Every cat, every day benefits from Winn funded research

Research Update

Over $518,000 in Feline Health Grants Awarded in last 2 Grant Cycles

Each year, Winn Feline Foundation receives proposals from veterinary researchers around the world who are interested in improving feline health. By May 2019, Winn's cumulative total in feline health research funding was more than $6.7 million at more than 30 partner institutions worldwide.

Feline Shelter Medicine Studies

W19-003 - Optimization of the Diagnosis of Feline Parvovirus (panleukopenia) Infection in a Shelter Environment
PI: Dr. Linda Jacobson, Toronto Humane Society; $21,500 (PetSmart Charities®)

The objective of this research is to determine how reliably the canine parvovirus test works to diagnose panleukopenia in shelters. The study will assess what diagnostic samples can be used to make an accurate diagnosis early in the disease. It will also look at how recent vaccination affects test results, given that cats in shelters are vaccinated earlier and more frequently than in a home. The ideal test protocol will allow rapid and accurate diagnosis, isolation and treatment of affected cats, and will help prevent cats being mistakenly isolated or even euthanized, as well as reducing potential for disease outbreaks. The ultimate goal is to save more lives.

W19-012 - Refining a Method to Measure Heart Rate Variability (HRV) in Freely Moving Cats to Assess Welfare
PI: Dr. Lynne A. Hart, University of California, Davis; $11,306 (PetSmart Charities®)

Chronic exposure to stressful environments can negatively affect cats' health and welfare in a variety of ways. Cardiac activity, particularly heart rate variability (HRV) is a non-invasive way to assess stress and emotional state in humans and non-human animals. HRV is a measure of the variation in time between each heartbeat, and is controlled by a primitive part of the nervous system called the autonomic nervous system (ANS). In this study, researchers propose to test feasibility of obtaining information on HRV of freely-moving cats using a readily available, inexpensive monitoring system and compare results with the standard, relatively expensive, Holter monitoring method. If the two methods of obtaining HRV data prove comparable, this practical, readily available, inexpensive method would be beneficial to the field of shelter medicine, and for demonstrating benefits of strategies designed to minimized stress in shelter cats.

W19-035 - Effects of a Surrogate Mother on Misdirected Oral Behaviors in Orphaned Neonatal Kittens
PI: Dr. Karen Vernau, University of California, Davis; $25,000 (PetSmart Charities®)

Around 20 percent of orphaned kittens, in search of an outlet for normal nursing behavior, will begin suckling on the bodies of other kittens. Kittens who are victims of this misdirected suckling may develop serious injuries that require medical care; some kittens may even be put to sleep. Kittens who suckle on their littermates often consume urine and feces, which can upset their stomachs and cause them to eat less formula. The proposed study will test the effectiveness of a surrogate mother, a stuffed animal with nipples attached, on preventing and reducing misdirected suckling behavior in orphaned kittens. We believe that providing young orphaned kittens with a safe outlet for nursing behavior will prevent or reduce harmful suckling on other kittens.

W19-041 - Screening Shelter Cats for FELV: Balancing Disease Control and Lifesaving
PIs: Dr. Alexis Bardzinski and Dr. Julie Levy, Austin Pets Alive! And University of Florida; $24,984 (PetSmart Charities®)

Millions of cats in North America are infected with feline leukemia virus. While this contagious infection is associated with disease and premature death in some cats, others live for many years. At this time, there is no way to predict which cats will survive. In addition, the blood tests used for diagnosis frequently have conflicting results or change between positive and negative over time. These uncertainties leave veterinary practitioners, shelters, and pet owners with inadequate guidance to properly respond to FeLV test results. As a result, many cats with a single positive screening test are routinely euthanized, even though a substantial, but as yet, unquantified proportion of such cats would likely enjoy many years of good quality of life at little risk to the health of other cats. The Austin Pets Alive animal shelter has developed an adoption and treatment program that enrolls hundreds of FeLV+ cats each year, providing an opportunity to monitor infected cats throughout their lives. This study will determine the optimum testing protocol for FeLV and the prognosis for long-term survival in cats with different testing patterns. The results will provide practitioners and shelter managers with the information they need to make evidence-based and cat-friendly decisions, potentially preventing the needless euthanasia of thousands of cats each year.

