



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

2018 Research Grants Portfolio



Introduction

December 1, 2017

For the past 22 years the AKC Canine Health Foundation (CHF) has remained committed to addressing the health needs of our closest companions through the funding of scientific research, and by providing educational resources for those dedicated to improving the health of dogs.

This grants portfolio represents active research projects, funded through CHF, categorized by research program area, and selected to advance the Foundation's Mission for the betterment of health for all dogs. Every grant proposal goes through a rigorous assessment by the CHF Scientific Review Committee (<http://www.akcchf.org/Scientific-Review-Committee>) and peer reviewers representing a diverse set of experts from within the scientific community. Each grant is assessed for scientific merit, impact in the field of study, and significance to dogs and their people through One Health. This review process ensures the contributions of our donors will be directed to studies that will have the greatest potential benefit for dogs. You will find the abstracts of awarded grants listed on the following pages represent cutting edge research as well as applied clinical studies chosen to improve the lives of dogs as well as contribute to our understanding of complex disease processes, including genetics. The program areas funded by CHF represent a broad range of concerns across general canine health as well as within specific breeds. Through defined research program areas, CHF considers areas of unmet health needs and areas of immediate opportunity, while applying recent advancements in science and technology to canine health research.

The recent research initiatives directed by CHF to address tick-borne diseases and epilepsy are reflected in this portfolio, and on our website. At these weblinks, [akcchf.org/ticks](http://www.akcchf.org/ticks) and [akcchf.org/epilepsy](http://www.akcchf.org/epilepsy), respectively, you will find the listing of all research projects, publication outcomes and educational resources compiled in one location. Additional work currently funded in oncology, cardiology, neurology and across all research program areas is contained within this portfolio and can also be searched online at [akcchf.org/research/our-research](http://www.akcchf.org/research/our-research).

In addition to CHF's wide array of research grants, the Foundation remains dedicated to educating the next generation of scientists by providing funds through the AKC Canine Health Foundation Clinician-Scientist Fellowship Program ([akcchf.org/about-us/who_we_are/Fellows/](http://www.akcchf.org/about-us/who_we_are/Fellows/)). Also, through the collaborative efforts of the American Kennel Club, AKC Canine Health Foundation and the Theriogenology Foundation, the AKC/AKCCHF/TF Theriogenology Residency Program increases the number of trained practitioners in the field of companion animal theriogenology. Through outreach to breeders, veterinarians and the general public, we also provide resources and communications on outcomes of research for canine health. (<http://www.akcchf.org/research/>)

As you look through the following pages please do so knowing these studies will lead to a better understanding of canine health concerns that will lead to improvements in the prevention, treatment and cures of canine diseases. To discuss a study or to learn about sponsoring research, please contact us at chfgrants@akcchf.org. We want to hear from you. Together, we are moving canine health research forward, benefiting the dogs who so enrich peoples' lives.

Because of the support of our partners at the American Kennel Club, Purina, Zoetis, and the many breed clubs, foundations and private donors whose support we so value, it has been another productive year for the AKC Canine Health Foundation.

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

Sincerely,

Diane Brown

Diane Brown, DVM, PhD, DACVP
Chief Executive Officer



Research Program Areas

Blood Disease	3
Cardiology	4
Dermatology & Allergic Disease.....	6
Endocrinology.....	7
Epilepsy Initiative.....	8
Gastrointestinal Disease	10
General Canine Health.....	11
Hepatic Disease	12
Immunology & Infectious Disease	13
Lung and Respiratory Disease.....	15
Musculoskeletal Conditions & Disease	16
Neurology.....	17
Oncology - General.....	19
Oncology - Hemangiosarcoma.....	22
Oncology - Lymphoma	22
Oncology - Osteosarcoma.....	24
Ophthalmology.....	25
Kidney and Urological Disease.....	27
Reproductive Conditions	29
Tick-Borne Disease Initiative	30
Clinician-Scientist Fellowship Program	32
Theriogenology Residency Program	33
Impact of Funding: Select 2017 Scientific Publications	34

Photo credits

Front cover, upper left: Kristin Marie Photography

Front cover, upper right: Lisa Croft-Elliott

Front cover, bottom: Sahar Sheikh-Ahmad

Back cover, upper left: Daniel Willis

Back cover, upper right: Teddy Lei

Back cover, bottom: Kristin Marie Photography

Blood Disease

02355-A

New

Hyperlipidemia in the Miniature Schnauzer: A Combined Metabolomic and Genomic Approach

Principal Investigator: Christopher A. O'Callaghan, MD, PhD; University of Oxford

Total Grant Amount: \$14,958

Grant Period: 8/1/2017- 7/31/2018

Project Abstract:

Miniature Schnauzers can be affected by a condition causing too much circulating lipid (fat) in the bloodstream, known as hyperlipidemia. The problem appears to worsen as dogs get older and may affect up to 3 in every 10 dogs. Affected dogs are more likely to suffer from other serious health conditions including pancreatitis and diabetes, and liver and kidney problems. Whilst an underlying genetic cause is suspected, the gene or genes responsible for this condition in Miniature Schnauzers have not been identified. At present, routine blood tests only allow veterinarians to measure 2 types of lipid - triglyceride and cholesterol. In contrast, in human lipid disorders, improved diagnosis and personalized treatment options have been achieved by measurement of a much wider variety of lipids in the bloodstream, combined with genetic testing. The investigators will measure over 2000 substances including lipid- and metabolism-related markers in the blood of Miniature Schnauzers to improve understanding of hyperlipidemia that may guide more specific treatment options. The researchers will also examine differences between genes of affected and unaffected Miniature Schnauzers, to try to identify important mutations associated with hyperlipidemia. These studies may lead to a genetic screening test and/or new targets for treatment of this condition.

01988

Identification of a Safe Storage Time for Canine Blood Used In the Treatment of Anemia

Principal Investigator: Mary Beth Callan, VMD; University of Pennsylvania

Total Grant Amount: \$113,499

Grant Period: 1/1/2014- 12/31/2017

Project Abstract:

Red blood cells (RBCs) can be refrigerator stored for up to 35 - 42 days in humans and dogs. Given that blood is a precious and limited resource, both human and veterinary blood banks typically dispense the oldest RBC units first to reduce waste. However, accumulating evidence suggests that transfusion of RBCs stored >14 days is associated with increased rates of complications and death in human patients. Preliminary data from a study of more than 2000 dogs receiving RBC transfusions suggest that administration of older RBCs to dogs with certain types of anemia negatively impact survival. Dr. Callan's goal is to conduct a randomized clinical trial in which dogs with anemia in need of RBC transfusions will receive either "fresh" RBCs (stored <7 days) or "old" RBCs (stored 21-28 days). If they document that administration of older RBCs is associated with increased inflammation and poorer outcome in dogs with anemia, the results of this study will have a significant impact on canine health and veterinary blood banks by changing current transfusion practices; that is, by providing fresh rather than older RBCs to anemic canine patients.

02343-A

New

Recognizing and Removing Lipemic Interferences for Accurate Laboratory Testing

Principal Investigator: Unity Jeffery, VetMB; Texas A&M University

Total Grant Amount: \$9,113

Grant Period: 5/1/2017- 4/30/2018

Project Abstract:

Over thirty percent of Miniature Schnauzers have primary hyperlipidemia, a disease in which fats (also termed lipids) are increased in the blood. Lipids are also increased in dogs who have recently eaten or are affected by disorders that alter lipid handling (e.g. diabetes, hypothyroidism, Cushing's disease). Blood samples collected from affected patients are milky and opaque due to large numbers of lipid droplets. Many blood tests rely on measuring a color change or light transmission through a sample, but lipid droplets absorb light and cause random light scatter preventing accurate measurement of these changes. High blood lipids may prevent clinically important tests from being performed or render their results inaccurate. Incorrect diagnosis or treatment may occur, or unnecessary invasive and expensive tests may be performed because of these inaccurate results. Two techniques are commonly used to reduce lipids before analysis: high-speed centrifugation or addition of a lipid extraction solution. For human samples, centrifugation is insufficient to remove lipid for some tests, but the lipid extraction solution produces inaccuracies in others. In dogs, the effect of the two techniques on subsequent analyses has not been well-established, preventing selection of the most appropriate lipid removal technique. The investigators will establish which biochemistry tests are altered by high lipids and determine the best means to remove interference, thereby improving the accuracy of laboratory testing and veterinary care.

