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

2017 Research Grants Portfolio

Introduction

December 1, 2016

For more than 21 years, the AKC Canine Health Foundation (CHF), with the support of our partners at the American Kennel Club, Purina, Zoetis, and many breed clubs and private donors, has worked for all dogs to live longer, healthier lives by funding much-needed research to address canine diseases. Together, we have made progress in addressing specific health needs of dogs through significant investments including mapping the canine genome, and studying the genetics of cancer and how these findings translate to the same cancers in people. CHF has also tackled emerging infectious diseases that strike dogs and, in some cases, their human companions. In 2016, CHF launched the Tick-Borne Disease Initiative, and we have already funded five grants (page 29) to improve the diagnosis and treatment of Lyme disease, Bartonellosis, and Ehrlichiosis – three diseases with potential devastating consequences to both dogs and people. CHF remains dedicated to this initiative, which will continue into 2017.

On the following pages you will find all new and active research grants, carefully selected through a stringent review process 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 dogs and their people by specialists in the research program area of interest. The CHF Scientific Review Committee, made up of external experts, is involved in the review and all recommendations for funding. Through defined research program areas, CHF considers areas of unmet need and areas of immediate opportunity, while looking to apply recent advancements in science and technology to canine health research. The information gathered from dog owners, veterinarians, breeders, and breed clubs about the most pressing health concerns in dogs is considered in selecting grants. 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.

Many technological and scientific innovations are being applied to canine health research through CHF funding. For example, new developments in stem cell research are being studied for canine joint disease, and advancements in human cancer are being employed to help dogs through new grants for canine lymphoma (page 22). 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. The philosophy of CHF in the selection of grants is to fill specific areas of unmet health needs, find medical breakthroughs for particularly stubborn diseases through new approaches, and to build upon the strengths and investments already made in CHF's canine health research portfolio. This body of work now equals more than $37.5 million in canine health research – our sole dedication to the dog allows us to be selective, and to provide a balanced approach to breed-specific and all-dogs health research. We find what is gained through this approach will provide the most benefit to dogs and often translates to human health.

This portfolio outlines CHF's currently active research projects, categorized by research program areas, allowing you to easily identify and support efforts important to you. These research program areas allow us to create in-depth areas of research and fund complementary studies to build a body of work that will more effectively advance health outcomes. Our entire history of funding in specific areas and for specific projects can be searched here: www.akcchf.org/research.

As the largest funder of health research focused solely on dogs, the AKC Canine Health Foundation believes in the advancement of science to meet the unmet medical needs of all dogs. We invite you to read through these project abstracts and to support this much-needed research with a donation today – in the manner that best works for you. Please contact us to discuss the many options available through matched funding initiatives, research program areas of particular interest to you, planned giving, or by supporting the CHF endowment. Together, we are moving canine health research forward, benefiting the dogs who so enrich peoples' lives.

We are pleased to announce, thanks to the generosity of the American Kennel Club, two major matched funding initiatives for 2017: first, for much-needed canine epilepsy research, and second, to continue our research efforts for tick-borne diseases. To discuss a study or to learn about sponsoring research, please contact: chfgrants@akcchf.org.

Thank you from the CHF staff and Board of Directors, and from the dogs whose lives will be positively impacted by this work and through your efforts and generosity.

Sincerely,

Diane Brown

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

Research Program Areas

All Dogs Health Research Program Area

02235-A

Medical Surveillance of Dogs Deployed to the World Trade Center and 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 – 12/31/2016
Project Abstract:

The investigators will complete the 14-15th years of the 9/11 Medical Surveillance Study. The initial study group was 95 deployed, and 55 non-deployed Search and Rescue dogs. Findings to date indicate overall good longevity and quality of life. This final phase of the study places emphasis on health issues 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. As the investigators further 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 will become clear. This study will provide 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 the years of this important work on behalf of Search and Rescue dogs from its inception in 2001.

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. Research conducted at Washington State University has enabled development of a simple cheek swab test (the MDR1 gene test) now being used 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 hope to identify the cause of extremely slow recovery from anesthesia (up to several days) in a high proportion of greyhounds and other sighthound breed dogs, such as Scottish Deerhound, Borzoi, Whippets, etc. The investigators have recently discovered a mutation in a gene known to be essential for metabolism of commonly used anesthetic drugs (such as propofol), as well as many other drugs used in dogs. In addition to sighthound breeds, this gene mutation is also found in 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 the study is to develop a genetic test to guide the safe use of these drugs in dogs with the gene mutation.

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 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 about 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 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.

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 employed 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. The investigators 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? 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 select dogs in order to increase the number of people assisted by service dogs. 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.

Bretagne. Courtesy Denise Corliss.

Blood Disease Research Program Area

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. 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 MultiplateTM 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. The investigators will measure the effect of low platelet counts on the reliability of this platelet function test in dogs. This project will contribute information to help veterinary clinicians accurately assess platelet function in dogs with low platelet counts, thus ensuring proper treatment of canine patients.


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Cardiology Research Program Area

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 – 5/31/2017
Project Abstract:

Pulmonic stenosis (PS) is an 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 five 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. The Bulldog is 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 to aid breeding decisions to reduce the prevalence of this condition. The investigators will perform clinical evaluation and genetic sample collection, followed by a genome wide association study to looks at genetic markers throughout the entire dog genome. Results from dogs with disease are then compared with healthy dogs. The investigators expect to identify a chromosomal region likely to contain a mutation for PS in this breed, the first step to reducing the prevalence of this disease.

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.

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, and has demonstrated that some Boxer dogs with the mutation have a more severe form of the disease and will become quite sick, while others 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 individual dogs which could include genetic or other factors including diet, exercise and hormone 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. The investigators hypothesize 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.

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.


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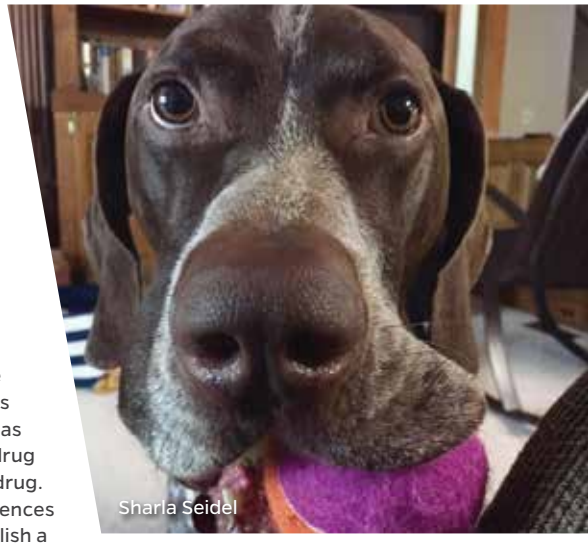
01982

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:


Sharla Seidel

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. The investigators 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 to the drug. The investigators will evaluate the responsiveness of dogs to sildenafil, and 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.

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 – 8/31/2018
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 current 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, the investigators 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 dogs 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

02261-MOU

Improvement of Risk Assessments for Dermatomyositis Testing

Principal Investigator: Dr. Leigh Anne Clark, PhD; Clemson University
Total Grant Amount: $11,704
Grant Period: 4/1/2016 - 3/31/2017
Project Abstract:

Dermatomyositis (DMS) is an autoimmune disease of the skin and muscle that is diagnosed almost exclusively in Shetland Sheepdogs and Collies. The onset of clinical signs of DMS can range from just a few months to several years of age, making elimination of DMS nearly impossible. The investigators have conducted genomic studies and identified genetic sequences that are highly associated with DMS development, which has led to a genetic test for risk alleles of three different genes. Availability of a genetic test will allow breeders to identify breeding pairs that will produce puppies having genotypic combinations associated with a low risk of disease development, and to gradually reduce the frequency of risk alleles in the population. To increase the utility of this test, the researchers must generate genotypes for a random population (i.e., not selected for or against DMS) for calculation of risk assessments. There are 18 possible genotypic combinations between the three genes, and they will study a large population to ensure that accurate risk assessments are available.

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

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 a 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 over time. 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 understand disease in underserved dogs in urban neighborhoods, and data to support keeping dogs and keeping them healthy to benefit both dogs and their owners.

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 - 6/30/2017
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 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 may open the way for a new 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.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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 - 1/31/2017
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. 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. 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 skin's ability to stimulate the immune system. This study will test an alternative route of administration using ASIT for canine atopic dermatitis.

Endocrinology Research Program Area

NEW

02298-MOU

Using OFA Testing to Assess Progression of Canine Autoimmune Thyroiditis

Principal Investigator: Dr. Brian Petroff, DVM, PhD; Michigan State University
Total Grant Amount: $35,630
Grant Period: 8/1/2016 - 7/31/2017
Project Abstract:

Hypothyroidism may be the most common endocrine disorder in adult dogs. As currently understood, a majority of cases are caused by autoimmune thyroiditis (AIT), a disorder in which the body's own immune system attacks the thyroid gland. This causes progressive, irreversible destruction of thyroid gland cells resulting in loss of thyroid hormone production. This disorder has similarities to Hashimoto's thyroiditis, an important cause of hypothyroidism in people. In dogs with AIT, low circulating concentrations of thyroid hormones are often seen in conjunction with increased autoantibodies against thyroglobulin, a large protein made by thyroid cells. Detection of thyroglobulin autoantibodies (TgAA) are the first marker of early stage of AIT, long before there is complete loss of thyroid function. Identification of elevated TgAA results with otherwise normal thyroid hormone concentrations is referred to as 'subclinical thyroiditis.' Dogs with subclinical thyroiditis are considered at risk of progression to hypothyroidism. It is assumed that while dogs with subclinical thyroiditis have increased TgAA, the rate of progression to hypothyroidism varies, and not all animals with increased TgAA will become hypothyroid. The investigators will study dogs with subclinical thyroiditis to better define what proportion develop hypothyroidism, and the timeline to disease progression.