New Feline Investigators Award

W19-005 - Gene Editing Strategies for Treatment of Feline Hypertrophic Cardiomyopathy
PI: Dr. Elliott Chiu, Colorado State University; $15,000 (Maine Coon Fund and Ricky Fund)

Feline hypertrophic cardiomyopathy (HCM)is a common disease of cats that results from heart muscle tissue thickening due to changes arising from genetic mutations in certain breeds. This thickening leads to improper blood flow, which may cause untreatable heart disease leading to mortality. While this disease is found in 10-15% of cats, HCM is more common in certain breeds like Maine Coon cats. One of these deleterious traits includes a mutation in a particular protein, which helps with the contractility of the heart, that is the result of a single gene mutation in

Maine Coon cats. This study proposes to use a new genetic therapy, CRISPR-Cas9, to replace a mutated gene with a normal gene. There are many potential benefits to using CRISPR-Cas9 to target HCM in Maine Coon cats. First and foremost, CRISPR technologies are very specific so there is unlikely to be non-specific targets. Second, HCM in Maine Coon cats is caused by a single point mutation, so there is a reduced chance to impact other parts of the genome. This study is designed to test this technique on cultured cells as a first step to potentially eradicating this devastating disease from the Maine Coon cat breed.

New Feline Investigators Award - Genomics

W19-010 - Annotation of Regulatory Regions in Feline Non-coding DNA via Tissue Specific ChIP-Seq
PIs: Dr. Alexandra N. Myers and Dr. William Murphy, Texas A & M AgriLife Research; $15,000 (Sponsored by Wisdom Health™ in honor of Fred Jacobberger)

Almost every cell in the body of living organisms contains DNA - the basis for life. From DNA, proteins are constantly being made that carry out cellular functions. Interestingly, only a small percentage of the genome codes for proteins (coding regions). What then, is the rest of the DNA (non-coding regions) for? Scientists once thought it was simply “junk,” but we now know that at least a portion of it serves a role in telling coding regions when and how fast to make proteins. This is accomplished via interactions of proteins with specific and relatively short DNA sequences in the non-coding regions, known as regulatory regions. Using a method called chromatin immunoprecipitation sequencing (ChIP-seq), these regulatory regions can be mapped or “annotated” across the entire genome so that their specific locations can be visualized. This allows researchers to determine if mutations in the vast expanse of non-coding DNA are likely to have any effect on the coding regions and thus on production of proteins important for cell function. ChIP-seq has been performed for humans and a variety of other species, and these species therefore have genomes that are well annotated for regulatory regions. For the cat genome, no such annotation exists. This study proposes to correct this deficit by performing ChIP-seq on eight different organs collected from cats after euthanasia for unrelated health reasons at the Texas A&M Veterinary Medical Teaching Hospital. This data would be made publicly available to aid in interpretation of feline genomic data.

Winn Grants

W19-002 - Diagnostic and Molecular Identification of Trypanosoma cruzi Infection in Cats from Animal Shelters in Southern Louisiana
PI: Dr. Eric Dumonteil, Tulane University; $24,937

This study will provide critical information to improve individual feline care as well as

population-level management of shelter felines. We will collect blood samples from 100 shelter cats from southern Louisiana to detect infection by laboratory analysis of their blood samples. We will also use genetic information of the parasite to identify the source of infection. These results will provide the baseline for the surveillance of T. cruzi infection in shelter cats in Louisiana, which will be key for the development of veterinary and public health interventions for the prevention of T.cruzi infection in both shelter animals and humans.

W19-014 - Targeted Intra-arterial Administration of Tissue Plasminogen Activator as a Treatment for Feline Distal Aortic Thromboembolism
PIs: Dr. Sigal Klainbart and Dr. Joshua Milgram, The Veterinary Teaching Hospital, Koret School of Veterinary Medicine; $24,950 (Ricky Fund)

Aortic thromboembolism (ATE) is a life-threatening condition in cats. Many cats with this disease die or are euthanized due to poor prognosis. In people the “state of the art” treatment is catheter-directed thrombolysis whereby a catheter is introduced into the blocked artery and a medication that dissolves the thromb is injected directly into the blockage. This is the preferred treatment for people with ATE, and it has been suggested that this treatment is more effective with fewer side effects than other treatments. The aim of this study is to determine the clinical response, side effects and outcome of targeted intra-arterial administration of tissue plasminogen activator (a blockage dissolving drug) as a treatment of ATE in cats.