02389-MOU

Characterization of Ventricular Arrhythmias in Rhodesian Ridgebacks**Principal Investigator:** Kathryn M. Meurs, DVM, PhD; North Carolina State University**Total Grant Amount:** \$26,919**Grant Period:** 9/1/2017- 8/31/2020**Project Abstract:**

The investigators recently identified a genetic mutation associated with heart arrhythmias in Rhodesian Ridgebacks. Dogs with the mutation appear to be at the most risk of developing an arrhythmia and suffering sudden death between 12-24 months of age, however, this timeline is variable, and some dogs appear to outgrow the arrhythmia. Due to the lack of knowledge of the specific at risk age, owners of dogs with the mutation must repeat the Holter monitor (a test to monitor heart rhythm) every few months to identify when their dog is at greatest risk and may need treatment. The objective of this study is to repeatedly perform regular Holter monitor testing on dogs with the mutation (including dogs with one copy and with two copies) every 4 months from 6-24 months of age with a final evaluation at 36 months to narrow in on the age when the arrhythmias appear to be the most severe. Gaining this increased clinical understanding of the disorder will decrease the risk of sudden death by helping owners and veterinarians in monitoring and providing treatment intervention for their dogs, and will further inform breeders and owners by characterizing the clinical and genetic manifestations of the disorder.

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

02388-MOU

Genetic Markers for Familial Subvalvular Aortic Stenosis in Newfoundlands**Principal Investigator:** Joshua A. Stern, DVM, PhD; University of California, Davis**Total Grant Amount:** \$58,949**Grant Period:** 9/1/2017- 8/31/2019**Project Abstract:**

Subvalvular Aortic Stenosis (SAS) is a heart defect characterized by a fibrous ridge located below the aortic valve. Affected dogs are at risk of developing heart valve infections, congestive heart failure or sudden death. Severely affected dogs have an average lifespan of 19 months. A previous study identified a single gene mutation associated with a cohort of Newfoundland dogs with SAS, however this mutation does not explain all SAS in the breed and requires further evaluation. Studying this disease in Newfoundlands has the potential to identify causative genetic mutations and develop a reliable genetic test for this condition to further aid breeders to reduce the prevalence of this condition. The investigators will study pattern of inheritance and use the most modern genetic techniques to identify the genetic cause of SAS in Newfoundlands, further expanding our understanding of this disease in dogs.

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

02327-MOU

Identification of Genetic Markers for Familial Subvalvular Aortic Stenosis in Bullmastiffs**Principal Investigator:** Joshua A. Stern, DVM, PhD; University of California, Davis**Total Grant Amount:** \$55,173**Grant Period:** 4/1/2017- 3/31/2019**Project Abstract:**

Subvalvular Aortic Stenosis (SAS) is a heart defect characterized by a fibrous ridge located below the aortic valve. Affected dogs are at risk of developing heart valve infections, congestive heart failure or sudden death. Severely affected dogs have an average lifespan of 19 months. SAS is an inherited heart problem reported in Bullmastiffs and other breeds. Studying this disease in Bullmastiffs has the potential to identify a genetic mutation and develop a test for this condition. Ultimately the identification of a mutation in Bullmastiffs would aid breeders in making decisions to reduce the prevalence of this condition. The objective of this study is to use the most modern genetic techniques to identify the genetic cause of SAS in Bullmastiffs. The investigators have collected DNA samples from affected and unaffected Bullmastiffs and will study inheritance to identify genetic variants associated with SAS.

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

02368

New

Identification of Mitral Valve Disease DNA variants in Miniature Schnauzers

Principal Investigator: Kathryn M. Meurs, DVM, PhD; North Carolina State University

Total Grant Amount: \$56,635

Grant Period: 8/1/2017- 7/31/2019

Project Abstract:

Mitral valve degeneration is the most common heart disease in the dog, and is particularly common in small breed dogs. Miniature Schnauzers are one of the most commonly affected breeds. Although some dogs live comfortably with the disease, many affected dogs die of congestive heart failure and sometimes sudden death due to rupture of a weakened heart. Mitral valve degeneration is thought to be an inherited disease in the dog although the causative mutation(s) have not been identified. Failure to understand the underlying cause of canine mitral valve degeneration has slowed the development of effective treatment and prevention plans. The investigators will identify genetic variants that lead to the development of mitral valve degeneration in Miniature Schnauzers, and use this information to develop treatment and prevention plans for dogs with high-risk DNA variants.

02163-MOU

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

Principal Investigator: Kathryn M. Meurs, DVM, PhD; North Carolina State University

Total Grant Amount: \$50,857

Grant Period: 1/1/2015- 12/31/2017

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. They have demonstrated that some Boxer dogs with the mutation have a more severe form of the disease and will become quite sick while others will remain free of clinical signs. The reason for the variability in clinical signs is unknown but is thought to be associated with concurrent factors for that individual dog which could include genetic or other more external factors including diet, exercise and hormonal levels. Genetic factors could include common variants in the nucleotide sequence of other cardiac modifying genes that have been shown to influence the severity of cardiac diseases. In addition, endocrine issues like hypothyroidism complicate ARVC and may play a role in disease progression. Dr. Meurs hypothesizes that low thyroid levels and/or other genetic variants may lead to the development of the more severe form of Boxer ARVC. Understanding the role of these factors in the severity of disease will greatly improve the ability to manage the common and sometimes fatal heart disease of ARVC.

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

01760-T

Use of Gene Therapy to Treat Dilated Cardiomyopathy

Principal Investigator: Margaret M. Sleeper, VMD; University of Florida

Total Grant Amount: \$146,774

Grant Period: 9/1/2016- 2/28/2019

Project Abstract:

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

02046

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

Principal Investigator: Janice McIntosh Bright, DVM, BSN, MS; Colorado State University

Total Grant Amount: \$33,060

Grant Period: 1/1/2014- 6/30/2018

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). Dr. Bright will evaluate dogs with naturally occurring atrial fibrillation and heart failure for their responsiveness to two drugs -- amiodarone, an antiarrhythmic agent, and ranolazine, a drug used in humans with coronary heart disease. She will 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.

Dermatology and Allergic Disease

02472-A

Effect of Lokivetmab on Tissue Biomarkers of Canine Atopic Dermatitis using RNA Sequencing

Principal Investigator: Frane Banovic, DVM, PhD; University of Georgia

Total Grant Amount: \$9,747

Grant Period: 12/1/2017- 11/30/2018

Project Abstract:

Atopic dermatitis (AD) is the most common, chronic, inflammatory and pruritic allergic skin disease that affects dogs worldwide. Treatment of canine AD has a high unmet need for effective and safe therapeutics. The transcriptome investigation of human AD tissues before and after treatment modalities has revolutionized the understanding of the molecular fingerprint of AD, further defining pathogenic immune pathways and identifying disease-specific biomarkers. In the early-phase trial, lokivetmab, a caninized monoclonal antibody targeting interleukin-31 (IL-31) cytokine, markedly improved disease activity, but the effect of IL-31 blockade on AD at the genomic level has not been characterized. The investigators will evaluate lokivetmab modulation of the canine AD transcriptome (defined as differentially expressed genes between lesional and non-lesional skin) using next-generation RNA sequencing (RNA-seq). Findings may suggest that inhibition of a single target has the potential to reverse AD pathomechanisms, opening the door for new targeted treatment for this common and debilitating inflammatory skin disease. Furthermore, transcriptome analysis using RNA-seq may identify novel pathogenic pathways of inflammatory biomarkers as canine AD disease drivers, with potential for development of novel targeted therapeutics.

