2004 Grant Awards
George and Phyllis Miller Trust
San Francisco Foundation
Five studies funded for a total of $68,730

The Winn Feline Foundation is pleased to announce the recent award of five grants funded by the George Sydney and Phyllis Redman Miller Trust. The Trust designated the Winn Foundation as one of its advisor organizations in their desire to "support medical research to investigate the causes, prevention and development of cures for diseases of . . . domestic cats."

Hyposensitization using allergen and CpG motifs for the treatment of feline allergic asthma. Carol Reinero, Leah Cohn; University of Missouri-Columbia; $12,500

Asthma is one of the most common types of lung disease in cats, and can be debilitating or occasionally fatal. There is no cure for this disease, and treatment often relies on high doses of steroids given for the remainder of the cat's life. Some cats become refractory to the effects of steroids and can develop life-threatening asthma attacks. In humans with life threatening allergies, a treatment option called rush immunotherapy (RIT) may be employed to attempt to quickly desensitize the patient to the allergen. High doses of the allergen are administered in the hospital under a doctor's supervision over one to a few days. This procedure causes the body to become resistant to a life-threatening reaction when exposed to the allergen again under natural conditions. Another novel treatment option for asthma is to give CpG motifs, which are components of bacteria that normally serve to warn the body that it has been invaded by potentially dangerous organisms. The body responds by mounting an immune response that also protects against asthma. We have previously shown in an experimental model of asthma that both of these treatments show promise individually. In this current study, we propose to combine both therapies in our model to determine if RIT combined with CpG motif administration is effective in ameliorating the signs of asthma.

Identification of in vitro correlates of differences in virulence between feline calicivirus strains - what determines the increased virulence of feline calicivirus isolated from cats with severe systemic disease? John Parker, Colin Parrish; Cornell University; $20,940

Highly virulent strains of feline calicivirus (FCV) have caused at least six outbreaks of a newly recognized fatal disease in cats. Although these outbreaks have been limited in extent, there is a real risk that these hypervirulent FCV strains will spread to the general cat population. FCV is highly contagious and may persist in the tonsils of infected cats that recover from disease. The goal of our proposed studies is to identify markers by which hypervirulent FCV can be distinguished from the more common, but less virulent FCV strains. Currently, there is no way to distinguish between strains of differing virulence; therefore, the prevalence of hypervirulent FCV in cats cannot be determined and consequently control measures cannot be undertaken to identify and isolate carrier cats. We propose to examine a large panel of FCV strains in the laboratory for differences in selected genetic, physical, and viral growth properties that correlate with their natural virulence for cats. In preliminary studies, we have found that a hypervirulent FCV strain is more stable at room temperature and grows more rapidly in cell culture than less virulent strains. We believe that these differences will be found in other hypervirulent strains. If we are correct, then we will use genetic techniques to identify the specific genome sequence(s) of FCV responsible for hypervirulence with the longer-term goal of developing a simple screening assay to identify hypervirulent strains and determine their prevalence in the general cat population, allowing more effective control programs to be developed.

Critical appraisal of zinc sulfate fecal flotation, enzyme-linked immunosorbent assay, and immunofluorescence for diagnosis of Giardia and Cryptosporidium spp. in naturally infected cats. Stanley Marks; University of California-Davis; $14,865

Diarrhea is an extremely common and clinically significant problem in cats, and the intestinal parasites, *Giardia* and *Cryptosporidium*, play an important role in many of these animals. The detection of these parasites in fecal specimens can be difficult, because the organisms can be shed intermittently, and because their detection can be confused with many artifacts such as grass, pollen, and yeast. The need for accurate identification of these parasites in diarrheic cats often leads to injudicious antibiotic therapy, which can exacerbate the diarrhea. Many veterinarians and reference laboratories have resorted to using alternate tests such as ELISA tests that rely upon a reaction between an antibody in the kit and antigen in the organism to cause a color change that denotes a positive test. However, virtually all of these tests are marketed for use in humans, and their performance characteristics have not been validated in the cat to date. Our preliminary studies have shown that many of these tests have unacceptably low sensitivities. The aim of this study is to evaluate and compare the performance characteristics of 5 ELISA tests with fecal flotation and immunofluorescence in 200 diarrheic cats for the detection of *Giardia* and *Cryptosporidium*. These results will have a direct impact on assisting veterinarians and reference laboratories in proper selection of

diagnostic tests to improve the diagnostic yield of these important parasites and facilitate their proper treatment.

