicated in the deaths of many common loons. A previous study showed that fungal infections were responsible for 7% of common loon mortalities. The proposed project will analyze historical records to see if there has been in an increased occurrence of these infections over the past 20 years.

A study conducted in the mid 1990s found no hemoparasites in common loons in the study area. As part of the proposed project, sampling will be conducted in conjunction with the seasonal banding to determine current levels of hemoparasites.

Awardee: Lori Newman V'13

Mentor: Dr. R. Alders

Award Type: NIH

Research Project: Prevalence of West Nile, Avian Influenza, and Newcastle Disease Viruses in Raptors in Beijin, China During Summer

Summary: Raptors play an important role in ecosystems and are known to be susceptible to a variety of panzootic diseases including West Nile virus (WNV), avian influenza viruses (AIV), and Newcastle Disease Virus (NDV). However, little is known about the prevalence, pathophysiology, or impact of these viruses in raptor populations outside the Western Hemisphere. In fact, WNV has not yet been investigated in China, and previous work on AIV and NDV in China has focused primarily on waterfowl and poultry. Clearly, more information is needed on the prevalence of these viruses in raptors in China.

The current project will screen raptors found in Beijing, China, for WNV, AIV, and NDV during summer 2010. Virus isolation, PCR, and serology will be used to determine seroprevalence of these viruses in these important predatory species.

Awardee: Jennifer Riley V'13

Mentor: Dr. M. Pokras

Award Type: NIH

Research Project: A Non-Invasive Assessment of Adrenal Activity in Malayan Sun Bears (*Helarctos malayanus*) in Relation to Common Stressors of Captivity

Summary: The stress associated with living in captive conditions has been shown to decrease resistance to disease, breeding success, and overall well-being in many species. I propose to study fecal cortisol levels in captive sun bears in Cambodia to learn more about determinants of fecal cortisol levels in this endangered species. The objectives of this study are 1) to establish baseline values for fecal glucocorticoid concentrations in sun bears and 2) to determine if fecal glucocorticoid levels are related to group size, age and gender differences, human-generated noise, and mixed-species housing. Fecal samples will be collected from at least 20 of the bears (more if possible) and the cortisol level in each sample will be measured using an enzyme immunoassay. The independent effect of the predictor variables on fecal cortisol levels will be analyzed with a multivariate linear regression model. The results

of this study may aid sanctuaries and rehabilitation centers in creating an optimal housing environment for their captive sun bears.

Awardee: Katherine Rodriguez V'12

Mentor: Dr. A. Karas

Award Type: NIH

Research Project: Nest Building Behavior as Indicator of Well-Being in Post-Surgical Mice

Summary: There are a number of proposed methods for evaluating the well-being of laboratory mice. However, many of these rely solely on the subjective opinion of the observer, are time consuming or not validated scientifically. The goal of our study is to test whether changes in laboratory mouse nesting behavior can indicate the impact of postsurgical pain. Our preliminary work supports that two nesting parameters are useful indicators of well being in chronically ill mice; the time to incorporate (TED) and the percentage of animals sniffing (%SED) additional nesting material added each day to a cage. In this study we intend to test the hypothesis that the TED and or %SED parameters are valid measures of morbidity following surgery, by measuring behavior changes prior to and after 2 different surgical procedures.

We will study two different groups of mice undergoing both minor (e.g. ovariectomy) and major surgery (e.g. thoracotomy). The mice will be having surgery for research purposes, i.e., there will be no additional animals who undergo surgery unnecessarily. The nesting material (ED) is a commercially available one that mice readily learn to incorporate into dome shaped nests. We will introduce mice to the ED material for a period of time before surgery and record TED and %SED scores for 2 days before and for up to 7 days after surgery. Each mouse or group of mice can thus be compared to itself pre and post surgery, and results for minor and major surgery groups compared between groups. We will also compare the recovery time (days until scores normalize) for both surgical groups.

TED and % SED scoring offer the potential advantage of being objective and simple parameters which can be measured for large groups of mice in a very short time period by observers of any skill. The initial results of our study may offer researchers a standardized technique for assessment of well-being and need for additional treatment with analgesics, supportive measures or humane euthanasia, and additional work would establish its relevance for additional strains and laboratory procedures.