New

02176-A

Intralymphatic Immunotherapy for the Treatment of Canine Atopic Dermatitis

Principal Investigator: Andrea Lam, DVM; Tufts University

Total Grant Amount: \$12,114

Grant Period: 7/1/2015- 1/31/2018

Project Abstract:

Atopic dermatitis (AD) is a genetically predisposed inflammatory skin condition affecting approximately 10% of dogs globally and is probably the most prevalent skin disease in all canines. Affected dogs manifest with itchy skin and ears and secondary infections. Clinical features are associated with IgE antibodies produced against indoor/outdoor environmental allergens. Breeds such as Boxers, Terriers, Retrievers, and Bulldogs are predisposed. Current treatment options include antihistamines, corticosteroids, cyclosporine, oclacitinib, and allergen-specific immunotherapy (ASIT), as well as adjunctive topical and antimicrobial therapy. Antihistamines are effective in about 25% of dogs. Corticosteroids are extremely efficacious; however, side effects are common, thus long-term use is strongly discouraged. Cyclosporine is effective in many dogs with few serious adverse effects, but cost can be a limitation in large breed dogs. Oclacitinib has been shown to have good efficacy, but long-term side effects have not been studied. ASIT appears as the only treatment that is able to induce a clinical cure. However, the percentage of atopic dogs that respond to this treatment is only 60-70% and in many, the response is only partial. It has been proposed that efficacy of subcutaneous ASIT is limited by the ability of the skin to stimulate the immune system. The investigators will test an alternative route of administration using ASIT for this important skin condition, to determine if direct administration of allergens into a peripheral lymph node may be more effective in stimulating an immunologic reaction, and thereby increasing the response rate, and potentially the cure rate, for canine atopic dermatitis.

02241

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

Principal Investigator: Meghan F. Davis, DVM, MPH, PhD; Johns Hopkins University

Total Grant Amount: \$158,367

Grant Period: 2/1/2016- 1/31/2019

Project Abstract:

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



Endocrinology

02342-A

Molecular Analysis of Giant Schnauzer-Type Congenital Hypothyroidism

Principal Investigator: John C. Fyfe, DVM, PhD; Michigan State University

Total Grant Amount: \$14,900

Grant Period: 6/1/2017- 5/31/2018

Project Abstract:

Isolated congenital hypothyroidism (CH) is a condition occurring at or near birth characterized by insufficient thyroid hormone production. The disorder in purebred dogs is usually inherited and leads to dwarfism and mental dullness. CH in Giant Schnauzers (GS) was first described in 1991 (Greco, et al) as a likely autosomal recessive disorder due to failed activity of the hypothalamus or pituitary gland. Since then the investigators have studied GS CH in three widely separated families and found pituitary failure of thyroid stimulating hormone (TSH) production beginning at birth in most affected dogs, but not until several months of age in a few. They mapped the genetic locus to a region of dog chromosome 28. The researchers will now perform DNA sequencing experiments of affected dogs and their parents and candidate variants will be assessed further by Sanger sequencing in all available members of the three families, as well as a large number of GS DNA samples available in the OFA CHIC repository. A successful outcome will lead to a reliable genetic test for GS CH, increased understanding of an essential pituitary function, and illumination of a highly similar condition reported in Miniature Schnauzers.



New

02417-A

Serum Total Histones in Dogs with Acute Pancreatitis, their Association with Laboratory Findings, Markers of Inflammation and Outcome: A Prospective Longitudinal Study

Principal Investigator: Ran Nivy, DVM; The Koret School of Veterinary Medicine, The Hebrew University of Jerusalem

Total Grant Amount: \$14,200

Grant Period: 12/1/2017- 11/30/2018

Project Abstract:

Acute pancreatitis (AP) is a common, potentially fatal, inflammatory disease in dogs. Miniature Schnauzers and several Terrier and non-sporting breeds are predisposed to develop AP. The spectrum of clinical signs greatly varies, from transient inappetence in mild cases, to intractable gastro-intestinal signs and jaundice in severe ones. The result of aberrant activation of pancreatic digestive enzymes, the ensuing inflammatory reaction within the pancreas and its surrounding tissues induces edema formation and tissue necrosis. In severe cases, inflammation spreads to other organs, leading to hemostatic disturbances, multi-organ dysfunction and ultimately, to death. Several measurable inflammation markers increase in canine pancreatitis. Recently, studies of human and murine AP have demonstrated significant increases in extracellular serum histones. Histones are evolutionally conserved nuclear proteins, constituting the basic structure with which DNA interacts. Histones exert proinflammatory properties, with many deleterious effects on various body cells, and hemostasis. Interestingly, their pernicious effects can be partly or completely abrogated therapeutically (e.g., administering heparin or activated protein C). Recently, circulating histones have shown excellent performance in predicting persistent organ failure and mortality in humans with AP. The investigators will measure, free total serum histones in dogs with naturally occurring AP, and examine their association with other laboratory analytes, and with the prognosis. Should serum histones be found to increase in canine AP, as in humans, this may open up new therapeutic and research avenues for this serious disease.



New

02298-MOU

Using OFA Testing to Assess Progression of Canine Autoimmune Thyroiditis

Principal Investigator: Brian K. Petroff, DVM, PhD; Michigan State University

Total Grant Amount: \$35,630

Grant Period: 8/1/2016- 12/31/2017

Project Abstract:

Hypothyroidism may be the most common endocrine disorder in adult dogs. As is 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) is used as a marker for how intensely the immune system is attacking the thyroid gland. Elevated TgAA results 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.

02366-A

Individualization of Pharmacological Interventions in Diabetic Dogs

Principal Investigator: Nicolas Villarino, Med.Vet.; Washington State University

Total Grant Amount: \$14,435

Grant Period: 5/1/2017- 4/30/2018

Project Abstract:

Diabetes mellitus is a disease of middle-aged to older dogs which means many affected dogs will develop other diseases such as arthritis, infections, and behavior disorders, all requiring drug therapy. Poor control of glucose levels in diabetic dogs can alter how drugs behave in the body, which can result in drug toxicities. This is an area of intense investigation in diabetic humans, but such effects have not been investigated in canine medicine, and prescribed treatments may result in individual dogs being under- or overdosed. The investigators intend to move from a 'one dose fits all' strategy to an individualized medical approach to ensure each patient receives optimal pharmacological therapy. Completion of this study is the first step toward establishing an in vitro method for evaluating the many drugs used in diabetic dogs. The long-term goal is to develop a free downloadable application for mobile devices (smartphones and tablets), for use by clinicians to make treatment selection, and to avoid drugs that may cause problems in diabetic patients. This research stands to play a substantial role in the clinical management of dogs with diabetes mellitus.

New

Epilepsy Initiative

02257

Identification of Genetic Risk Factors for Canine Epilepsy

Principal Investigator: Gary S. Johnson, DVM, PhD; University of Missouri, Columbia

Total Grant Amount: \$102,081

Grant Period: 5/1/2016- 4/30/2018

Project Abstract:

Epilepsy is one of the most common neurologic diseases of dogs and a top concern of dog breeders. 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 novel 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 that have been shown to alter the seizure threshold in humans or rodents. 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.

02323

New

Efficacy of Cannabidiol (CBD) for the Treatment of Canine Epilepsy**Principal Investigator:** Stephanie McGrath, DVM, MS; Colorado State University**Total Grant Amount:** \$356,022**Grant Period:** 12/1/2017- 11/30/2020**Project Abstract:**

Epilepsy is the most common neurologic condition in dogs. Approximately 20-30% of dogs receiving standard therapy remain uncontrolled for their seizures. Additionally, the side effects of the antiepileptic drugs (AED) are often unacceptable. Thus, there is a need for an AED that is efficacious with minimal side effects. Cannabidiol (CBD), a prominent non-psychotropic component of the Cannabis sativa plant, has been shown to have anti-convulsant properties. While CBD offers promise as a treatment for canine epilepsy, controlled studies are needed to prove its effectiveness. In this randomized, double-blinded, placebo-controlled, crossover clinical trial, client-owned dogs with uncontrolled epilepsy will be enrolled following a full seizure evaluation, including bloodwork and magnetic resonance imaging. The canine patients will first receive either a placebo or CBD in addition to their standard AED protocol and then the opposite drug in this crossover designed study. Seizure frequency and medication side effects will be monitored by owners using a seizure log and questionnaire. Regular CBD plasma concentrations, routine bloodwork and serial physical examinations will be monitored by the investigator. The primary goal of the study is to determine the efficacy of CBD in the treatment of canine epilepsy. If CBD is effective in decreasing seizure frequency, it has the potential to improve the quality and length of life for dogs with uncontrolled epilepsy, and add a much-needed tool for veterinarians in the treatment of canine epilepsy.

