AMERICAN KENNEL CLUB
CANINE HEALTH FOUNDATION
PREVENT TREAT & CURE
SINCE 1995

2016 Research Grants Portfolio

Introduction

Science is moving rapidly in this era of modern technology. While human biomedical research progresses at breakneck speed with more than $30 billion spent annually in the United States alone, our canine partners are often left behind. The AKC Canine Health Foundation (CHF) believes in the advancement of science to meet the unmet medical needs of the dogs who are such an important part of our daily lives.

For 20 years, CHF, with your support, has worked for all dogs to live longer, healthier lives by funding cutting-edge canine health research. Together, we have made progress in addressing specific health needs of dogs through disease surveillance and the development of vaccines to prevent diseases before they strike; the use of novel technologies to diagnose and treat cancer and heart disease, arthritis and epilepsy; and by studying the health and well-being of working dogs – but the needs remain great.

On the following pages, we are proud to present new and active grants, carefully selected and awarded by CHF for the betterment of all dogs. Each grant is reviewed for scientific merit, impact in the field of study, and the significance to our dogs and their people. Through defined program areas of funding, we take into account the information gathered from breeders, dog owners, veterinarians and dog clubs about the most pressing health concerns in dogs. This way, we are confident our research is doing the most good for the most dogs, and making the best use of our donors' contributions.

Science does not work in isolation, but builds from each new finding to bring about better treatments, more accurate diagnoses and an improved understanding of the mechanisms that cause disease. New grants are selected to fill specific areas of unmet need, find medical breakthroughs for particularly stubborn diseases through innovative approaches, and to complement ongoing studies in CHF's canine health research portfolio.

For your ease of review, our grants are classified by research program area, allowing you to identify and support efforts important to you. Program areas also allow us to create depth in areas of research and fund complementary studies that will build a body of work to more effectively advance health outcomes.

We invite you to support these research projects with a donation today – in the manner that best works for you. Please contact us to discuss the many options available. Together, we can move canine health research forward, benefitting the dogs we love today, and the dogs we will love tomorrow.

To discuss a study or to learn about sponsoring research, contact **chfgrants@akcchf.org**.

To view all completed CHF grants, please visit **akcchf.org/research**.

Thank you from our staff, and from the dogs whose lives will be positively impacted by your generosity,

Diane E. Brown, DVM, PhD, DACVP
Chief Executive Officer

Research Program Areas

All Dogs Health Research Program Area

NEW

02235-A

Medical Surveillance of Dogs Deployed to the World Trade Center and the Pentagon on 9/11/01

Principal Investigator: Dr. Cynthia M. Otto, DVM, PhD; University of Pennsylvania
Total Grant Amount: $11,340
Grant Period: 12/1/2015 - 11/30/2016
Project Abstract:

As the investigators wrap up the 14th year of the 9/11 Medical Surveillance Study, they continue to follow 2 surviving deployed dogs and 1 surviving control dog, each of them now 16 years of age. The initial study group consisted of 95 deployed and 55 non-deployed Search and Rescue dogs. Findings to date indicate that overall these dogs have demonstrated good longevity and quality of life. This final phase of the study will monitor the remaining dogs, placing emphasis on health issues occurring in later years of life and necropsy evaluations at time of death. This vital information will allow for a comprehensive understanding of the impact of the deployment and a life spent working Search and Rescue on long-term canine health.

The rate of cancer in deceased deployed dogs to date is not different than in deceased control dogs. Of note, within the deployed dogs, the median age at death was significantly lower for dogs with cancer than the non-cancer group; however, this was not the case with the control group. As the final three dogs approach the end of their natural lives, the investigators will further define any effects of the 9/11 deployment in the full cohort of study dogs. As they analyze the data, a full picture of causes of death and types and incidences of cancer, and long-term impacts of the 9/11 deployment may become clear. Seeing this study through to completion, and publishing the long term findings will provide critical information to canine health that may impact future tactics employed in Search and Rescue missions.

The AKC Canine Health Foundation is proud to have funded Dr. Otto through all 14 years of this important work on behalf of Search and Rescue dogs from its inception in 2001.

Bretagne. Courtesy Denise Corliss.

01943-A

In Support of Our Working Dogs: Medical Surveillance of Dogs Deployed to the World Trade Center and the Pentagon 2013-2014

Principal Investigator: Dr. Cynthia M. Otto, DVM, PhD; University of Pennsylvania
Total Grant Amount: $12,960
Grant Period: 6/1/2013 - 5/31/2016
Project Abstract:

In its twelfth year, the 9/11 Medical Surveillance Study continues to follow the surviving dogs. Of the initial group consisting of 95 deployed and 55 non-deployed search and rescue dogs, 9 deployed dogs and 12 control dogs remain. As these dogs age Dr. Otto will be placing emphasis on health issues occurring in later years of life. Dr. Otto's goal is to obtain a complete picture of causes of death and incidences of cancer so that the long-term impact of September 11th will become visible. This vital information will provide the most inclusive understanding of the impact of the deployment on long-term canine health and will be critical to the future tactics employed in Search and Rescue missions.

NEW

02242

Understanding the Genetics of Adverse Drug Reactions in Sighthounds

Principal Investigator: Dr. Michael H. Court, BVSc, PhD; Washington State University
Total Grant Amount: $150,000
Grant Period: 2/1/2016 - 1/31/2018
Project Abstract:

Life-threatening unanticipated reactions to drugs with a narrow margin of safety (such as those used for anesthesia and to treat cancer) are a common concern for dog owners and veterinarians. However, research conducted at Washington State University has enabled development of a simple cheek swab test (the MDR1 gene test) that is now being used by veterinarians to identify dogs that should either avoid or have reduced doses of certain drugs used to treat cancer and parasite infections. Using a similar strategy the investigators have been conducting research to identify the cause of extremely slow recovery from anesthesia (up to several days) in a high proportion of greyhounds, and also in other sighthound breed dogs (such as Scottish Deerhound, Borzoi, Whippets, etc.). The investigators have recently discovered a mutation in a gene that is known to be essential for metabolism (breaking down) many commonly used anesthetic drugs (such as propofol), as well as many other drugs used in dogs. Interestingly in addition to sighthound breeds, this gene mutation is also found in some other breeds such as Border Collies. The purpose of this research project is to prove that this mutation can cause decreased drug metabolism, while also determining which drugs and which dog breeds are likely to be most impacted. The ultimate goal of this study is to develop a genetic test that could be used by veterinarians to guide the safe use of these drugs in dogs with the gene mutation.

NEW

02231-A

Bioavailability of Suppository Acetaminophen for Treatment of Pain in Healthy and Critically Ill Dogs

Principal Investigator: Dr. Jonathan F Bach, DVM; University of Wisconsin, Madison
Total Grant Amount: $12,761
Grant Period: 10/1/2015 - 9/30/2016
Project Abstract:

Pain control is one of the most important aspects of therapy in aging, critically ill, and hospitalized veterinary patients. Uncontrolled pain in dogs can increase stress, delay recovery, prolong hospitalization, and contribute to complications. Uncontrolled or chronic pain can also be detrimental to a patient's immune system, which further complicates recovery. Because of nausea, vomiting, or reluctance to swallow, geriatric ill dogs may be unable to take pain medication orally. This usually requires veterinarians to administer pain medication by injection, which can be more expensive, create anxiety in the patient, and is difficult in the home environment. Geriatric dogs often do not tolerate other analgesics such as nonsteroidal anti-inflammatory drugs due to vomiting, diarrhea, or gastrointestinal ulceration, and may exacerbate underlying kidney disease. Opioid pain relievers may not be tolerated well in geriatric dogs due to sedation, dysphoria, anorexia, nausea, and vomiting. Acetaminophen (the active ingredient in Tylenol) is effective in treating mild to moderate pain in dogs, and is often administered orally, but can also be administered by rectal suppository. There are no current data on the absorption of suppository acetaminophen in healthy dogs or ill hospitalized dogs to guide dosages. If absorbed well by this route, this medication would provide a practical and inexpensive approach to pain control in dogs that cannot take medication by mouth. This study will assess the absorption and plasma concentrations of acetaminophen as administered rectally by suppository in both healthy and clinically ill canine patients to determine dosing recommendations as a much-needed treatment for pain.

NEW

02228-MOU

Assessing the Genetic Diversity of North American Golden Retrievers

Principal Investigator: Dr. Joshua A Stern, DVM, PhD; University of California, Davis
Grant Amount: $27,612
Grant Period: 1/1/2016 - 12/31/2016
Project Abstract:

The Golden Retriever is a breed of extreme popularity and utility. However, the breed carries an increased risk for disease processes that are either believed or proven to have an inherited/genetic origin. These conditions are often discussed as being linked to a lack of genetic diversity. As the breed strives for type, the diversity may decrease in general, and genetic diseases may inadvertently increase in frequency. This important study will survey the genetic landscape in North American Golden Retrievers to assess the breed's genetic diversity in a sample size of at least 500 dogs. The dogs are from diverse geographic regions and functions, and results will be reported for the entire population as well as by geographic and functional subpopulation. This study will fill in much-needed data around internal relatedness, and develop a genetic test of internal relatedness that may serve as a breeding tool to preserve and maximize genetic diversity within the Golden Retriever breed moving forward in a concerted effort to improve canine health overall.

Funding for the research is provided through the efforts and generosity of the Golden Retriever Foundation. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.

Courtesy AKC Family Dog Photo Contest

02161-A

Supporting the Evidence-Based Use of Antibiotic Gels after Extensive Dental Plaque Removal in Dogs

Principal Investigator: Dr. Django Martel, DVM; The Animal Medical Center
Total Grant Amount: $12,156
Grant Period: 11/1/2014 - 10/31/2016
Project Abstract:

Canine periodontal disease (gum disease) is the most common cause of tooth loss and is a source of chronic bacterial infection, contributing to adverse health conditions including kidney failure and endocarditis. Treatment options are limited and their benefits remain uncertain due to a lack of evidence-based research. The cause of canine periodontal disease is accumulation of plaque under the gum line that leads to inflammation and progressive erosion of normal periodontal structures, including the gums, tooth root and supporting facial bones. The first step in the evolution of gum disease is development of a periodontal "pocket;" a gap between the gum line and tooth margin that traps food and bacteria and promotes continued destruction of these supporting structures. In healthy gums the depth of the periodontal space measures less than 2 mm. With periodontal disease this space becomes larger, and consensus opinion is that deep pockets promote rapid progression of gum disease. Detection of mild pockets (measuring 3-5 mm) indicates that dental disease is present and progressing. A treatment technique called root planing (deep plaque removal) can slow the deepening of periodontal pockets, and veterinarians often consider use of local antibiotic gel therapy placed into the pockets after root planing under the assumption that they retard plaque regrowth and potentially reduce pocket depth. However, this benefit has not been clearly demonstrated in the dog through studies funded independent of corporate-sponsored studies. Dr. Martel and colleagues will establish whether the use of antibiotic gel therapy (doxycycline hyclate gel or clindamycin hydrochloride hydrogel) reduces periodontal disease and provide veterinarians with the evidence needed for effective periodontal disease management.

02103-A

Development of an Effective Canine Periodontal Disease Vaccine

Principal Investigator: Dr. Paola Massari, PhD; Tufts University
Total Grant Amount: $5,630
Grant Period: 1/1/2016 - 4/30/2016
Project Abstract:

Eighty percent of dogs will experience some form of periodontal disease in their lifetime. Halitosis (bad breath) is a minor side effect of disease, but in its more severe form disease can cause gum inflammation, oral bone and tooth loss, all of which are painful and debilitating. Current treatment options include manual removal of plaque and tartar; however, this only delays disease progression and often must be supplemented with antibiotics, anti-inflammatory and pain medications. Periodontitis is caused by infection with oral pathogens including *Fusobacterium nucleatum* and *Porphyromonas gulae*. The most effective targeted interventions against periodontal pathogens will be through effective immunization, directing a dog's own immune system to combat the bacteria responsible for disease. At the current time research efforts on vaccine strategies against canine periodontitis are still scarce compared to human disease. Dr. Massari will investigate a novel vaccine containing purified *Fusobacterium nucleatum* and Porphyromonas gulae bacterial proteins. She believes that dogs immunized with these bacterial proteins and an effective adjuvant (immune enhancer) will generate antibodies against the pathogens. Further, her research group believes that the ideal adjuvant must enhance vaccine efficacy by driving an antibody-mediated response that will not cause cell-mediated inflammation, thereby preventing the exacerbation of oral tissue disruption and pain. Rigorous testing of efficacy and safety of this vaccine in a laboratory setting is required prior to immunization of animals. Therefore, Dr. Massari will conduct proof-of-principle studies with candidate antigens and adjuvants in cell culture, as well as conduct a laboratory mouse model study to determine if their candidate vaccine has the potential to prevent oral infection. This study will guide future studies for vaccine trials designed to prevent periodontal disease in dogs.

Behavior Research Program Area

01995

Understanding the Flexibility and Limitations of How Dogs Acquire Knowledge and Understanding: Application to Service Dog Emotional Health and Selection

Principal Investigator: Dr. Evan L. MacLean, PhD; Duke University
Total Grant Amount: $97,809
Grant Period: 1/1/2014 - 12/31/2016
Project Abstract:

Dogs are being used to help people with mental and physical disabilities in more ways than ever before. There is increasing evidence that trained dogs can dramatically improve the lives of people with a wide variety of disabilities, and the demand for these dogs climbs higher each year. The biggest challenge is increasing the supply of well-trained dogs to serve individuals who will benefit from their help, while at the same time ensuring the reciprocal emotional health of the dogs chosen for service. Dr. MacLean and his colleagues aim to increase the supply of these dogs by improving the ability to identify and train dogs with the greatest potential for success. The Duke Canine Cognition Center and Canine Companions for Independence will work together to identify cognitive traits that predict success during service dog training. They will pose the question: Do a dog's communicative abilities, memory, empathy for humans, or ability to independently solve problems predict success? For the first time, a series of cognitive games will be used to determine which dogs have the cognitive abilities that best predict their abilities to help humans. With this new tool they will be able to more rapidly identify and train the best dogs in order to increase the number of people assisted by our best friends. This research will ensure that we begin to take the steps to understand canine emotional health and well-being in the service dog selection process and beyond.

Blood Disease Research Program Area

NEW

02238-A

Effect of Platelet Count on Platelet Function Tests in Dogs

Principal Investigator: Dr. Elizabeth Spangler, DVM, PhD; Auburn University
Total Grant Amount: $7,650
Grant Period: 1/1/2016 - 12/31/2016
Project Abstract:

Platelets are small blood cells that function to stop excessive bleeding by forming blood clots when injury occurs. Diseases can affect both the number of platelets in the blood stream, as well as how well these platelets work. Both types of disease can cause bleeding which can be life threatening in any dog. Tests that measure platelet function can be affected when the number of platelets is also low. This makes it difficult to assess platelet dysfunction in healthy or sick dogs that also have low platelet counts. The Multiplate™ platelet analyzer is used to measure platelet function. This test is commonly performed in people and there has been much research into interpreting results from human patients with different diseases, including low platelet counts. While

reference intervals exist for healthy dogs, there is no available data on its use in dogs with decreased platelet counts. This study is important because the effect of low platelet counts on the reliability of this platelet function test has not been studied in dogs. This project will contribute important information to help veterinary clinicians accurately assess platelet function in dogs with low platelet counts, thus ensuring proper treatment of canine patients.