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

Epilepsy Research Program Area

Epilepsy is the most common neurological disease in dogs, and affects almost all breeds.

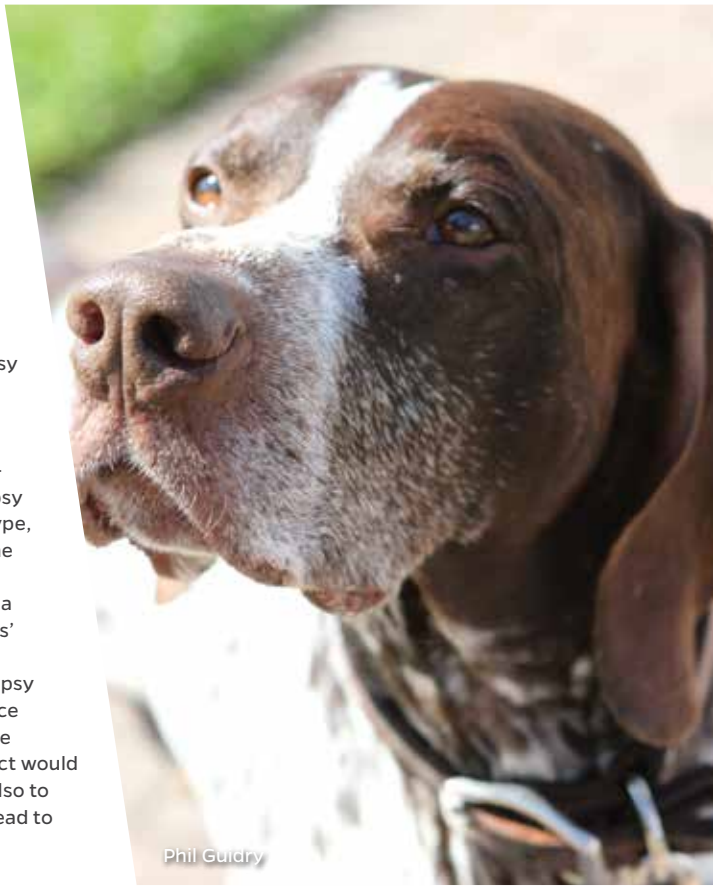
NEW

02248

Identification of a Novel Juvenile Myoclonic Epilepsy Gene and Its Underlying Disease Mechanism

Principal Investigator: Dr. Hannes T Lohi, PhD; University of Helsinki and the Folkhälsan Institute of Genetics
Total Grant Amount: $82,240
Grant Period: 5/1/2016 - 10/31/2017
Project Abstract:

Genetics is likely to play a major role in seizure risk, and gene discovery remains as an important goal to better understand epilepsy and its treatment. Genetic breakthroughs have been rare partially due to incomplete clinical diagnostics to identify true cases and controls, or to distinguish specific syndromes for genetic analyses. The investigators have recently utilized an advanced wireless video-EEG approach in clinical studies to identify juvenile myoclonic epilepsy (JME) in Rhodesian Ridgebacks with characteristic epilepsy phenotype, age of onset and photosensitivity. The pedigree established using the JME cases suggests a strong genetic contribution and is supported by preliminary genetic data that proposes a novel disease locus and a deleterious mutation in a neuronal candidate gene. The investigators' objectives are to: i) further characterize EEG, imaging and disease features of JME, ii) confirm the presence and segregation of an epilepsy gene, iii) investigate the breed-specificity, prevalence and penetrance of the mutation, iv) conclude the inheritance model, and v) define the pathogenicity of the mutation. The confirmation of the genetic defect would allow for development of a genetic test for breeding purposes and also to understand how myoclonic seizures develop. This could ultimately lead to improved treatments for canine epilepsy.


Phil Guidry

NEW

02249-A

Studying the Role of the Gastrointestinal Tract in Canine Epilepsy

Principal Investigator: Dr. Karen R. Munana, DVM, MS; North Carolina State University
Total Grant Amount: $14,995
Grant Period: 6/1/2016 - 11/30/2017
Project Abstract:

Approximately one-third of dogs with epilepsy fail to achieve adequate seizure control with anti-seizure medication, and are considered to have drug resistant epilepsy. The mechanisms that lead to drug resistance are poorly understood. Alterations in the population of intestinal bacteria in the Lactobacillus group are believed to play a role in the development and progression of several human diseases of the nervous system, and an association between epilepsy and both celiac disease and inflammatory bowel disease has been identified in humans, which suggests that changes in intestinal bacteria might play a role in the progression of epilepsy. The investigators hypothesize that dogs with epilepsy have an altered population of Lactobacillus species in their gastrointestinal tracts compared to normal dogs, thus influencing the course of disease. Using molecular genetics and bacterial culture techniques, the investigators will determine differences in bacterial populations, and quantify the Lactobacillus component of the feces of untreated epileptic and control dogs, and determine the effect of antiepileptic medication on Lactobacillus growth rates. By providing preliminary information on the role of gastrointestinal tract bacteria in canine epilepsy, information can be gained to further our understanding of epilepsy and drug resistance in dogs, and ultimately lead to more successful management of the disorder.

NEW

02252

Investigating a Ketogenic Medium-Chain Triglyceride (MCT) Supplement for the Treatment of Drug-Resistant Canine Idiopathic Epilepsy and Its Behavioral Comorbidities

Principal Investigator: Dr. Holger Andreas Volk, DVM, PhD; Royal Veterinary College
Total Grant Amount: $107,697
Grant Period: 5/1/2016 - 10/31/2017
Project Abstract:

Canine epilepsy often requires lifelong medication with anti-epileptic drugs (AEDs). Despite appropriate treatment with available AEDs, seizure freedom may not always be achievable. Over two-thirds of dogs with epilepsy continue to have seizures long-term and around 20-30% remain poorly controlled on standard AEDs. There is an urgent need to develop alternative treatments to improve the quality of life (QoL) of drug-resistant patients. The ketogenic diet, originally characterized as high in fat and low in carbohydrates, has been a successful treatment in children with epilepsy. Recent research has identified a component of the ketogenic diet, a medium-chain fatty acid (MCT) called C10, has direct anti-seizure effects on the brain. The investigators will assess whether dietary supplementation with MCT oil containing C10 for dogs with drug-resistant epilepsy will reduce seizure frequency and/or severity. As epilepsy has multiple impacts on QoL beyond seizure frequency, the researchers will also investigate whether the MCT supplement alters the side effect profile of AEDs, improves behavioral problems associated with epilepsy (e.g. anxiety) and cognition, and improves the stress levels of the affected dog. If successful, MCT supplements could provide a new tool for canine epilepsy treatment.

NEW

02257

Identification of Genetic Risk Factors for Canine Epilepsy

Principal Investigator: Dr. Gary S. Johnson, DVM PhD; University of Missouri, Columbia
Total Grant Amount: $84,121
Grant Period: 5/1/2016 - 4/30/2017
Project Abstract: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Despite strong evidence that genetics is important in determining the risk of idiopathic epilepsy, numerous gene mapping studies have failed to identify a locus that accounts for that risk in either dogs or humans. Seizures occur when excessive activity goes beyond the normal threshold for brain function. Many factors contribute to that level of activity, and therefore, mutations in numerous genes may collectively contribute to increased activity until that threshold is exceeded, resulting in epilepsy. Any one of these mutations may be present in non-epileptic dogs, but because it only partially alters activity, it would not produce seizures. Therefore, traditional gene mapping studies might overlook that mutation. Using a whole genome sequencing approach the investigators hope to identify DNA variations in epileptic dogs that could affect the function of genes such as ion channels and neurotransmitter receptors. The frequency of such variations in populations of epileptic and non-epileptic dogs will be directly compared rather than the indirect markers used in traditional mapping studies. The increased power provided by looking for specific gene candidate variations rather than linked markers will aid the identification of epilepsy risk factors, perhaps leading to development of DNA tests to enable breeders to select against such risk factors.

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 – 12/31/2016
Project Abstract:

Epilepsy has a prevalence of 0.5 - 5.7%, resulting in approximately 2 million affected dogs in the USA. Dogs with drug-resistant epilepsy have frequent seizures even when treated with two or more anti-epileptic drugs. The cross-disciplinary investigative 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; and 3) Perform initial testing of two new potential drugs for the emergency treatment of canine epilepsy.

