WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

Research Update

$397,009 in Feline Health Study Grants Awarded in 2014/2015

Each year, Winn Feline Foundation receives proposals from veterinary researchers around the world who are interested in improving feline health. By May 2015, Winn's cumulative total in feline health research funding exceeds $5 million at more than 30 partner institutions world-wide.

Winn Feline Foundation funded the following feline health studies in August 2014: Winn Feline Foundation announced the award of three feline medical research grants in a special research review made possible by the generous support of Zoetis.

***WZ14-005* Indicators of inflammation in painful cats with degenerative joint disease (DJD)**
Principal Investigator: Duncan Lascelles; North Carolina State University; *$22,815*
There is a critical need for safe and effective analgesics treating pain associated with the most common disease of cats - degenerative joint disease (DJD). This is particularly important in such populations of cats with chronic kidney disease (CKD) where current analgesics (pain-killers) are considered to be associated with a risk of toxicity. The biggest impediment to development of analgesics in cats has been the difficulty in measuring pain. Several sources of evidence suggest that DJD-pain in cats is due to an altered state of immune function, resulting in inflammatory mediators (such as substances called cytokines and chemokines) building up in the body and producing pain. Researchers here believe cytokine/chemokine profiles in the blood can be used as a measure of DJD-associated pain, and further, that cytokine/chemokine profiles will lead them to novel targets for the development of effective, safe analgesics in cats, especially in cats with concurrent DJD and chronic kidney disease (CKD). In this study, the proposal is to measure these inflammatory mediators in groups of cats from which they have extremely detailed clinical information and have already collected the samples. The pilot data indicates they will successfully identify differences, and the results of this study may lead to a biomarker (or biomarker profile) measurement of chronic pain associated with DJD or DJD and CKD – essentially, a 'blood test' for chronic pain.

***WZ14-009* Defining biomarkers involved in the development and progression of feline chronic kidney disease (CKD)**
Principal Investigators: Paola Scarpa, Saverio Paltrinieri; Dept. of Veterinary Sciences & Public Health, Milan, Italy; $34,887
Chronic kidney disease (CKD) is a common disease of older cats that has a progressive course and a high mortality rate. The development and the progression of CKD depend upon the presence of complications such as proteinuria or hypertension. Therefore an early diagnosis of CKD or of hypertension and proteinuria associated with CKD may allow veterinarians to prevent progression of the disease and ultimately improve the quality of life of affected feline patients. In people, several recognized biomarkers serve as early, measurable indicators of CKD or of disease progression. Unfortunately only some of these have been deeply investigated in cats with CKD. Therefore, this study will assess how biomarkers in blood [such as homocysteine (Hcy), endothelin-1 (ET-1), aldosterone, angiotensin II], or in urine [such as urinary protein to creatinine (UPC) ratio, presence of tubular proteins, or alpha-1-macroglobulin (A1M)], may allow an early diagnosis of CKD or identify cats at risk of severe worsening of the disease. To this aim, privately owned cats routinely admitted to their clinical services will have samples tested to assess the serum or urinary levels of these biomarkers. Biomarker levels in cats with CKD of differing severity will be compared with indicator values from cats with non-azotemic CKD and with clinically healthy cats. Moreover, non-azotemic cats at risk to develop CKD will have repeated samples tested over the next 18 months. This planned process will determine the time-based appearance of azotemia and changes in the biomarker levels thus allowing the identification of an early indicator of CKD.

***WZ14-011* Identification of osteoarthritis related biomarkers in the cat**
Principal Investigators: Drs. Thierry Beths, Jennifer Carter, Sebastien Bauquier; University of Melbourne; $37,266
The radiographic prevalence of osteoarthritis (OA) in cats is estimated to be as high as 90% of the population. However, radiographic evidence has a very poor correlation with clinical signs (either pain or dysfunction). The reasons behind this poor correlation include practical ones such as the fact that cats hide "pain" as well as the more clinical issues such as the lack of specific and validated tools identifying and quantifying such pain or dysfunction. There is currently one validated multifactorial scale for identifying acute pain in the cat but there are no good tools for chronic pain. The gold standard for identification of OA in the cat is currently through radiography. Obtaining full radiographs of cats involves deep sedation or full general anaesthesia which is not ideal for many situations. The goal of this study is to develop a blood test biomarker for osteoarthritis in order to

diagnose OA earlier, treat OA earlier, and possibly even to use the biomarker as a gauge of the effectiveness of treatment. The advantage of a blood test, especially if used as a screening tool, would eliminate the need for sedation and anaesthesia along with decreasing costs for the owner.

Winn Feline Foundation funded the following feline health studies in November 2014:

Winn Feline Foundation announced the award of seven feline medical research grants funded in partnership with the George Sydney and Phyllis Redman Miller Trust.