Cardiology Research Program Area

NEW

02227-MOU

Identification of Genetic Markers of Pulmonic Stenosis in Bulldogs

Principal Investigator: Dr. Joshua A Stern, DVM, PhD; University of California, Davis
Total Grant Amount: $19,512
Grant Period: 12/1/2015 - 11/30/2016
Project Abstract:

Pulmonic stenosis (PS) is a devastating inherited heart disease of dogs and children. PS is caused by an abnormal fusion or anatomy of the pulmonic valve that limits ejection of blood into the lungs and has severe consequences to the heart muscle and function. Untreated dogs are at risk of sudden death or congestive heart failure, and may die before 5 years of age. Treatment is palliative and aims to stretch or open the narrowed valve region. This treatment is expensive and not always effective at resolving this clinical condition.


Courtesy AKC Family Dog Photo Contest

The Bulldog is extremely overrepresented for cases of PS and the disease is familial. Studying this disease in Bulldogs has the potential to identify a genetic mutation leading to a genetic test for this condition. Ultimately the identification of a mutation in Bulldogs would aid breeders in making responsible decisions to reduce the prevalence of this condition. The first step in this study will be clinical evaluation and genetic sample collection to be followed by a genome wide association study, which looks at genetic markers throughout the entire dog genome. The results from dogs that have the disease are then compared with healthy dogs. The investigators expect to identify a chromosomal region that is likely to contain a mutation for PS in this breed, the first step to reducing the prevalence of this devastating disease in dogs.

Funding for the research is provided through the efforts and generosity of the Bulldog Club of America Charitable Fund. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.

01753

Identification of Genetic Factors That Alter the Severity of Cardiomyopathy

Principal Investigator: Dr. Kathryn M Meurs, DVM, PhD; North Carolina State University
Total Grant Amount: $73,343
Grant Period: 1/1/2013 - 6/30/2016
Project Abstract:

Arrhythmogenic right ventricular cardiomyopathy is a genetic-based heart disease in adult dogs that was recently found to be due to a deletion mutation in the striatin gene. Dogs with this genetic mutation can suffer from irregular heartbeat, loss of consciousness and sudden death. Dr. Meurs' lab has demonstrated that Boxer dogs with 2 copies of a genetic deletion (homozygous) are most likely to have the more severe form of the disease, however dogs with 1 copy of the mutation are more likely to have variable disease wherein some will become quite sick while others will remain free of clinical signs. The mechanism for the variability in clinical signs is unknown, but is thought to be associated with the concurrent inheritance of other genetic factors. Dr. Meurs' research will determine if additional genetic factors exist, thus greatly improving our ability to use and interpret the genetic test for the striatin mutation.

01982

Personalized Medicine: The Intersection of Genotype and Drug Responsiveness in the Treatment of Canine Pulmonary Hypertension

Principal Investigator: Dr. Joshua A Stern, DVM, PhD; University of California, Davis
Total Grant Amount: $27,971
Grant Period: 1/1/2014 - 12/31/2016
Project Abstract:

Genetic background is thought to alter the way animals and humans respond to disease and drug therapy. The unique DNA signature of an individual is now recognized to have a pivotal influence on disease outcome during treatment, and has become the central concept propelling the study of pharmacogenomics and individualized medicine. Dr. Stern will apply this cutting-edge knowledge to pulmonary hypertension in dogs, a common disease with serious consequences including exercise intolerance, respiratory distress, and sudden death. Dr. Stern has identified a mutation in the gene phosphodiesterase 5A (PDE5A), the target of a drug called sildenafil, and believes this mutation may influence

responsiveness of dogs to the drug. Dr. Stern will evaluate the responsiveness of dogs to sildenafil through pre- and post-echocardiogram, identification of biological markers of disease, and quality of life questionnaires. Differences between treatment responses will be compared to genotype with an aim to establish a diagnostic test that allows clinicians to tailor treatment recommendations for individual dogs with pulmonary hypertension.

02046

Using a Novel Combination of Drugs to Treat Arrhythmia and Heart Failure in Dogs

Principal Investigator: Dr. Janice McIntosh Bright, DVM, BSN; Colorado State University
Total Grant Amount: $33,060
Grant Period: 1/1/2014 - 12/31/2016
Project Abstract:

Atrial fibrillation is a common heart rhythm abnormality (arrhythmia) in dogs. This arrhythmia affects all dog breeds and frequently coexists with heart failure causing worsening of disease and high mortality. Atrial fibrillation may be managed by administering drugs to slow heart rate or by restoring normal rhythm (cardioversion). The investigators will evaluate dogs with naturally occurring atrial fibrillation and heart failure for their responsiveness to two drugs -- amidodarone, an antiarrhythmic agent, and ranolazine, a drug used in humans with coronary heart disease to determine whether ranolazine given with amiodarone prolongs normal rhythm compared to amiodarone alone, and whether ranolazine also improves heart function. Results will validate combined ranolazine/amiodarone administration as an improved new treatment for atrial fibrillation in dogs with heart failure, extending their quality of life.

02163-MOU

Is Hypothyroidism a Contributor to Progression of Arrhythmogenic Right Ventricular Cardiomyopathy?

Principal Investigator: Dr. Kathryn M Meurs, DVM, PhD; North Carolina State University
Total Grant Amount: $50,857
Grant Period: 1/1/2015 - 12/31/2016
Project Abstract:

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) in the Boxer dog is an adult onset, familial disease characterized by the presence of ventricular arrhythmias, fainting and sudden death. Dr. Meurs' research group identified a causative mutation in the cardiac Striatin gene that is highly associated with the development of Boxer ARVC. The investigators have demonstrated that some Boxers with the mutation have a more severe form of the disease and will become quite sick while others will remain free of clinical signs. The reason for the variability in clinical signs is unknown but is thought to be associated with concurrent factors for that individual dog which could include genetic or more external factors including diet, exercise and hormonal levels. Genetic factors could include common variants in the nucleotide sequence of other cardiac modifying genes that have been shown to influence the severity of cardiac diseases. In addition, endocrine issues like hypothyroidism complicate ARVC and may play a role in disease progression. Dr. Meurs hypothesizes that low thyroid levels and/or other genetic variants may lead to the development of the more severe form of Boxer ARVC. Understanding the role of these factors in the severity of disease will greatly improve the ability to manage the common and sometimes fatal heart disease of ARVC.

Funding for the research is provided through the efforts and generosity of the American Boxer Charitable Foundation. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.

01760

Use of Gene Therapy to Treat Dilated Cardiomyopathy

Principal Investigator: Dr. Margaret M. Sleeper, VMD; University of Florida
Total Grant Amount: $146,774
Grant Period: 1/1/2015 - 12/31/2016
Project Abstract:

Dilated cardiomyopathy (DCM) is the second most common cause of heart disease in dogs, and medical management of the secondary signs is the only therapeutic option. The outcome for affected dogs depends on the stage of disease and the breed. Once diagnosed, dogs typically exhibit rapid and uniform progression to congestive heart failure (CHF), with most living less than 6 months. Previous research has shown that heart function is critically dependent upon calcium channel function. These gate-like channels found within the wall of cardiac muscle cells open and close, allowing calcium ions to flow into the cell. Calcium influx then regulates muscle contraction. Heart disease is strongly associated with malfunctioning calcium channels within cardiac cells. Gene transfer strategies to reduce calcium cycling abnormalities improve heart function in animal models as well as in human clinical trials. In this study, Dr. Sleeper will conduct a placebo-controlled, double blinded study to evaluate gene delivery approaches for treatment of Doberman Pinschers affected with DCM and CHF. If results show that the gene delivery slows progression of heart failure in Dobermans with DCM, the results will have significant ramifications for all dogs with heart disease, as calcium handling proteins are abnormally expressed in dogs with heart disease of varying causes.

Dermatology and Allergic Disease Research Program Area

NEW

02176-A

Intralymphatic Immunotherapy for the Treatment of Canine Atopic Dermatitis

Principal Investigator: Dr. Andrea Lam, DVM; Tufts University
Total Grant Amount: $12,113
Grant Period: 7/1/2015 - 7/31/2016
Project Abstract:

Atopic dermatitis (AD) is a genetically predisposed inflammatory skin condition affecting approximately 10% of dogs globally and is probably the most prevalent skin disease in all canines. Affected dogs manifest with itchy skin and ears and secondary infections. Clinical features are associated with IgE antibodies produced against indoor/outdoor environmental allergens. Breeds such as Boxers, Terriers, Retrievers, and Bulldogs are predisposed. Current treatment options include antihistamines, corticosteroids, cyclosporine, oclacitinib, and allergen-specific immunotherapy (ASIT), as well as adjunctive topical and antimicrobial therapy. Antihistamines are effective in about 25% of dogs. Corticosteroids are extremely efficacious; however, side effects are common, thus long-term use is strongly discouraged. Cyclosporine is effective in many dogs with few serious adverse effects, but cost can be a limitation in large breed dogs. Oclacitinib has been shown to have good efficacy, but long-term side effects have not been studied. ASIT appears as the only treatment that is able to induce a clinical cure. However, the percentage of atopic dogs that respond to this treatment is only 60-70% and in many, the response is only partial.

It has been proposed that efficacy of subcutaneous ASIT is limited by the ability of the skin to stimulate the immune system. This study will test an alternative route of administration using ASIT for this important skin condition. The investigator will test if direct administration of allergens into a peripheral lymph node may be more effective in stimulating an immunologic reaction, and thereby increasing the response rate, and potentially the cure rate, for canine atopic dermatitis.

NEW

02182-A

Is Defective Secretion of Antimicrobial Peptides Associated with Reduced Microbicidal Effects in Atopic Keratinocytes?

Principal Investigator: Dr. Domenico Santoro, DVM; University of Florida
Total Grant Amount: $12,959
Grant Period: 7/1/2015 - 6/30/2016
Project Abstract:

Antimicrobial peptides (AMPs) are small proteins produced by many organisms. They have multiple functions, the most important of which is the defense against pathogens. The antimicrobial activity of such proteins has been demonstrated against multiple microorganisms. Recently, a lack of secretion of AMPs, after exposure to bacteria in human skin cells harvested from allergic patients, has been hypothesized as a possible cause of recurrent infections in allergic skin conditions. Allergies are common in dogs and frequently associated with recurrent, antibiotic-resistant skin infections. Thus, the identification of ways to boost ability to fight bacteria is important. The investigation of possible changes between healthy and atopic skin cells is fundamental in order to be able to intervene, and make such secretion more effective without the use of synthetic antimicrobials. Thus, the goal of this study is to determine if, like in people, lower AMP secretion is present in skin cells harvested from allergic dogs after stimulation with common cutaneous pathogenic bacteria. The hypotheses to test are 1) whether a lower amount of AMPs are secreted by allergic skin cells compared with healthy ones, and consequently, bacteria are not effectively killed; and 2) if a higher amount of AMPs is retained within the allergic cells. This study has the potential to open the way for a revolutionary approach to treating skin infections that occur secondary to allergies in dogs by increasing the secretion of natural antimicrobial defenses, and thus reducing the use of synthetic and expensive antimicrobials with potential side effects.

NEW

02241

The City Dog Study: Dermatologic and Respiratory Disease among Inner-City Dogs Living in the Homes of Children with Asthma

Principal Investigator: Dr. Meghan F. Davis, DVM, MPH, PhD; Johns Hopkins University
Total Grant Amount: $158,367
Grant Period: 2/1/2016 - 1/31/2019
Project Abstract:

Children who live in inner-city households of low economic means suffer disproportionately from skin and lung diseases, including asthma. This study will evaluate the burden of skin and respiratory disease among the dogs who live with them. These dogs often can be hard to study because their owners may not have the means or access to take them to the veterinarian. As an adjunct to a funded public health research effort targeting 200 children with asthma, Dr. Davis and her team will enroll 100 dogs and follow their health at three home visits over six months, and perform two additional evaluations. First, they will study the microbial (bacterial) communities on the dogs to determine how these change over time, and if the changes are associated with skin or respiratory diseases in the dogs. Then, the investigators will look at how the children and dogs share bacteria (i.e. microbiome). Early life exposures to dogs may protect children against the development of asthma, so next will be to investigate if dogs also have a beneficial impact when the children are older and have existing disease. This study will provide knowledge needed to help understand disease in underserved dogs in urban neighborhoods, providing data to support keeping dogs and keeping them healthy to benefit both dogs and their owners.

Endocrinology Research Program Area

01602

Defining the Cause of Hyperadrenocorticism

Principal Investigator: Dr. Kurt Zimmerman, DVM, PhD; Virginia-Maryland Regional College of Veterinary Medicine
Total Grant Amount: $66,226
Grant Period: 1/1/2012 - 6/30/2016
Project Abstract:

Hyperadrenocorticism (HAC) is a chronic debilitating disorder in dogs and contributes to the development of negative health and behavior outcomes including diabetes mellitus, obesity, musculoskeletal weakness, immune system dysfunction, and inappropriate urination. Increased serum alkaline phosphatase (ALP) activity and increased non-cortisol steroids are associated with HAC. By studying Scottish Terriers (due to their predisposition to atypical HAC), Dr. Zimmerman will: 1) determine if the severity of the HAC increases over time; 2) determine if HAC is due to a functional problem of the brain or adrenal gland itself; and 3) determine if there is a problem with steroid production in the adrenal gland. These efforts will help us understand breed predisposition to developing atypical HAC, and how to best treat and screen for this disorder.

02138

Development of Accurate Diagnostic Tests for Canine Hypothyroidism

Principal Investigator: Dr. Jan A Mol, PhD; University of Utrecht
Total Grant Amount: $48,195
Grant Period: 11/1/2014 - 4/30/2016
Project Abstract:

Primary hypothyroidism is one of the most common endocrine disorders in dogs. The insufficient secretion of thyroid hormones may result in severe physical and mental changes, such as lethargy, alopecia, obesity, decreased cardiac output, and decreased renal perfusion. The diagnosis of hypothyroidism is sometimes problematic. The circulating thyroxin (T4) concentration is below the reference range in most dogs with primary hypothyroidism, but T4 is not very specific as it can also be low in sick dogs with a normal thyroid function, i.e., dogs with non-thyroidal illness (NTI). However, a combination of a low T4 concentration and a clearly elevated plasma thyroid stimulating hormone (TSH) concentration is a definitive proof of hypothyroidism. Unfortunately, about 30% of dogs with primary hypothyroidism have a TSH concentration within the reference range and therefore cannot be distinguished from dogs with NTI. Consequently, either dogs with NTI are unnecessarily treated with thyroxin supplementation or dogs with primary hypothyroidism may lack proper treatment. Dr. Mol and colleagues propose to investigate 3 methods that may provide a more accurate diagnosis than the currently available tests for practitioners. They will test whether 1) a stimulation test with measurements of plasma growth hormone and TSH concentrations, 2) the plasma TRH or ghrelin concentration, or 3) a reporter assay for plasma thyroid hormone bioactivity, can be used to differentiate between dogs with primary hypothyroidism and dogs with NTI.