02131

Neurostimulation: A Groundbreaking New Treatment for Canine Epilepsy

Principal Investigator: Dr. Sam Nicholas Long, BVSc, MVM, PhD, MRCVS; University of Melbourne
Total Grant Amount: $116,000
Grant Period: 10/1/2014 – 3/31/2017
Project Abstract:

Epilepsy is a debilitating condition, and for many dogs, the underlying cause is unknown. In people with epilepsy, advances in some types of imaging have identified subtle brain abnormalities that can be surgically addressed to improve the control of seizures. This project will apply the same advanced techniques to examine the brains of dogs with epilepsy to determine whether such abnormalities exist. In those dogs in which no abnormalities can be found, the investigators will study a new form of treatment, known as neurostimulation, which has been shown to reduce the frequency of seizures in humans. A surgically implanted device called the Brain Radio can provide controlled electrical stimulation to parts of the brain while simultaneously recording the brain's activity. This device is one of the first that could potentially provide successful therapy only when needed to treat imminent seizures, and if proven successful in dogs, may also help people with epilepsy.

Gastrointestinal Disease Research Program Area

02002

Defining the Genetic Basis of Inflammatory Bowel Disease

Principal Investigator: Dr. Karin Allenspach, DVM, PhD; Royal Veterinary College
Total Grant Amount: $119,268
Grant Period: 10/1/2014 - 9/30/2017
Project Abstract:

Inflammatory Bowel Disease (IBD) is a group of disorders in which the intestinal tract has become inflamed. Over time, this inflammation causes the intestine to become less efficient at absorbing nutrients, and weight loss and vomiting or diarrhea often result. Currently, IBD can be controlled, but not cured. The cause of IBD is poorly understood, and it appears genetics, diet, intestinal bacteria, and abnormalities of the dog's immune system all may play a role. The investigator 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, and will investigate underlying genetic factors that could contribute to disease, thus leading to the development of new diagnostic and therapeutic avenues for canine IBD.

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 – 12/31/2016
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 intestinal bacteria contribute to chronic intestinal inflammation. Recent studies have shown that dogs with IBD have 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 insight into the anti-inflammatory effects of probiotics for treatment of human and canine IBD.

Bloat Initiative Grants

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. Rapid and effective decompression of the stomach is critical for successful treatment of dogs with GDV. Current 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. A new, minimally-invasive technique, similar to that used in human medicine, will be tested for its ability to immediately and continuously alleviate gas distention in the stomach of GDV patients using a specialized catheter, thus allowing the patient to be stabilized and/or transported for surgery.

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 – 12/31/2016
Project Abstract:

Gastric dilatation-volvulus (GDV or bloat) is 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. 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 has been shown to, in some instances, be associated with abnormalities in the motilin gene. Motilin is an important driver of stomach contraction. The investigators will study the relationship between abnormal stomach contraction and GDV, and 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 to allow for early detection, and offer selective breeding as an option to eliminate the condition and determine 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 common in large and giant breed dogs with an unacceptably high morbidity and mortality rate. Several studies have investigated potential risk factors for GDV. There is no known single cause for GDV; its occurrence is multifactorial, with both genetic and environmental factors likely contributing. The investigators will study 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 to identify differences in genetic makeup, 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). Using genomic, epigenomic, transcriptomic, proteomic and metabolomic strategies, the investigators hope to understand what causes GDV, and guide more effective preventive and treatment strategies.

Courtesy of Bad Wolf Digital Images

Hepatic Disease Research Program Area

NEW

02297-MOU

Understanding the Genetics of Hepatic Copper Toxicosis in the Dalmatian

Principal Investigator: Dr. Andrew Lawrence Mason, PhD; University of Alberta
Total Grant Amount: $100,000
Grant Period: 12/1/2016 - 11/30/2018
Project Abstract:

Copper toxicosis, leading to early death from liver disease, was first described in Bedlington Terriers in 1975, with similar diseases described in other dog breeds including the Labrador Retriever, West Highland White Terrier, Skye Terrier, and Doberman Pinscher. Genes have been linked to copper toxicosis in the Bedlington Terrier and the Labrador Retriever, but the genes differ by breed. In most breeds the genes are not known. Symptomatic dogs may be misdiagnosed as having other liver diseases, never appropriately diagnosed or only diagnosed with copper overload at a terminal stage. The investigators aim to identify the faulty gene(s) in Dalmatians using a whole genome sequencing strategy to obtain the genome sequences of carefully selected members of an affected Dalmatian pedigree. Identification of the problem gene is the first step towards genetic testing and to improved breeding practices necessary to eradicate hepatic copper toxicosis from the Dalmatian breed. Gene identification will help raise awareness of copper toxicosis, lead to more rapid diagnosis of the condition, and support the search for the most effective therapy.

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

Immunology and Infectious Disease Research Program Area

NEW

02245-MOU

Genetic Predisposition to Avian Tuberculosis in Miniature Schnauzers and Basset Hounds

Principal Investigator: Dr. Urs Giger, DVM, PhD; University of Pennsylvania
Total Grant Amount: $106,858
Grant Period: 5/1/2016 - 4/30/2017
Project Abstract:

While people and dogs are generally resistant to avian tuberculosis infections, there are individuals that lack proper host defense against these intracellular bacteria. The precise molecular basis is unknown, but there is much interest because of the major morbidity and mortality in susceptible patients. The investigators have recognized that many young adult Miniature Schnauzers (and few Basset Hounds) succumb to systemic avian tuberculosis (referred to as Mycobacterium avium complex or MAC), characterized by enlarged lymph nodes, fever, diarrhea and respiratory signs. Based upon pedigree analysis, this appears to be a simple autosomal recessive trait. Preliminary pedigree and limited molecular genetic data suggest a strong signal for one specific small chromosomal region, which the investigators will substantiate using whole genome sequencing. Identification of the molecular basis of this genetic predisposition will allow for the development of a DNA screening test to identify animals at risk and carriers. As avian tuberculosis is a zoonotic disease, the findings should provide insight into genetic determinants of host microbe interaction and resistance in dogs and people, and thereby could have an impact on comparative medicine.

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

NEW

02299-A

Investigating Recovery of the Skin Microbiota after Surgery

Principal Investigator: Dr. Julie Horvath, PhD; North Carolina Museum of Natural Sciences
Total Grant Amount: $9,605
Grant Period: 8/1/2016 - 7/31/2017
Project Abstract:

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

Microbes that live on the skin of humans and animals include bacteria, Archaea, and fungi. These microbes contribute to the overall health and wellness of animals including humans, and have been shown to influence the wound healing process. Antibiotic resistant bacteria are a growing threat to good health. Therefore, while it is not yet understood how microbes play a role in wound healing, a better understanding would allow potential new treatments to emerge using either the microbes themselves, and/or microbial products. This project brings together collaborators from the NCMNS, North

Carolina Central University, North Carolina State University (NCSU) and the NCSU College of Veterinary Medicine to investigate ecological changes in skin microbe composition of dogs following elective surgery. The dogs in this study receive veterinary care at NCSU's College of Veterinary Medicine, undergoing surgery as part of their care, and are given antibiotics. The study's investigators will assess the presence of antibiotic resistant bacteria on dog skin before and after surgery and evaluate the impacts on wound healing.

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 – 12/31/2016
Project Abstract:

The Major Histocompatibility Complex (MHC) genes encode proteins critical for a wide range of biological functions, from immune protection against infectious disease to the predisposition to develop diabetes and autoimmune diseases. The MHC genes in the dog are incompletely characterized, thereby severely limiting the ability to fully define causes of many canine diseases. The investigators have developed improved methods for identifying canine MHC genes in a large number of dogs of diverse breeds. The investigators will characterize MHC genetic variation in over 1200 dogs from at least 50 breeds using a high throughput sequencing strategy. 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 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

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:

Upper airway issues in Norwich Terriers (NTUAS) 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), however, recent evidence shows changes in the larynx including redundant tissue at the top of the larynx, and narrowing of the larynx behind the glottis. The investigators will characterize NTUAS in detail through comprehensive history, oral examination and upper airway endoscopy in US Norwich Terriers. Results will be used to create a NTUAS severity grading system. A subset of dogs will undergo computed tomography and nasal airflow measurements. Results will be compared for Norfolk Terriers, brachycephalic and 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.

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

02275

Disease Risks Associated with Spay and Neuter: A Breed-Specific, Gender-Specific Perspective

Principal Investigator: Dr. Benjamin L Hart, DVM, PhD; University of California, Davis
Total Grant Amount: $61,784
Grant Period: 9/1/2016 - 8/31/2017
Project Abstract:

This study extends the previously completed AKC Canine Health Foundation-funded study of 12 dog breeds to identify differences in the degree to which spay or neuter may be related to joint disorders (hip dysplasia; cranial cruciate ligament tear) and/or cancers (lymphoma; hemangiosarcoma; and mast cell tumor). The original breeds studied were: Labrador Retriever, Golden Retriever, German Shepherd Dog, Rottweiler, Boxer, Bulldog, Doberman Pinscher, Dachshund, Corgi (both breeds), Chihuahua, Yorkshire Terrier and Shih Tzu. The study did not find disease association in the small breeds with spaying or neutering, while in larger breeds

disease risk was dependent upon gender, and whether the spay or neuter procedure was performed before or after one year of age (Hart, B.L., et al. 2014. Long-term health effects of neutering dogs: Comparison of Labrador Retrievers and Golden Retrievers. PLoS ONE 9(7): 10.1371/journal.pone.0102241). In this second phase, the following breeds will be studied: Great Dane, Australian Shepherd, Bernese Mountain Dog, Cocker Spaniel, Border Collie, Beagle, St. Bernard, Irish Wolfhound, Jack Russell Terrier, Pug, Maltese, Pomeranian, Miniature Schnauzer, Boston Terrier, Australian Cattle Dog, Shetland Sheepdog, English Springer Spaniel, Cavalier King Charles Spaniel, and West Highland White Terrier. Upon completion, the major publisher, Wiley, has agreed to place the total data set of all 31 breeds on an open access website as a resource for breeders, dogs owners, researchers and veterinarians.