Determination of in vitro susceptibility of feline Tritrichomonas foetus to nitroimidazoles and novel antimicrobials. Stanley Marks; University of California-Davis; $5,425

Tritrichomonas foetus is a parasite that has been identified as an important cause of diarrhea in domestic cats. Infection with *T. foetus* is characterized by a waxing and waning large bowel diarrhea that occasionally contains fresh blood and mucus. The prevalence of *T. foetus* infection at an international cat show was found to be 31% (36 out of 117 cats), with 28 out of 89 catteries affected. Risk factors for protozoal shedding and exacerbation of diarrhea included concurrent infection with *Cryptosporidium* spp., and cats living in close proximity with one another. There is currently no therapy for elimination of the organism and cats may shed protozoa continually in spite of feces returning to normal consistency. A recent report showed that 57% of cats diagnosed with *T. foetus*-associated diarrhea were still shedding the organism up to 3 years following diagnosis, and diarrhea persisted for up to 2 years in many cats, despite aggressive antimicrobial administration. Cats infected with *T. foetus* have failed treatment with recommended and higher dosages of conventional antimicrobial drugs, including metronidazole, fenbendazole, sulfadimethoxine, furazolidone, tylosin, amoxicillin, and paromomycin. The goal of this study is to evaluate the *in vitro* susceptibility of feline *T. foetus* strains to conventional and novel antimicrobial agents in an effort to find a safe and efficacious treatment for elimination of the organism. The novel compounds that will be studied have already demonstrated excellent efficacy *in vitro* against *T. foetus* strains isolated from cattle.

Phase I studies on the heritability of resistance/susceptibility to feline enteric coronavirus infection in randomly-bred, colony reared, domestic cats. Niels Pedersen, Leslie Lyons; University of California-Davis; $15,000

Vaccines have proven ineffective in protecting cats against either feline enteric coronavirus infection (FECV), or its most serious sequel - feline infectious peritonitis (FIP). However, preliminary studies indicate that genetic selection for resistance may be possible. Ten to 20% of FECV infected cats will develop strong immunity and no longer shed virus, while an equal proportion will become persistent fecal shedders. The remainder of cats have an intermediate disease course, i.e. alternating between infection, immunity, loss of immunity and reinfection. These patterns of infection and immunity are best explained by genetic differences in susceptibility/resistance. If so, genetic selection for resistance to FECV might be the most effective means to eliminating or minimizing FIP mortality. The goal of this study is to tap into the resources of a large specific pathogen free domestic cat-breeding colony on the U.C. Davis campus. Accurate records are kept of the matings and progeny of cats in the colony. In a pilot study, 7 adult cats from this colony were experimentally exposed to FECV and their pattern of fecal

shedding followed over 3-1/2 months. One of 7 cats rapidly cleared the infection and remained immune (strong immunity), 4/7 cats underwent repeated cycles of reinfection (waxing and waning immunity), and 2/7 cats became persistent virus shedders (poor immunity). The goal of this phase I study is to create two cohorts of breeding cats, representing the extremes in immunity; 1) cats that develop strong immunity, and 2) cats that remain chronically infected. Cats in each colony will then be bred and kittens tested for their pattern of FECV immunity. Hopefully, progeny will eventually breed true for either resistance or susceptibility. If this can be achieved, future phase II and III studies will look at the genetic basis for resistance and susceptibility. Hopefully, genetic markers may some day be available to identify breeding cats that have excellent or poor FECV immunity.

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