Epilepsy Research Program Area

02131

Neurostimulation: A Groundbreaking New Treatment for Canine Epilepsy

Principal Investigator: Dr. Sam Nicholas Long, BVSc, MVM, PhD, MRCVS; The University of Melbourne
Total Grant Amount: $116,000
Grant Period: 10/1/2014 - 9/30/2016
Project Abstract:

Epilepsy is a debilitating condition that affects a large number of dogs, resulting in premature death and distress for their owners. For many dogs the underlying cause is unknown. In people, advances in some types of imaging have identified subtle abnormalities, including abnormal development and shrinkage of particular regions in the brain of some people with epilepsy that can be surgically removed to improve the control of seizures. This project will apply the same advanced techniques to the brains of dogs with epilepsy to determine whether those same abnormalities exist in dogs. In those dogs in which no abnormalities can be found, this project will investigate a new form of treatment, known as neurostimulation, which has been shown to reduce the frequency of seizures dramatically in human clinical trials. This involves surgically implanting a new, highly sophisticated device called the Brain Radio that can provide controlled electrical stimulation to parts of the brain while simultaneously recording the brain's activity. This device is one of the very first that could potentially provide successful therapy only when needed to treat imminent seizures, and if it proves successful in dogs, will enter clinical trials in people with epilepsy.

02133

Canine Epilepsy: Genetic Variants, Biomarkers, and New Therapies

Principal Investigator: Dr. Ned E. Patterson, DVM, PhD; University of Minnesota
Total Grant Amount: $104,781
Grant Period: 10/1/2014 - 9/30/2016
Project Abstract:

Epilepsy is a significant seizure disorder affecting all dog breeds. It is the most common chronic nervous system disorder in dogs, with a prevalence of 0.5% - 5.7%, resulting in approximately 2 million affected dogs in the USA. We have assembled a cross-disciplinary team in an effort to improve the fate of dogs that have epilepsy, with a special emphasis on dogs with drug-resistant epilepsy. Dogs with drug-resistant epilepsy have frequent seizures even when treated with two or more anti-epileptic drugs. The team includes Veterinarians, Canine Geneticists, Pharmacologists, Human Neurologists, Basic Scientists and Biomedical Engineers from the University of Minnesota College of Veterinary Medicine, College of Pharmacy, Institute for Engineering in Medicine, Departments of Neurology and Surgery, and Mayo Clinic in Rochester, MN. Under the guidance of Dr. Patterson, the collaborative group will evaluate traditional DNA genetic markers, blood biomarkers called microRNAs (miRNAs), and potential new drugs for the emergency treatment of seizures in dogs.

In phase 1 of the study, the team will 1) Identify genetic markers associated with epilepsy in Australian Shepherds and Vizslas, and identify markers associated with epileptic dogs that are unresponsive to anti-epileptic drug therapy to develop genetic screening tests in phase 2; and 2) Document microRNA levels in the blood of dogs with epilepsy to develop potential blood markers that vary between epileptic and non-epileptic dogs, and dogs with drug-resistant epilepsy; and 3) Perform initial testing of two new potential drugs for the emergency treatment of canine epilepsy.

Gastrointestinal Disease Research Program Area

01609

Use of Probiotic to Reduce the Symptoms of Inflammatory Bowel Disease

Principal Investigator: Dr. Albert E. Jergens, DVM, PhD; Iowa State University
Total Grant Amount: $97,416
Grant Period: 1/1/2012 - 6/30/2016
Project Abstract:

Idiopathic inflammatory bowel disease (IBD) is a common cause of chronic gastrointestinal disease in dogs. Accumulating evidence in human IBD and animal models suggests that imbalances in composition of the intestinal microbiota contribute to the pathogenesis of chronic intestinal inflammation. Recent studies have also shown that dogs with IBD have distinctly different duodenal microbial communities compared to healthy dogs. Current treatments for IBD include the administration of nonspecific anti-inflammatory drugs which may confer serious side effects and do not address the underlying basis for disease, namely, altered microbial composition. Use of probiotics (viable, non-pathogenic bacteria that exert health benefits beyond basic nutrition) offers an attractive, physiologic, and non-toxic alternative to shift the balance to protective gut bacterial species to treat IBD. The researchers will study the clinical, microbiologic, and anti-inflammatory effects of probiotics for the treatment of canine IBD. These studies will provide highly relevant insight into the anti-inflammatory effects of probiotics for treatment of human and canine IBD.


Courtesy AKC Family Dog Photo Contest

02002

Defining the Genetic Basis of Inflammatory Bowel Disease

Principal Investigator: Dr. Karin Allenspach, DVM, PhD; Royal Veterinary College, University of London
Total Grant Amount: $119,268
Grant Period: 10/1/2014 - 9/30/2016
Project Abstract:

Inflammatory Bowel Disease (IBD) is a group of disorders in which the intestinal tract has become invaded with the dog's own white blood cells, leading to inflammation. Over time, this inflammation causes the intestine to become less efficient at absorbing nutrients from digested food, and weight loss and vomiting or diarrhea often result. Currently, IBD can be controlled, but not cured. The cause of IBD is poorly understood, but it appears that genetics, diet, intestinal bacteria, and abnormalities of the dog's immune system all may play a role. Dr. Allenspach has recently identified genetic markers known as SNPs (single nucleotide polymorphisms) which she believes contribute to disease susceptibility. Beyond genetics, this research group has mechanistic data showing one of the putative mutations contributes to the inflammation seen in the intestine of dogs with IBD. In order to find all underlying genetic factors that could contribute to disease, they will perform a genome-wide association study. This study will lead to the development of new diagnostic and therapeutic avenues for canine IBD as has already been ongoing in people with IBD.

02050

Defining the Genetic Susceptibility to Granulomatous Colitis, a Severe Form of Inflammatory Bowel Disease

Principal Investigator: Dr. Kenneth W. Simpson, BVMS, PhD; Cornell University
Total Grant Amount: $187,730
Grant Period: 1/1/2014 - 6/30/2016
Project Abstract:

Granulomatous colitis is a severe inflammatory bowel disease (IBD), usually diagnosed in young dogs. Affected dogs present with hemorrhagic diarrhea, often progressing to weight loss and debilitation. Recent studies have identified invasive *Escherichia coli (E. coli)* bacteria within macrophages in the inflamed large intestine, and eradication of *E.coli* induces dramatic clinical and histologic improvement. Unfortunately, the emergence of antimicrobial resistance has greatly reduced our ability to treat this disease, and persistently affected dogs are frequently euthanized. The type of *E.coli* isolated from dogs with granulomatous colitis is very similar to adherent and invasive *E.coli*(AIEC) associated with IBD in people. This type of *E.coli* is considered opportunistic, and can exploit genetic defects in bacterial killing in an IBD susceptible individual. Dr. Simpson suspects this is due to a heritable abnormality that confers susceptibility to invasion and persistence of *E.coli*. In preliminary studies his research group has identified a region of the canine genome that is associated with granulomatous colitis in affected dogs. This region contains candidate genes associated with IBD in people and mouse models, and has been specifically linked to sensing and killing of *E.coli*. In this study, the investigators will identify the gene(s), causal variant(s) and cellular pathways involved in the development of granulomatous colitis. This will enable the development of screening tests to eradicate this disease, and advance understanding of the development of IBD in dogs and people.

Bloat Initiative Grants

01935-B

Abnormalities in the Stomach's Ability to Contract Predisposes Large-Breed Dogs to Bloat

Principal Investigator: Dr. Laura L. Nelson, DVM; Michigan State University
Total Grant Amount: $233,774
Grant Period: 1/1/2014 - 6/30/2016
Project Abstract:

Gastric dilatation-volvulus (GDV or bloat) is a devastating disease common in large and giant-breed dogs. Occurring most frequently in older dogs with a close relative who has also suffered the condition, the stomach becomes both displaced and distended with air. Without emergency medical stabilization and surgical intervention, affected dogs quickly experience shock, damage to the stomach wall, and death. Most of the research relating to GDV has described risk factors for the disease, determinants of outcome with treatment, and the effectiveness of preventive surgery (gastropexy). However, the underlying cause of GDV remains unknown. Abnormalities in the ability of the stomach to contract have been documented in dogs after naturally-occurring GDV. An analogous stomach condition in cattle, left-sided displacement of the abomasum (LDA) has been shown to, in some instances, be associated with abnormalities in the motilin gene. Motilin is an important driver of stomach contraction. This suggests that LDA and potentially GDV may be primarily caused by a stomach that does not properly contract, and that this condition may be inherited. This study will help to determine the relationship between abnormal stomach contraction and GDV, and to define the biochemical and genetic alterations that may be associated with these stomach abnormalities. The long term goal is to develop a test to identify dogs at high risk for GDV. This would allow for early detection and offer selective breeding as an option to eliminate the condition and determine best preventive therapies.

01937-B

Evaluating the Complex Genetic Basis of Bloat

Principal Investigator: Dr. Elizabeth A Rozanski, DVM; Tufts University
Total Grant Amount: $251,097
Grant Period: 1/1/2014 - 12/31/2016
Project Abstract:

Gastric dilatation and volvulus (GDV), or bloat, is a common condition in large and giant breed dogs with an unacceptably high morbidity and mortality rate. Due to the importance of GDV in many dog breeds, several previous studies have investigated potential risk factors for the development of GDV. It is known that there is no single cause for GDV, rather its occurrence is multifactorial, with both genetic and environmental factors likely contributing. This study will allow for further investigation of how these risk factors cause GDV through the application of genomic and molecular methods. Samples from purebred dogs with

GDV will be analyzed and compared to control dogs of similar age and breed that have not developed GDV. A genome wide association study (GWAS) will help to identify differences in the genetic makeup of dogs with GDV, and see which genes are turned on and off in GDV (epigenomics). The study will also determine if dogs with GDV have different types or amounts of proteins, hormones and other molecules in their blood and tissues (transcriptomics, proteomics and metabolomics). The investigators hypothesize that only when all of this information is considered together (genomic, epigenomic, transcriptomic, proteomic and metabolomic) will we truly understand what causes GDV, and guide more effective preventive and treatment strategies.

NEW

02233-A

Evaluation of a Novel Technique for Gastric Decompression in Dogs with Gastric Dilatation and Volvulus

Principal Investigator: Dr. J. Brad Case, DVM, MS; University of Florida
Total Grant Amount: $12,960
Grant Period: 11/1/2015 - 4/30/2017
Project Abstract:

Gastric dilatation-volvulus (GDV) is a common medical and surgical emergency that involves severe gas distention and malposition of the stomach in dogs. GDV results in profound distension of the stomach which compresses vital blood vessels and organs within the abdomen, thus reducing oxygen delivery to these organs. The ultimate result is tissue death and toxins in the blood stream. Surgery is necessary to correct the condition, and overall mortality rates range from 10-50% depending on severity and duration of gastric dilatation. For this reason, rapid and effective decompression of the stomach is critical for successful treatment of dogs with GDV. Currently, approaches to decompression have a temporary effect and gas can re-inflate the stomach within minutes. Oftentimes affected dogs are not near a facility with surgical capabilities when they develop signs of GDV. Owners may then need to drive hours to a facility in which emergency stabilization and surgery can be performed.

A new, minimally-invasive technique, similar to that used in human medicine, will be tested for its ability to immediately and continuously alleviate the gas distention in the stomach of GDV patients using a specialized catheter, thus allowing the patient to be stabilized and/or transported for surgery. This much-needed, relatively inexpensive and rapid procedure could have far-reaching impact for dogs with this devastating condition.

Courtesy AKC Family Dog Photo Contest

Immunology and Infectious Disease Research Program Area

02128-A

Redefining the Recommendations for Prevention of Infectious Disease at Dog Shows and Other Areas Where Dogs Meet and Compete

Principal Investigator: Dr. Jason Stull, VMD, PhD; Ohio State University
Total Grant Amount: $11,942
Grant Period: 7/1/2014 - 8/31/2016
Project Abstract:

Collaborative Grant between the Orthopedic Foundation for Animals and AKC Canine Health Foundation

The AKC Canine Health Foundation and the Orthopedic Foundation for Animals have a long standing commitment to support research that aims to prevent, treat, and cure canine disease. As the sport of dogs increases in popularity, we realized that one major gap in our current body of knowledge is how to reduce the risk of infectious disease spread at the intersection of the dog and the environment. Put another way, now that more and more large groups of dogs congregate at dog shows, agility events, field trials, animal shelters and dog parks, where are the risks and how should we manage them? Dr. Jason Stull and colleagues at the Ohio State University and Ontario Veterinary College will conduct a retrospective analysis of the veterinary infectious disease literature in order to provide updated recommendations for mitigation of risk of contraction of infectious disease at events where dogs congregate. Lead by Dr. Stull, this influential collaborative group of veterinary epidemiologists, infectious disease experts, immunologists, and internal medicine specialists will evaluate peer reviewed studies defining the incidence, clinical presentations, and outcomes of diseases; mechanism of infection, replication, spread and/or pathogenesis of diseases, computer modeling of disease transmission, characterization of susceptible cohorts for particular pathogens, and emerging concerns for novel pathogens to assess risk and develop management strategies. They will also include major stakeholders within the dog community in the process, guaranteeing that recommendations made at the outcome of this study will be practical and possible to accomplish in the 'real world'. The end result will be a peer-reviewed publication defining an up-to-date risk assessment and management recommendations, and most importantly, a white paper that can be used by dog owners and organizers of canine events and facilities. Finally, the researchers aim to create an open-access website that will be an interactive, living document, helping all those involved with dogs reduce the risk and spread of infectious disease where dogs meet and compete.

NEW

02180-A

Exploring the Canine Immune System for New Treatments

Principal Investigator: Dr. Christine A Petersen, DVM, PhD; University of Iowa
Total Grant Amount: $12,960
Grant Period: 10/1/2015 - 9/30/2016
Project Abstract:

Recent studies show the presence of resistant infections in dogs and the ability of these infections to spread between a dog and its family. New treatment options are needed, and development of non-antibiotic antibacterial agents, or immunotherapy, is critical to progressing treatment for potentially fatal infections. This project will use cutting edge immunology to better understand how special regulatory immune cells (B10 B cells) in hunting Foxhounds with naturally-occurring Leishmania infections might be reprogrammed to help fight infections. These unique immune cells are thought to alter the course of human diseases such as malaria, lupus, and arthritis. Dogs have an immune system very similar to humans and, unlike mice, represent a way to investigate and further understand these cells in naturally-occurring infections in dogs; findings that will also translate to human health. This innovative research will expand our understanding of how regulatory B cells could be modulated to control infections, ameliorate canine allergy and dampen autoimmune diseases like lupus and thyroid disease, and thus may also identify targets for much-needed new therapies for dogs.

