



WINN FELINE FOUNDATION

For the Health and Well-being of All Cats

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2010 FELINE HEALTH GRANT AWARDS 16 projects funded for a total of \$183,391

The Winn Feline Foundation receives proposals from veterinary researchers around the world who are interested in improving feline health. Out of 50 proposals for 2010, our team of expert veterinary consultants helped the Foundation select 16 projects for funding for a record-breaking total of \$183,391. The Winn Foundation looks forward to seeing the results of these projects and to sharing them with the veterinary community as well as with cat owners and pedigreed cat breeders.

RICKY FUND PROJECTS

10-013: *Plasma homocysteine concentrations after methionine challenge in cats with and without hypertrophic cardiomyopathy*

Karl E. Jandrey, DVM, MAS, DACVECC; Mark Kittleson, DVM, PhD, DACVIM; Jennifer Larsen, DVM, PhD, DACVN; University of California-Davis: \$5,694

Hypertrophic cardiomyopathy (HCM) is the most important cause of cardiovascular morbidity and mortality in the cat. Cats with heart disease are at risk of sudden death from several possible causes. One cause is the formation of blood clots that block blood vessels that supply oxygen and nutrients to tissues. A similar problem is associated with humans with heart disease, heart attack, and/or stroke. This common emergency causes illness and death in both cats and humans. People at high risk for formation of blood clots have higher blood concentrations of an amino acid called homocysteine. In addition, low blood concentrations of B vitamins have been shown to be associated with the high concentrations of homocysteine in humans.

This study will document the blood concentrations of homocysteine and B vitamins in a group of cats that have heart disease and are at risk for the development of blood clots. This study will also correlate the concentration of homocysteine to measurements of clot formation. The goal of our research is to identify the underlying cause and develop a novel therapy to prevent or reduce the incidence of thromboembolism. The identification of an early marker of clot formation may give veterinarians evidence to begin preventative therapy minimizing these fatal complications of heart disease in cats and humans.

BRIA FUND PROJECTS

10-036: *Molecular prevalence and viral load of replicating feline coronavirus in the bloodstream of healthy shelter cats in southern California*

Pedro Paulo Diniz, DVM, PhD; Yvonne Drechsler, PhD; Linda Kidd, DVM, PhD, DACVIM; Frank Bossong, DVM; Ellen Collisson, MS, PhD; Western University of Health Sciences: \$10,000

Feline infectious peritonitis (FIP) is a generalized disease caused by a coronavirus (FCoV). It causes subtle onset of clinical signs, persistent fever that does not respond to treatment, inflammatory nodular tissue reaction with pus, and accumulation of inflammatory fluids in the abdomen. FIP has a high mortality rate, and it occurs more frequently among young cats. Despite improvement in laboratory methods, FIP remains one of the most difficult diseases to diagnose definitively in feline

medicine. A new technique based on DNA detection has been suggested as an improved way to identify cats with FIP. However, it is not clear how many healthy cats are considered positive using this technique, because two different studies reported discrepant results. No such study has ever been conducted in cats in the United States. The objective of this study is to determine the frequency of healthy cats in southern California that are infected with FCoV, and the relative number of viruses in their bloodstream. The results of this study will provide epidemiological data about healthy but infected cats in the U.S. and select these cats to participate in a future study about early detection of FIP.

10-037: *Development of feline infectious peritonitis therapeutics in a mouse model*

Gary R. Whittaker, BSc (Hon), PhD; Cornell University: \$15,000

Feline infectious peritonitis (FIP) is a deadly disease of cats, caused by infection with a coronavirus. The virus normally resides in the gut of the cat, but can mutate and so infect the immune system of certain cats. By use of feline cells grown in the laboratory, the investigators have identified a key factor in feline immune cells (a protease that activates the deadly form of the virus), which could be a potential target for drug therapy. The goal of the project is to test the activity of these protease inhibitors in a mouse model of FIP, as a first step to developing effective therapeutics for use in cats.