02249-A

Studying the Role of the Gastrointestinal Tract in Canine Epilepsy**Principal Investigator:** Karen R. Munana, DVM, MS; North Carolina State University**Total Grant Amount:** \$14,995**Grant Period:** 6/1/2016- 2/28/2018**Project Abstract:**

Epilepsy is the most common nervous system disorder of dogs. 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, including anxiety/depression, autism, multiple sclerosis and Alzheimer's disease. An association between epilepsy and both celiac disease and inflammatory bowel disease has been identified in humans, which suggests that changes in intestinal bacterial might play a role in the progression of epilepsy as well. 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.

02252

Investigating a Ketogenic Medium-Chain Triglyceride (MCT) Supplement for the Treatment of Drug-Resistant Canine Idiopathic Epilepsy and Its Behavioral Comorbidities**Principal Investigator:** Holger Andreas Volk, DVM, PhD; Royal Veterinary College, University of London**Total Grant Amount:** \$107,697**Grant Period:** 5/1/2016- 3/31/2018**Project Abstract:**

Canine epilepsy is a chronic neurological condition, often requiring lifelong medication with anti-epileptic drugs (AEDs). Despite appropriate treatment with available AEDs, seizure freedom may not always be achievable. Indeed, over two thirds of dogs with epilepsy continue to have seizures long-term and around 20-30% remain poorly controlled on standard AEDs. The hardest to treat dogs are termed 'refractory' or 'drug-resistant' patients. 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 for several decades, decreasing seizure activity and even leading to seizure freedom in drug-resistant patients. Recent research has identified that 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 ACT 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.

01935-B

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

Principal Investigator: Laura L. Nelson, DVM; Michigan State University

Total Grant Amount: \$233,774

Grant Period: 1/1/2014- 6/30/2018

Project Abstract:

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

01937-B

Evaluating the Complex Genetic Basis of Bloat

Principal Investigator: Elizabeth A. Rozanski, DVM; Tufts University

Total Grant Amount: \$251,097

Grant Period: 1/1/2014- 12/31/2018

Project Abstract:

Gastric dilatation-volvulus (GDV), or bloat, is a common condition in large and giant breed dogs with an unacceptably high morbidity and mortality rate. Due to the importance of GDV in many dog breeds, several previous studies have investigated potential risk factors for the development of GDV. It is known that there is no single cause for GDV, rather its occurrence is multifactorial, with both genetic and environmental factors likely contributing. This study will allow for further investigation of how these risk factors cause GDV through the application of genomic and molecular methods. Samples from purebred dogs with GDV will be analyzed and compared to control dogs of similar age and breed that have not developed GDV. A genome wide association study (GWAS) will help to identify differences in the genetic makeup of dogs with GDV, and see which genes are turned on and off in GDV (epigenomics). The study will also determine if dogs with GDV have different types or amounts of proteins, hormones and other molecules in their blood and tissues (transcriptomics, proteomics and metabolomics). The investigators hypothesize that only when all of this information is considered together (genomic, epigenomic, transcriptomic, proteomic and metabolomic) will we truly understand what causes GDV, and guide more effective preventive and treatment strategies.

02338

The Genetics of Bloat in German Shepherd Dogs: The Roles of Immune System Genes and the Gut Microbiome

Principal Investigator: Michael Alan Harkey, PhD; Fred Hutchinson Cancer Research Center

Total Grant Amount: \$152,270

Grant Period: 6/1/2017- 5/31/2019

Project Abstract:

While gastric dilatation-volvulus (GDV or bloat) is a serious problem for many large canine breeds, little is known about the causes of this deadly disease. The most significant factors may be genetic, since certain breeds are more susceptible than others, and strong familial predispositions are seen within breeds. The investigators have recently shown a significant association of three immune genes with bloat in Great Danes. For each of the three genes, one allele (variant) is found at unusually high frequency in dogs that have been treated for bloat, and the presence of any one of these "risk" alleles triples the chance that the dog will experience bloat at some time in its life. The research team also showed that the bacterial population living in the gut (the gut microbiome) is altered in dogs with bloat, and in dogs that carry these "risk" alleles, which may predispose these dogs to bloat. It is not known if other breeds show this same association of genetics and microbiome with bloat. The team will investigate whether bloat in German Shepherd Dogs is associated with the same risk alleles and the same microbiome profiles as were seen in Great Danes. The results of this work could lead to genetic tests for at-risk dogs, as well as dietary or probiotic therapies to prevent bloat.

New

General Canine Health

02322

Analysis of the Health, Behavioral, and Longevity Data Collected in the 9/11 Medical Surveillance Longitudinal Study

Principal Investigator: Cynthia M. Otto, DVM, PhD; University of Pennsylvania

Total Grant Amount: \$37,672

Grant Period: 2/1/2017- 1/31/2019

Project Abstract:

Following the attacks of September 11, 2001 on the World Trade Center and Pentagon, the AKC Canine Health Foundation awarded funds the only lifetime longitudinal study tracking the medical and behavioral impacts of a major national disaster on the health and behavior of search & rescue (SAR) dogs. On June 6, 2016, the last study dog was laid to rest and data collection for the 9/11 Medical Surveillance Study was concluded. With 15 years of data, including annual radiographs, bloodwork, and handler surveys (health, performance, and behavior), the opportunity for in-depth analysis and discovery of new best practices and protocols for SAR dogs has never been greater. Data collected from deployed dogs will be compared to data collected from control SAR dogs that underwent similar training and careers, but did not deploy to 9/11. The investigators will explore three key areas of data: behavior, occupational hazards, and longevity related to health and work. Critical information gleaned from this study will have major implications applicable to the development, training, and care of our nation's SAR dogs, other working canines, and even companion dogs. Results will improve our understanding of traits of successful SAR dogs and thus influence dog selection. Importantly, following characterization of trait heritability, this data could be critical to a focused breeding program. The complete analysis of the occupational hazards of SAR dogs will shape preventive practices to allow these dogs to safely and effectively fulfill their mission of saving human lives.

New

02353-A

Characterization of Naturally-Occurring Neuropathic Pain in Dogs

Principal Investigator: Paulo V. Steagall, DVM, MSc, PhD; University of Montreal

Total Grant Amount: \$14,753

Grant Period: 11/1/2017- 10/31/2018

Project Abstract:

Clinical experience demonstrates that canine patients commonly suffer from neuropathic pain and little is known to address this issue. The researchers will investigate different tools for the recognition, diagnosis and treatment of neuropathic pain using a multidisciplinary approach. A two-phased study will include client-owned healthy dogs as controls and dogs with naturally-occurring neuropathic pain (Neuropathic Group-NG). In a prospective, randomized, masked clinical trial using appropriate inclusion and exclusion criteria, dogs in the NG group will be assigned to receive treatment with a drug for neuropathic pain (gabapentin), or gabapentin in combination with an anti-inflammatory drug (meloxicam) in a cross-over design (dogs will receive both treatments during the study). Placebo will be administered between treatments to assess placebo effect; additional analgesics will be administered if needed. Quality of life, pain scores, client-specific outcome measures, biomarkers of inflammation and quantitative sensory testing will be evaluated and compared with controls for observation of treatment effect, and blood concentrations of gabapentin will be measured. This multidisciplinary research may have a timely, immediate impact in veterinary medicine, canine health and welfare by providing important insight into diagnosis and therapeutic options for neuropathic pain.