NEW

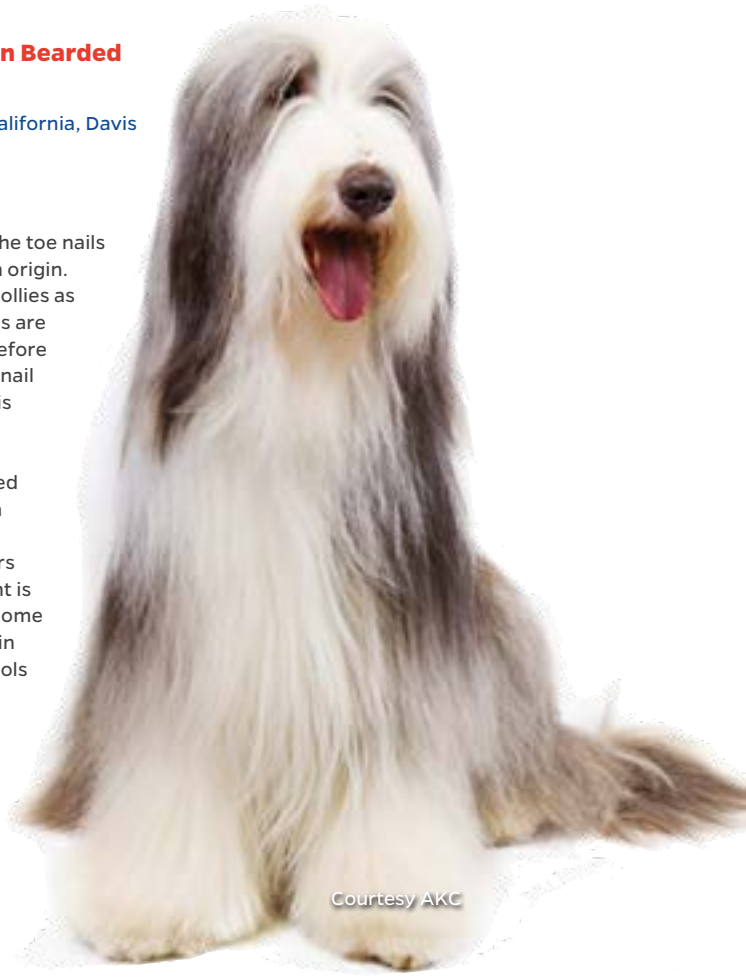
02187-MOU

Investigating Symmetrical Lupoid Onychodystrophy in Bearded Collies

Principal Investigator: Dr. Anita M. Oberbauer, PhD; University of California, Davis
Total Grant Amount: $9,072
Grant Period: 7/1/2015 - 6/30/2016
Project Abstract:

Symmetrical lupoid onychodystrophy (SLO) is a chronic problem of the toe nails seen in a number of dog breeds, and is believed to be autoimmune in origin. It is the second most common autoimmune disease in the Bearded Collies as per the Bearded Collie BeaCon's Open Health Registry: ~3.5% of dogs are reported as having the condition and of those, 88% are diagnosed before the age of 8 years. Affected dogs display loose nails, bleeding at the nail beds, loss of nails, splitting nails, and significant pain. The condition is difficult to treat showing variable response to treatment. In all cases the nails must be removed when the condition first presents. Some dogs show complete recovery (rare) whereas others require sustained treatment with immune modulators, whereas others show remission followed by recurrence with nails needing to be removed again. The precise cause of the condition remains unclear with numerous factors potentiating expression of the disease although a genetic component is strongly suspected. In this study, Dr. Oberbauer will undertake a genome wide association study to identify genetic regions that underlie SLO in the Bearded Collie. The ultimate goal will be to develop diagnostic tools to aid in reducing the incidence of SLO through genetic testing.

Funding for the research is provided through the efforts and generosity of the Bearded Collie Foundation for Health. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.



Courtesy AKC

01771

Defining the Unique Genetic Markers in Dogs That Define Immune Function, Disease Resistance and Tissue Transplantation

Principal Investigator: Dr. Beverly Torok-Storb, PhD; Fred Hutchinson Cancer Research Center
Total Grant Amount: $178,200
Grant Period: 1/1/2013 - 6/30/2016
Project Abstract:

The Major Histocompatibility Complex (MHC) genes encode proteins that are critical for a wide range of biological functions, from immune protection against infectious disease to the predisposition of an individual to develop diabetes and auto immune diseases. The MHC genes in the dog are incompletely characterized, thereby severely limiting our ability to fully define the cause of many canine diseases. The investigators have developed improved methods for identifying the different forms of canine MHC genes in a large number of dogs of diverse breeds. In this study they will characterize the patterns of MHC genetic variation in over 1200 dogs from at least 50 breeds using a high throughput sequencing strategy. The distribution and frequency of different forms of each of these genes and their specific clustering among different breeds will greatly enhance our knowledge of the genetic diversity among breeds. The methodology and data gained from this study will enhance the power of association studies between MHC types and canine diseases. Such a database will also enable tissue transplantation from unrelated but matched donors as a treatment for advanced malignancies (stem cell transplants) and other diseases (tissue transplantation). Fully defining the canine MHC will have broad impact across canine health, including oncology, immunology and infectious disease.

Lung and Respiratory Disease Research Program Area

NEW

02232-MOU

Characterization of Upper Airway Syndrome in Norwich Terriers

Principal Investigator: Dr. Bryden J. Stanley, BVMS; Michigan State University
Total Grant Amount: $74,496
Grant Period: 11/1/2015 - 10/31/2017
Project Abstract:

Breeders have long known of upper airway issues in Norwich Terriers (NTUAS) while veterinary awareness and recognition of NTUAS, has often lagged behind. Signs of disease can vary from mild airway noise to severe distress with heat and exercise intolerance, and death. Descriptions of NTUAS have focused on everted laryngeal saccules (outpouched laryngeal tissue), likening it to issues seen in brachycephalic dogs. However, recent evidence shows changes in the larynx that are not seen in brachycephalic dogs: redundant tissue at the top of the larynx, and narrowing of the larynx behind the glottis. The entire upper airway needs to be clearly described for NTUAS, and it is likely that the condition is separate from brachycephalic airway syndrome, with distinctive, primary changes arising in the larynx.

In this study, NTUAS will be characterized in detail through comprehensive history, oral examination and upper airway endoscopy in 150 US Norwich Terriers. Results will be used to create a NTUAS severity grading system. A subset of 25 of the dogs will additionally undergo computed tomography and nasal airflow measurements. Results will be compared for 25 Norfolk Terriers, 25 brachycephalic and 25 mesaticephalic dogs of similar ages from a separately funded study. Identifying the contributory components of NTUAS is the first step in determining prognosis and evaluating treatment options. This work will lay the groundwork for future research to follow the youngest dogs in the study throughout their lives, and to examine the effect of time and treatment on NTUAS.

Funding for the research is provided through the efforts and generosity of Norwich Terrier Club of America. The AKC Canine Health Foundation supports this effort and will oversee administration of funds and scientific progress reports.

Musculoskeletal Conditions and Disease Research Program Area

NEW

02226-A

Pilot Clinical Trial to Test the Efficacy of Mesenchymal Stem Cells Over-Expressing IL-10 to Treat Osteoarthritis in Elbows of Senior Dogs

Principal Investigator: Dr. Fernando A Fierro, PhD; University of California, Davis
Total Grant Amount: $12,954
Grant Period: 10/1/2015 - 8/31/2016
Project Abstract:

Osteoarthritis (OA) is characterized by both chronic inflammation and structural defects in cartilage and subchondral bone. Mesenchymal stem cells (MSC) have become ideal candidates for therapy, because these cells could contribute to the treatment of OA in two ways: they can differentiate and replace the damaged cartilage and bone, but also secrete key signals that regulate the immune system. In fact, at least 13 early-stage human clinical trials are underway and three canine trials have been completed testing the delivery of MSCs into patients with OA. Certainly, this approach has, and is expected to demonstrate, a satisfactory safety profile. However, to date, clinical efficacy has been poor, due to an insufficient contribution from the cells. Dr. Fierro and team propose an optimized treatment for OA by combining cell and gene therapies which will induce the expression of the anti-inflammatory cytokine interleukin 10 (IL-10) in canine adipose tissue derived-MSCs. This approach is based on the research team's experience on a planned first-in-human Phase I clinical trial with a very similar approach, strictly adhering to the same safety profile requested by both clinicians and regulatory agencies. The main goal of this proposal is to conduct a pilot study in four senior dogs, injecting 5-7 million MSC/IL-10 cells (carried in 0.5 ml hyaluronic acid) into one elbow with more severe OA. The proposed outcome measurements are objective and rely on the latest technology. With this pilot study, the investigators expect to demonstrate both safety and efficacy of MSC therapy for this important unmet clinical need, and ultimately find a cure for OA in senior dogs.

NEW

02229-A

TPLO Surgery and Recovery: A Comparison of Arthroscopy and Arthrotomy

Principal Investigator: Dr. Andrea Sundholm-Tepper, DVM; Washington State University
Total Grant Amount: $12,960
Grant Period: 11/1/2015 - 8/31/2016
Project Abstract:

Cranial cruciate ligament (CrCL) rupture is the most common stifle (knee) condition in many breeds of dogs. Surgery is recommended to provide stabilization of the stifle and allow the patient to be free of lameness. Although several surgical procedures are available, all require examination and potential manipulation of damaged ligaments and cartilage inside the stifle joint. Traditionally, an incision (arthrotomy) into the joint was required; however, since the late 1990's, arthroscopy (using a small fiber optic camera placed into the joint) has been available in veterinary surgery. In human patients, arthroscopy is associated with lower costs and infection rates, and decreased morbidity (patient-related negative effects) compared to arthrotomy. Arthroscopy in dogs can be combined with many CrCL rupture surgeries including the Tibial Plateau Leveling Osteotomy (TPLO). Currently, clinical impressions are that dogs undergoing stifle arthroscopy are more comfortable and using their limbs sooner post-operatively than dogs undergoing arthrotomy for CrCL rupture surgery. To date, there is limited evidence to support this claim. This study will objectively measure and compare the recovery of dogs with CrCL rupture treated by TPLO with arthroscopy or arthrotomy. These findings will inform the decision-making process for stifle surgical procedures (arthrotomy or arthroscopy) to the veterinary and dog-owning communities.

01828

Mapping of Genetic Risk Factors for Canine Hip Dysplasia

Principal Investigator: Dr. Antti Iivanainen, DVM, PhD; University of Helsinki and the Folkhälsan Institute of Genetics
Total Grant Amount: $79,488
Grant Period: 1/1/2014 - 12/31/2016
Project Abstract:

Canine hip dysplasia is a common developmental disorder of the hip joint that severely affects a dog's quality of life. As the disease has several genetic risk elements and is influenced by environmental factors like diet and exercise, it is of paramount importance that genetic association studies are conducted using adequately-sized cohorts of genotyped diseased and healthy animals. Dr. Iivanainen will sample a large population of dogs (>300-400 dogs) so that contributing genetic loci can reliably be discovered. This research group expects that with such a strongly powered study all major genetic risk factors can be uncovered with a high statistical significance. Investigators expect that identified loci will be discovered across breeds. The identification of genetic risk elements will allow the development of genetic tests that can be used in breeding programs to control the disease incidence, as well as further studies regarding the possible role of diet and exercise in hip dysplasia development.

CANINE ATHLETE INITIATIVE!

02078

Development of a Regenerative Medicine Technique to Treat Cartilage Disorders in Dogs

Principal Investigator: Dr. William Brian Saunders, DVM, PhD; Texas A&M AgriLife Research
Total Grant Amount: $120,872
Grant Period: 1/1/2014 - 12/31/2016
Project Abstract:

Osteochondrosis is a common and debilitating disease affecting large, athletic dogs. Osteochondrosis is caused by abnormal endochondral ossification, the process by which growth plate cartilage adjacent to joint surfaces transitions from cartilage to bone. The result is excessively thickened cartilage that partially or completely separates from surrounding bone. Cartilage separation exposes the joint to underlying bone and creates a large loose body, termed a joint mouse, within the joint. Surgical or medical treatment results vary widely based on the affected joint, size of the osteochondrosis defect, and intended purpose for each dog. Treatment options for osteochondrosis have remained essentially unchanged for decades. Tissue engineering represents a promising treatment alternative for dogs suffering from osteochondrosis. Dr. Saunders believes the key to successful tissue engineering involves generation of regenerative osteochondral plugs, or ROPs. ROPs are tri-layered cylindrical plugs composed of hydrogels seeded with adult mesenchymal stem cells (MSCs). Each ROP layer is composed of materials that closely mimic specific zones of the joint and adjacent bone. ROP layers are bioactive, directing encapsulated MSCs to differentiate into specific tissues to more efficiently restore normal joint anatomy. Dr. Saunders will optimize the materials used to generate ROP layers and will determine if MSCs from tissue lining the joint (synovium) or inner cavity of bones (bone marrow) more effectively reconstruct native cartilage, transitional tissue, or bone. This work represents an important advance in canine regenerative medicine and is highly applicable to dogs with osteochondrosis or other common joint ailments such as osteoarthritis.

CANINE ATHLETE INITIATIVE!

02107

Landmark Clinical Trial to Establish the Evidence-Based Use of Regenerative Medicine to Treat Tendon Injury in Dogs

Principal Investigator: Dr. Jennifer G. Barrett, DVM, PhD; Virginia-Maryland Regional College of Veterinary Medicine
Total Grant Amount: $254,509
Grant Period: 7/1/2014 - 6/30/2016
Project Abstract:

Regenerative medicine is a rapidly developing field with the potential to transform the treatment of canine disease. The ability to repair damaged tissue and treat diseases once believed to be incurable may soon be a reality. However, there are concerns that some techniques are being used prematurely. Due to the lower regulatory barriers in veterinary medicine, company-sponsored

regenerative medicine products and techniques are currently used in general practice and specialty hospitals without the benefit of having been preceded by stringently controlled, independently funded clinical trials. As a result, techniques vary widely and the evidence that they work is anecdotal at best. The AKC Canine Health Foundation has made the evidence-based practice of regenerative medicine a major focus within our research portfolio. Through an ongoing commitment to fund research studies that will inform the veterinary community in the use of safe and effective regenerative medicine techniques, we intend to protect dog owners and support veterinarians with innovative technology that will consistently improve outcomes for dogs.

In support of our effort to provide evidence-based regenerative medicine research, CHF is funding this landmark study to evaluate the effectiveness of Platelet-Rich Plasma (PRP) and stem cells in the treatment of the most common sporting injury in dogs: supraspinatus tendinopathy (similar to the rotator cuff injury in humans). Tendon injuries in dogs often progress undiagnosed and result in chronic lameness and pain. Ultimately, unassisted tendon healing results in scar formation and reduced function of the joint and surrounding muscle tissue. PRP and stem cell therapies aim to accelerate and promote healing through tissue regeneration and reduced scarring. The investigators will conduct the first randomized, placebo-controlled clinical trial evaluating the effectiveness of PRP, adipose-derived, cultured stem cells (ASC) and commonly used stromal vascular fraction (SVF) cells. This will be the first study to directly compare efficacy of intratendinous injection of ASC versus SVF, both of which are currently commercially available despite having limited scientific evidence of efficacy. The study will be conducted to recruit real-world cases in a clinically relevant, state of the art canine sports medicine environment. Using the gold-standard 'Blinded, Placebo Controlled' clinical trial design, Drs. Barrett and Canapp will not only identify an effective treatment for supraspinatus tendon injury, but their research will have a profound impact on the treatment of a wide array of musculoskeletal conditions affecting dogs and humans.