10-038: *Polyprenyl immunostimulant for the treatment of the dry form of feline infectious peritonitis*

Alfred Legendre, DVM, MS, DACVIM; University of Tennessee: \$14,825

Feline infectious peritonitis (FIP) is a devastating, fatal disease of cats that responds poorly to treatment. It is believed that the disease occurs when there is a mutation of the common intestinal coronavirus. There is a depression of the cell-mediated immune response to the mutated virus, which results in an overproduction of antibodies and a loss of the cell-mediated immunity needed to destroy coronavirus-infected macrophages. The polyprenyl immunostimulant (PI) stimulates cell-mediated immunity. Since the publication of an article on the response of three cats with FIP to PI, we have received requests for the PI from owners and veterinarians from throughout the United States. The investigators will treat 20 cats diagnosed with FIP with PI to validate the responses previously seen.

10-039: *Development of a novel treatment strategy to inhibit the immune evasion mechanism of feline infectious peritonitis virus (FIPV)*

Sabine Gleich, DVM; Hannah Dewerchin, DVM; Hans Nauwynck, DVM; Ghent University: \$12,700

Feline coronavirus exists in two forms: a less harmful (avirulent) strain that can cause mild enteritis and a highly pathogenic (virulent) strain that causes a progressive and usually fatal disease known as feline infectious peritonitis (FIP). Cats living in multi-cat environments (e.g., shelter cats or cats in catteries) are at increased risk to develop FIP. An effective therapy is currently not available and affected cats usually succumb to their disease. In the past, the mechanisms describing how the virus can hide from the host's immune system have been discovered by this research group. These mechanisms can be inhibited by specific compounds, as has been shown *in vitro*. These inhibitors could be potential candidates for a new therapy for FIP and could help to make the virus visible to the host's immune system. Virus-infected cells could then be identified and effectively eliminated. The goals of this project are the development of a novel therapeutic approach for FIP, the optimization of detection methods of this therapeutic compound in feline plasma, the determination of its pharmacokinetic characteristics, and, finally, to evaluate its efficacy in FIP-infected feline patients.

NEW PROJECTS

10-008: *Antinociceptive effects of fentanyl administered transdermally in cats*

Bruno H Pypendop, DrMedVet, DrVetSci, DACVA; Jan E. Ilkiw, BVSc, PhD, DECVA; University of California-Davis: \$5,670

Opioids are commonly used for the treatment of pain in cats. While they are considered to be highly efficacious, one main disadvantage to their use is their relative short duration of action, and therefore the need for repeated administration. Fentanyl is a potent opioid with a short duration of action. It is commercially available in patches, which are applied on the skin and provide continuous release for up to three days. They are therefore expected to produce continuous pain relief, with a single, non-invasive administration. While fentanyl patches are commonly used to treat pain in feline patients, their analgesic effect has not been studied using objective methods, leading to uncertainties as to onset and duration of effect. This is important, since practitioners using these patches may rely on the effect, and may not have the opportunity to reassess their feline patients often enough to detect inadequate analgesia early. The study proposed here will examine the effect of fentanyl patch application on an established model of pain in cats.

10-009: *Treatment for visceral pain with the new NK-1 receptor antagonist maropitant in cats*

Pedro Boscan DVM, MSc, PhD, DACVA; David Twedt DVM, DACVIM; Eric Monnet DVM, PhD, DACVS; Colorado State University: \$9,905

Pain deteriorates the quality of life, induces behavioral abnormalities, and increases morbidity and mortality in animals, including cats. At present, there are limited therapeutic choices, as well as limited knowledge on how to treat visceral pain in cats. Available analgesics often have detrimental effects. Maropitant is a newly developed drug shown to be effective in treating vomiting in cats by blocking certain receptors (NK-1) in the central nervous system. These receptors are also involved in pain pathways. The study will investigate the use of maropitant to promote analgesia in cats. This study will test the analgesic effect of maropitant in cats during spay surgeries. Maropitant should decrease the anesthetic requirements, suggesting an analgesic effect. Maropitant is an important anti-nausea drug in cats but has the potential to also become an important analgesic drug without side effects. This will be the first study addressing the potential use of maropitant to manage painful diseases or procedures such as pancreatitis, chronic gastrointestinal disease, renal failure, and abdominal surgeries, including spays.