MT14-002 Assessment of an imaging chamber for handling cats in respiratory distress
Principal Investigator: Elizabeth Riedesel; Iowa State University; $3133
Handling unanesthetized cats in order to obtain high quality X-rays or CT scans can be a challenge. When the cat has respiratory symptoms, the stress of restraint can be life threatening. A tube for cat restraint has been developed to provide a low stress environment for the cat and allow for the administration of oxygen during imaging. This device will be evaluated during this study.

MT14-005 Comparison of two treatment options for a tick borne blood parasite
Principal Investigator: Leah A. Cohn; University of Missouri; $23,023
Cytauxzoon felis is a deadly tick borne parasite of cats that is increasing in prevalence. Traditional treatment regimens are difficult to administer and prohibitively expensive for many owners. Under this study, the traditional treatment regimen will be compared to a lower cost orally administered anti-malarial drug: Coartem®.

MT14-009 Improving the quality of the feline reference genome
Principal Investigator: William J. Murphy; Texas A&M University; $25,000
Sequencing of the cat genome has resulted in numerous breakthroughs in the understanding of feline genetic disease. However, over 1000 genes (about 10% of the genome) remain unplaced or unresolved. This project will improve the quality of the feline reference genome and bring it more in line with the dog, human and mouse genomes.

MT14-010 Development of a genetic test for silver coat color
Principal Investigator: Barbara Gandolfi; University of Missouri; *$10,000*
Mutations have been identified through whole genome sequencing appear to be correlated with silver coat color in cats. This study will evaluate whether these mutations are present in 300 cats of known coat color to establish which mutation causes this trait. This will enable the development of a genetic test for silver, one of the few remaining cat colors for which there is no genetic test.

MT14-013 Improving the effectiveness of chemotherapy on feline injection site sarcomas
Principal Investigator: Kelly Hume; Cornell University; $12,969
Feline injection site sarcomas (ISS) are aggressive cancers that can occur at the site of injections. They grow quickly and invasively. Radical surgery and/or radiation therapy are often required and still do not necessarily result in cures. The role of chemotherapy in treatment is not well defined and there is little data supporting a positive impact on outcome. This study looks at ways to increase the beneficial effect of chemotherapy by evaluating a variety of therapeutic combinations on cancer cells. The combinations are designed to inhibit the way cancer cells recognize and respond to DNA damage inflicted by the chemotherapeutic.

MT14-017 Improving the safety of a drug used for sedation or pre-anesthesia, Phase Two
Principal Investigator: Bruno Pypendop; University of California-Davis; $12,479
Dexmedetomidine is a drug commonly used in cats for its calming and pain-relieving effects. It is also sometimes used prior to general anesthesia. However, its use is mostly indicated in relatively young, healthy cats, because it produces severe effects on the cardiovascular system. MK-467 is a drug that is expected to prevent these cardiovascular effects, while preserving the beneficial effects of dexmedetomidine when administered simultaneously. It has been studied in dogs and sheep, but not in cats.

MT14-018 Changes in bacterial and fungal flora on the skin of cats with skin allergies from normal cats
Principal Investigator: Aline Rodrigues-Hoffman; Texas A&M University; $24,788
This study will use DNA sequencing technology to identify the normal bacterial and fungal organisms present on the skin of healthy cats. These species will be compared to those found on cats with skin allergies. This will aid in the identification of therapeutic approaches in the treatment of skin allergies and other skin diseases.

Winn Feline Foundation funded the following feline health studies in March 2015:

Winn Feline Foundation awarded eleven feline medical research grants funded through the generous support of private and corporate donations from around the world. This year Winn awarded $190,649 in grants for studies on a variety of diseases including tests for ringworm, diagnosing and treating *Tritrichomonas foetus*, kidney disease, liver disease, urethral obstruction, heart disease in Birman cats and four FIP projects. In addition, Winn renewed its support for continued mapping of the cat genome.

GENERAL STUDIES

W15-001 Comparing a polymerase chain reaction (PCR) test with fungal culture for ringworm

Principal Investigators: Linda Jacobson, Lauren McIntyre; Toronto Humane Society; $15,375

Ringworm is currently diagnosed by culturing infected hairs and skin scrapings and observing for growth of fungal colonies. If ringworm is confirmed, the animal needs two negative cultures to confirm a cure. Even if the first culture is negative, the cat needs to be held back from adoption for 2 or 3 weeks while waiting for the result. IDEXX Laboratories® has recently developed a rapid test for ringworm that identifies ringworm DNA in hair samples and skin scrapings. The PCR test results are available within 3 business days thus cats could potentially be confirmed ringworm-free, or cured, a full 11-18 days sooner. The goal of this study is to compare the IDEXX Laboratories® PCR test with fungal culture in an animal shelter, to see if the PCR test could replace fungal culture for early diagnosis of ringworm and for showing that the animal has been cured after treatment. This could save the lives of many shelter cats.