Neurology Research Program Area

02165-MOU

Identification of Biomarkers and Therapeutic Targets for Canine Degenerative Myelopathy: The Search for A Cure

Principal Investigator: Dr. Joan R. Coates, DVM; University of Missouri, Columbia
Total Grant Amount: $154,077
Grant Period: 1/1/2015 - 12/31/2016
Project Abstract:

Degenerative myelopathy (DM) is an adult onset disease of the spinal cord causing progressive weakness and paralysis of the hind limbs and eventually all limbs. Mutations in an enzyme that converts superoxide to water and hydrogen peroxide, superoxide dismutase 1 (SOD1), have been linked to DM and amyotrophic lateral sclerosis (ALS-Lou Gehrig's disease). DM is associated with degenerative loss of axons, which transmit signals from the brain and spinal cord to their targets (muscle). Currently no diagnostic test exists that would allow for repeated measurements with minimal invasiveness. Dr. Coates will develop a test to assay the blood and cerebrospinal fluid (CSF) for proteins that are exclusively found in axons under non-disease conditions, referred to as neurofilament proteins. They will correlate the concentrations of neurofilament proteins in CSF and blood with disease stage, and anticipate that neurofilament protein concentration in blood and CSF will increase as disease progresses. Such a test will allow for minimally invasive monitoring of disease. Furthermore, such a diagnostic test could be used to measure the success of therapy, which is underway in a cohort of DM-affected dogs [Boxers and Pembroke Welsh Corgis (PWC)] (funded by NIH/NINDS). They will complement the test for neurofilament proteins with other studies that measure disease progression such as specific MRI techniques to evaluate the brain and spinal cord and electrical testing of the muscle and nerves. These functional disease markers are also being studied in human ALS patients.

Funding for the research is provided through the efforts and generosity of the American Boxer Charitable Foundation. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.

NEW

02210

Gene Therapy for Canine Degenerative Myelopathy

Principal Investigator: Dr. Brian K Kaspar, PhD; The Research Institute at Nationwide Children's Hospital
Total Grant Amount: $50,000
Grant Period: 1/1/2016 - 12/31/2018
Project Abstract:

Degenerative myelopathy (DM) is a devastating neurodegenerative disease that affects multiple breeds of dog. DM is an adult-onset disease that manifests at the later stages of life. It is characterized by progressive weakness and inability to control the hind limbs, ultimately leading to involvement of forelimbs and complete paralysis. With no current treatments available, euthanasia is the only option available for DM-affected dogs. Recent studies have identified mutation in the Superoxide dismutase 1 (SOD1) gene to be a high risk factor associated with canine DM. In humans, mutations in the same SOD1 gene cause Amyotrophic Lateral Sclerosis (ALS), a neurodegenerative disorder very similar to canine DM. It is also shown that reduction of mutant SOD1 in ALS mouse models provides beneficial effects. Hence, therapeutic approaches to reduce the expression of mutant SOD1 in DM-affected dogs may improve survival and preserve neurologic function. In this study, a viral-based gene therapy approach to treat DM will be evaluated, utilizing Adeno-associated Virus 9 (AAV9) mediated delivery of shRNA to reduce the mutant SOD1 in DM affected dogs. AAV9 is a safe, well tolerated and widely used

vector for gene therapy in animals as well as for humans. If successful, this one-time treatment with AAV9 SOD1 shRNA will result in improved quality of life, and significantly extend the survival of dogs affected with this previously hopeless disease.

NEW

02172-MOU

Understanding Hereditary Deafness in Dogs

Principal Investigator: Dr. George M. Strain, PhD; Louisiana State University
Total Grant Amount: $120,015
Grant Period: 11/1/2015 - 10/31/2017
Project Abstract:

Hereditary deafness associated with white pigmentation occurs in numerous dog breeds. The breeds most affected are the Dalmatian (Dal, 22% unilaterally deaf, 8% bilaterally deaf) and the Australian cattle dog (ACD, 11.4% and 3%). The mechanism of inheritance is unknown, and previous studies to determine the mode of inheritance and locate the causative gene(s) have thus far been unsuccessful.

Using a modified twin study approach, full-sibling littermates will be clinically and genetically evaluated. Like human twins, full siblings should have very similar DNA, which will reduce the variability of their DNA when compared to studies of unrelated dogs. Using the Illumina CanineHD Beadchip, which contains 172,115 DNA markers (SNPs) spread uniformly across the canine chromosomes, markers will be compared between the sibling pairs, and differences between siblings at individual markers will thus be identified. Using this approach candidate deafness genes can be identified and will advance the current understanding of this heritable disorder.

Funding for the research is provided through the efforts and generosity of the Australian Cattle Dog Health, Education, and Welfare, Australian Cattle Dog Club of America, Dalmatian Club of America, and the Dalmatian Club of America Foundation. The AKC Canine Health Foundation supports this effort and will oversee administration of funds and scientific progress reports.

02157-MOU

Genomics of Deafness in the Dalmatian

Principal Investigator: Dr. Claire M Wade, PhD; University of Sydney
Total Grant Amount: $120,960
Grant Period: 1/1/2015 - 12/31/2016
Project Abstract:

Congenital deafness is a health issue that has higher prevalence in certain breeds, including the Dalmatian. Other studies in this breed have found the trait to be inherited in a complex rather than simple Mendelian manner. Using a large number of samples from animals that have been tested for hearing status, Dr. Wade will employ the latest genomic technologies and computational analyses to conduct this study. The ultimate goal is to identify mutations underlying the trait of congenital deafness in the Dalmatian breed and work towards a genetic testing solution for the Dalmatian breeding community.

Funding for the research is provided through the efforts and generosity of the Dalmatian Club of America Foundation. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.


Courtesy AKC Family Dog Photo Contest

02139-A

Development of a Neuromusculoskeletal Computer Simulation Gait Model to Characterize Functional Recovery in Dogs with Intervertebral Disk Herniation

Principal Investigator: Dr. Gina E Bertocci, PhD; University of Louisville
Total Grant Amount: $12,740
Grant Period: 9/1/2014 - 8/31/2016
Project Abstract:

Intervertebral disk herniation (IVDH) leads to spinal cord injury (SCI) in dogs. The most commonly affected breed is the Dachshund, of which 19% develop IVDH. IVDH compresses the spinal cord and can lead to paralysis, incontinence, reduced quality of life, permanent neurological deficits and secondary conditions. Dogs that receive decompressive surgery (standard of care) and rehabilitation immediately following IVDH may regain the ability to walk. Certain aspects of recovery, such as muscle activation patterns, are not clearly understood and play a pivotal role in whether dogs regain full function of their limbs. Scientists know that neurologic disruption following IVDH alters muscle recruitment strategies leading to compensatory changes in muscle function post-injury. An improved understanding of muscle activation during walking following IVDH-associated SCI is paramount to developing strategies to enable full recovery. The goal of Dr. Bertocci's study is to characterize individual muscle activation patterns during walking. Her research group is responsible for development of landmark computer simulation techniques that have transformed our understanding of Cranial Cruciate Ligament Disease. She will now apply this successful methodology to IVDD and assess muscle function in: 1) a healthy Dachshund, and 2) a Dachshund with moderate IVDH-associated SCI following surgical decompression at multiple time points during recovery. Proof-of-principle computer models will be developed based on medical imaging, and hind-limb motion, ground reaction forces, and body weight support provided during walking. They will characterize differences in hind-limb motion and muscle activation patterns during walking between the healthy dog and dog with SCI, as well as differences in the dog with SCI throughout recovery. Their outcomes will enhance understanding of functional recovery following surgical treatment of IVDH, which will provide a foundation for improved clinical decision-making for treatment options and investigating future therapeutic interventions.

02141-A

Describing the Kinetic and Kinematic Recovery of Dachshunds with Spinal Cord Injury

Principal Investigator: Dr. Gwendolyn J. Levine, DVM; Texas A&M AgriLife Research
Total Grant Amount: $12,935
Grant Period: 9/1/2014 - 8/31/2016
Project Abstract:

Intervertebral disk herniation (IVDH) is common in dogs and results in injury by compressing and bruising the spinal cord. The most frequently affected breed is the Dachshund, with as many as 19% of Dachshunds developing IVDH. Effects of IVDH include paralysis, paresis, incontinence, reduced quality of life, and permanent neurological disabilities; these facets of injury place a tremendous burden on caregivers. Traditionally, qualitative scoring systems have been used to determine injury severity, recovery, and identify if therapies are effective. More recently, computerized gait assessment (kinematics) has been applied to dogs with IVDH. These studies have examined dogs at single time points and suggest that kinematics is more sensitive than traditional scoring in detecting changes in gait. The goal of Dr. Levine's research is to characterize gait recovery in Dachshunds with IVDH using kinematics. She will utilize dogs with moderate and severe injury to capture the spectrum of dysfunction and recovery that occurs following injury. All dogs will receive spinal decompression surgery (standard) and be assessed at 5 time points: pre-surgery and 7, 14, 30 and 90 days post-surgery. Information will be compared to the gait of healthy Dachshunds. This work is novel based on the quantitative, kinematic and longitudinal characterization of locomotion in healthy and spinal cord injured Dachshunds. The major outcomes will be: 1) an enhanced understanding of natural recovery post-IVDH; 2) improved clinical decision making with respect to treatment options; 3) identification of effective assessment parameters; and 4) creation of a baseline for future clinical trials assessing therapies.

02162-MOU

Defining the Genetic Foundations of Chiari-Like Malformation and Syringomyelia as a Tool to Better Treat Neuropathic Pain in the Dog

Principal Investigator: Dr. Natasha J Olby, VetMB, PhD; North Carolina State University
Total Grant Amount: $37,530
Grant Period: 1/1/2015 - 6/30/2016
Project Abstract:

Chiari-like malformations and syringomyelia (CM/SM) are a common problem in Cavalier King Charles Spaniels (CKCS) causing severe neuropathic pain. The morphometry of the skull has been examined in detail and the development of clinical signs and syringomyelia has been correlated to reduced caudal fossa to cranial cavity volume ratios and stenosis of the jugular foramen respectively. There is evidence this disorder is a complex hereditary trait, but attempts to identify genetic causes have been hampered by assigning an affected or normal phenotype. Use of quantitative data from magnetic resonance imaging (MRI) will allow us to perform a more appropriate genetic analysis of this important and common disease. Quantification of neuropathic pain is challenging and while owners of affected CKCS frequently complain that their pet is experiencing significant pain, a routine evaluation by palpation does not always correlate well to their history. Humans with CM report increased sensitivity to touch and temperature. During case phenotyping for the genetic study, Dr. Olby will also investigate sensory thresholds in affected and normal CKCS to improve the ability to document and treat pain in these patients. This project will define the genetic etiology of this disease with the long-term aim of developing genetic tests for use by breeders, and will quantify the sensory dysfunction experienced by these dogs to facilitate objective therapeutic trials.


Courtesy AKC Family Dog Photo Contest

Funding for the research is provided through the efforts and generosity of the American Cavalier King Charles Spaniel Club Charitable Trust. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.

Oncology Research Program Area

NEW

02171-MOU

Histiocytic Sarcoma in Bernese Mountain Dogs: Novel Approaches To Treatment

Principal Investigator: Dr. Vilma Yuzbasiyan-Gurkan, PhD; Michigan State University
Total Grant Amount: $43,661
Grant Period: 7/1/2015 - 6/30/2016
Project Abstract:


Courtesy AKC Family Dog Photo Contest

Canine histiocytic sarcoma (HS) is a highly aggressive cancer that affects primarily Bernese Mountain Dogs (BMD), with a prevalence that ranges from 15 to 25% of the population. The current treatment options for HS are based on the administration of conventional chemotherapeutic drugs, to which dogs respond poorly and only for a short period of time. Dr. Yuzbasiyan-Gurkan and her team will evaluate a novel modality of treatment for HS using small molecule inhibitors of key cancer pathways. The research team will evaluate three inhibitors, which have shown promising results in cell culture studies, in an immunodeficient mouse model. They will also focus on the gene expression associated with the response to treatment in order to better understand the events leading to the development of HS in BMD, and therefore, develop better therapeutic strategies. The investigators expect the drugs to be effective without any significant drug-related toxic effects, so further safety and clinical efficacy studies can be pursued in dogs. The treatment of dogs with HS remains challenging, and additional therapeutic options are needed. The study of novel small molecule inhibitors for this malignancy may contribute to improvement of quality of life and survival time of dogs with HS.

Funding for the research is provided through the efforts and generosity of the Bernese Mountain Dog Club of America. The AKC Canine Health Foundation supports this effort and will oversee administration of funds and scientific progress reports.

NEW

02204

Using Enhanced Imaging to Evaluate Tumor Margins for Canine Mammary Cancer and Soft Tissue Sarcoma

Principal Investigator: Dr. Laura Selmic, BVetMed; University of Illinois
Total Grant Amount: $46,358
Grant Period: 1/1/2016 - 12/31/2017
Project Abstract:

Surgery is the primary treatment for many common tumors affecting dogs including mammary tumors and soft tissue sarcomas (STS). For these tumors, the best chance of cure is offered if the surgeon can fully remove both visible and microscopic traces of the tumor. Unfortunately, to do this, surgeons must rely on indirect and crude methods to assess the extent of the tumor during surgery. The success of the procedure will not be known until several days later, following sample assessment by the pathologist. After surgery, decisions regarding the necessity of further treatment and the patient's prognosis are often determined from the pathology results. For malignant tumors, if the disease is minimally or incompletely removed, further surgery or radiation therapy is often required. Additional treatments such as these can result in further risk and discomfort for the patient as well as present emotional and financial costs for owners. Optical coherence tomography (OCT) is an emerging diagnostic imaging tool that uses light waves to generate real-time, high-resolution images of tissue at a microscopic level. These images can be used to evaluate for residual disease at the time of surgery giving immediate feedback to the surgeon. This study will focus on validating this technology for the imaging of surgical margins of two important canine cancers - mammary tumors and STS. If successful, this technology can be used to assess for residual cancer during surgery to benefit patients by guiding accurate treatment recommendations and attempting to reduce the need for additional treatments or surgery, and thus advancing the standard of care for canine patients.