10-014: *Cat Phenotypic Health and Information Registry (Cat PHIR)*

Leslie A. Lyons, PhD; University of California-Davis: \$14,000

Approximately 32% of households in the United States have a cat. While cats generally succumb to renal disease and cancer in old age, they are also plagued by a variety of infectious diseases. Cats suffer from many behavioral disorders, which are so significant that undesired behavior is one of the leading causes for cats to be placed in animal shelters. The cat lifestyle has become sedentary and indoor, mimicking that of humans. Thus, as found in humans, diabetes, obesity, and asthma are increasing in incidence in cats and are becoming chronic health concerns. As a result, veterinarians are beginning to perform genetic studies in cats. Improved electronic resources, the interest in obtaining genetic information about pets by owners and breeders, and the feasibility of retaining sufficient DNA sources all support the establishment of a focused system that can be used by researchers to develop disease projects in the cat. Here we propose to coordinate the

health information, DNA banking, and cat pedigrees into an electronic, online database system that will assist the collection of individual data for complex disease studies. The resource development proposed will augment research for feline diseases, support clinical and laboratory-based research, and teaching within the veterinary community, and support the development of grant applications to funding agencies. This proposal will continue to develop resources that can be used not only by veterinary researchers, but will also be at the cutting edge of genomic technologies for more complex studies in the cat. The proposed name for the database system is the Cat Phenotypic and Health Information Registry (Cat PHIR).

10-015: *Health concerns of dominant traits in domestic cats*

Robert A. Grahn, PhD; Leslie A. Lyons, PhD; University of California-Davis: \$15,000

While cats have been living with humans for nearly 10,000 years, selection for specific traits has only recently occurred. While many of these traits are innocuous, others occasionally have associated deleterious phenotypes. These include deafness in dominant white cats, lameness in Manx and Cymrics, and joint problems in Scottish Folds. These are all dominant traits and, in the case of Manx, Cymrics, and Scottish Folds, manifestation of the disease occurs when both maternal and paternal genes are affected. The genes and associated mutations that result in these phenotypes have yet to be identified. Similarly, the genetic mutation for dominant white and the allele for deafness have yet to be determined. This proposal will obtain sample sets sufficient for determining the causative genes for both dominant white/deafness and taillessness. Deaf cats will be determined via hearing tests by qualified veterinarians and small pedigrees, sufficient for candidate gene exclusion, will be established. Using available genetic resources, the samples collected will be used for case control studies to identify candidate genes.

10-016: *Ability of a novel probiotic *Lactobacillus acidophilus* NCK2025 to colonize and stimulate mucosal IL-10 synthesis in healthy and immunosuppressed cats*

Gregg A. Dean, DVM, PhD, DACVCP; Allison S. W. Mazepa, DVM; Todd R. Klaenhammer, PhD; North Carolina State University: \$15,000

Feline idiopathic inflammatory bowel disease (IBD) is a common diagnosis in cats with chronic vomiting, diarrhea, and/or weight loss. The exact cause is unknown, but excessive inflammation in the gastrointestinal tract (GIT) resulting from genetic abnormalities, or loss of tolerance to normal bacteria are possible triggers. Current therapies include novel diets, antibiotics, and drugs that suppress the immune system. Probiotics are increasingly popular for the treatment of IBD. *Lactobacillus acidophilus* NCK2025 is an exciting probiotic candidate IBD therapy. Our goal is to investigate its immune effects on the GIT, persistence in the host, and potential adverse effects. Goals of this study include: demonstrating the ability of *L. acidophilus* NCK2025 to colonize the feline GIT, documenting induced synthesis of IL-10 by the GIT in response to the bacterium, and documenting the absence of adverse effects or induction of an undesirable immune response. The clinical relevance of this study is the potential to develop a new, effective therapy for feline idiopathic inflammatory bowel disease.