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 - 8/31/2017
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. 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. 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 in dogs.


Courtesy of Joyce Baker Brown

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 - 6/30/2017
Project Abstract:

This study will 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 a randomized, placebo-controlled clinical trial evaluating the effectiveness of PRP, adipose-derived, cultured stem cells (ASC) and commonly used stromal vascular fraction (SVF) cells 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 investigators hope to identify an effective treatment for supraspinatus tendon injury.

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 debilitating disease affecting large, athletic dogs, 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 separates from surrounding bone, exposing the joint to underlying bone.

Treatment options for osteochondrosis have remained essentially unchanged for decades. Tissue engineering represents a promising treatment alternative for dogs suffering from osteochondrosis. The investigators will study 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. The investigators will optimize materials used to generate ROP layers to determine if MSCs from tissue lining the joint (synovium) or inner cavity of bones (bone marrow) more effectively reconstruct cartilage, transitional tissue, or bone. This work represents an important advance in canine regenerative medicine and is applicable to dogs with osteochondrosis or other common joint ailments such as osteoarthritis.


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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 important that genetic association studies are conducted using adequately-sized cohorts of genotyped diseased and healthy animals. The investigators will sample a large population of dogs so that contributing genetic loci can reliably be discovered. This research group expects that with such a strongly powered study, major genetic risk factors can be uncovered with a high statistical significance. Investigators expect to identify loci 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 of the possible role of diet and exercise in development of hip dysplasia.

Neurology Research Program Area

02210

Gene Therapy for Canine Degenerative Myelopathy

Principal Investigator: Dr. Brian K Kaspar, PhD; 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 dog breeds. DM is an adult-onset disease that manifests at the later stages of life, characterized by progressive weakness and inability to control the hind limbs, ultimately leading to involvement of forelimbs and complete paralysis. There are no current treatments available. Recent studies have identified mutation in the Superoxide dismutase 1 (SOD1) gene as 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. 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. 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 disease.

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 called 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 muscle. Currently no diagnostic test exists that would allow for repeated measurements with minimal invasiveness. The investigator 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, to 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, and could be used to measure the success of therapy. The investigator will complement the test for neurofilament proteins with other studies to measure disease progression.

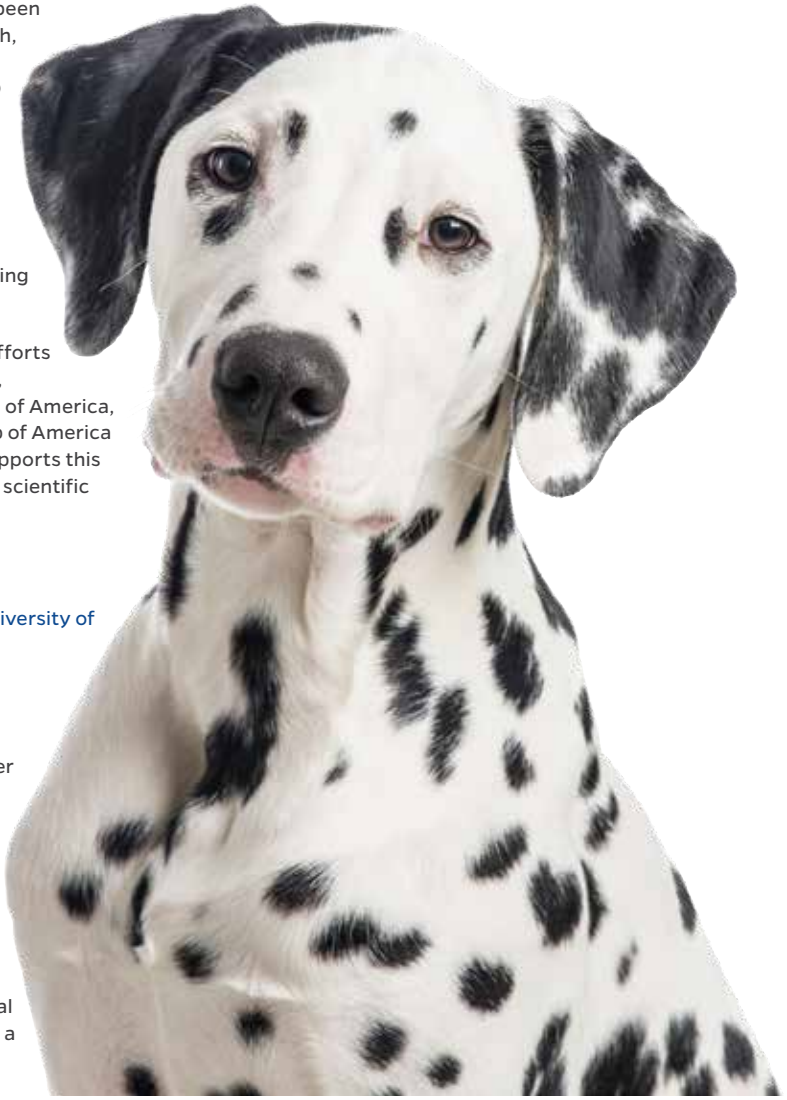
Funding for the research is provided through the efforts and generosity of the American Boxer Charitable Foundation. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.

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, including Dalmatians and Australian Cattle Dogs. The mechanism of inheritance is unknown, and previous studies to determine the mode of inheritance and locate the causative gene(s) have been unsuccessful. Using a modified twin study approach, full-sibling littermates will be clinically and genetically evaluated. 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 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. Other studies in Dalmatians, for example, 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 test.

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.

NEW

02290-MOU

Further Studies to Identify the Mutation Responsible for DUNGd

Principal Investigator: Dr. Dennis P. O'Brien, DVM, PhD; University of Missouri, Columbia
Total Grant Amount: $14,904
Grant Period: 7/1/2016 - 6/30/2017
Project Abstract:

A hereditary disease that breeders called DUNGd was recognized in Gordon Setters in the early 1990s and reported in the veterinary literature in 2000 (Journal of Veterinary Diagnostic Investigation 12:570–573). Affected pups develop normally until 3-4 weeks of age when they show progressive behavioral changes, gait abnormalities and weakness. By 5-6 weeks of age, they are recumbent and must be euthanized. The investigators will utilize next-generation whole genome sequencing and gene mapping to identify genes associated with the disease. If a mutation that appears to cause the disease is found, they will develop a DNA test to identify carriers of the mutation, and thus permit breeders to avoid producing affected pups in the future.

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

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 - 8/31/2017
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. Traditionally, qualitative scoring systems have been used to determine injury severity, recovery, and to 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 gait changes. The investigators will characterize gait recovery in Dachshunds with IVDH using kinematics and compared to the gait of healthy Dachshunds. The major outcomes will be: 1) an enhanced understanding of natural recovery post-IVDH; 2) improved clinical decision making for treatment options; 3) identification of effective assessment parameters; and 4) creation of a baseline for future clinical trials assessing therapies.

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 – 8/31/2017
Project Abstract:

Intervertebral disk herniation (IVDH) leads to spinal cord injury (SCI) in dogs. 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. An improved understanding of muscle activation during walking following IVDH-associated SCI is paramount to developing strategies to enable full recovery. The goal of this study is to characterize individual muscle activation patterns during walking. The investigators will apply computer simulation techniques 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. Computer models will be developed to characterize differences in hind-limb motion and muscle activation patterns during walking between the healthy dog and dog with SCI throughout recovery. The goal is to enhance understanding of functional recovery following surgical treatment of IVDH, and to provide a foundation for improved clinical decision-making for future therapeutic interventions.

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 – 12/31/2016
Project Abstract:

Chiari-like malformations and syringomyelia (CM/SM) are a problem in Cavalier King Charles Spaniels (CKCS) causing severe neuropathic pain. 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. Humans with CM report increased sensitivity to touch and temperature. During case phenotyping for the genetic study, Dr. Olby will investigate sensory thresholds in affected and normal CKCS to improve the ability to document and treat pain in these patients. The goals of this project are to define the genetic etiology of this disease with the long-term aim of developing genetic tests, and to quantify the sensory dysfunction experienced by these dogs to facilitate objective therapeutic trials.

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

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 – 12/31/2016
Project Abstract:

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

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 – 5/31/2017
Project Abstract:

Like their human owners, many dogs suffer from cancer, which is often malignant, spreading through the body via blood. Once tumors have spread, the usual result is a poor outcome. Tumor cells in circulation (CTCs) can be counted in the blood of people with cancer using immunocapture devices, and 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 dogs. Development of an assay for counting CTCs in canine blood would be of benefit to canine patients because, from a simple blood test, we could detect hidden tumors and gather information on tumor severity and the likelihood of metastasis. The investigators will test a novel immunocapture microdevice - the GEDI - for counting tumor cells in canine blood. 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 with cancer, paving a path to early detection of canine cancer.

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 tumors including mammary tumors and soft tissue sarcomas (STS). The best chance of cure is offered if the surgeon can fully remove all traces of the tumor. 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. For malignant tumors, if the disease is minimally or incompletely removed, further surgery or radiation therapy is often required. Additional treatments 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. The investigators will validate this technology for 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, thus advancing the standard of care for canine patients.