Awardee: Paula Shover V'13/The University of North Carolina

Mentor: Dr. R. Boudrieau and Dr. M. Kowaleski

Award Type: Merial Veterinary Scholars

Research Project: Biomechanical Evaluation and Comparison of Veterinary Orthopedic Plate/Constructs in Cyclic Fatigue Four-Point Bending and Torsion Testing

Summary: The specific aim is to evaluate and compare the biomechanical properties of locking plating systems and conventional plates in cyclic fatigue four-point bending torsion failure. Currently, fracture fixation methods have evolved to a more biologic, as opposed to anatomic, focus for fracture stabilization methods. This has resulted in a plethora of implant systems designed with locking screw fixation, with the proposed advantages less vascular damaged and improved stability due to the fixed angle, locked construct. All of these systems have markedly different designs, i.e., very different material strengths and locking mechanisms. At this time there is only limited information available on their respective strengths, and no information as to their respective strengths in an unstable fracture model. Additionally, there is no information available on cyclic fatigue of these constructs, which is the clinical mode of failure after fracture fixation.

Eight different designs of plates will be evaluated in this study; 5 locking plate designs: 3.5 mm stainless steel locking compression plate (SS LCP®; Synthes Vet®, Paoli, PA); 10 mm and 11 mm titanium advanced locking plate system (Ti ALPS; Kyon, Zürich, SW)); 3.5 mm String of Pearls (SOPTM; Orthomed Ltd., Halifax, UK); 3.5 mm Fixin (TraumaVet; Rivolito, Italy), and 3 conventional designs: 3.5 mm SS Dynamic Compression Plate (DCP®; Synthes Vet®) and 3.5 mm SS Low Contact Dynamic Compression Plate (LC-DCP®; Synthes Vet®), and 3.5 mm Ti LC-DCP® (Synthes Vet®). Shortfiber filled epoxy hollow cylinders (SFE), 3 mm thickness, 40 mm OD (Pacific Research Laboratories, Inc.; Vashon Island, WA) will be used as the bone construct. The cylinders will be cut into 6-in lengths with a 1" central gap; the gap will be spanned with the appropriate plate and screws. The constructs will be tested using a servohydraulic testing machine.

A total of 96 constructs will be subjected to cyclic load in four-point bending at a frequency of 5 Hz. Another total of 96 constructs will be subjected to cyclic torque at a frequency of 2 Hz. The staircase method will be used to determine fatigue limits of four-point bending as well as torque. Generally, 12 samples are required for each test to achieve run-out.

This study will determine fatigue strength and mode of failure for each plate design in this model. The results of this study will allow an across the board comparison of the very different designs of the newly developed locking plate systems. This information will allow selection of the most appropriate plate for fracture stabilization based upon experimental results rather than anecdotal clinical information. Plate section will then be performed such that the mechanical properties are considered under the varying fracture configurations; this should lead to improved and more appropriate plate selection and improved healing with fewer complications.

Awardee: Samantha Swisher V'12

Mentor: Dr. S. Ayres

Award Type: NIH

Research Project: Comparison of Short and Long Progesterone Priming Protocols in Goats

Summary: Progesterone priming is an important tool used to synchronize goats for breeding. Recent evidence suggests that the current priming protocols are unnecessarily long, and we propose to compare the conventional protocol with a new, shorter protocol. The protocols will be compared based on progesterone levels, number of follicles, and number and quality of embryos produced in does that have been superovulated and hand-bred. Validation of the shorter progesterone priming protocol for use outside of the breeding season could increase productivity and reduce the amount of hormones used in food animals.

Awardee: Jana Thomas V'12

Mentor: Dr. F. Tseng

Award Type: NIH

Research Project: Evaluation and Management of Pain in Injured Red-Tailed Hawks (*Buteo jamaicensis*)

Summary: Analgesia in hospitalized birds is of critical importance, both in improving recovery and as a measure of humane care. However, many recommended drug regimens are based on limited data, and even where clinical studies have been performed, they are primarily on domestic chickens or pigeons, or, more rarely, on psittacines or birds of prey. Given the documented differences between opioid responses between the orders of birds already studied (Galliformes, Psittaciformes, Falconiformes, Strigiformes), the assumption that those data can be directly extended to clinical practice in all birds is not justified. In this study, we intend to first quantify and localize the three antinociceptive classes of opioid receptors within the brains of Red-tailed Hawks, allowing us to determine which classes of opioids are most likely to be effective for analgesia in this species. Simultaneously, we will obtain pilot data towards the design and validation of a model for evaluating pain in Red-tailed Hawks, using a combination of behavioral assessment and clinical measures. These studies will later be combined to allow comparison of analgesic regimens in the control of pain following orthopedic injury.