New

02242

Understanding the Genetics of Adverse Drug Reactions in Sighthounds

Principal Investigator: Michael H. Court, BVSc, PhD; Washington State University

Total Grant Amount: \$150,000

Grant Period: 2/1/2016- 1/31/2018

Project Abstract:

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

02434-A

New

Characterization of the Anal Sac Microbiota in Dogs with Sacculitis

Principal Investigator: Marcio Costa, DVM, PhD; University of Montreal

Total Grant Amount: \$14,709

Grant Period: 12/1/2017- 11/30/2019

Project Abstract:

Anal sacs are two small cavities found adjacent to the anus in dogs, and accumulate secretions from the ad-anal glands. Inflammation of the anal sac (sacculitis) is a frequent condition affecting up to 12% of dogs and is mainly caused by bacterial infection. Therefore, treatment of this disease requires antibiotics, but reoccurrence can occur and often culminates with surgery. During the last decades, the development of new methods for DNA sequencing has allowed a better characterization of bacterial communities, since only the minority of those organisms grow in culture media. Imbalances of the normal populations are related to predisposition to certain diseases. Risk factors for sacculitis in dogs are still uncertain, but studies investigating the role of bacteria in this disease are rare. The investigators will characterize the microbiota present in the anal sac of dogs affected by sacculitis and compare it to the healthy contra-lateral sac using next generation DNA sequencing (NGS). In addition, factors such as antibiotic use, severity of inflammation and clinical response to treatment will be followed. Understanding the physiopathology of sacculitis in dogs may lead to increased success rates following conservative treatment, reducing the need for invasive surgery.

02328-A

New

Harmonization of Genetic Testing for Dogs

Principal Investigator: Brenda Bonnett, DVM, PhD; International Partnership for Dogs

Total Grant Amount: \$15,000

Grant Period: 1/1/2017- 12/31/2018

Project Abstract:

The ever-increasing number of canine DNA tests and testing laboratories has made choosing quality DNA testing providers and the right DNA tests for health and breeding decisions challenging for dog owners, breeders and veterinarians. With no existing national or international standards of genetic testing for laboratory accreditation, or a standardization oversight group, there is a growing need for a neutral organization that can provide guidance about test reliability and laboratory quality assurance. In response to this need, and with initial funding provided through generous contributions from the Orthopedic Foundation for Animals (OFA), the AKC Canine Health Foundation (CHF) and the founding partners of the International Partnership for Dogs (IPFD), a new initiative has been launched. Called the "IPFD Harmonization of Genetic Testing for Dogs," the initiative will provide practical support to address the challenges associated with the often confusing world of canine DNA testing. It will also strive to support consumer confidence in DNA testing, educate consumers in the use of these tests as tools to reduce the incidence of inherited disease, and reduce redundant international efforts. The initiative's aim is to create an open access, searchable and sustainable online resource for the international dog world, including breeders, dog owners and veterinarians that will: catalog information provided voluntarily from commercial test providers for genetic testing in dogs; describe expertise, quality assurance, activities and resources of the laboratories/test providers; host expert panel reviews of genetic tests, their reliability, and applicability; coordinate a program for standardized proficiency testing, and peer review; and link to and share existing and new resources for genetic counseling and education. The online resource will be hosted and available online to the public on the IPFD's DogWellNet.com platform. The initiative will be guided by IPFD CEO Brenda Bonnett and Project Director Aimee Llewellyn-Zaidi, and will be overseen by a multi-stakeholder steering committee.

Hepatic Disease

02363-A

New

Platelet Function in Dogs with Chronic Liver Disease

Principal Investigator: David L. Panciera, DVM, MS; Virginia-Maryland Regional College of Veterinary Medicine

Total Grant Amount: \$14,904

Grant Period: 6/1/2017- 5/31/2018

Project Abstract:

Chronic liver disease is common among adult dogs with numerous breeds being predisposed. Liver biopsy is usually required to identify the underlying cause of liver disease in these patients, and is often recommended to monitor response to treatment. Because dogs with liver disease have abnormal clotting activity, bleeding is a substantial risk of biopsy. Routine screening for clotting abnormalities in dogs with liver disease is accomplished using blood tests including prothrombin time, partial thromboplastin time, and platelet count. Unfortunately, these routine tests do not necessarily correlate with excessive biopsy-induced bleeding, which makes predicting and preventing hemorrhage during liver biopsy difficult. Humans with liver disease have abnormal platelet function that contributes to abnormal coagulation. Because standard diagnostics do not assess platelet function, we propose to evaluate platelet function in dogs with chronic liver disease. The investigators will determine if dogs with chronic liver disease have platelet dysfunction and if there is a correlation between platelet function and bleeding after liver biopsy. The research team will use two methods to evaluate platelet function in canine patients with chronic liver disease undergoing ultrasound guided liver biopsies to determine if there is a relationship between platelet function and hemorrhage after biopsy.

01986

Profiling the Metabolic and Lipid Imbalances that are Causative of Gallbladder Disease in Dogs

Principal Investigator: Jody L. Gookin, DVM, PhD; North Carolina State University

Total Grant Amount: \$135,354

Grant Period: 1/1/2014- 12/31/2017

Project Abstract:

The gallbladder mucocele (GBM) is one of the most common, poorly understood and deadliest biliary diseases of dogs. A GBM develops when the gallbladder secretes abnormal mucus that eventually obstructs or ruptures the gallbladder. GBM formation afflicts all dogs, but especially Shetland Sheepdogs, Miniature Schnauzers and Cocker Spaniels, and in general, dogs with disorders of steroid hormone or lipid metabolism. By the time a diagnosis of GBM is made, emergency surgery to remove the gallbladder is often required. After surgery only 22-50% of dogs survive to be discharged from the hospital. There is a critical need to determine why dogs form a GBM so we can prevent the high cost and lost lives of these dogs. Based on the breeds and diseases that predispose to GBM, Dr. Gookin hypothesizes these dogs have a unique disturbance in cholesterol or lipid metabolism. If the cause of this disturbance can be identified we will be able to understand why GBM form, develop tests for early diagnosis and design diets or drugs to prevent GBM formation.

02297-MOU

Understanding the Genetics of Hepatic Copper Toxicosis in the Dalmatian

Principal Investigator: Andrew Lawrence Mason, PhD; University of Alberta

Total Grant Amount: \$100,000

Grant Period: 3/1/2017- 2/28/2019

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. Copper toxicosis was considered rare in the Dalmatian but may be more common than previously believed. 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 an advanced 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 in the Dalmatian breed, 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 and 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.

Immunology and Infectious Disease

01771

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

Principal Investigator: Beverly Torok-Storb, PhD; Fred Hutchinson Cancer Research Center

Total Grant Amount: \$178,200

Grant Period: 1/1/2013- 6/30/2018

Project Abstract:

The Major Histocompatibility Complex (MHC) genes encode proteins that are critical for a wide range of biological functions, from immune protection against infectious disease to the predisposition of an individual to develop diabetes and auto immune diseases. The MHC genes in the dog are incompletely characterized, thereby severely limiting our ability to full define the cause of many canine diseases. Dr. Ramakrishnan has developed improved methods for identifying the different forms of canine MHC genes in a large number of dogs of diverse breeds. In this study he will characterize the patterns of MHC genetic variation in over 1,200 dogs from at least 50 breeds using a high throughput sequencing strategy. The distribution and frequency of different forms of each of these genes and their specific clustering among different breeds will greatly enhance our knowledge of the genetic diversity among breeds. The methodology and data gained from this study will enhance the power of association studies between MHC types and canine diseases. Such a database will also enable tissue transplantation from unrelated but matched donors as a treatment for advanced malignancies (stem cell transplants) and other diseases (tissue transplantation). Fully defining the canine MHC will have broad impact across canine health, including oncology, immunology and infectious disease.

02380-A

New

Estimating Prevalence and Identifying Risk Factors for Canine Leptospirosis in North America

Principal Investigator: Jason Stull, VMD, PhD; Ohio State University

Total Grant Amount: \$14,990

Grant Period: 5/1/2017- 10/31/2018

Project Abstract:

Leptospirosis is an important and re-emerging disease of dogs, humans and other species that is transmitted by contact with infected urine. Infected dogs can develop severe illness, including death. Despite being recognized as a disease that appears to be increasing in frequency in dogs across the United States and Canada, many areas important to dog health are unknown. Regions of greatest canine leptospirosis risk, dog factors that increase risk and the most important prevention methods remain unclear. The investigators will use an existing large international database of dogs to determine the occurrence and changes over time and region of this disease. Current "hot spots" for canine leptospirosis will be determined. These "hot spots" will be further evaluated in detail by enrolling dogs and their owners in a follow-up study component to identify key behaviors and practices that can be used to successfully reduce the risk of leptospirosis in dogs. Maps will be created for use by dog owners and veterinarians to identify areas of greatest risk and concern for this disease. Together, maps and risk reduction data will allow for targeted education to individuals with dogs living or traveling to higher-risk areas to protect dogs against leptospirosis.