NEW

02237-A

Capturing Tumor Cells in Canine Blood

Principal Investigator: Dr. Tracy Stokol, BVSc, PhD; Cornell University
Total Grant Amount: $10,239
Grant Period: 1/1/2016 - 12/31/2016
Project Abstract:

Just like their human owners, many dogs suffer from cancer, which is often malignant, spreading through the body via blood. Once tumors have spread, they usually result in a poor outcome, including death. The tumor cells in circulation (CTCs) can be counted in the blood of people with cancer using immunocapture devices. The number of CTCs in blood can tell the clinician how aggressive the tumor is, its potential to spread, and how long a patient might survive. There is currently no such way of detecting CTCs in our canine companions. Development of an assay for counting CTCs in canine blood would be of tremendous benefit to our canine patients because, from a simple blood test, we could detect hidden tumors and gather information on tumor severity and the likelihood of spread or metastasis. The investigators will test a novel immunocapture microdevice - the GEDI - for counting tumor

cells in canine blood. This device can capture CTCs from blood in human patients with various cancers. This study will test its potential to do the same for dogs. In this pilot study, blood samples from healthy dogs will be manipulated to test the ability to count how many added tumor cells are captured by the GEDI device. If the GEDI does capture the tumor cells, the next step will be to determine if the device can capture CTCs from the blood of dogs that are known to have cancer, paving a path to early detection of cancer in dogs.

NEW

02244-A

Beyond Peto's Paradox with the Geriatric Peromyscus

Principal Investigator: Dr. Corbin D. Jones, PhD; University of North Carolina
Total Grant Amount: $8,500
Grant Period: 1/1/2016 - 6/30/2016
Project Abstract:

Collaborative Grant between Triangle Center for Evolutionary Medicine and AKC Canine Health Foundation

Cancer is a heterogeneous or widely divergent collection of diseases with a similarly wide variety of outcomes, natural histories and responses to therapy. While new medical and genomic data have shed light on the molecular mechanisms causing cancer, why cancer should occur in the first place remains unclear. Equally perplexing is why some organisms or individuals seem more or less likely to get cancer. This project uses the unique biology of deer mice *(Peromyscus)* species to identify the genes contributing to longevity and cancer resistance in *P. leucopus*, the white-footed deer mouse. Since the 1950s it's been known that *P. leucopus* is very long lived for such a small rodent and has a similarly low rate of cancer compared to common or laboratory mice. Our project will use comparative genomic comparisons between *P. leucopus* and its close relatives to discover the extraordinary ways animals have "invented" to reduce cancer. These findings will inform the field of cancer genetics, and will be translatable to larger mammalian species such as dogs and humans.

01889-G

Innovations in Prevention, Diagnosis, and Treatment of Cancer - Goldens Lead the Way

Principal Investigator: Dr. Jaime F Modiano, VMD, PhD; University of Minnesota
Total Grant Amount: $360,933
Grant Period: 1/1/2014 - 12/31/2016
Project Abstract:

Collaborative Grant between the Golden Retriever Foundation and AKC Canine Health Foundation

Lymphoma and hemangiosarcoma are major health problems in Golden Retrievers, causing both suffering and premature death. Through ongoing collaboration, Drs. Jaime Modiano, Matthew Breen, and Kerstin Lindblad-Toh have identified several regions of the genome that contain genetic heritable risk factors for lymphoma and hemangiosarcoma in Golden Retrievers. They have tumor-specific mutations that occur recurrently in both cancers, some of which are linked to duration of remission when treated with standard of care. Their results indicate that a few heritable genetic risk factors account for as much as 50% of the risk for these cancers. These findings offer the potential to develop tests and strategies for DNA tests that can predict risk for individual dogs, as well as to manage risk across the population as a whole. Indeed, both the inherited risk factors and tumor mutations point to pathways that have been implicated in the pathogenesis of lymphoma and hemangiosarcoma, and thus should inform the development of targeted therapies. In the current study, Drs. Modiano, Breen, and Lindblad-Toh will find the precise mutations for the heritable genetic risk factors and to validate markers (mutations) used to determine risk at the heritable loci in a larger independent population of Golden Retrievers from the United States and Europe in order to develop robust risk prediction tools and an accompanying DNA test. Further, they will identify and characterize tumor mutations and study their relationship to heritable risk factors, tumor pathogenetic mechanisms, and disease outcome.


Courtesy AKC Family Dog Photo Contest

01826

A Novel Treatment for Brain Tumors Using a One Medicine Approach

Principal Investigator: Dr. Simon R. Platt, BVMS; University of Georgia
Total Grant Amount: $119,065
Grant Period: 1/1/2013 - 12/31/2016
Project Abstract:

Drs. Simon Platt (University of Georgia College of Veterinary Medicine) and Costas Hadjipanayis (Emory University School of Medicine) will take a One Medicine approach to treating canine glioma brain tumors. Brain tumors in humans and animals are often devastating and fatal diseases. Many are not accessible to surgical removal which is the main treatment option. Likewise, chemotherapy has traditionally been ineffective because systemic delivery is prevented by the blood-brain barrier. In an effort to deliver chemotherapy drugs directly into brain tumors, a procedure called convection-enhanced delivery (CED) has been developed. This procedure utilizes small catheters, placed directly into tumors which allow direct drug delivery, limiting systemic drug concentrations, and therefore minimizing side effects. In this study dogs will undergo CED treatment with the monoclonal antibody cetuximab conjugated to magnetic iron-oxide nanoparticles (IONPs). Cetuximab is a monoclonal antibody specific to the epidermal growth factor receptor (EGFR) which is over-expressed in the majority of canine gliomas. Cetuximab is FDA-approved for use in several cancers in humans. When combined with IONPs, cetuximab can be visualized utilizing MRI. The dogs will be monitored clinically and with MRI over twelve months. The aim is a significant decrease in MRI volume of the tumors and ultimately, tumor-free survival of patients.

02071

Development of a Therapeutic Brain Tumor Vaccine

Principal Investigator: Dr. Grace Elizabeth Pluhar, DVM, PhD; University of Minnesota
Total Grant Amount: $130,572
Grant Period: 1/1/2014 - 6/30/2016
Project Abstract:

Meningiomas are the most common primary brain tumor in dogs that affect more than 10,000 dogs in the U.S. annually. These tumors occur most frequently in older dogs and in certain breeds -- Golden Retrievers, Labrador Retrievers, Boxers, German Shepherd Dogs and Collies -- causing uncontrolled generalized grand mal seizures in most cases. Although the biological behavior of these tumors is generally considered benign, most meningiomas recur less than one year after either surgery or radiation therapy. Furthermore, radiation therapy is expensive, involves many repeated episodes of general anesthesia, and causes severe adverse effects. Longer survival times can be achieved through special techniques, but most dogs treated undergo more standard surgical removal and/or radiation therapy. Clearly, there is an urgent need for novel therapies to prevent tumor recurrence and increase survival time after surgery. Dr. Pluhar has developed immunotherapy protocols for dogs with gliomas, and recently assessed this strategy in a pilot study treating meningiomas with tumor lysate vaccines. Her data for six dogs showed this approach was safe, feasible and effective. Dr. Pluhar will now conduct a larger clinical trial treating 30 dogs with meningioma by surgery alone or surgery followed by vaccines. They expect to see a specific immune response to the vaccines that prevents tumor recurrence. The data from the proposed study will provide further proof of safety and efficacy of vaccine-based therapy to support: 1) more widespread use in dogs, and 2) initiation of a Phase I trial for high grade and recurrent meningioma in humans.

01787

Clinical Advancement of a Cancer Vaccine in Dogs

Principal Investigator: Dr. Nicola J Mason, BVetMed, PhD; University of Pennsylvania
Total Grant Amount: $96,660
Grant Period: 1/1/2013 - 12/31/2016
Project Abstract:

Canine lymphoma is the most common blood-based cancer in dogs with an estimated annual incidence of 30/100,000. Chemotherapy induces remission in 75-85% of patients; however, the majority of patients relapse with drug-resistant lymphoma within 8-10 months of diagnosis and most dogs die of their disease shortly thereafter. Cell-based vaccine strategies that stimulate anti-tumor immunity have shown promise in the treatment of many different cancer types including non-Hodgkin's lymphoma (NHL) in humans. In a previous study Dr. Mason developed a cell-based vaccine to induce anti-tumor immunity in dogs with NHL. Initial studies were hopeful as this early vaccine significantly prolonged second remission duration and overall survival, but ultimately the vaccine did not prevent relapse. These early findings suggest that while the lymphoma vaccine stimulated anti-tumor immunity it will require immunological boosting to achieve prolonged cancer-free survival. In the current study, Dr. Mason will optimize her cell-based vaccine approach to induce functional, long lasting tumor-specific immune responses that will prevent relapse and prolong survival in dogs with NHL.

01689-A

Increasing the Effectiveness of Radiation Therapy in Treatment of Mast Cell Tumors

Principal Investigator: Dr. Keijiro Shiomitsu, DVM; University of Florida
Total Grant Amount: $1,603
Grant Period: 8/1/2015 - 3/31/2016
Project Abstract:

Canine mast cell tumors are the most common cutaneous malignant tumors in dogs. Histologic grades, I, II, and III, provide very useful information because they are indicative of a patient's prognosis. Treatment options depend on negative prognostic factors, but in general surgery and radiation therapy are very effective. Chemotherapy could be applied if the patient has either systemic disease or a grade III mast cell tumor. The most commonly used chemotherapy drugs for mast cell tumors are CCNU and vinblastine. A new therapeutic agent, Palladia, targets a receptor on mast cell tumors called c-kit (CD117). Dr. Shiomitsu will investigate if Palladia can enhance the radiosensitivity of canine mast cell tumor cells in vitro and determine the mechanism of radiosensitization when it occurs. Radiosensitization by Palladia may be able to improve local tumor control, and hopefully prolong survival time for radiation oncology patients.

Oncology - Hemangiosarcoma Research Program Area

NEW

02217

A Novel Mechanism to Regulate the Growth of Canine Hemangiosarcoma

Principal Investigator: Dr. Erin B. Dickerson, PhD; University of Minnesota
Total Grant Amount: $86,206
Grant Period: 1/1/2016 - 12/31/2017
Project Abstract:

Hemangiosarcoma is an extremely aggressive cancer that is rapidly fatal in dogs. While the lifetime risk is alarmingly high for some breeds such as Golden Retrievers and German Shepherd Dogs, the disease does not discriminate, and it can strike any dog at any time. Despite considerable efforts by veterinarians and scientists to find effective treatments, the outcome for dogs with hemangiosarcoma has changed very little over the past few decades. Recent evidence provides essential clues into how these tumors grow and progress, generating new ideas for treatment approaches. Such new evidence suggests that hemangiosarcoma

cells rely on the metabolism of lipids or fatty acids to supply energy for tissue invasion or continued tumor growth. To obtain these lipids, hemangiosarcomas may take over the metabolic machinery of neighboring cells, forcing them to produce nutrients for the tumor cells to help them proliferate and grow. This study will verify that tumor cells rely on lipid metabolism for growth, and determine if tumor cells alter the metabolism of fat cells to obtain cellular nutrients and accelerate tumor cell lipid metabolism. Identifying and exploiting a novel mechanism that may disrupt this process by inhibiting the interactions between tumor cells and cells in the tumor environment will speed clinical investigations, and ultimately lead to improved outcomes for dogs with this devastating disease.

NEW

02234-MOU

A Novel Approach for Prevention of Canine Hemangiosarcoma

Principal Investigator: Dr. Jaime F Modiano, VMD, PhD; University of Minnesota
Total Grant Amount: $432,000
Grant Period: 1/1/2016 - 12/31/2018
Project Abstract:

Courtesy AKC Family Dog Photo Contest

Hemangiosarcoma, an aggressive form of cancer in dogs, is the cause of death for one out of every five Golden Retrievers in the United States. Portuguese Water Dogs and Boxers also have an especially high risk for this disease which is devastating for all dogs. Hemangiosarcoma is incurable partly because the cancer is detected at a very advanced stage when it is resistant to conventional therapies. Thus, an unconventional approach to improve outcomes for hemangiosarcoma patients will involve effective methods for early detection and for disease prevention. This project will pair two novel technologies consisting of a patented test to detect hemangiosarcoma cells in blood samples, and a treatment that attacks the cells that establish and maintain the disease. Three milestones will be met: first, will be to expand understanding of the performance and utility of the blood test for cancer in dogs with active disease; second will be to confirm the utility of the test to predict disease progression in treated dogs. And third will be to establish the performance of the test in the “early detection” setting (dogs at high risk without evidence of active cancer), and thus measure hemangiosarcoma prevention through eradication of the tumor initiating cells with the targeted, investigational drug. This project will create tools to guide further development, licensing and deployment of these paired technologies against cancer, specifically hemangiosarcoma, with an ultimate goal for disease prevention in all dogs.

Funding for the research is provided through the collaborative efforts and generosity of the American Boxer Charitable Foundation, Golden Retriever Foundation, and Portuguese Water Dog Foundation. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.

Oncology - Lymphoma Research Program Area

01918-G

Discovery of Biomarkers to Detect Lymphoma Risk, Classify For Treatment, and Predict Outcome in Golden Retrievers

Principal Investigator: Dr. Jeffery N. Bryan, DVM, PhD; University of Missouri, Columbia
Total Grant Amount: $404,813
Grant Period: 7/1/2013 - 6/30/2016
Project Abstract:

Collaborative Grant between the Golden Retriever Foundation and AKC Canine Health Foundation

Lymphoma strikes 1 in 8 Golden Retrievers, approximately one-third of the cases being B-cell. While T-cell classifications currently inform therapy choices for dogs, B-cell classifications have been investigated little in Golden Retrievers. Dr. Jeffrey Bryan, in collaboration with Drs. Anne Avery and Heather Wilson will focus their efforts on an area of emerging importance in cancer: epigenetics. Epigenetics is defined as stable and heritable patterns of gene expression that do not entail any alterations to the original DNA sequence. Epigenetic DNA methylation changes clearly underlie development of lymphoma in humans, but have been evaluated minimally in dogs. These investigators will improve diagnostic, classification, and prognostic ability by using flow cytometry paired with biopsy to characterize the B-cell lymphomas of Golden Retrievers. They will identify DNA methylation changes in lymphoma cells not present in normal cells to develop biomarkers of each class of lymphoma, and identify new therapy targets for affected Golden Retrievers. More significantly, because DNA methylation changes occur so early in the process of cancer formation, they hypothesize that they could

serve as biomarkers of risk, allowing medicine or diet to prevent lymphoma in Golden Retrievers before it develops. Finally, they propose to identify tumor initiating cells (TIC) in lymphoma biopsies to characterize stem-like cells by surface markers and DNA methylation changes. Identifying these cells will aid therapeutic strategy development. Each project advances a current frontier of research; performing them in parallel, the markers from each can be combined, correlated, and translated into biomarkers of risk, diagnosis, and prognosis to advance the prevention and management of lymphoma in Golden Retrievers.