Cindy Vogels

02071 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 – 12/31/2016
Project Abstract:

Canine histiocytic sarcoma (HS) is an aggressive cancer that affects Bernese Mountain Dogs (BMD) with a prevalence that ranges from 15 to 25% of the population. Current treatment options for HS are conventional chemotherapeutic drugs, to which dogs respond poorly and only for a short period of time. The investigators will evaluate a modality of treatment for HS using small molecule inhibitors of key cancer pathways. They will also focus on the gene expression associated with the response to treatment to better understand the events leading to the development of HS in BMD, and therefore, develop better therapeutic strategies.

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.

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 – 12/31/2016
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. Radiation therapy is expensive, involves 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 therapy. There is an urgent need for novel therapies to prevent tumor recurrence and increase survival time after surgery. The investigator has previously developed immunotherapy protocols for dogs with gliomas, and will now conduct a larger clinical trial treating 30 dogs with meningioma by surgery alone or surgery followed by vaccines, hoping to see a specific immune response to the vaccines that prevents tumor recurrence. The data from the study will provide further proof of safety and efficacy of vaccine-based therapy to support: 1) more widespread use in dogs, and 2) a Phase I trial for high grade and recurrent meningioma in 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; Dr. Matthew Breen, PhD, North Carolina State University; Dr. Elinor Karlsson, PhD, Broad Institute
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. Through ongoing collaboration, the investigative team has identified several regions of the genome that contain genetic heritable risk factors for lymphoma and hemangiosarcoma in Golden Retrievers. Tumor-specific mutations occur recurrently in both cancers, some linked to duration of remission when treated with standard of care. Their results indicate that a few heritable genetic risk factors may account for as much as 50% of the risk for these cancers. The investigators hope to develop DNA tests that can predict risk for individual dogs, and to manage risk across the whole population. 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. The investigators propose to find precise mutations for heritable genetic risk factors and to validate markers (mutations)

used to determine risk in a 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.

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, many of which are not accessible to surgical removal. 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 using small catheters, placed directly into tumors to allow direct drug delivery to minimize side effects. The investigators will study 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, and is FDA-approved for use in several cancers in humans. When combined with IONPs, cetuximab can be visualized utilizing MRI. The aim is a significant decrease in MRI volume of the tumors and ultimately, tumor-free survival of patients.

Oncology - Hemangiosarcoma Research Program Area

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:

Hemangiosarcoma is an aggressive form of cancer in many dogs, with Golden Retrievers, Portuguese Water Dogs and Boxers at an especially high risk. Hemangiosarcoma is incurable partly because the cancer is detected at a very advanced stage when it is resistant to conventional therapies. To improve outcomes for hemangiosarcoma patients will involve effective methods for early detection and disease prevention. The investigators will use 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, to expand understanding of the performance and utility of the blood test for cancer in dogs with active disease; second, to confirm utility of the test to predict disease progression in treated dogs, 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 has 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.

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. 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, 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 to the tumor. To obtain these lipids, hemangiosarcomas may take over the metabolic machinery of neighboring cells, forcing them to produce nutrients for the tumor. 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 may speed clinical investigations and lead to improved outcomes for dogs.

Oncology - Lymphoma Research Program Area

Canine lymphoma is one of the most common cancers in all dogs.

NEW

02304-A

Investigating a Biomarker and Novel Therapeutic Target for Canine Diffuse Large B Cell Lymphoma

Principal Investigator: Dr. Jennifer A. Luff, VMD, PhD; North Carolina State University
Total Grant Amount: $14,509
Grant Period: 12/1/2016 - 11/30/2017
Project Abstract:


Mary Bloom © AKC

Canine diffuse large B-cell lymphoma (DLBCL) is a common, aggressive cancer in dogs, with an average survival time after initial diagnosis of one year. The diagnosis of DLBCL is often made late in disease when the cancer is advanced, which negatively impacts survival. There is a need to 1) develop non-invasive screening methods for early diagnosis, and 2) identify novel therapies to treat this cancer. In human oncology, the discovery of a new type of gene called long non-coding RNA (lncRNA) has led to the development of non-invasive screening methods for certain cancers. These lncRNAs are also being explored as new cancer targets for drug development, which are expected to have fewer side effects than current treatments. These lncRNA can be detected in blood of cancer patients, so can be used in non-invasive, early detection assays. Recently, human DLBCLs were shown to express high levels of the lncRNA HOX transcript antisense RNA (HOTAIR), and its expression was predictive of a poor prognosis; human HOTAIR is also being explored as a new target for cancer therapy. The investigators will study canine lncRNA HOTAIR to determine expression and blood detection in canine DLBCL patients. If successful, this research will advance the detection and treatment of DLBCL.

NEW

02309

Targeting the Cancer Epigenome: The Effect of Specific Histone Lysine Methyltransferase Inhibition in Canine B-Cell Lymphoma

Principal Investigator: Dr. Angela McCleary-Wheeler, DVM, PhD; Cornell University
Total Grant Amount: $78,069
Grant Period: 1/1/2017 - 12/31/2018
Project Abstract:

While often treatable, canine lymphoma can rarely be cured. A continued understanding of the mechanisms causing lymphoma in dogs and identification of novel therapies are needed to improve survival. Research that has been actively explored and provided exciting breakthroughs for human lymphoma is epigenetics, or alterations in how genes are turned on and off independent of the DNA sequence. One way this occurs is through modifications of proteins that interact with DNA called histones. Modifications to these histones can result in genes being turned on or off, leading to the development of cancer. One enzyme that modifies histones, EZH2, has been found to play a role in some human lymphomas. Given the striking similarities between human and canine lymphoma, the objective of this study is to characterize the function and role of EZH2 in canine lymphoma. The investigators will utilize an EZH2 inhibitor to study EZH2 in canine lymphoma cells, and help guide the future development of this targeted inhibitor for use as a novel therapy for canine lymphoma.

NEW

02315-A

Discovering Peptide Targets for Development of Adoptive Cell Therapy for Peripheral T-Cell Lymphoma

Principal Investigator: Dr. Paul R. Hess, DVM PhD; North Carolina State University
Total Grant Amount: $14,990
Grant Period: 12/1/2016 - 11/30/2017
Project Abstract:

T cells (a type of white blood cell known as a lymphocyte) constitute the immune system's most potent weapons against cancer, but growing malignant cells can quickly outpace and overwhelm these defenses. In the most advanced form of cancer immunotherapy, these T cells can be isolated from the body, reinvigorated and expanded in the test tube, and then given back to patients -- in some cases, leading to years-long remissions of advanced cancers, usually melanomas, resistant to other treatments. There is tremendous enthusiasm to extend this approach to lymphoma and other incurable malignancies, which has proved difficult because T cells also recognize and attack normal tissues, causing patient death. Because the therapy involves living cells, and is personalized -- T cells typically target a marker unique to a specific patient's tumor -- the complexity and cost is enormous. Efforts to make this immunotherapy safer and readily available are being pursued, focused on finding cancer proteins recognized by T cells that are 1) shared between patients with the same cancer, and 2) not expressed by normal tissues, sparing them from inappropriate attack. The investigators recently discovered a protein expressed by lymphoma cells across multiple canine patients; importantly, normal tissue expression appears minimal. This study's goal is to identify the correct tiny fragment (peptide) of this protein that T cells directly recognize, which then will be used to extract these T cells from patients for development of immunotherapy for dogs.

NEW

02316

Genetic Risk Factors for Canine T zone Lymphoma

Principal Investigator: Dr. Anne A. Avery, DVM PhD; Colorado State University
Total Grant Amount: $52,894
Grant Period: 1/1/2017 - 12/31/2017
Project Abstract:

The Golden Retriever is a breed that develops a variety of cancers at a high frequency. One type of cancer, T zone lymphoma, is so common that 40% of cases are seen in Golden Retrievers. This observation suggests a genetic predisposition. The investigators have completed an environmental risk factor study and the first phase of a genetic risk factor study to better understand the causes of this disease. Two key findings from this work are, 1) The same genetic region associated with risk for mast cell tumors was identified as conferring risk for T zone lymphoma, and 2) The presence of hypothyroidism was protective for T zone lymphoma, and genes associated with thyroid function are also found in the risk regions. The goal of this study is to complete the genetic risk factor study by identifying specific genetic mutations associated with the disease, to improve understanding of the mechanisms that lead to T zone lymphoma as well as mast cell tumors in dogs.