02461-A

New

Innate Immune Response to Leptospira in Naturally Exposed Dogs

Principal Investigator: Sreekumari Rajeev, BVSc, PhD; Ross University School of Veterinary Medicine

Total Grant Amount: \$15,000

Grant Period: 12/1/2017- 11/30/2018

Project Abstract:

Leptospirosis is a zoonotic disease of global occurrence and may result in life threatening illness in animals and humans. *Leptospira* may also reside in the kidney of many animal species including dogs without causing disease. Factors predisposing to clinical disease, carrier stage, or protection needs to be clarified. Dog are susceptible to fatal illness and at the same time may serve as asymptomatic reservoirs. Protection from vaccines is short-lived and suboptimal. Information available on immune response in naturally infected dogs is sparse. The investigators hope to unravel the host and pathogen factors in *Leptospira* infection that leads to fatal disease, chronic asymptomatic infection, or bacterial clearance. Innate immune cells are the first line of defense against *Leptospira* infection, initial experiments will determine the response of innate immune cells of dogs. The knowledge acquired from this study will be beneficial for the development of control and treatment strategies for this problematic and life-threatening disease. As leptospirosis is a zoonotic disease where animal, human and environmental interface is essential for transmission, the findings from this study will have a "One Health" impact.

02245-MOU

Genetic Predisposition to Avian Tuberculosis in Miniature Schnauzers and Basset Hounds

Principal Investigator: Urs Giger, DVM, PhD; University of Pennsylvania

Total Grant Amount: \$106,858

Grant Period: 5/1/2016- 4/30/2018

Project Abstract:

While people and dogs are generally resistant to avian tuberculosis (*Mycobacterium avium*) infections, there are certain individuals that lack proper host defense against these intracellular bacteria. The precise molecular basis is still 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 further samples and whole genome sequencing. Identification of the molecular basis of this genetic predisposition will allow for a better understanding of the disease and the development of a DNA screening test to identify animals at risk as well as carriers, thereby reducing the production of dogs predisposed to this fatal disease in future generations. 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.

02299-A

Investigating Recovery of the Skin Microbiota after Surgery**Principal Investigator:** Julie Horvath, PhD; North Carolina Museum of Natural Sciences**Total Grant Amount:** \$9,605**Grant Period:** 8/1/2016- 7/31/2018**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 are microscopic organisms including 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 the 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 will assess the presence of antibiotic resistant bacteria on dog skin before and after surgery and evaluate the impacts on wound healing.

02404-A

The Impact of Lidocaine Administration on Natural Killer Cell Populations in Canine Sepsis**Principal Investigator:** Mandy L. Wallace, DVM, MS; University of Georgia**Total Grant Amount:** \$14,896**Grant Period:** 11/1/2017- 4/30/2019**Project Abstract:**

Sepsis is a life-threatening condition that results from an excessive systemic inflammatory response to infection. This can occur due to infections in various parts of the body including the chest, abdomen, or bloodstream. Pure-bred dogs are overrepresented in clinical studies of abdominal sepsis due to gastrointestinal blockage or rupture. Dogs and humans with sepsis have up to a 50% mortality rate, with most dying from organ system failure. This high mortality rate has been linked to the dysfunction of several types of immune cells. One of these cell types, Natural Killer (NK) cells, plays a critical role in the killing of bacteria within the body, but their role has not been evaluated in dogs with sepsis. Administration of the local anesthetic lidocaine, a drug that can decrease pain and correct cardiac arrhythmias, has been shown to increase survival in dogs with sepsis. This study seeks (1) to determine the relationship between Natural Killer cell numbers and phenotype in the blood and disease severity in dogs with abdominal sepsis and (2) to evaluate if the administration of lidocaine during surgery changes NK cell numbers or affects survival rates in dogs with sepsis from abdominal infection.

New

Lung and Respiratory Disease

02232-MOU

Characterization of Upper Airway Syndrome in Norwich Terriers**Principal Investigator:** Bryden J. Stanley, BVMS; Michigan State University**Total Grant Amount:** \$74,497**Grant Period:** 11/1/2015- 12/31/2017**Project Abstract:**

Breeders have long known of upper airway issues in Norwich Terriers (NTUAS) while veterinary awareness and recognition of NTUAS, has lagged behind. Signs of disease can vary from mild airway noise to severe distress with heat and exercise intolerance, and death. Descriptions of NTUAS have focused on everted laryngeal sacculles (outpouched laryngeal tissue), likening it to issues seen in brachycephalic dogs. However, recent evidence shows changes in the larynx that are not seen in brachycephalic dogs: redundant tissue at the top of the larynx, and narrowing of the larynx behind the glottis. The entire upper airway needs to be clearly described for NTUAS, and it is likely that the condition is separate from brachycephalic airway syndrome, with distinctive, primary changes arising in the larynx. In this study, NTUAS will be characterized in detail through comprehensive history, oral examination and upper airway endoscopy in 150 US Norwich Terriers. Results will be used to create a NTUAS severity grading system. A subset of 25 of the dogs will additionally undergo computed tomography and nasal airflow measurements. Results will be compared for 25 Norfolk Terriers, 25 brachycephalic and 25 mesaticephalic dogs of similar ages from a separately funded study. Identifying the contributory components of NTUAS is the first step in determining prognosis and evaluating treatment options. This work will lay the groundwork for future research to follow the youngest dogs in the study throughout their lives, and to examine the effect of time and treatment on NTUAS.

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

02346-A

New

Blood Culture and Blood Microbiome as Minimally Invasive Diagnostics for Canine Bacterial Pneumonia

Principal Investigator: Carol R. Reiner, DVM, PhD; University of Missouri

Total Grant Amount: \$11,394

Grant Period: 6/1/2017- 5/31/2018

Project Abstract:

Canine bacterial pneumonia is a common and serious respiratory infection. Pneumonia can develop from contagious environmental bacteria or from the dog's own bacteria gaining access to the lungs (e.g., after accidentally inhaling food, liquids or vomit). Diagnosis relies on clinical signs, x-rays, and lung fluid (bronchoalveolar lavage fluid or BALF) analysis. Analysis of BALF helps identify the causative bacteria and aids in appropriate antibiotic selection. While key to definitive diagnosis and management of bacterial pneumonia, collection of BALF requires general anesthesia, which can be especially risky in dogs with severe lung disease. To address the clinical need for a minimally invasive diagnostic test, the first study objective is to determine if blood cultures, acting as a surrogate for BALF analysis, can identify the bacteria causing pneumonia and provide antibiotic susceptibility information. In addition, the investigators will employ molecular means of identification of bacterial populations in samples, so called "microbiome" analysis. Researchers will compare BALF and blood microbiomes to determine sample relatedness and then to the bacteria identified via BALF culture to determine if lung bacteria appear in the blood in minute quantities and whether the predominant cultured bacteria is reflected in the blood microbiome.

Musculoskeletal Conditions and Disease

02275

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

Principal Investigator: Benjamin L Hart, DVM, PhD; University of California, Davis

Total Grant Amount: \$61,784

Grant Period: 9/1/2016- 2/28/2018

Project Abstract:

This study extends the investigator's recently completed AKC Canine Health Foundation-funded project studying 12 dog breeds to identify major differences in the degree to which spay or neuter may be related to an increase in 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. Findings did not associate an increase in 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., L.A. Hart, A.P. Thigpen and N. H. Willits. 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 have been added to the study: 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 of the study, 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: Andrea Sundholm-Tepper, DVM; Washington State University

Total Grant Amount: \$12,960

Grant Period: 11/1/2015- 12/31/2017

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

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: Natasha J. Olby, VetMB, PhD; North Carolina State University

Total Grant Amount: \$78,786

Grant Period: 1/1/2015- 6/30/2018

Project Abstract:

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

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.

02290-MOU

Further Studies to Identify the Mutation Responsible for DUNGd

Principal Investigator: Dennis P. O'Brien, DVM, PhD; University of Missouri, Columbia

Total Grant Amount: \$14,904

Grant Period: 7/1/2016- 12/31/2017

Project Abstract:

A hereditary disease that the 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 the latest genomic techniques (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.

