



THE WINN FELINE FOUNDATION

For the Health and Well-Being of All Cats

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2009 FELINE HEALTH GRANT AWARDS 12 projects funded for a total of \$127,411

The Winn Feline Foundation receives proposals from veterinary researchers around the world who are interested in improving feline health. Out of 36 proposals for 2009, our team of outstanding veterinary consultants helped the Foundation select twelve projects for funding, as well as an additional project approved pending further fund-raising. 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.

APPROVED PENDING FUNDING

#09-008: *SNP analysis in rapidly progressing feline autosomal dominant polycystic kidney disease*
Robert Grahn, PhD; University of California, Davis; \$13,557

Polycystic kidney disease (PKD) in the domestic cat results from a mutation in the gene PKD1. Knowing a cat has this gene does not tell a veterinarian how severe the disease will become or how long the animal will live a comfortable life, however, because other genes influence the progression of the disease. Several of the other genes that contribute to the proliferation of the disease have been identified in humans. These genes have yet to be investigated in the cat. This study will identify mutations that are correlated with severe disease progression. Knowing which genes are affected may impact the course of therapy and will aid in decisions regarding treatment of cats with polycystic kidney disease. **[For information on how to donate to this study, please contact the Winn Feline Foundation.]**

BRIA FUND PROJECTS

09-027: *Determining genetic correlates of FIP susceptibility*

Jacqueline Norris, BVSc, MVS, MASM, PhD; Steven A. Holloway BVSc, MVS, MACVSc, DACVIM, PhD; Craig McLure, BSc, PhD; The University of Sydney, Australia; \$12,240

Feline infectious peritonitis (FIP) is a fatal disease of cats involving variants of feline coronavirus, commonly called feline infectious peritonitis virus (FIPV). The disease tends to be sporadic and is more common in certain pedigreed cats and in cats from multi-cat environments. This study uses molecular biology methods to examine areas of variability in the cat genetic code that may be associated with susceptibility to FIP. In particular, the study will compare genes from cats with FIP to those of older breed-matched cats that have not developed FIP. The genes selected for examination are known to be involved in coronavirus attachment to cells or to form part of the immune response against the virus. The genes have been selected based upon examination of the complete sequence of the feline genome for areas that are likely to be variable between individual cats. In this manner, the investigators can look for genetic differences between cats that develop FIP and those that are resistant. This information will improve understanding of FIP and may provide genetic tests that will assist breeders in avoiding the use of cats with susceptibility to FIP for breeding.

RICKY FUND PROJECTS

09-017: *Feline hypertrophic cardiomyopathy: five year outcomes and risk assessment*

Philip Fox, DVM, MS, DACVIM, DECVIM, DACVECC; The Animal Medical Center; \$14,050

Hypertrophic cardiomyopathy (HCM) is the most important cause of cardiovascular morbidity and mortality in the cat. Nevertheless, its natural history is unresolved, and factors that promote heart failure and cardiac death remain unidentified. Risk factor identification in human HCM patients has greatly improved patient health and survival. Of particular relevance are positive family history of cardiac morbidity, genetic mutations, presence of cardiac outflow tract obstruction and arrhythmias, and magnitude of ventricular thickening. This study is the first comprehensive clinical analysis of feline HCM by virtue of evaluating a large population of 1,200 cats to assess risk factors for heart failure and death. The investigators will identify cats that were diagnosed five years ago with asymptomatic and symptomatic forms of HCM, as well as healthy cats that were examined over the same period for comparison. They will prospectively analyze their echocardiograms, review their history and medical record data, and then conduct follow up health surveys with their owners. Results of this study should contribute meaningfully to developing more useful and cost effective disease monitoring, improving treatment strategies, enhancing ability to assess cardiac risk, and improving accuracy for prognosis.

NEW PROJECTS

#09-002: Nutritional adequacy and performance of raw food diets in kittens

Beth Hamper, DVM; Claudia Kirk, DVM, PhD, DACVN, DACVIM; Joseph Bartges, DVM, PhD, DACVN, DACVIM; University of Tennessee; \$14,878

There are many benefits claimed for feeding raw food diets to cats, including improved immune function. Although 4% of U.S. cat owners feed raw diets as all or part of their cat's diet, there are no published studies examining whether these diets are complete and balanced for feeding cats or whether immune function is improved in cats on a raw food diet. The goal of this study is to determine whether a commercially produced raw food diet and a homemade raw diet are nutritionally adequate for feedings kittens and whether these diets enhance immune function and improve digestibility. The outcomes to be measured include growth rate, feed efficiency, digestibility, and various blood and immune status parameters. The long term goal is to evaluate ways of improving feline immune function through diet.