W19-024 - Identification of Diagnosis Biomarkers of Feline Infectious Peritonitis
PIs: Dr. Gregg Dean and Dr. Kelly Santangelo, Colorado State University; $25,000 (Bria Fund)

Feline infectious peritonitis (FIP) is perhaps the most devastating infectious disease of cats and there remains a desperate need for a fast and reliable diagnostic test. FIP is caused by the Feline Infectious Peritonitis Virus (FIPV), which has undergone subtle mutations from its normal gastrointestinal counterpart, Feline Enteric Coronavirus (FECV). Clinical signs in the cat are vague and nonspecific, and can include inappetence, lethargy, disorientation, vomiting and diarrhea. Unfortunately, a definitive diagnosis of FIP is often challenging and is typically a diagnosis of exclusion, which is frustrating for owners and veterinarians, alike. While several assays capable of confirming FIP have been developed, these tests can require invasive methods and lengthy wait times for results. We have employed a powerful new technology to simultaneously measure more that 1300 proteins in the blood of cats with FIPV. We compared these results to normal cats and cats infected with other viruses to identify unique proteins that might allow diagnosis of FIPV. We then evaluated a total of 56 cats and utilized statistical modelling to reduce the number of candidate proteins from >1300 to 18. Our current plan is to further evaluate these 18 proteins for accuracy with feline samples prior to ultimately validating a diagnostic test for FIPV.

W19-025 - Generating an Attenuated Feline Infectious Peritonitis (FIP) Vaccine by Inactivating EndoU
PIs: Dr. Gary R. Whittaker and Dr. Susan G. Baker, Cornell University and Loyola University Chicago; $25,000 (Bria Fund)

Feline infectious peritonitis (FIP) is an important cause of death in cats and is caused by a coronavirus. There are currently no effective treatments or vaccines for FIP. Based on new information demonstrating that mutation of a specific viral gene allows for a robust immune response to coronavirus infection without causing disease, we propose to develop a new live-attenuated vaccine for FIP.

W19-026 - Developing a Safe and Effective Anticoronaviral Therapy for Cats with FIP (continuation)
PIs: Dr. Brian Murphy and Dr. Niels C. Pedersen, University of California Davis; $23,779 (Bria Fund)

Feline infectious peritonitis (FIP), caused by mutant feline coronavirus known as FIPV, is a common and generally lethal disease of domestic cats. Over the past 3 years, and with the help of funds provided by Winn Feline Foundation, our research group at University California Davis has conclusively demonstrated that naturally acquired FIP is a curable disease using a nucleoside analog called GS-441524 (Gilead). However, this drug is not yet available for use in cats. In its place, Gilead has provided 48 related nucleoside analogs and if any are found to be equivalent, they have agreed to provide the necessary animal rights. Preliminary data indicates that 3 or more of these drugs will have potent anti-FIPV properties and be non-cytotoxic in feline cells. The most promising of these compounds will be synthesized in much larger amounts and ultimately tested in cats for safety and efficacy. Another collaborator, Mark Olsen (Midwestern University) is creating a set of drug compounds targeting a different viral protein. The results of our initial studies, although not immediately yielding a marketable drug for cats, lead us to conclude that that FIP is in fact a curable disease.

W19-027 - Determining the Pharmacokinetic Profile of Mefloquine in Clinically Normal Cats as a Preliminary In-Vivo Study Towards a Potential Treatment for Feline Infectious Peritonitis
PIs: Dr. Merran Govendir and Dr. Jaqueline Norris, university of Sydney; $24,624 (Bria Fund)

Our recently completed study investigated whether mefloquine was likely to accumulate in the cat; as some other medicines, such as acetaminophen, accumulate with resultant toxic effects. This preclinical study incubated mefloquine with feline liver metabolism enzymes (known as microsomes) acquired from medical suppliers. The results demonstrated that mefloquine did not have delayed elimination in the cat compared to other species such as the dog and rat. The next stage is to conduct a clinical study to determine mefloquine's actions in the clinically normal cat. Therefore, a conventional human pediatric dose of an oral mefloquine syrup will be

administered to cats to determine how well it is absorbed, how fast it is eliminated and whether it has any adverse effects. Such information will be used to formulate a mefloquine dose-rate and dosing frequency, to medicate cats with FIP. This study will also provide information on whether mefloquine results in short-term adverse effects and whether this poses an acceptable risk that can be mitigated, when mefloquine is administered to sick cats.