02210

Gene Therapy for Canine Degenerative Myelopathy

Principal Investigator: Kathrin Meyer, PhD; The Research Institute at Nationwide Children's Hospital

Total Grant Amount: \$50,000

Grant Period: 1/1/2016- 12/31/2018

Project Abstract:

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

02165-MOU

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

Principal Investigator: Joan R. Coates, DVM, MS; University of Missouri, Columbia

Total Grant Amount: \$154,077

Grant Period: 1/1/2015- 12/31/2017

Project Abstract:

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

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

02157-MOU

Genomics of Deafness in the Dalmatian

Principal Investigator: Claire M. Wade, PhD; University of Sydney

Total Grant Amount: \$120,960

Grant Period: 1/1/2015- 12/31/2017

Project Abstract:

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

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

02387-MOU

Hereditary Deafness in Dogs – Genomic Studies in English Setters Using Full Sibling Pairs

Principal Investigator: George M. Strain, PhD; Louisiana State University

Total Grant Amount: \$12,960

Grant Period: 9/1/2017- 8/31/2018

Project Abstract:

Hereditary deafness associated with white pigmentation occurs in several dog breeds. The mechanism of inheritance is unknown, but does not appear to be simple Mendelian. Numerous studies to determine the mode of inheritance and locate the causative gene(s) have thus far failed. The investigators will use a unique modified twin study approach in an effort to determine the mode of inheritance and locate the causative gene(s). Full-sibling littermates will be identified, where one puppy has normal hearing and one is deaf. Like human twins, full siblings should have very similar DNA, which will reduce the variability of the DNA samples when compared to studies of unrelated dogs. The study of pairs of English Setters will be added to an ongoing study examining differences in Dalmatian and Australian Cattle Dog pairs. Identifying candidate deafness genes will be an important breakthrough to understanding deafness in dogs and people, with a goal to establish a genetic test to reduce or eliminate deafness in these canine populations.

Funding for the research is provided through the collaborative efforts and generosity of the English Setter Association of America. 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: George M. Strain, PhD; Louisiana State University

Total Grant Amount: \$120,015

Grant Period: 11/1/2015- 4/30/2018

Project Abstract:

Hereditary deafness associated with white pigmentation occurs in numerous dog breeds. The breeds most affected are the Dalmatian (Dal, 22% unilaterally deaf, 8% bilaterally deaf) and the Australian cattle dog (ACD, 11.4% and 3%). The mechanism of inheritance is unknown, and previous studies to determine the mode of inheritance and locate the causative gene(s) have thus far been unsuccessful. Using a modified twin study approach, full-sibling littermates will be clinically and genetically evaluated. Like human twins, full siblings should have very similar DNA, which will reduce the variability of their DNA when compared to studies of unrelated dogs. Using the Illumina CanineHD Beadchip, which contains 172,115 DNA markers (SNPs) spread uniformly across the canine chromosomes, markers will be compared between the sibling pairs, and differences between siblings at individual markers will thus be identified. Using this approach candidate deafness genes can be identified and will advance the current understanding of this heritable disorder.

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

02452-A

Targeting the T helper Inflammatory Pathway in Meningoencephalomyelitis of Unknown Origin (MUO)

Principal Investigator: Renee Barber, DVM, PhD; University of Georgia

Total Grant Amount: \$8,845

Grant Period: 1/1/2018- 6/30/2019

Project Abstract:

Meningoencephalomyelitis of unknown origin (MUO) is a common neurological disorder of dogs that results in inflammation of the brain and/or spinal cord causing depression, seizures, blindness, difficulty walking, and death. All dogs can be affected but young to middle aged small and toy breed dogs (such as the Chihuahua, Maltese, Pug, and Yorkshire Terrier) are often affected. Currently, brain biopsy is the only means of definitive diagnosis prior to death and the ideal treatment is not known. There is a critical need to improve diagnosis and treatment of MUO. The investigators will identify changes in the immune system associated with inflammation that occurs in the brains and spinal cords of affected dogs, looking for specific products of the immune response, such as interferon-gamma and interleukin 17, in blood and cerebrospinal fluid. Identification of these products could lead to development of new diagnostic tests, strategies for more effective treatment, and improved prognosis prediction.

New

Oncology

02237-A

Capturing Tumor Cells in Canine Blood

Principal Investigator: Tracy Stokol, BVSc, PhD; Cornell University

Total Grant Amount: \$10,239

Grant Period: 6/1/2016- 5/31/2018

Project Abstract:

Just like their human owners, many dogs suffer from cancer, which is often malignant, spreading through the body via blood. Once tumors have spread, they usually result in a poor outcome, including death. The tumor cells in circulation (CTCs) can be counted in the blood of people with cancer using immunocapture devices. The number of CTCs in blood can tell the clinician how aggressive the tumor is, its potential to spread, and how long a patient might survive. There is currently no such way of detecting CTCs in our canine companions. Development of an assay for counting CTCs in canine blood would be of tremendous benefit to our canine patients because, from a simple blood test, we could detect hidden tumors and gather information on tumor severity and the likelihood of spread or metastasis. The investigators will test a novel immunocapture microdevice - the GEDI - for counting tumor cells in canine blood. This device can capture CTCs from blood in human patients with various cancers. This study will test its potential to do the same for dogs. In this pilot study, blood samples from healthy dogs will be manipulated to test the ability to count how many added tumor cells are captured by the GEDI device. If the GEDI does capture the tumor cells, the next step will be to determine if the device can capture CTCs from the blood of dogs that are known to have cancer, paving a path to early detection of cancer in dogs.

02171-MOU

Histiocytic Sarcoma in Bernese Mountain Dogs: Novel Approaches To Treatment

Principal Investigator: Vilma Yuzbasiyan-Gurkan, PhD; Michigan State University

Total Grant Amount: \$43,661

Grant Period: 7/1/2015- 12/31/2017

Project Abstract:

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

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

02321

Clinical Trial of Procaspace-3 Activator (PAC-1) in Combination with Hydroxyurea for Treatment of Canine Meningioma

Principal Investigator: Timothy M. Fan, DVM, PhD; University of Illinois

Total Grant Amount: \$51,191

Grant Period: 2/1/2017- 1/31/2019

Project Abstract:

Primary brain tumors are a significant cause of illness and death in pet dogs, with meningioma accounting for approximately half of the cases seen by veterinary neurologists and oncologists. Although surgery remains the best treatment for dogs with meningioma, some dogs are not good candidates for this approach based on their tumor size and/or location. Dogs also may experience tumor regrowth after an attempt is made to surgically remove the tumor. In these situations, effective treatment options are limited. Thus, new treatments that are both safe and effective are needed for dogs with meningioma. A team of investigators from the National Cancer Institute's Comparative Oncology Program (NCI-COP) and selected veterinary academic centers will work together using state-of-the art imaging and a novel therapeutic approach for dogs with meningioma that are good surgical candidates. Dogs enrolled in this study will receive an investigational combination of chemotherapy agents (PAC-1 + hydroxyurea) and will be monitored with magnetic resonance and non-invasive molecular imaging techniques. Dogs will then undergo tumor removal and tissue analysis. This approach is the first to validate and advance a new therapy that is directly applicable to dogs, and potentially also to humans, with advanced, locally-recurrent, and/or non-resectable meningioma.