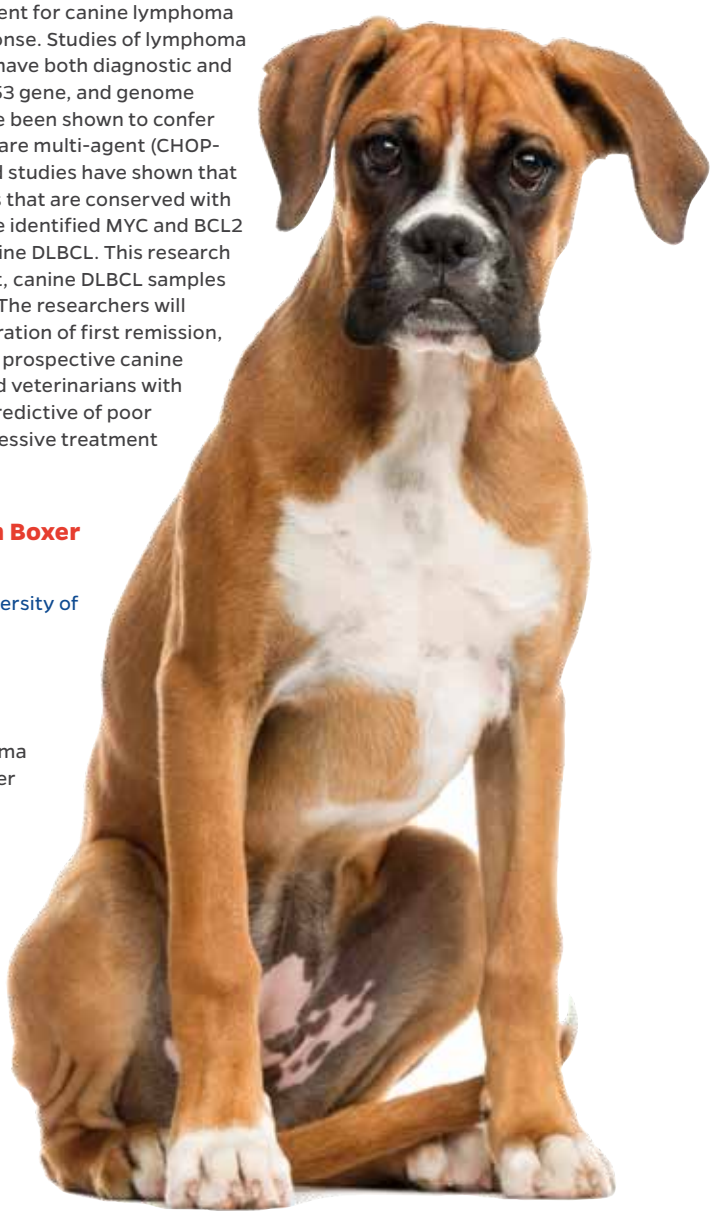
NEW

02317

The Role of Complex Translocations Associated with TP53 Somatic Mutations for Aiding Prognosis of Canine Diffuse Large B-cell Lymphoma

Principal Investigator: Dr. Matthew Breen, PhD; North Carolina State University
Total Grant Amount: $177,327
Grant Period: 1/1/2017 - 12/31/2018
Project Abstract:

Lymphoma accounts for up to 24% of all cancers diagnosed in pet dogs; diffuse large B-cell lymphoma (DLBCL) is the most common subtype. The response to treatment for canine lymphoma remains highly variable with no reliable means to predict response. Studies of lymphoma in people have identified characteristic genome changes that have both diagnostic and prognostic significance. In human DLBCL, mutations in the TP53 gene, and genome rearrangements involving the MYC, BCL2 and BCL6 genes have been shown to confer particularly poor prognosis in cases treated with standard of care multi-agent (CHOP-based) chemotherapy. The investigator's previous CHF-funded studies have shown that canine cancers, including lymphoma, exhibit genomic changes that are conserved with those observed in the corresponding human cancers, and have identified MYC and BCL2 rearrangements and a high frequency of TP53 mutation in canine DLBCL. This research will screen a well-defined collection of over 450 pre-treatment, canine DLBCL samples to determine accurate frequencies of these genome changes. The researchers will investigate the correlation of these target aberrations with duration of first remission, and identify key genomic signatures that may aid prognosis of prospective canine lymphoma cases. The data generated should assist owners and veterinarians with decisions regarding treatment, and patients with signatures predictive of poor response to CHOP chemotherapy may benefit from more aggressive treatment to improve outcomes.



NEW

02318

Genetic and Environmental Risk for Lymphoma in Boxer Dogs

Principal Investigator: Dr. Lauren A Trepanier, DVM PhD; University of Wisconsin, Madison
Total Grant Amount: $112,861
Grant Period: 1/1/2017 - 12/31/2018
Project Abstract:

Lymphoma is a fatal cancer that can occur in any dog. Lymphoma is more common in Boxers, Golden Retrievers, and several other purebreds, which suggests involvement of inherited genes. Recent research has focused on gene mutations in the tumors of dogs with lymphoma. However, we do not understand why these mutations accumulate in certain dogs, and this understanding is essential for disease prevention. Canine lymphoma resembles Non-Hodgkin lymphoma (NHL) in humans, which is more common in industrialized countries and is associated with chemicals found in tobacco smoke, certain household products, pesticides, herbicides, and fungicides. Glutathione-S-transferases (GSTs) are enzymes that can break down toxic chemicals in the body and prevent tumor mutations. Inherited gene defects in the 3 major GST enzymes, GST-theta, GST-pi and GST-mu, each increase NHL risk. Simultaneous defects in more than one enzyme further increase NHL risk. The investigators have characterized two GST-theta enzymes in dogs, and both have defective gene

variants. Findings suggest one variant is a risk factor for lymphoma in dogs of varying breeds. This research will determine whether defective GST genes along with certain household and yard chemicals are associated with lymphoma in dogs, with a focus on the high-risk Boxer breed. The overall goal of this study is to identify combinations of genes and environmental chemicals that contribute to the development of lymphoma in dogs, so that better cancer prevention strategies can be developed.

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 - 6/30/2017
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. The investigative team will focus their efforts on an area of emerging importance in cancer: epigenetics, 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 use flow cytometry paired with biopsy to characterize 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. Because DNA methylation changes occur so early in the process of cancer formation, these could serve as biomarkers of risk, allowing medicine or diet to prevent lymphoma in Golden Retrievers before it develops. Finally, they will identify tumor initiating cells (TIC) in lymphoma biopsies to characterize stem-like cells by surface markers and DNA methylation changes to aid therapeutic strategy development and to advance the prevention and management of lymphoma in Golden Retrievers.

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. 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 to prevent relapse and prolong survival in dogs with NHL.

Oncology - Osteosarcoma Research Program Area

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. A large number of 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. Developing an osteosarcoma cancer vaccine holds promise as an adjunct treatment to surgery and chemotherapy. In a previous study of 400 dogs with melanoma the investigators 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, dogs with osteosarcoma will be randomly assigned to two treatment groups with the outcomes of dogs receiving the vaccine plus standard of care compared to dogs who receive standard of care without vaccination. Vaccines will be administered monthly for 4 treatments and the dogs monitored for life. 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.

Ophthalmology Research Program Area

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 - 12/31/2017
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, resulting in corneal swelling, 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 compared to other breeds, thus 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, evaluating the entire canine genome for an association with CED to identify the gene(s) responsible for this condition in these 3 breeds, and to develop a genetic test for CED.


Supreme Point's Peanuts and Cracker Jacks

02164-MOU

Determining the Genetic Contribution to Boxer Corneal Ulcers

Principal Investigator: Dr. Kathryn M Meurs, DVM, PhD; North Carolina State University
Total Grant Amount: $68,053
Grant Period: 1/1/2015 - 12/31/2016
Project Abstract:

Spontaneous chronic corneal epithelial defects (SCCEDs) are commonly seen in Boxers. The predilection for Boxers suggests that SCCEDs is inherited in this breed. Affected dogs develop spontaneous corneal ulcers that are often exceptionally painful and persist for weeks to months. Most dogs require surgical therapy and experience corneal scarring as a result. The impact on the quality of life for dogs during episodes of ulceration has led to increased interest in disease prevention. However, since SCCEDs is an adult onset disease, many dogs are selected for breeding before they are diagnosed. Early testing could identify affected animals and greatly decrease the prevalence of SCCEDs. In a previous study funded by the AKC CHF, the investigators performed a genome wide association study in Boxers. They will now perform whole genome sequencing on a subset of affected and unaffected dogs, using data from the GWAS. Variants of interest will be used to determine the gene and ultimately the causative genetic mutation. The identification of a genetic cause for SCCEDs in the Boxer can be used to reduce the prevalence of this disease in this breed and others.

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.

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 – 5/31/2017
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. 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, suggesting a genetic component. The investigators hope to identify the region of the dog genome associated with KCS in the West Highland White Terrier. The entire canine genome will be evaluated for an association with KCS 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 with an increased risk of KCS.

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 – 12/31/2016
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 prevention or effective treatment for pigmentary uveitis. Evidence strongly suggests pigmentary uveitis is an inherited disease 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. 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. The investigators will perform a genome-wide association study (GWAS) to identify a chromosomal region associated with Golden Retriever pigmentary uveitis, and use high-throughput DNA sequencing to allow identification of the causative mutation. Identification of the gene responsible for pigmentary uveitis would permit development of a genetic test to inform breeding decisions. Knowing the molecular basis underlying pigmentary uveitis may allow researchers to develop more effective treatments for dogs to possibly prevent the blindness, cataracts, and glaucoma caused by pigmentary uveitis.