Oncology - Osteosarcoma Research Program Area

NEW

02215

A Cancer Vaccine for Canine Osteosarcoma

Principal Investigator: Dr. Rowan J Milner, BVSc; University of Florida
Total Grant Amount: $80,974
Grant Period: 1/1/2016 - 12/31/2017
Project Abstract:

Osteosarcoma is a malignant cancer that carries a very poor prognosis in most large breeds of dogs. The standard of care treatment for osteosarcoma is surgery followed by chemotherapy. Unfortunately, a large number of these osteosarcomas undergo early metastasis (spread) even with early surgical intervention and chemotherapy. Infections of the surgery site, especially when limb-sparing surgery is used, have been known to stimulate the immune system post-operatively in dogs, resulting in improved survival. Since overall survival is bleak in patients with osteosarcoma, developing an osteosarcoma cancer vaccine holds promise as an adjunct treatment to surgery and chemotherapy. In a previous study of 400 dogs with melanoma we showed that a vaccine containing the ganglioside (GD3) causes a measurable immune response in normal dogs and dogs with melanoma, and prolonged survival. In this study, 40 dogs with osteosarcoma presenting to the University of Florida Small Animal Hospital will be randomly assigned to two treatment groups. Twenty dogs will be vaccinated using a ganglioside-based cancer vaccine following standard of care treatment. The outcome of the dogs receiving the vaccine plus standard of care will be compared to 20 dogs who receive standard of care without vaccination. Vaccines will be administered monthly for 4 treatments and the dogs monitored every 3-6 months for life or until lost to follow-up. The outcome of this study will help us understand the immune process associated with cancer vaccines for osteosarcoma and with an ultimate goal to improve survival for dogs with this aggressive form of cancer.

Ophthalmology Research Program Area

NEW

02105-A

The Genetics of Keratoconjunctivitis Sicca in West Highland White Terriers

Principal Investigator: Dr. Christopher J Murphy, DVM, PhD; University of California, Davis
Total Grant Amount: $5,000
Grant Period: 6/1/2015 - 5/31/2016
Project Abstract:

Dry eye disease or keratoconjunctivitis sicca (KCS) is a devastating disease in dogs and humans where inadequate tear production can result in ocular pain, corneal ulceration and even blindness. The most common cause for KCS in dogs is immune-mediated, which means that the dog's immune system attacks the tear-producing glands. However, the exact mechanism by which this inflammatory process occurs is poorly understood. A variety of treatments for KCS exist including immunomodulators, tear replacements, and surgical interventions, but are often incompletely effective in dogs and humans.

Several dog breeds including West Highland White Terriers are seen more commonly for KCS in comparison to other breeds. This observation suggests that this disease may have a genetic component. We propose to identify the region of the dog genome associated with KCS in the West Highland White Terrier. In order to do this, we will perform thorough eye examinations and use multiple tests to assess the tear film in normal and affected West Highland White Terriers. We will then collect blood from these dogs. The entire canine genome will be evaluated for an association with KCS. This work will be used to identify the gene(s) responsible for this condition in West Highland White Terriers and help us understand KCS better in dogs and humans. The ultimate goal will be to develop a genetic test for KCS in West Highland White Terriers and possibly other breeds such as Bulldogs, Shih Tzus, and Clumber Spaniels with an increased risk of KCS.

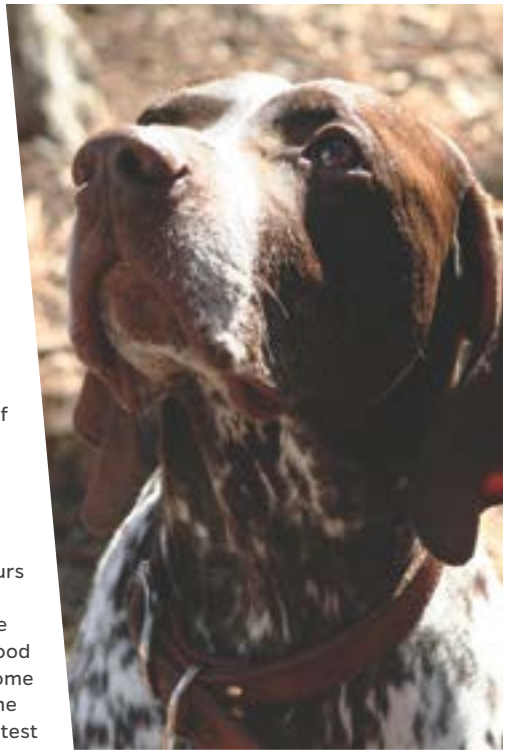
Courtesy AKC Family Dog Photo Contest

NEW

02243-A

Genomic Profiling of Canine Corneal Endothelial Dystrophy

Principal Investigator: Dr. Sara M Thomasy, DVM, PhD; University of California, Davis
Total Grant Amount: $12,960
Grant Period: 1/1/2016 - 12/31/2016
Project Abstract:



Corneal endothelial dystrophy (CED) is a disease in dogs that can result in blindness and ocular pain. The endothelial cells comprise the most inner aspect of the cornea and are responsible for maintaining a proper fluid balance and thus corneal transparency. In dogs with CED, the endothelial cells degenerate prematurely until the remaining cells no longer function properly. This results in corneal swelling, and secondary vision compromise and corneal ulceration. The only definitive treatment for CED is a corneal transplant. Unfortunately, corneal transplants are rarely performed in canine patients with CED due to the expense of the surgery and follow-up care, high risk of complications, and lack of appropriate donor tissue.

Several dog breeds including Boston Terriers, German Shorthaired Pointers and German Wirehaired Pointers are seen more commonly for CED in comparison to other breeds. This observation suggests that this disease may have a genetic basis. A similar condition called Fuchs endothelial corneal dystrophy (FECD) occurs in humans and several genes associated with FECD have been identified. This project will investigate the genetics of CED in dogs, and will include thorough eye examinations and advanced ocular imaging as well as extraction of DNA from blood collected from dogs with CED and age-matched controls. The entire canine genome will be evaluated for an association with CED. This work will be used to identify the gene(s) responsible for this condition in these 3 breeds and to develop a genetic test for CED.

02057

Identification of the Genetic Cause of Corneal Ulcers

Principal Investigator: Dr. Kathryn M Meurs, DVM, PhD; North Carolina State University
Total Grant Amount: $27,201
Grant Period: 1/1/2014 - 6/30/2016
Project Abstract:

Spontaneous chronic corneal epithelial defects (SCCEDs) describe an eye disorder characterized by chronic corneal ulcers that fail to undergo normal healing. The predilection of certain breeds suggests that SCCEDs is inherited. Affected dogs develop spontaneous corneal ulcers that are often exceptionally painful and persist for weeks to months. Most dogs require surgical therapy to heal the corneal ulcer and experience corneal scarring as a result. Although SCCEDs can be effectively treated, some dogs develop additional episodes of corneal ulcers during their lifetime. The impact on the quality of life for dogs during episodes of ulceration has led to increased interest in disease prevention. However, since SCCED is an adult onset disease, many dogs are selected for breeding before they are diagnosed. A blood test that could identify affected animals before they are used for breeding would greatly decrease the prevalence of SCCEDs. The investigators will use a genome wide association approach to identify an association of a genetic region to SCCEDs. They will then more closely evaluate the chromosomal region of interest to determine the gene and ultimately the causative genetic mutation. They believe that the identification of a genetic cause for SCCEDs can be used to reduce the prevalence of this disease in multiple affected breeds.

02061

Emergence of Pigmentary Uveitis as a Potential Cause of Cataracts and Glaucoma

Principal Investigator: Dr. Wendy M. Townsend, DVM, MS; Purdue University
Total Grant Amount: $74,070
Grant Period: 1/1/2014 - 6/30/2016
Project Abstract:

Pigmentary uveitis affects 10% of senior Golden Retrievers and frequently results in blindness due to cataracts and/or glaucoma. The pain of glaucoma often leads to removal of the eye. Currently there is no way to prevent or effectively treat pigmentary uveitis. Evidence strongly suggests pigmentary uveitis is an inherited disease: it is observed exclusively in the Golden Retriever breed, and family members (parents/offspring, full- and half-siblings) can be affected. Complicating the phenotype is the fact that most dogs are 8 years or older before developing clinical signs of pigmentary uveitis. Therefore, affected dogs may be used extensively in a breeding program before being diagnosed. This has frustrated conscientious breeders in their efforts to decrease the prevalence of pigmentary uveitis. Dr. Townsend and her team hypothesize that a genome-wide association study (GWAS) will identify a chromosomal region associated with Golden Retriever pigmentary uveitis, and that high-throughput DNA sequencing will allow identification of the causative mutation. Previous CHF funding helped establish a bank of Golden Retriever DNA for use in the present proposal. Identification of the gene responsible for pigmentary uveitis would permit development of a genetic test whereby affected individuals can be identified at a young age, allowing breeders to make informed breeding decisions. In addition, knowing the molecular basis underlying pigmentary uveitis may allow researchers to develop more effective treatments for dogs already affected by or genetically destined to develop pigmentary uveitis; this could possibly prevent the blindness, cataracts, and glaucoma caused by pigmentary uveitis.

Renal Disease Research Program Area

01844

Treatment of Urinary Incontinence with Multipotent Muscle Cells: A Regenerative Medicine Approach to a Common Canine Health Problem

Principal Investigator: Dr. Shelly Vaden, DVM, PhD; North Carolina State University
Total Grant Amount: $116,184
Grant Period: 1/1/2013 - 12/31/2016
Project Abstract:

Urinary incontinence affects more than 20% of spayed female dogs, with medium and large breeds more commonly affected. In the majority of the cases urinary incontinence is caused by dysfunction of the muscles controlling the urethral sphincter. This results in uncontrolled loss of urine and can lead to serious bladder and kidney infections, in addition to irritation and/or ulceration of the skin in contact with the urine. Treatment can include hormone therapy, drugs designed to strengthen the muscle tone of the urethral sphincter, collagen injections, or surgery. Recently, Dr. Vaden's lab has reported that injection of muscle progenitor cells into damaged urethral sphincters can restore normal function in dogs. The purpose of this project is to extend those observations and examine the usefulness of cultured muscle cells for the restoration of function of the urethral sphincter in dogs with naturally occurring urinary incontinence. The effects of the procedure will be determined by owner reported continence scoring, as well as urodynamic testing that will provide an objective measurement for how well the bladder, sphincters, and urethra are storing and releasing urine.


Courtesy AKC Family Dog Photo Contest

02066

Identification of Novel Biomarkers and Therapeutic Targets for Chronic Kidney Disease in Dogs

Principal Investigator: Dr. Mary B Nabity, DVM, PhD; Texas A&M AgriLife Research
Total Grant Amount: $108,243
Grant Period: 1/1/2014 - 6/30/2016
Project Abstract:

Chronic kidney disease is a significant cause of illness and death in dogs. Early treatment can prolong the lives of dogs with chronic kidney disease, but timely detection can be difficult. The outcome for each patient using current, early non-invasive testing is unpredictable. Therefore, improvements in tests to detect kidney damage at an earlier stage would allow veterinarians to provide dogs with appropriate treatments in a more timely fashion to slow disease progression and improve quality and length of life. Further, better treatments are needed to prevent disease progression. MicroRNAs (miRNAs) are small molecules that can regulate gene expression by up or down regulation of messenger RNA transcripts and proteins in target tissues. Many studies have found that increases or decreases in miRNAs can serve as biomarkers of diseases, including human chronic kidney disease. They also contribute to the development of diseases. Dr. Nabity will evaluate miRNAs in the serum and urine of dogs with chronic kidney disease to determine their use as biomarkers of kidney injury and their potential as targets for future therapeutics. They will evaluate kidney tissue, urine, and serum samples from dogs with a hereditary disease that causes early-onset chronic kidney disease, as well as serum and urine from dogs with a variety of other naturally occurring kidney diseases to identify miRNAs that may be useful as biomarkers of kidney damage. Gene and protein targets of altered miRNAs will also be evaluated to learn more about the mechanisms that contribute to the development of chronic kidney disease in dogs.

02152

Translation of MicroRNA into an Early Diagnostic Test for Chronic Kidney Disease

Principal Investigator: Dr. Mary B Nabity, DVM, PhD; Texas A&M AgriLife Research
Total Grant Amount: $26,988
Grant Period: 1/1/2015 - 6/30/2016
Project Abstract:

Chronic kidney disease (CKD) is a significant cause of illness and death in dogs and is often due to glomerular diseases. Dogs with glomerular disease often have poor outcomes with standard therapy, and specific treatment recommendations are difficult without performing a kidney biopsy to determine the type of glomerular disease present, since treatment and outcome among these diseases differ substantially. Even then, we lack an understanding of the mechanisms driving these diseases, limiting our ability to optimally treat these dogs. Therefore, tests to non-invasively diagnose the type of glomerular disease would help veterinarians more appropriately treat these patients and provide insight into the mechanisms that cause the diseases. This could lead to better therapies that slow disease progression and improve quality and length of life in dogs with CKD.

One area of emerging importance in CKD is the role of microRNAs (miRNAs) in disease pathogenesis and progression. miRNAs are small molecules that can regulate gene expression by up or down regulation of messenger RNA transcripts and proteins in target tissues. Many studies have found that increases or decreases in miRNAs can serve as biomarkers of diseases, including human CKD.

They also contribute to the development of diseases. The goal of Dr. Nabity's study is to identify miRNAs in serum and urine of dogs that are specific for the three major causes of glomerular disease in this species. They also aim to identify miRNAs associated with disease progression for each of these diseases. Successful completion of these goals will support the translation of miRNAs into diagnostic tests and viable targets for future drug development.

Reproductive Conditions and Disease Research Program Area

Preventing Inaccurate Diagnosis of Brucellosis

01699-A

Principal Investigator: Dr. Christina M Larson, DVM; University of Minnesota
Total Grant Amount: $10,567
Grant Period: 3/1/2012 - 8/30/2016
Project Abstract:

Brucellosis testing is often made difficult due to the fact that the most commonly-used Brucellosis test, the Rapid Slide Agglutination Test (RSAT) also gives false positive results when the dog has recently experienced a bacterial infection due to *Bordetella bronchiseptica*, which is one of the common causes of kennel cough. Vaccinating the dog by injection of Bordetella (kennel cough) vaccine is likely to cause false positive results on the RSAT. This study will evaluate whether false positive RSAT results are obtained after vaccinating the dog via nasal spray with a commercially-available Bordetella (kennel cough) vaccine.

Development of a Brucellosis Vaccine for Dogs

NEW

02175-A

Principal Investigator: Dr. Angela M Arenas, DVM, PhD; Texas A&M AgriLife Research
Total Grant Amount: $12,952
Grant Period: 10/1/2015 - 9/30/2016
Project Abstract:

Brucella infections constitute a serious problem for dog breeders, pet owners, and kennels, leading not only to economic costs associated with reproductive loss, but also a public health concern because of the zoonotic potential. The disease, once established, is difficult to control due to the lack of a protective vaccine for canine use. Historically, brucellosis control efforts have demonstrated that the spread of the disease is preventable or significantly reduced in association with vaccination. Unfortunately, efforts to develop a brucellosis vaccine that is safe and effective for dogs have been unsuccessful to date. The goal of this research is to develop a safe and efficacious *Brucella canis* vaccine using a genetic mutant that has been shown to be safe and efficacious for controlling infection against other Brucella species. The development of a safe and highly protective brucellosis vaccine for dogs will significantly impact canine and human health by limiting the spread of disease.