W15-010 Evaluating new drug compounds for treating feline coronavirus (Sponsored)

Principal Investigators: Brian Murphy, Niels Pedersen; University of California-Davis; $14,970

Given successes in antiviral therapeutics for HIV, many researchers studying feline infectious peritonitis (FIP) consider antiviral therapy the brightest hope for successful treatment. In addition, rapidly emerging research into related human-animal coronaviruses SARS and MERS has paved the way for dramatic advances in FIP therapeutics. Through optimizing laboratory methods, drug compounds with demonstrated effects against SARS and MERS will be tested for their efficacy against FIP. A FIP-specific enzyme will also be isolated and produced to create a more sophisticated screening test for such drug compounds. Although FIP is a great challenge, the intent is to identify drug compounds that will successfully treat FIP.

W15-011 Diagnosis and treatment of feline Tritrichomonas foetus through target surface antigens

Principal Investigators: M. Katherine Tolbert, Emily Gould; The University of Tennessee; $16,000

Tritrichomonas foetus (Tf) is a protozoal parasite that is a prevalent cause of chronic diarrhea in domestic cats globally. No rapid, bedside assays are available to diagnose this infection. Moreover, only one drug is available to treat feline Tf and this drug is associated with increasing treatment failure and unacceptable side effects. As feline Tf closely resembles other intestinal infections of cats, it can be challenging for veterinarians to rapidly diagnose and treat Tf infection. This research group has previously demonstrated that cat and cattle Tf share common strategies for infecting their hosts. Two surface markers (1.15, 1.17) on bovine Tf participate in establishment of infection and induction of clinical signs. Thus, the aims of this study are to evaluate the expression of 1.15 and 1.17 in feline Tf and to determine if these markers play a role in injury of the intestine. A vaccine against 1.17 is commercially available against bovine Tf. The ultimate result of this study could lead to the development of a novel therapy and/or diagnostic strategy for cats infected with feline Tf.

W15-018 Transdermal mirtazapine as an appetite stimulant in cats with chronic kidney disease

Principal Investigator: Jessica Quimby; Colorado State University; $10,000

Chronic kidney disease (CKD) is a common progressive disease in elderly cats and inappetence is frequently reported as a clinical sign. Mirtazapine is an appetite stimulant that a previous Winn study demonstrated it to be useful in the management of appetite and weight in cats with CKD. Since poor body condition is associated with a poor prognosis, maintaining nutrition is a key goal of medical management. The medication is currently available in pill form, which presents a problem for cats resistant to pill administration, and potentially interferes with the bond between owner and pet. The purpose of this study is to assess the efficacy of transdermal mirtazapine in stimulating appetite in cats suffering from inappetence associated with CKD.

W15-037 Feline liver organoids for the study of liver disease

Principal Investigators: Bart Spee, Hedwig Kruitwagen; Utrecht University; $25,000

Liver diseases such as fatty liver disease and inflammatory liver disease are common in cats. Adult stem cells from the liver can be successfully isolated from cat livers and cultured in the laboratory as organoids. These organoids have the same function as the liver and can therefore be used to study diseases and test the effects – and possible side effects – of newly developed drugs. This proposal aims to establish and fully characterize feline liver organoid cultures and test their application to study liver diseases. This study has the potential to greatly advance feline health as these organoids can be used to test new drugs before their application in the clinic.

W15-042 Effect of Prazocin on recurrence of feline urethral obstruction

Principal Investigators: Kayla Hanson, Andrew Linklater; Lakeshore Veterinary Specialists; $9,000

Urethral obstruction (UO) is a common emergency in male cats, having many causes, and although life-threatening, is treatable with appropriate care. There is a high percentage of recurrent urethral obstruction (rUO), defined as the presence of a non-expressible bladder or observed as non-productive straining to urinate as documented by a veterinarian. Most cases of rUO occur within 2 weeks of discharge and can lead to the need for reconstructive surgery or euthanasia. Prazosin is one of several bladder relaxing drugs used by veterinarians to help treat rUO but there are no controlled clinical studies evaluating the drug in management of feline UO and its use is not considered standard of care at all institutions. This study is a clinical trial evaluating rUO rates in cats treated with a standardized protocol, receiving either prazosin or a placebo (inactive drug) for 7 days following initial presentation. The goal of this study is to provide valuable information regarding the role of prazosin in prevention of short-term rUO and will help guide its use in future cases, perhaps reducing the need for reconstructive surgical procedures and euthanasia.