Location and relative density of μ, κ, and δ receptors in the supraspinal CNS will be evaluated using immunocytochemistry. This technique has not been used extensively in birds, so validity of commercially available antisera will first be demonstrated by comparison of mammalian and avian brainstems (where density and distribution of opioid receptors is conserved across phyla). If indicated,

this study will be followed by investigation into the pharmacodynamics of a specific opioid in Red-tailed Hawks, to allow us to better determine the appropriate dose.

Evaluation of pain and analgesia is controversial, espcially in the case of birds, and even more so in birds of prey. Whether tests of withdrawal from a noxious stimuli actually correlate to experienced pain is questionable. Evaluation via behavioral observation may more closely correlate to the actual experience of the observed animal, but requires carefully designed validation. During the summer, we will begin by using videorecording to develop a behavioral assessment protocol for healthy and injured raptors. Each subject will be placed into identical testing cages, then evaluated for appetite, frequency of motion, respiratory rate and other potential objective behavioral markers. This pilot data will be used to direct research to take place from Sept. 2010 to August 2011 in fulfillment of the DVM/MS.

Awardee: Deborah Thomson V'12

Mentor: Dr. R. Alders

Award Type: US Army

Research Project: Identification of Priority Diseases in Village Chicken Flocks Vaccinated Against Newcastle Disease in Tanzania.

Summary: Newcastle disease (ND) is considered the most important disease of village poultry in Tanzania. A current study is being conducted in Tanzania's Central zone (Singida region) which is vaccinating village chicken for ND. My project will build on this study and will determine what diseases are the most prevalent in the animals once ND is no longer a concern. A haemagglutination inhibition test will verify sufficient antibody levels against Newcastle disease in my sample population. A survey will be conducted to assess the farmers' concerns about their chickens' health and productivity. Physical examinations will be performed to determine the general well-being of the animals. If dead chickens are found upon arrival, and the farmer would allow a sample to be taken, further tissue analysis will be done at the Central Veterinary Laboratory by resident veterinarians. The results will expose early potential disease outbreaks in the poultry population of central Tanzania. Preventative measures will then be taken to control future outbreaks.

Awardee: Lauren Wedig V' 12

Mentor: Dr. A. Koong and Dr. J. Keating

Award Type: NIH

Research Project: Evaluating the Ability of a Novel Group of Compounds, Irestatins to Inhibit Multiple Myeloma Tumor Growth in a Mouse Xenograft Model

Summary: As tumors grow, they initially outgrow their blood supply, causing hypoxia and nutrient deprivation. This causes endoplasmic reticulum (ER) stress, but tumor cells have a mechanism, called the unfolded protein response (UPR), to survive the effects of ER stress and continue to grow and divide. One important molecular branch of the UPR, inositol-requiring kinase 1 (IRE1), is required to activate the transcription factor, X-box binding protein 1 (XBP1), which mediates survival of cells under hypoxic conditions and is essential for tumor growth. Development of a chemical inhibitor of IRE1 is a promising anti-cancer therapeutic strategy. Dr. Koong's lab has completed a high throughput screen for small molecule inhibitors of this pathway, and has identified several classes of compounds of the IRE1-XBP1 pathway, termed Irestatins. The goal of my project is to test 2 of the most active compounds in a mouse multiple myeloma xenograft model in order to determine how effective they are in inhibiting the growth of these tumors. My project will include determining the most effective dose to use and optimal frequency of administration, using transgenic XBP1-luciferase mice and an imaging system to quantify bioluminescence. I also plan to necropsy the mice used in the xenograft study and use a molecular marker for apoptosis (TUNEL staining) to determine the efficacy of the Irestatins and toxicity to normal tissues.