Combined Anti-Müllerian Hormone and Progesterone Testing for the Diagnosis of Canine Ovarian Remnant Syndrome

NEW

02188-A

Principal Investigator: Dr. Ned J Place, MD, PhD; Cornell University
Total Grant Amount: $8,165
Grant Period: 7/1/2015 - 12/31/2016
Project Abstract:

Canine ovarian remnant syndrome (ORS) is a diagnosis that veterinarians consider when a spayed bitch shows signs that she is still under the influence of ovarian hormones. This would indicate that she has retained some functional ovarian tissue. Before surgical exploration is considered, the veterinarian will want to have strong evidence that an ovarian remnant is present. Current diagnostic tests for ORS have limitations, and Dr. Place and team are proposing to thoroughly evaluate a new line of testing: anti-Müllerian hormone (AMH) combined with progesterone. Dr. Place's laboratory was the first to demonstrate that AMH effectively distinguishes between spayed and intact dogs. When combined with progesterone testing, their preliminary data suggest that AMH is also effective in determining if a spayed bitch has an ovarian remnant. The ovaries are the sole source of AMH in mammals, and therefore a positive AMH test indicates the presence of ovarian tissue. Interestingly, the ovarian structure that develops after ovulation, the corpus luteum, does not produce AMH, but it does produce large amounts of progesterone. These researchers have identified a few cases of ORS for which the AMH test was negative, but the progesterone test was positive. In these cases, microscopic exam showed that the ovarian remnant was almost entirely luteal tissue. This grant will evaluate the efficacy of an AMH+progesterone test for the diagnosis of canine ORS, and perform histopathological examination of any tissue that is surgically removed from bitches that have undergone AMH+progesterone testing in their lab. If successful, this testing will help to reduce the number of unnecessary exploratory surgeries in dogs.

NEW

02192-A

Advanced Semen Analysis in Labrador Retrievers

Principal Investigator: Dr. Stuart Meyers, DVM, PhD; University of California, Davis
Total Grant Amount: $12,960
Grant Period: 10/1/2015 - 9/30/2016
Project Abstract:


Courtesy AKC Family Dog Photo Contest

With the growing use of artificial insemination and frozen semen in dog breeding, the level of predictability of fertile matings for any breed of dogs, particularly with age, is largely unknown. The researchers are currently developing a database with CHF funding to determine the relationship of sperm characteristics to pregnancy outcome in a large population of Labrador Retrievers. In this follow up study, the researchers will recruit and obtain semen samples from Labrador Retriever stud dogs with a history of subfertility or infertility and evaluate a wide array of routine and advanced semen quality measures including sperm viability, motility, lipid peroxidation, oxidative metabolism, acrosomal integrity, sperm chromatin structure assay (SCSA), mitochondrial DNA, and reactive oxygen species generation. The two databases will be compared using a powerful epidemiological approach to determine sperm effects on fertility. The relationship of sperm factors and male age to pregnancy will be measured. This project will result in improved accuracy to predict fertility for valuable stud dogs, and improve analysis of transported and frozen semen for Labrador Retrievers that will likely benefit all breeds.

NEW

02193-A

Identifying the Genetic Basis of Fetal Anasarca in Bulldogs/Canines

Principal Investigator: Dr. Anna V. Kukekova, PhD; University of Illinois
Total Grant Amount: $12,960
Grant Period: 10/1/2015 - 9/30/2017
Project Abstract:

Dystocia is one of the most significant reproductive health concerns for dog owners and breeders. While there can be many causes of dystocia, the occurrence of so-called “water” or “walrus” puppies is one of the more common reasons within particular breeds. Water puppies suffer from the abnormal accumulation of body fluids, called anasarca, resulting in a generalized swelling of the body. Normal delivery through the birth canal then becomes difficult or even impossible, oftentimes requiring intervention by caesarean section. Water puppies are generally stillborn or die shortly after birth. While anasarca affects many dog breeds, it appears to be more frequent in the brachycephalic breeds including the Bulldog, French Bulldog, Pug, Boston Terrier and others. Due to the known genetic relationship between these breeds and the recurrence of anasarca puppies in specific matings, it is strongly believed that there is a significant genetic risk factor associated with this problem. Modern genetic tools and techniques have greatly improved the ability to identify specific variations in DNA which may be responsible for such traits. Thus, in an effort initiated by the Bulldog Club of America and Bulldog Club of America Charitable Health Fund, samples from newborn puppies with anasarca, their parents, and non-affected puppies have been collected, and will be utilized to analyze for a genetic basis of anasarca in an effort to develop a DNA-based test that can be used to screen for and reduce the incidence of this devastating disease.

02123-A

Identifying the Gene Responsible For Inherited Infertility and Sterility in 28 Breeds

Principal Investigator: Dr. Vicki Meyers-Wallen, VMD, PhD; Cornell University
Total Grant Amount: $12,960
Grant Period: 7/1/2014 - 6/30/2016
Project Abstract:

In a previous study, Dr. Meyers-Wallen demonstrated that canine XX Disorder of Sexual Development (DSD) is a sex-limited autosomal recessive trait. Affected dogs develop testes or ovotestes and are masculinized in proportion to the amount of testis. Those having bilateral testes are sterile. Dogs with ovotestes range from sterile to fertile, with most developing female genitalia. Fertile affected dogs transmit the mutation to all their offspring. Carrier sires are fertile, and by founder effect, have increased mutation frequency in some breeds. Elimination of this mutation would reduce inherited female sterility and infertility in 28 breeds.

Dr. Meyers-Wallen hypothesizes that the XX DSD mutation is ancient, and therefore identical in most breeds. This predicts an identical XX DSD mutation in most, if not all breeds. In previous genomic studies, her research group identified a chromosomal region containing more than 16-fold enrichment for DNA sequence variants associated with XX DSD in the study pedigree. Using a custom designed array of 80 priority SNPs located in that region, they will now genotype affected dogs of 22 breeds and controls to identify variants that are identical in affected dogs. At the study conclusion, researchers are hopeful they will have an identical mutation candidate and be poised to develop a single DNA test for affected and carrier dogs in all breeds having this mutation.

Clinician-Scientist Fellowship Research Program Area

To sustain future advancements in canine and human health, the AKC Canine Health Foundation makes it a priority to encourage and support the next generation of canine health researchers, understanding the impact of present fiscal restraints on research and development. To help diminish this impact, the AKC Canine Health Foundation Clinician-Scientist Fellowship Program supports young scientists. Through these efforts the AKC Canine Health Foundation's ongoing mission to prevent, treat and cure canine disease will endure for years to come.

Resident recipients are selected based upon the following criteria:

1)A resident who has shown promise and enthusiasm for pursuing a career in canine health research.

2)A resident who will conduct research in line with the CHF's mission to advance the health of all dogs and their owners.

3)A resident who will conduct research that will abide by CHF policies, including our Humane Use of Animals Policy.

Three promising researchers have been named 2016 Clinician-Scientist Fellows:

Vincent Baldanza, VMD; Cornell University

Dr. Baldanza is a veterinary oncology resident at Cornell University's College of Veterinary Medicine. He will be working under the mentorship of Dr. Angela McCleary-Wheeler on 'The Role of Canonical Hedgehog Signaling in Canine Osteosarcoma'.

Project Abstract:

Canine osteosarcoma (cOSA), the most common primary bone cancer in dogs, is a highly aggressive tumor with an estimated spread (or metastasis) rate of approximately 90%. Even with surgery and chemotherapy, the median survival time remains only 10-12 months. The pathogenesis, disease course, and treatment response of cOSA closely parallels that of human pediatric OSA (hOSA), and it has thus been proposed as a spontaneous animal model of the disease. In hOSA, the Hedgehog (HH) developmental and cellular signaling pathway has been documented to contribute to the pathogenesis of the disease, impacting genes responsible for tumor formation and metastasis. While a critical pathway during development and maintenance of normal bone, increased activity of HH signaling can lead to tumor formation. Building off of the data in hOSA, Dr. Baldanza's study will address the hypothesis that HH signaling is also active in cOSA, and targeted inhibition of the pathway will negatively impact and slow OSA cell growth and survival. They will study canine genes of interest to this pathway in both cOSA tumor specimens and cOSA cell lines in culture.

The results provided by these studies will further explore the role of HH signaling in cOSA and act as a foundation for future experiments and clinical trials exploring more efficacious, targeted therapeutics for the treatment of this devastating disease in dogs. This work may also provide more evidence for this comparative model of cancer to benefit both human and canine cancer research.

Shirley Chu, DVM; University of Missouri

Dr. Chu is a medical oncology resident and PhD student in the Comparative Oncology and Epigenetics laboratory of Dr. Jeffrey Bryan at the University of Missouri. The focus of her research, 'Examination of the Methylome of Golden Retriever B cell lymphoma', is applying massively parallel sequencing (MPS) or next generation sequencing techniques to determine the genetic makeup of cancer. MPS will help us understand breed/genetic predisposition, environmental causes, classification, genetic evolution and drug targets, in canine and feline cancers.

Project Abstract:

Lymphoma is one of the most common cancers in people and in dogs, and Diffuse Large B cell Lymphoma (DLBCL) is the most common aggressive lymphoma in these species. Dr. Chu's project is to further understand the effects of DNA methylation on cancer, using epigenetics, the study of potentially reversible changes to nuclear material that ultimately determine DNA expression. DNA methylation is the most permanent epigenetic mark and has been the most widely studied. DLBCL is the subject of this study to elucidate the first methylome in the canine species (specifically in Golden Retrievers). MIRA-seq (methylated CpG island recovery assay) is an enrichment technique that was used to collect genome wide DNA methylation information. The methylomes will be analyzed to determine if a distinct fingerprint can be seen in DLBCL in Golden Retrievers, if this fingerprint models human DLBCL, and if a diagnostic panel can be produced for early diagnosis and aid in prognostication.

Other future projects to understand the genetic landscape of cancer in dogs include a parallel whole genome, exome (allows increased sequencing coverage of the part of the genome that contains known genes) and RNA-sequencing of DLBCL for the identification of actionable somatic mutations, biomarkers of minimal residual disease, tumor subtyping, tumor heterogeneity, structural variants and breed-related susceptibility. The bioinformatics pipeline that will be developed for these projects can then be readily applied to other canine cancers.

Emily Rout, DVM; Colorado State University

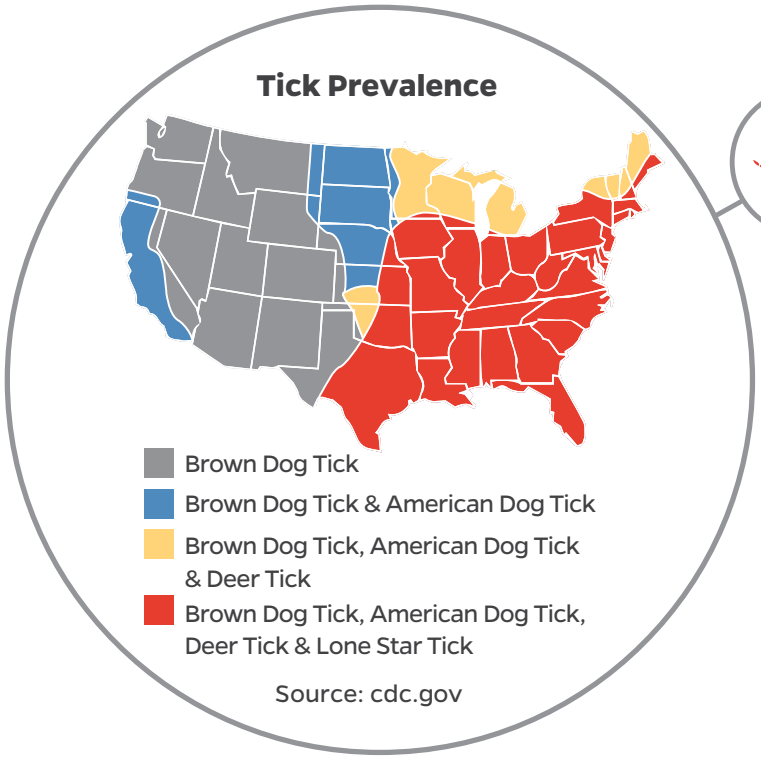
Emily Rout, DVM, is a clinical pathology resident and graduate student pursuing her PhD in the laboratory of Dr. Anne Avery at the College of Veterinary Medicine and Biomedical Sciences at Colorado State University. She is investigating variable heavy chain polymorphisms in canine chronic lymphocytic leukemia, having recently been recognized for her work on 'Preferential Usage of a Single Immunoglobulin Heavy Chain Variable Gene in Boxers with Chronic Lymphocytic Leukemia'.

Project Abstract:

B cell chronic lymphocytic leukemia (B-CLL) is a cancer of lymphocytes (B cells) in the blood. Although this disease is frequently seen in dogs, B-CLL has not been fully characterized. This Fellow will study the clinical features, pathogenesis, genetics and outcomes of B-CLL in dogs, particularly in two high-risk breeds, Boxers and English Bulldogs. B-CLL is the most common blood cancer affecting humans in the developed world. Human patients are generally divided into two subsets with very different clinical outcomes based on genetics. Analysis of gene mutation status (VH) is one of the best prognostic factors for predicting outcome in human B-CLL patients. By further investigating B-CLL in the Boxer and English Bulldog, Dr. Rout and the team hope to have a better understanding of B-CLL, and how it may differ across breeds, studying gene expression to identify potential differences in tumor biology between breeds, and further validating canine B-CLL as a naturally occurring model of a common human cancer.

Finally, the investigators have launched a large study to correlate breed, clinicopathologic findings and gene mutations with outcome. This study may also identify certain types of patients with a unique outcome, which would be important for further understanding this disease and guiding appropriate and improved treatment.

Tick Talk



Tick-borne diseases are found in all

50

states

Tick-borne diseases:
A growing threat to ALL dogs and their people

Disease can be transmitted within 3-6 hours of a tick bite

AKC Canine Health Foundation Launches 2016 Tick-Borne Disease Initiative

All donations will be matched dollar for dollar up to $250,000 thanks to the generosity of the American Kennel Club!

What are the goals of CHF's Tick-Borne Disease Initiative?

EDUCATION

An educational series including free webinars will outline important tick-borne diseases, their diagnosis and treatment in your dog. Join us to learn from internationally recognized infectious disease expert and internal medicine specialist, Dr. Ed Breitschwerdt, and veterinary practitioner and parasitologist, Dr. Chris Adolph, who will address biology of ticks to help you understand the "how" and "why" of tick distribution, disease prevention and spread. Contact us to receive educational materials about these life-threatening diseases to share with clients or your breed clubs. Learn how to keep your dog safe, about regional prevalence and incidence maps and how everyone can join this fight!

RESEARCH

CHF will help tackle the growing problem of tick-borne diseases in dogs by funding critical research to find new ways to prevent infections, and to recognize, diagnose and treat tick-borne diseases before they become debilitating or fatal to dogs. Innovative new research proposals will be solicited and awarded later this spring to address these important diseases: ehrlichiosis, anaplasmosis, Rocky Mountain spotted fever, hepatozoonosis, babesiosis, bartonellosis, hemotropic mycoplasmosis and Lyme disease.

ACT NOW for you and your dog!
Join CHF's Tick-Borne Disease Initiative:
akcchf.org/ticks

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SINCE 1995

Your gift to CHF helps dogs live longer, healthier lives and supports cutting-edge research to prevent, treat and cure canine diseases.

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