Renal Disease Research Program Area

NEW

02263-MOU

Characterization of Kidney Disease in Dalmatians

Principal Investigator: Dr. Rachel E Cianciolo, VMD, PhD; Ohio State University
Total Grant Amount: $31,434
Grant Period: 5/1/2016 - 4/30/2018
Project Abstract:

Chronic kidney disease is a significant progressive problem in dogs. Two different hereditary diseases of the urinary system are being studied in Dalmatian dogs: urinary stone formation (urolithiasis) and glomerular disease. These diseases cause distinct clinical signs: urolithiasis leads to urinary tract obstruction while glomerular disease results in protein loss into the urine (proteinuria). The genetic cause of urolithiasis is known while the genetic cause of glomerular disease has not yet been identified. Preliminary investigations indicate that there may be multiple causes of proteinuria in Dalmatians. Evaluation of kidney tissue by the International Veterinary Renal Pathology Service has revealed diverse types of glomerular diseases in Dalmatians, at least 4 of which might be hereditary. Therefore, the most common disease type is unknown and must be identified and characterized. A detailed review of necropsy and biopsy sample archives previously obtained from Dalmatians with proteinuria will be performed. Next, prospective examination of select kidney samples using advanced techniques (electron microscopy and immunofluorescence) will ensure an accurate diagnosis of the glomerular disease. Ultimately, genetic analyses performed on related dogs could demonstrate similar glomerular lesions to identify candidate genes.

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.

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 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. Treatment can include hormone therapy, drugs designed to strengthen the muscle tone of the urethral sphincter, collagen injections, or surgery. The investigator has reported that injection of muscle progenitor cells into damaged urethral sphincters can restore normal function in dogs. This project will 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.

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 - 6/30/2017
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. Improvements in tests to detect kidney damage at an earlier stage would allow veterinarians to provide dogs with 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. 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. The investigator 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. 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 – 12/31/2016
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. 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 disease. 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. The goal of this study is to identify miRNAs in serum and urine of dogs that are specific for the three major causes of canine glomerular disease. They also aim to identify miRNAs associated with disease progression. 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

NEW

02264-A

Role of *E. Coli* Biofilm in Canine Pyometra

Principal Investigator: Dr. Marco A Coutinho da Silva, DVM, PhD; Ohio State University
Total Grant Amount: $14,731
Grant Period: 5/1/2016 - 4/30/2017
Project Abstract:

Pyometra is a potentially life-threatening infection of the canine uterus by bacteria, most commonly *Escherichia coli (E. coli)*. In humans with recurrent infections, *E. coli* produces a biofilm, a layer of polysaccharide that protects the organism from the host immune system as well as antibiotic agents, decreasing treatment efficacy. The investigators postulate that biofilm production by *E.coli* within the endometrium of the bitch may be responsible for perpetuating the disease and making treatment difficult. In this pilot study, the potential of *E. coli* obtained from clinical cases of canine pyometra to produce biofilm will be evaluated in vitro and in vivo. Endometrial samples from clinical cases of pyometra will be evaluated for the presence of biofilm in situ, as well as the ability of the isolated bacteria to produce biofilm in vitro. If successful, demonstration of the presence of biofilm in the endometrium of bitches affected by pyometra could lead to development of new therapeutics targeted to disrupt the biofilm, resulting in improved treatment for canine pyometra.

NEW

02267-A

An Epidemiological Study of *Brucella canis*

Principal Investigator: Ms. Tory V Whitten, MPH; Minnesota Department of Health
Total Grant Amount: $14,986
Grant Period: 11/1/2016 - 10/31/2017
Project Abstract:

Canine brucellosis is a reproductive disease caused by the bacterium *Brucella canis (B. canis)* that can cause infertility, abortion and severe spinal infections in dogs. Though well understood in the context of canine breeding operations, this disease is an under-recognized public health issue in the canine rescue and shelter populations, and may constitute a source of infection to dog and human populations. In 2015 there was an increase in the number of rescue dogs identified with canine brucellosis in Minnesota where, prior to 2015, there had been no cases of canine brucellosis identified in a dog not used in a breeding program. This study will measure exposure to this disease in rescue and shelter dogs entering Minnesota, as a first step to understanding prevalence of this important reproductive disease. The results of this study

will be used to determine prevalence and raise awareness of this disease in rescue and shelter dog populations, help identify risk factors for canine brucellosis, and develop a diagnostic PCR test for canine brucellosis. An important outcome of this study will be to create prevention and control measures applicable to all dogs.

02175-A 01699-A

Preventing Inaccurate Diagnosis of Brucellosis

Principal Investigator: Dr. Christina M Larson, DVM; University of Minnesota
Total Grant Amount: $10,567
Grant Period: 3/1/2012 - 8/30/2017
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

Principal Investigator: Dr. Angela M Arenas, DVM, PhD; Texas A&M AgriLife Research
Total Grant Amount: $12,952
Grant Period: 10/1/2015 – 1/31/2017
Project Abstract: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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 dogs. Historically, brucellosis control efforts have demonstrated that the spread of the disease is preventable or significantly reduced in association with vaccination. 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.

02188-A

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

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. Before surgical exploration is considered, the veterinarian wants to have strong evidence that an ovarian remnant is present. Current diagnostic tests for ORS have limitations, and the research team will thoroughly evaluate a new line of testing: anti-Müllerian hormone (AMH) combined with progesterone. AMH effectively distinguishes between spayed and intact dogs, and when combined with progesterone testing, the investigator's preliminary data suggest that AMH is also effective in determining if a spayed bitch has an ovarian remnant. This project 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.

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 – 6/30/2017
Project Abstract:

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 an 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 male fertility, and improve analysis of transported and frozen semen for Labrador Retrievers that will likely benefit all breeds.

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 a significant reproductive health concern 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 becomes difficult or even impossible, often 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 genetic risk factor associated with this problem. 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 will be analyzed 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 disease.

Tick-Borne Disease Initiative Grants

NEW

02284-A

Lyme Disease in Dogs: Prevalence, Clinical Illness, and Prognosis

Principal Investigator: Dr. Jason Stull, VMD, PhD; Ohio State University
Total Grant Amount: $14,148
Grant Period: 7/1/2016 - 6/30/2018
Project Abstract:

Lyme disease (or Borreliosis) is a bacterial disease of dogs and humans that is transmitted by tick bites. While most common in the northeastern coastal states and the upper Midwest, Lyme disease is moving into other regions of the U.S. and Canada. Dogs infected with Lyme disease rarely show signs of illness (typically lameness), but illness can be severe (e.g., kidney disease). Diagnosis, treatment and prevention of Lyme disease in dogs are complicated by limited research and conflicting professional guidance. Current practices may unnecessarily place dogs at risk for illness and negative outcomes. The investigators will follow a large group of dogs from different regions of the U.S. and Canada to determine how often healthy dogs test positive for Lyme disease (meaning they have been bitten by an infected tick) and identify how often they later develop a Lyme-related illness. The risks and benefits of management strategies for Lyme-positive dogs and obstacles to effective tick prevention will be determined to help clarify unmet pet owner education needs. Collectively, this research will allow us to identify, define and improve upon best practices for prevention and control of Lyme disease in areas with different Lyme risks, ultimately improving the health of dogs and people.

NEW

02285-A

Thrombocytopenia and Occult Vector-Borne Disease in Greyhound Dogs: Implications for Clinical Cases and Blood Donors

Principal Investigator: Dr. Linda Kidd, DVM, PhD; Western University of Health SciencesSciences
Total Grant Amount: $12,960
Grant Period: 7/1/2016 - 6/30/2017
Project Abstract:

Retired racing Greyhounds (RRG) are popular pets, and also commonly serve as blood donors to treat all types of dogs. Not all Greyhounds are RRG; show-bred Greyhounds (SBG) have traceable pedigrees verifying they do not descend from racing lines. Low platelet (thrombocytopenia) and white blood cell counts are considered normal findings in Greyhounds, and protein in the urine is common. Because these findings can also be caused by infection with vector-borne disease agents, Greyhounds can present clinicians with a diagnostic dilemma. Racing Greyhounds are commonly exposed to the brown dog tick, which transmits many agents that can cause disease. Vector-borne diseases are also transmitted by the lone star tick, also common in the region of the U.S. where racing farms are located. Because these pathogens can cause chronic, clinically silent infection, the investigators hypothesize that infection occurs in, and contributes to blood and urine abnormalities in some healthy-appearing RRG. This study will compare the prevalence of vector-borne diseases in RRG and SBG, determine whether thrombocytopenia, low white blood cell counts and protein in the urine are associated with vector-borne disease in RRG, and whether blood and urine abnormalities occur with the same frequency in RRG and SBG. The results will help veterinarians decide when to pursue infectious disease testing, and whether more aggressive infectious disease screening for both pet and blood donor Greyhounds is warranted based on lineage.

NEW

02287

Enhanced Testing for the Diagnosis of Bartonellosis in Dogs

Principal Investigator: Dr. Edward B Breitschwerdt, DVM; North Carolina State University
Total Grant Amount: $103,013
Grant Period: 8/1/2016 - 7/31/2017
Project Abstract:

Bartonellosis, a zoonotic bacterial disease of worldwide distribution, is caused by approximately 10 different Bartonella species. Bartonella are transmitted to canines and humans by ticks, fleas, lice, mites, and sand flies. Bartonella species have been associated with an expanding spectrum of important disease manifestations including anemia, endocarditis, hepatitis, lymphadenitis, myocarditis, thrombocytopenia and vascular tumor-like lesions. Infections can be life-threatening. Due to a lack of sensitive and reliable diagnostic assays, definitive diagnosis of bartonellosis in dogs remains a significant problem. Because these bacteria invade cells and infect tissues throughout the body, this chronic intracellular infection is difficult to cure with currently used antibiotic regimens. This study will develop improved serodiagnostic tests for bartonellosis in dogs. These assays can also be used for world-wide sero-epidemiological prevalence studies, and to establish early and accurate diagnosis. Dr. Breitschwerdt's research group has described concurrent infection in dogs, their owners and veterinary workers; this allows for a One Health approach to this important emerging infectious disease.