#09-009: *Linkage disequilibrium in the domestic cat and its breeds*

Leslie Lyons, PhD; University of California, Davis; \$15,000

The cat lifestyle has evolved to be sedentary and indoor, and diabetes, obesity, and asthma are increasing in incidence, becoming chronic health concerns. The National Institutes of Health (NIH) is sponsoring a more thorough genome sequencing project for the cat. Studies to determine the genetic variation within cat breeds have started. This sequencing effort will promote the development of resources (DNA chips) for genetic studies of conditions that are influenced by many genes. To study both simple and complex diseases and traits in cats, DNA chips generally make use of unrelated individuals, known as cases, that have the trait of interest, and unrelated individuals, known as controls, that do not have the trait but otherwise mimic all other aspects of the cases, including age, gender, breed and environment. The number of cases and controls needed for a study is directly correlated to the amount of inbreeding and selection within the cat population that the cases and controls represent. Inbreeding is also considered in developing an efficient DNA chip. The stronger the inbreeding, the fewer cases and controls required, as well as fewer DNA mutations required for an efficient DNA chip. An adequate estimation of inbreeding of cat breeds has not been accomplished. This project will determine the amount of inbreeding in domestic cat breeds and random bred cat populations. This study will provide the necessary background information needed by all researchers to conduct effective case - control studies in all cat populations and help to develop the appropriate and sufficient DNA chip for the cat.

09-013: Identification of a biomarker for masked renal failure in hyperthyroid cats

Thomas Schermerhorn, VMD, DACVIM; Gary Gadbury, PhD; Ruth Welti, PhD; Richard Jeannotte, PhD; Kansas State University; \$15,000

Hyperthyroidism is a common ailment of older cats. The presence of hyperthyroidism can make it difficult to determine whether or not a cat has another common ailment, loss of kidney function. One common treatment for hyperthyroidism is radioactive iodine, and the treatment typically includes a weeklong hospital stay. Kidney problems, masked by the hyperthyroid state and discovered only after treatment, may make the cat ill, may require chronic treatment, and can reduce life expectancy. The aim of this project is to discover a measurable component of a hyperthyroid cat's urine that is associated with hidden kidney failure. To do this, the team will apply mass spectrometry, a technique that is capable of identifying thousands of urine components. The long-term goal is to devise a test to accurately assess the presence of hidden kidney problems in hyperthyroid cats before treatment is undertaken, thus maximizing the chances for a successful outcome.

09-015: The incretin effect: A potential role for GLP-1 analogues in the treatment of feline diabetes

Chen Gilor, DVM, DACVIM; Thomas Graves, DVM, PhD, DACVIM; University of Illinois Urbana-Champaign; \$12,638

Incretin hormones are secreted from the intestinal tract in response to ingestion of nutrients. They play a major role in augmenting insulin secretion and in controlling blood glucose concentrations after meals in healthy animals. Drugs that mimic the action of incretin hormones are effective in the treatment of diabetes in humans. Little is known about these hormones in cats. This project will measure the physiologic effect of incretin hormones in healthy cats by comparing the effects of oral glucose to intravenous glucose on the secretion of incretin hormones and on the stimulation of insulin secretion. After showing that incretins have a similar biologic effect in cats as in other species, the investigators will study the effect of exenatide on augmentation of insulin secretion. This drug mimics the effect of the incretin hormone GLP-1, but it is much more resistant to degradation in the body and thus it is long-acting. Exenatide is as effective as insulin in diabetic humans and is associated with fewer side effects. The goal of this study is to generate data to be used as baseline for clinical trials of exenatide in diabetic cats.

09-022: Prevalence, identity, and antimicrobial susceptibility of enteroadherent *Enterococcus* spp. infection in kittens with and without diarrhea – A new pathogen?

Jody L. Gookin, DVM, PhD; North Carolina State University; \$14,918

Kitten diarrhea is a frustrating problem for which few causes, and therefore few treatments, have been identified. Although the intestinal tract is well populated by many healthy bacteria, certain strains can adhere to the lining of the intestine and are strongly associated with diarrhea. The investigators have identified five unrelated kittens aged 3-10 weeks with massive numbers of Gram-positive bacteria adhering to the lining of the intestine. Each kitten had died in a shelter or foster care facility. The bacteria were identified as *Enterococcus*. These bacteria could not be demonstrated in five age-matched kittens euthanized or dying for reasons unrelated to diarrhea. It is suspected that these *Enterococcus* bacteria are a potentially significant cause or complicating factor for diarrhea in weaning-age kittens. In this study, the investigators aim to determine 1) whether *Enterococcus* infection is more common in kittens with diarrhea compared with age-matched controls, 2) what specific strain of *Enterococcus* is responsible for these infections, and 3) what kind of antibiotics are effective against the bacteria. The relevance of this study is its potential to identify a new bacterial culprit that may cause or significantly contribute to diarrhea, death and euthanasia of weaning-age kittens in shelter or animal control facilities.