10-017: *Management of feline acromegaly with a long-acting somatostatin receptor ligand*

Katharine F. Lunn, BVMS, MS, PhD, MRCVS, DACVIM; Colorado State University: \$7,302

Acromegaly is a hormonal disease of cats in which excessive growth hormone (GH) is produced from a tumor in the pituitary gland. Although previously considered to be rare, there is now evidence that acromegaly may be under-diagnosed in cats. One reason for this is that there are currently few effective therapies for feline acromegaly, and therefore veterinarians may not test for the disorder. Acromegaly is important in cats because it causes diabetes mellitus with severe insulin resistance. It also causes weight gain, enlarged organs, thickened bone and soft tissues, and heart and kidney disease. Cats with acromegaly often die or are euthanized because of heart or kidney disease, or the complications of uncontrollable diabetes mellitus. Acromegaly is diagnosed by measuring GH, and a related hormone called insulin-like growth factor-1 (IGF-1). The latter is responsible for tissue and organ growth in these patients. In this study we propose to evaluate a drug that is commonly used in human patients with acromegaly. The drug is a long-acting form of octreotide, which acts to decrease GH production from the pituitary tumor. This medication has not been previously evaluated in cats. The goals of the study are to determine if the medication safely reduces insulin dose, GH and IGF-1 levels in cats when given monthly for six months. The appropriate dose of the medication will also be determined. If effective, this medication will provide a more accessible therapy for cats with acromegaly and may increase awareness and diagnosis of this serious condition.

10-020: *Pharmacokinetics of pioglitazone in lean and obese cats*

Levent Dirikolu, DVM, PhD; Margarethe Hoenig, Dr med vet, PhD; Duncan C. Ferguson, VMD, PhD, DACVIM, DACVCP; University of Illinois: \$13,100

Diabetes mellitus and hepatic lipidosis (fatty liver disease) are commonly encountered medical problems in pet cats. Both are associated with obesity. Prevention of these diseases by maintenance of an appropriate body weight would be ideal; however, weight control is difficult in many cats, and overweight cats with diabetes or fatty liver disease need specific treatments for these potentially life-threatening disorders. Current treatment options for diabetes in cats are limited to insulin, which must be given by injection, and to glipizide, a drug that exhausts the insulin-secreting cells of the pancreas over time. The only treatment that has improved survival rates in feline hepatic lipidosis is aggressive nutritional support via a feeding tube. In humans, relatively new anti-diabetic drugs called thiazolidinediones (TZDs) have been shown to improve insulin sensitivity and reverse fatty changes in the liver, not only in diabetics, but also in people with non-alcoholic fatty liver disease. Non-alcoholic fatty liver disease in people is similar in several ways to hepatic lipidosis in cats. Because of this, human TZDs such as pioglitazone would presumably be beneficial for treatment of diabetes and fatty liver disease in cats. The purpose of this project is to begin investigation of this drug in cats, so that it can later be used for clinical trials in cats with diabetes mellitus and hepatic lipidosis.

10-043: *PET-CT of feline oral squamous cell carcinoma*

Elissa K. Randall, DVM, MS, DACVR; Colorado State University: \$8,103

Squamous cell carcinoma is the most common oral tumor in cats, and accounts for approximately 10% of all feline tumors. So far, all attempted treatments have met with limited success and limited survival times. This study will use PET-CT before and after stereotactic radiosurgery (SRS) to evaluate the primary tumor and to detect spread of the tumor (metastasis). PET-CT provides a combination of a metabolic scan (the PET portion) as well as a detailed CT scan that is good for anatomic and structural detail of organs. SRS is a type of radiation therapy that

allows for fewer days of anesthesia as the treatment is delivered in several larger doses instead of smaller doses over several weeks. The post treatment scan will be used to evaluate response to treatment, and will be compared to biopsies. This study will provide multiple benefits. It will allow evaluation of a new imaging modality in the veterinary profession and give information on the efficacy of PET-CT for staging this particular type of cancer. Additionally, it will provide information about tumor response to SRS and the appearance of tumors post-SRS on PET-CT scans. The data gained could assist in the treatment planning of cats with this difficult-to-treat cancer, by better detecting metastasis and evaluating tumor response to this treatment regimen. This is a pilot study and will, it is hoped, provide information that will lead to further developments in the fields of veterinary PET-CT, SRS, and oral squamous cell carcinoma.