NEW

02292

Broad-Range Detection of Canine Tick-Borne Disease and Improved Diagnostics Using Next-Generation Sequencing

Principal Investigator: Dr. Pedro Paul Diniz, DVM, PhD; Western University of Health Sciences
Total Grant Amount: $60,717
Grant Period: 9/1/2016 - 8/31/2017
Project Abstract:

Diagnostic tests based on the detection of DNA of infectious organisms from clinical samples have revolutionized veterinary medicine in the last decades. Currently, diagnostic panels for several tick-borne organisms are available through universities and private laboratories in the USA and abroad. However, the vast majority of results from clinically ill dogs are negative for tick-borne diseases, which frustrates veterinarians and dog owners trying to reach a definitive diagnosis and improve treatment options. These panels are based on the detection of previously known DNA sequences of each pathogen, with little room for detecting new organisms. Using an innovative approach, the investigators will employ next-generation sequencing (NGS) to overcome the limitations of current diagnostic technology and generate millions of individual gene sequencing reads from each clinical sample, allowing for the identification and characterization of multiple organisms from a single sample. Testing samples from dogs naturally exposed to tick-borne diseases, NGS will detect not only new organisms but also characterize genetic differences among known organisms. The resulting dataset of a large number of DNA sequences of known tick-borne organisms and previously undetected organisms in naturally-infected dogs will support the development of diagnostic tools to simultaneously advance canine and human health.

NEW

02295-A

The Role of Lymphocytes in Canine Monocytic Ehrlichiosis

Principal Investigator: Dr. Mary Anna Thrall, DVM, MS; Ross University School of Veterinary Medicine
Total Grant Amount: $15,000
Grant Period: 7/1/2016 - 6/30/2017
Project Abstract:

Canine monocytic ehrlichiosis (CME) is a serious disease of dogs, caused by the intracellular bacteria *Ehrlichia canis* that is transmitted by a tick bite. There is no vaccine for CME, and the pathophysiology of why the disease is more serious in some dogs is not understood. CME is very common in St. Kitts, home to Ross University School of Veterinary Medicine. The large numbers of affected dogs are a valuable resource for studies of this important disease. Lymphocytes (a type of white blood cell) appear to be related to the pathophysiology of CME. The investigators will study the types of lymphocytes present in dogs with both mild and severe disease and compare them to non-affected dogs. Lymphocytes will be identified by type as B or T cells using antibody markers for lymphocytes and flow cytometry. The investigators will determine if an increase in lymphocyte counts (lymphocytosis) is associated with severity of disease, and whether clonality (having a large number of the exact same type of lymphocyte) is associated with severity of disease. Fifty Ehrlichia-positive dogs admitted to Ross University will be evaluated for their number of lymphocytes by blood cell counts, by flow cytometry to determine their lymphocyte subsets, and by PCR and antibody testing for the presence of tick-borne disease. These dogs will be compared to healthy control dogs. The researchers will also evaluate 50 dogs presenting with persistent lymphocytosis and determine the percentage of those dogs that are Ehrlichia positive. The findings of this study will advance understanding of the pathophysiology and diagnosis of ehrlichiosis and lymphocytosis.

Clinician-Scientist Fellowship Training Program

To sustain future advancements in canine and human health, the AKC Canine Health Foundation encourages and supports 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 this effort the AKC Canine Health Foundation's mission to prevent, treat and cure canine disease will endure for years to come.

Recipients are selected based upon the following criteria for a resident/graduate student:
1)Who has shown promise and enthusiasm for pursuing a career in canine health research,
2Who will conduct research in line with CHF's mission to advance the health of all dogs and their people,
3)Who will conduct research that will abide by CHF policies, including our Humane Use of Animals Policy.

Three promising researchers have been named 2017 Clinician-Scientist Fellows:

Dr. Jeanie Lau, BVSc; North Carolina State University
Mentor: Dr. Karen R. Munana, DVM, MS, DACVIM

Dr. Lau received her bachelor's degree in Neuroscience from Dartmouth College and her veterinary degree from the University of Sydney. Upon graduation from veterinary school, Dr. Lau practiced as an associate veterinarian before completing both a rotating small animal internship and a neurology specialty internship. Dr. Lau is now in a residency training program in Neurology and Neurosurgery at North Carolina State University College of Veterinary Medicine.

Dr. Lau's research on Steroid Responsive Meningitis-Arteritis (SRMA) in dogs will involve characterizing the clinical and diagnostic findings and response to therapy in a population of dogs with SRMA in North America. Comparisons will be performed to identify any differences in the disease with respect to breed.

Dr. Jennifer Reinhart, DVM, DACVIM; University of Wisconsin
Mentor: Dr. Lauren A. Trepanier, DVM, PhD, DACVCP, DACVIM

Dr. Reinhart received her veterinary degree from the University of Illinois, completed a small animal internship at Cornell University, and a small animal internal medicine residency at Kansas State University. She is a diplomate of the American College of Veterinary Internal Medicine and is currently pursuing a PhD at the University of Wisconsin School of Veterinary Medicine.

The focus of Dr. Reinhart's research is the identification of genetic and breed risk factors for sulfonamide hypersensitivity in dogs. She has identified a candidate gene and is working to validate this finding in hypersensitive dogs. This work also entails determining susceptibility in specific breeds (particularly the Doberman Pinscher).

Dr. Takashi Taguchi, DVM; Western University of Health Sciences
Mentor: Dr. Dominique Griffon, DMV, MS, PhD, DECVS, DACVS

Dr. Taguchi received his veterinary degree from the Osaka Prefecture University in Japan and completed a small animal surgery internship at Tokyo University of Agriculture and Technology.

Dr. Taguchi will study the influence of donor's age on canine adipose-derived mesenchymal stem cells at Western University of Health Sciences College of Veterinary Medicine, where he is currently a graduate student. Dr. Taguchi's long-term goals are to address challenges currently faced in orthopedics as a clinician scientist, using sound research design to advance the prevention, diagnosis, treatment, and well-being of small animals.

2016 Theriogenology Residency Program

This program is a collaboration between the American Kennel Club, the AKC Canine Health Foundation, and the Theriogenology Foundation to increase the number of trained practitioners in companion animal theriogenology. Theriogenology is the branch of veterinary medicine concerned with reproduction, including the physiology and pathology of male and female reproductive systems, and the clinical practice of veterinary obstetrics, gynecology, and andrology.

Dr. Carla Barstow, DVM; Auburn University (CHF Grant 02282-E)
Residency Coordinator: Dr. Robyn R. Wilborn, DVM, MS, DACT; Auburn University
Total Grant Amount: $100,000; Grant Period: 7/1/2016 - 6/30/2019

Dr. Carla Barstow has been showing and breeding Samoyeds for over 20 years. Prior to obtaining her DVM degree, she spent 10 years working in the veterinary field as a technician. Dr. Barstow then pursued her DVM degree at the University of Minnesota, where she received mentorship from Dr. Peggy Root Kustritz who further cultivated her love of theriogenology. Upon graduation, Dr. Barstow returned to Tampa to join a private practice which emphasized reproduction, and enjoyed a heavy theriogenology caseload prior to starting her residency.

Dr. Tessa Fiamengo, DVM; Ohio State University (CHF Grant 02294-E)
Residency Coordinator: Dr. Marco A. Coutinho da Silva, DVM, PhD, DACT; Ohio State University
Total Grant Amount: $100,000; Grant Period: 7/1/2016 - 6/30/2018

Dr. Tessa Fiamengo graduated with honors from Colorado State University with a major in Biology and minors in Biomedical Sciences and Philosophy. She earned her veterinary degree from Oregon State University, and has worked as a small animal general practitioner in Portland, OR.

Dr. Victor Stora, DVM; University of Pennsylvania (CHF Grant 02283-E)
Residency Coordinator: Dr. Margret L. Casal, DVM, PhD, DECAR; University of Pennsylvania
Total Grant Amount: $100,000; Grant Period: 7/1/2016 - 6/30/2018

Dr. Victor Stora received his Bachelor of Science from Wagner College, Staten Island, NY, with a double major in Molecular and Cellular Biology and Biochemistry. He received his veterinary degree from the School of Veterinary Medicine, Louisiana State University. He completed a small animal medicine and surgery internship at Virginia-Maryland College of Veterinary Medicine. Dr. Stora breeds Shetland Sheepdogs.

Dr. Karen Von Dollen, DVM; North Carolina State University (CHF Grant 02281-E)
Residency Coordinator: Dr. Scott Bailey, DVM, MS, DACT; North Carolina State University
Total Grant Amount: $100,000; Grant Period: 7/1/2016 - 6/30/2019

Dr. Von Dollen attended Bryn Mawr College in Pennsylvania, where she majored in chemistry with minors in mathematics and biology and was a member of the varsity lacrosse team. She returned to California to earn her DVM degree from the University of California - Davis. Following graduation, she completed internships at Alamo Pintado Equine Medical Center in Los Olivos, California and Goulburn Valley Equine Hospital in Victoria, Australia.

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