09-028: *Cyclosporine blood levels after subcutaneous administration in cats*

Sandra F. Diaz, DVM, MS; David L. Panciera, DVM, MS, DACVIM; James Blair Meldrum, DVM, PhD; VA-MD Regional College of Veterinary Medicine; \$5,947

Cyclosporine A (CsA) is an immune-modulating medication. In veterinary medicine, CsA has been classically used as an immunosuppressive agent in kidney transplantation in cats. More recently, CsA has been reported to be effective for the management of several skin diseases, including allergic skin diseases. Allergy is a chronic, frustrating disease to manage, with few effective treatments available. Although steroids are an effective therapy for allergy in cats, side effects are common. A recent study reported CsA as an effective alternative to prednisolone in cats with allergic skin disease. Absorption of CsA is variable when given by mouth, making monitoring strategies difficult to implement. Additionally, for clients with cats that are difficult to medicate, giving medications by mouth for several weeks or longer, which is often the case with cyclosporine treatment, can be a problem leading to poor compliance and treatment failure. CsA injected under the skin may allow more steady blood concentrations, facilitating monitoring and dose adjustment. In addition, because of the small volume needed, this type of administration is expected to be well tolerated in cats. The objective of this study is to determine blood levels of CsA after subcutaneous administration. It is anticipated that subcutaneous administration will result in more predictable blood cyclosporine concentrations, reduce side effects, and decrease the need for expensive monitoring.

09-030: *PCR amplification and sequence analysis of exon 9 and exon 12 of the c-KIT gene in feline soft tissue fibrosarcomas*

Amanda J. Smith; Bradley L. Njaa, DVM, DACVP; Catherine G. Lamm, DVM, DACVP; Oklahoma State University; \$1,932

Fibrosarcoma is an aggressive cancer of cats that is difficult to treat effectively. Some of the cancer cells found within these tumors produce a protein called KIT. Studies involving several types of cancer in people and dogs have shown mutations in this protein. These mutations can lead to cancer formation and increased tumor growth. Successful treatment of these cancers in people and dogs has been achieved through chemotherapy directed at the KIT protein. The purpose of this study is to determine whether these mutations are also present in the cancer cells of cats with fibrosarcoma. If mutations are found, it is possible that use of the same chemotherapy may improve the treatment outcome in cats with fibrosarcomas.

09-031: *Investigation of myxoma virus as an oncolytic agent in feline cancer cell cultures*

Amy L. MacNeill, DVM, PhD, DACVP; University of Illinois Urbana-Champaign; \$15,000

The purpose of this project is to determine whether poxviruses can be used to eliminate cancer cells. Poxviruses have several characteristics that make them ideal cancer therapeutics. Currently this lab has tested several tumor cell lines and many support growth of a poxvirus called myxoma virus. Myxoma virus does not cause disease in any animal except the rabbit; however, it was recently shown that myxoma virus grows in some cancer cell lines. Since myxoma virus only grows in abnormal cells, virus replication in healthy tissue should not occur. Vaccinia virus is another virus that may be useful as a cancer treatment. The effects of virus infection on a large number of feline cancer cell lines will be studied extensively. The investigators hope to show that poxviruses are safe and effective treatments for several types of feline cancer.

09-032: *Molecular pathology of feline oral squamous cell carcinomas*

Susan M. LaRue DVM, PhD, DACVS, DACVR; E.J Ehrhart, DVM, PhD; Colorado State University; \$5,808

Feline oral squamous cell carcinomas (SCCs) account for approximately 10% of all feline tumors. Cats will often have mucosal ulceration and bone necrosis that is painful and interferes with eating and drinking. Cats with these devastating tumors are often euthanized with progression of local disease. The historical failure of treatment of this disease with surgery, chemotherapy, or radiation therapy discourages owners and veterinarians from pursuing treatment. This project will evaluate archived tissue biopsy samples from oral SCCs using immunohistochemistry. Several factors will be analyzed to help characterize the behavior of these tumors. This information can be used to develop more effective treatment protocols using radiation or chemotherapy. There is also the potential for use on pre-treatment biopsies as predictive assays. This will help develop more effective treatment protocols based on tumor biology.

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