W19-030 - Accuracy and Precision of Compounded Famciclovir for Treatment of Cats Affected with Feline Herpesvirus Type-1
PI: Dr. Louise O'Leary, Iowa State University; $8,587

Veterinarians and owners are increasingly reaching for compounded famciclovir for treatment of feline herpesvirus. Unlike their FDA-approved counterparts, compounded drugs seldom undergo any quality control testing. In fact, many compounded formulations are ineffective according to recent veterinary literature. For famciclovir, such erroneous formulations would mean prolonged clinical signs, increased shedding and spread of virus, and promotion of antiviral resistance. Using Famvir® as the control, we hypothesize that compounded formulations of famciclovir will have decreased accuracy (drug content), decreased stability (fast degradation), and decreased precision (high variability). This will be verified by analyzing compounded famciclovir at different doses, from different pharmacies and at different times. Results of this study will enable veterinarians and owners to make informed decisions when prescribing famciclovir-ensuring cats only receive effective treatments.

W19-037 - The Pharmokinetics of Single Oral Dose Extended-Release Topiramate and Adverse Effects After Multi-Dose Administration in Healthy Cats
PIs: Dr. Kari Foss and Dr. Jennifer M. Reinhart, University of Illinois; $18,800

Topiramate is a newer anti-epileptic drug that has shown efficacy in the treatment of seizures in people. However, there is limited data on this medication in veterinary medicine. In order to use a medication appropriately, an accurate dosage and dosing frequency must be determined. This study will be performed in two phases. Phase one will establish the dosing parameters for extended release topiramate in cats. Phase two will establish plasma levels following multiple doses as well as identify any side effects related to the medication.

W19-038 - Evaluation of Feline Urine Concentration of Amoxicillin and Clavulanate
PIs: Dr. Kate Kukanich and Dr. Butch KuKanich, Kansas State University; $7,275 (Feline Kidney Disease in honor of Dr. Vicki Thayer)

The current study goals are to measure the urine concentration of amoxicillin and clavulanate in 12 cats after oral dosing, so that a urine-specific cutoff dose for determining resistant bacteria can be determined. We anticipate this would result in many feline urine culture isolates being

usceptible for these two antibiotics, lowering the use of critical antibiotics. Veterinarians will gain more options for first line, oral, well-tolerated, and affordable treatment of UTIs in cats.

W19-039 - Assessment of Transdermal Penetration of Gabapentin in Cats
PI: Dr. Jennifer E. Slovak, Animal Medical Center; $11,937

Little is known about the therapeutic potential of gabapentin administered via the transdermal route in cats. Therefore, the goal of this study is to determine if therapeutic plasma levels can be reached in cats administered gabapentin at a 10mg/kg transdermal dose applied initially to the inside of the ear flap and then to a shaved region of the neck.

2018 George Sydney and Phyllis Redman Miller Trust Grant Awards

MT18-003 - Metagenomic and Metabolomic Analysis of the Short-Term and Long-Term Effects of Antibiotic Therapy on the Intestinal Microbiota in Growing Kittens and Their Relation to the Overall Health Status of These Kittens
PIs: Jan Suchodolski, DVM, PhD, DACVIM, Texas A & M University and Panagiotis Xenoulis, DVM, PhD, University of Thessaly, Greece; $34,800

The potential hazardous effects of antibiotic administration to kittens has received limited attention and no such studies exist in cats. The purpose of this study is to identify the differences that exist in fecal and blood samples between healthy kittens and kittens receiving antibiotics, and to investigate whether cats receiving antibiotics will more commonly develop certain disease conditions (such as obesity or episodes of diarrhea) during their first year of life. Kittens with upper respiratory tract disease (URTD) will be included and receive either amoxicillin-clavulanic acid or doxycycline, as part of their standard treatment. Bacterial communities will be investigated in fecal samples by performing state-of-the-art metagenomic analysis. The metabolic products of these bacterial communities in the gut (i.e., their metabolites) will be identified and compared by untargeted metabolomic analysis.

MT18-004 - Evaluating the Efficacy of Novel Gastroprotectants in Cats
PIs: M. Katherine Tolbert, DVM, PhD, DACVP, University of Tennessee and Adesola Odunayo, DVM, MS, DACVECC; $18,080

Veterinarians are increasingly prescribing newer proton pump inhibitors that are more effective, longer acting, and, in humans, can be given with food. However, the efficacy of these novel PPIs has not yet been evaluated in cats. Although we believe that some of these drugs will be more effective and replace the use of omeprazole, we have concerns that some will be no better than placebo in cats and therefore do not improve the cat's condition. This would be the first study to investigate the impact of these novel drugs in cats.