10-044: *Evaluation of the effects of the retinoid isotretinoin and feline recombinant interferon- ω on a feline squamous cell carcinoma cell line*

Carlos H. de M. Souza, DVM, MS, DACVIM; Sharon Stack, PhD; Carolyn J. Henry, DVM, MS, DACVIM; Kim Selting, DVM, MS, DACVIM; Sandra Axiak, DVM, DACVIM; University of Missouri-Columbia: \$11,210

Oral cancer is common, representing 10% of all tumors in cats. Squamous cell carcinoma is the most common of them, comprising approximately 65% of all oral cancers. Because of its location (tongue, mandible, or maxilla) and aggressiveness, oral SCC usually leads to loss of appetite, pain, and overall dramatic decrease in quality of life. Despite treatment, most cats will die from progression of their disease, and survival beyond a few months is not commonly seen. New therapies must be investigated in order to improve quality of life and survival rates of cats affected by this tumor. Two of these new therapies are retinoids and interferon. Retinoids, such as isotretinoin, are synthetic derivatives of vitamin A and have been successfully used against many different cancers in people. When combined with interferon (an immunostimulant and growth-inhibiting drug), synergistic effects have been seen in a number of human cancers. Side effects of either drug or their combination are uncommon and are usually manageable. This study will evaluate the effects of these drugs in SCC cell cultures, and intends to answer two main questions: does isotretinoin have an effect against oral SCC, and does this effect increase by combining it with interferon? The long-term goal of the study is to provide the basis for a new, safe, and efficient modality of treatment for cats affected by this dreadful disease.

10-045: *New staging techniques and evaluation of therapies for oral squamous cell carcinomas*

Maria Cekanova, MS, RNDr, PhD; Alfred Legendre, DVM, MS, DACVIM; Amy LeBlanc, BS, DVM; University of Tennessee: \$15,000

Oral squamous cell carcinoma (SCC) develops in the jaw, gum, and under the tongue of cats. Oral SCC aggressively invades local tissue, causes bone destruction, and spreads to other parts of the body. The options for the treatment of oral SCC are limited and less than 10% of cats survive one year from the time of diagnosis. In most cases, the treatment goals are to palliate pain until the oral tumor has advanced to a stage where comfortable eating and breathing are not possible. Cyclooxygenase (COX) enzyme is important for inflammation and tumor growth. It has been shown that COX-2 inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs, such as piroxicam, meloxicam, and celecoxib) could be used for the detection of the COX-2 in tumors. This study will use new COX-2 inhibitors labeled with fluorescence or radio-tracers to detect the oral SCC as well as

metastatic sites. In addition, the study will assess *in vitro* potential treatment with different COX-2 inhibitors alone or in combination with a tyrosine kinase inhibitor, masitinib, using the cells originated from the cat's SCC tumors. Masitinib inhibits epidermal growth factor receptor, which is also responsible for the growth of SCC. The most effective treatment in cells will be used to treat cats with oral SCC.

10-049: Investigation of *in vitro* enzymatic and cytotoxic activity of L-asparaginase (Elspar®) in feline lymphoma after cold storage

Jackie Wypij, DVM, MS, DACVIM; University of Illinois at Urbana-Champaign: \$10,882

Hematopoietic tumors such as lymphoma are common in cats, accounting for nearly one-third of all cancer in this species. Lymphoma affects all breeds, including Siamese and Oriental Shorthairs, and causes significant impact on quality of life as well as mortality. The incidence of feline lymphoma is increasing, with more and more cats developing this deadly but treatable cancer every year. The use of L-asparaginase (Elspar®), an effective chemotherapeutic agent, is limited in cats because of expense. The drug is packaged in human-sized doses, and unused drug must be discarded resulting in the majority of the drug being wasted in cats. Similar to other drugs, L-asparaginase may retain enzymatic and biologic cell-killing abilities against tumor cells after refrigeration and/or freezing. The goal of this research is to establish a scientific basis for the practice of long-term cold storage of L-asparaginase. This may provide multiple doses from one vial, decreasing costs for pet owners and improving medical care for cats with lymphoma.

FOR FURTHER INFORMATION

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