BRIA FUND STUDIES

W15-013 A feline tumor necrosis factor inhibitor for feline infectious peritonitis

Principal Investigator: Yunjeong Kim; Kansas State University; $23,758

FIP is caused by a variant of a feline coronavirus and cats can develop FIP when their cellular immunity is insufficient to fight the virulent disease. As FIP progresses, lymphocyte loss occurs due to increased cell death impairing the cat's ability to check virus replication. Lymphocyte loss in FIP is reported to be cause by tumor necrosis factor (TNF) -α. The researcher postulates that combined treatment with specific antiviral drugs that inhibit the replication of virus and direct counteraction of the detrimental effects of TNF-α by an inhibitor may lead to a better clinical outcome. The goal of this study is to evaluate suitable expression systems and biological function of a feline TNF-α inhibitor.

W15-026 Systemic feline coronavirus and its relationship to FIP

Principal Investigator: Gary R. Whittaker; Cornell University; $24,967

A critical determinant of feline infectious peritonitis (FIP) is the ability of the virus to infect white blood cells. The key differences between the viruses infecting the gastrointestinal tract (FECV), white blood cells, and other tissues and organs (FIPV), however, are still not well understood. The goal of this study is to understand the virus present in blood samples, and to identify the viral mutations responsible for spread in the blood. We expect the work proposed here to advance our understanding of both early and late events in FIP disease and to provide critical information on a diagnostic test currently under development in this lab The researcher also hopes to develop a novel, early, therapeutic interventions for treating FIP in the future.

W15-030 Using small interfering RNA for treatment of feline infectious peritonitis

Principal Investigators: Emin Anis, Rebecca Wilkes; The University of Tennessee; $16,500

Feline infectious peritonitis (FIP) is a fatal disease that is caused by feline coronavirus (FCoV). Cats lack an effective immune response (IR) to the virus and cats with FIP have a profound reduction in a specific white blood cell type (WBCs) that is important for protection of cats from infection. In this study, it is proposed that death of these important WBCs is due to activation of a response called "programmed death" within the cells. Initiation of this response is thought to be due to an overexpression of two proteins on the surface of the WBCs and the interaction of these two proteins. Preliminary evidence supports this hypothesis therefore the study's goals are to confirm these findings by testing more samples and to evaluate whether blocking WBCs death will enhance the survival of the white blood cells. If shown to be effective, programmed death pathway blocking could be a useful addition to any therapy that specifically targets the virus.

ABYSSINIAN HEALTH FUND STUDY

W15-008 Improving the Feline Reference Genome with PacBio sequencing, a continuation study

Principal Investigator: William J. Murphy; Texas A&M University; $24,910

Sequencing of the cat genome has resulted in numerous breakthroughs in the understanding of feline genetic disease. DNA from the female Abyssinian cat, "Cinnamon", who was used to create the original reference genome will be used to build a single library and generate 8X sequence coverage on the PacBio instrument. This process will help improve the reliability of the feline reference genome and bring it more in line with dog, human and mouse genomes. As a continuation of a funded project from Fall 2014, the results of this study will significantly increase the quality of the feline genome sequence assembly and also sequence the Y chromosome which is less than 10% complete. This new technology will fill gaps in genes and resolve a large number of duplicated gene regions into their proper structure and copies. The results of this study will significantly improve the quality of the feline genome assembly, and increase our ability to map genes that contribute to traits and diseases in different cat breeds.

BIRMAN HEART DISEASE FUND AND RICKY FUND

W15-044 Phenotypic characteristic of cardiomyopathy in Birman cats

Principal Investigator: Virginia Luis Fuentes; Royal Veterinary College, University of London; $10,169

Birman cats, primarily in Europe, are predisposed to heart muscle disease (cardiomyopathy). A crucial question that must be answered before a genetic mutation can be identified is whether the three forms of heart muscle disease are three different diseases with three different causes or whether they are part of a spectrum of one disease with one genetic cause. The plan here is to study Birmans with cardiomyopathy using a combination of cardiac ultrasound (echocardiography), pathology and pedigree analysis, so that the research team can determine the features of these heart muscle diseases. If there is substantial overlap in their ultrasound and pathology characteristics, or they find families of Birmans with multiple members affected by more than one type of cardiomyopathy, they can be more confident that they are dealing with one disease, and so can proceed to genetic research.

For more information www.winnfelinefoundation.org

Winn Feline Foundation
637 Wyckoff Ave., Suite 336
Wyckoff, NJ 07481
Telephone: 201.275.0624; Toll free: 888.963.6946
Email: info@winnfelinefoundation.org

Winn Feline Foundation is a non-profit organization [501(c)(3)] established in 1968 that supports studies to improve cat health.

Member Combined Federal Campaign #10321