MT18-005 - Estimating the Significance of a Novel Feline Hepadnavirus in Hepatitis and Liver Cancer
PI: Patricia Pesavento, DVM, PhD, DACVP, University California - Davis; $34,880

Recently, a feline virus has been discovered that is a hepatitis B-like virus. Importantly, in humans and other animals, hepatitis B viruses cause liver inflammation (hepatitis) that can progress to cirrhosis and fatal liver cancer. We urgently need to understand whether cat hepatitis B virus causes liver cancer and other liver diseases in cats. We will test archived feline liver biopsies for the cat hepatitis B-like virus. Because we are investigating a newly discovered feline virus, we will custom-design probes that bind specifically to the virus genes. Cancer cells and liver cells infected with the virus will show up under the microscope as different colors. These probes will be made available to all researchers. The greatest significance of this work for cat health is that we will define whether cat hepatitis B virus contributes to liver inflammation and cancer in the cat. The long-term goal of our research is to develop novel treatments for feline liver diseases and cancer-preventing vaccines specifically for cats.

MT18-009 - Precision Medicine Genomics for Cats
PI: Leslie Lyons, University of Missouri - Columbia; $12,648

The objective is to develop automated workflows that can process and combine these data efficiently. With this workflow, researcher participants can then more easily find DNA changes that likely cause the diseases in their submitted cat. The analysis of these cat genetic data is complex, but similar to techniques used in human genetics. Recently, there was a major improvement in the reference assembly of the DNA in cat chromosomes, making assembly version 9.0 one of the best genetic references of all species. The genetic data from the 99 Lives project (almost 200 cats) now needs to be compared to this new reference to identify DNA differences between a study cat and the reference. These DNA differences can then be compared to other databases to help determine if newly identified DNA variants are “good variants” for genetic diversity”, or “bad variants” that cause disease. If successful, the Lyons laboratory can update the genetic data to the new reference and share the results with the research community.

MT18-010 - The Effects of Brachycephalic Conformation on Cardiopulmonary Health in Cats
PIs: Heidi Phillips, VMD, ACVS and Hadley Gleason, VMD, University of Illinois; $31,696

Brachycephalic cat breeds, such as Persian, Himalayan, and Exotic Shorthair cats, can suffer from breathing problems that can have a negative impact on heart and lung function. In this study, researchers will evaluate the respiratory tract by head, neck, and chest computed tomography (CT) and by direct endoscopic visualization. Heart and lung gas exchange parameters will be determined by blood gas analyses. Ultrasonography of the heart will be used to determine the impact that brachycephalic conformation has on heart function. Benefit of surgically opening the nostrils will also be assessed.

MTW18-001 - Evaluation of Commercial Feline Diets for Calcium, Phosphorous, and the Calcium and Phosphorous Ratio
PI: Jonathon Stockman, DVM, ACVN, Colorado State University; $9,103 (Feline Kidney Disease)

Kidney disease is a common malady in senior cats with an estimation of approximately 35% of cats older than 12 y being affected. Recently, several studies have shown that foods with high phosphorus content and low calcium-to-phosphorus ratios can be detrimental to the kidneys and possibly contribute to the development of chronic kidney disease. Surprisingly, there is lack of published information regarding phosphorus content in commercial foods, and while some manufacturers state the calcium and phosphorus content on food labels, they are not obliged to do so. Therefore, in this study, researchers propose to sample assorted commercially available adult maintenance cat foods and to perform laboratory analysis of the phosphorous and calcium content. They will further evaluate whether certain types of food such as canned, dry, grain-free, or raw products are higher (or lower) in their phosphorous content, and whether the calcium-to-phosphorous ratio differs between them. For this purpose, 60-100 cat food samples will be purchased from local retail stores or online, and sent to analysis. The calcium and phosphorus contents will be determined to identify products with high phosphorous content, and products with low calcium to phosphorous ratio.

For more information visit www.winnfelinefoundation.org

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Winn Feline Foundation is a non-profit orgranization [501(c)(3)] that was established in 1968 that support studies to imporove cat health.

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