New

01889-G

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

Principal Investigator: Jaime F. Modiano, VMD, PhD; University of Minnesota; Matthew Breen, PhD, North Carolina State University; Elinor Karlsson, PhD, Broad Institute

Total Grant Amount: \$360,933

Grant Period: 1/1/2014- 12/31/2017

Project Abstract:

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

02405-A

New

Transcriptome Based Diagnostics in Canine Soft Tissue Sarcoma

Principal Investigator: Andrew D. Miller, DVM; Cornell University

Total Grant Amount: \$14,880

Grant Period: 11/1/2017- 10/31/2018

Project Abstract:

Sarcomas are malignant cancers that can arise in any part of the body; however, in the dog, a subset referred to as soft tissue sarcomas account for 10-15% of all skin and subcutaneous cancers. Traditionally biopsy and subsequent histology have been the primary means of diagnosing these cancers. The histology is assigned to one of three grades ranging from low (grade I), intermediate (grade II), and high (grade III). Currently, histologic grade is the key criterion for guiding treatment and determining patient outcome. However, in human medicine and pathology, soft tissue sarcomas are diagnosed with a hybrid approach that involves both histologic features and genetic analysis of the tumor sample. This genetic analysis guides further treatment, aids in developing accurate follow-up information, and has been shown to have a positive effect on patient outcome and survival. Unfortunately, despite how common soft tissue sarcomas are in the dog, we still rely solely on the histologic grade, which is subjective at best, and we do not incorporate any genetic data into our diagnostic plan. The objective of this grant is to develop a validated test to analyze the genes present in canine soft tissue sarcoma. This will allow for future prospective studies in which genetic analysis will be used to guide treatment in dogs afflicted with this cancer, lead to more refined care, and ultimately improve patient outcome.

02455-A

New

Identification of Genetic Mutations in Anal Sac Carcinoma in English Cocker Spaniels

Principal Investigator: Shaying Zhao, PhD; University of Georgia

Total Grant Amount: \$15,000

Grant Period: 12/1/2017- 11/30/2018

Project Abstract:

English Cocker Spaniels (ECSs) are about 7 times more likely than other dog breeds to develop anal sac carcinoma (ASC). Hence, there appears to be a genetic basis for this disease development in ECSs. The investigators will sequence the genomes and transcriptomes of blood and ASC tumor samples collected from ECS dogs across the US. The samples will be studied alongside the pedigree information and medical records. Using dog-human comparative genomics and oncology strategy for cancer-causative mutation discovery, successful identification of mutations in ASC development in ECSs may lead to the development of genetic tests of this aggressive disease in ECSs and yield targets for therapeutic intervention.

02204

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

Principal Investigator: Laura E. Selmic, BVetMed; University of Illinois

Total Grant Amount: \$46,358

Grant Period: 1/1/2016- 12/31/2018

Project Abstract:

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

Oncology - Hemangiosarcoma

02234-MOU

A Novel Approach for Prevention of Canine Hemangiosarcoma

Principal Investigator: Jaime F. Modiano, VMD, PhD; University of Minnesota

Total Grant Amount: \$432,000

Grant Period: 3/1/2016- 2/28/2019

Project Abstract:

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

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

02217

A Novel Mechanism to Regulate the Growth of Canine Hemangiosarcoma

Principal Investigator: Erin B. Dickerson, PhD; University of Minnesota

Total Grant Amount: \$86,206

Grant Period: 1/1/2016- 12/31/2017

Project Abstract:

Hemangiosarcoma is an extremely aggressive cancer that is rapidly fatal in dogs. While the lifetime risk is alarmingly high for some breeds such as Golden Retrievers and German Shepherd Dogs, the disease does not discriminate, and it can strike any dog at any time. Despite considerable efforts by veterinarians and scientists to find effective treatments, the outcome for dogs with hemangiosarcoma has changed very little over the past few decades. Recent evidence provides essential clues into how these tumors grow and progress, generating new ideas for treatment approaches. Such new evidence suggests that hemangiosarcoma cells rely on the metabolism of lipids or fatty acids to supply energy for tissue invasion or continued tumor growth. To obtain these lipids, hemangiosarcomas may take over the metabolic machinery of neighboring cells, forcing them to produce nutrients for the tumor cells to help them proliferate and grow. This study will verify that tumor cells rely on lipid metabolism for growth, and determine if tumor cells alter the metabolism of fat cells to obtain cellular nutrients and accelerate tumor cell lipid metabolism. Identifying and exploiting a novel mechanism that may disrupt this process by inhibiting the interactions between tumor cells and cells in the tumor environment will speed clinical investigations, and ultimately lead to improved outcomes for dogs with this devastating disease.

Oncology - Lymphoma

02316

Genetic Risk Factors for Canine T zone Lymphoma

Principal Investigator: 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 in this breed that 40% of all cases are seen in Golden Retrievers. This observation suggests a clear 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. This research will improve understanding of the mechanisms that lead to T zone lymphoma as well as mast cell tumors in dogs.

New

01918-G

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

Principal Investigator: Jeffery N. Bryan, DVM, PhD; University of Missouri, Columbia

Total Grant Amount: \$404,813

Grant Period: 7/1/2013- 12/31/2017

Project Abstract:

Lymphoma strikes 1 in 8 Golden Retrievers, approximately one-third of the cases being B-cell. While T-cell classifications currently inform therapy choices for dogs, B-cell classifications have been investigated little in Golden Retrievers. Dr. Jeffrey Bryan, in collaboration with Drs. Anne Avery and Heather Wilson-Robles will focus their efforts on an area of emerging importance in cancer: epigenetics. Epigenetics is defined as stable and heritable patterns of gene expression that do not entail any alterations to the original DNA sequence. Epigenetic DNA methylation changes clearly underlie development of lymphoma in humans, but have been evaluated minimally in dogs. Dr. Bryan and collaborators propose to improve diagnostic, classification, and prognostic ability using flow cytometry paired with biopsy to characterize the B-cell lymphomas of Golden Retrievers. They will identify DNA methylation changes in lymphoma cells not present in normal cells to develop biomarkers of each class of lymphoma and identify new therapy targets for affected Golden Retrievers. More significantly, because DNA methylation changes occur so early in the process of cancer formation, they hypothesize that they could serve as biomarkers of risk, allowing medicine or diet to prevent lymphoma in Golden Retrievers before it develops. Finally, they propose to identify tumor initiating cells (TIC) in lymphoma biopsies to characterize stem-like cells by surface markers and DNA methylation changes. Identifying these cells will aid therapeutic strategy development. Each project advances a current frontier of research. By performing them in parallel, the markers from each can be combined, correlated, and translated into biomarkers of risk, diagnosis, and prognosis to advance the prevention and management of lymphoma in Golden Retrievers.

02318

New

Genetic and Environmental Risk for Lymphoma in Boxer Dogs

Principal Investigator: 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 of the blood cells 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, and 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. So far, their findings suggest one variant is a risk factor for lymphoma in dogs of varying breeds. However, the genes for canine GST-pi and GST-mu enzymes have not yet been explored. 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.

01418

Harnessing a Dog's Own Immune System to Kill Lymphoma Tumor Cells

Principal Investigator: Heather M. Wilson-Robles, DVM; Texas A&M Research Foundation

Total Grant Amount: \$150,000

Grant Period: 1/1/2011- 6/30/2018

Project Abstract:

Lymphoma is the most common malignancy of dogs representing up to 25% of diagnosed cancers. Dogs often develop an aggressive form of lymphoma that is rarely curable, with most unfortunately succumbing to disease within 12 months of diagnosis despite best-available chemotherapies. Dr. Wilson will develop a new treatment to re-train the dog's own immune system to attack the most common type of canine lymphoma, B-cell lymphoma. In order to accomplish this they will obtain a small number of circulating white blood cells, called T cells, from the blood of affected dogs and insert a gene that will cause the T cell to express a receptor which recognizes the tumor "fingerprint". After docking with the lymphoma, the T cell will be triggered to mount an immune response against the tumor cells with the specific fingerprint. This therapy could be used alone or in combination with chemotherapy. Their preliminary data demonstrate that it is possible to genetically modify T cells. Further, they have been able to successfully harvest and grow T cells in the laboratory and return them safely to the dog. These infused cells can be found in the blood and tumor weeks after infusion, showing that it is possible for these cells to survive in the dog. If successful this study will be the first to develop an "in-dog" T-cell therapy targeting a tumor that has historically thought to be untreatable.

02309

New

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

Principal Investigator: Angela McCleary-Wheeler, DVM, PhD; Cornell University

Total Grant Amount: \$78,069

Grant Period: 1/1/2017- 12/31/2018

Project Abstract:

Canine lymphoma is one of the most common cancers in dogs. While some breeds appear more at risk than others, all can be affected. 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 in dogs with lymphoma. One area of 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 in which this occurs is due to modifications of the proteins that interact with DNA called histones. Various modifications to these histones can result in genes being turned on or off, leading to the development of cancer. One particular enzyme that modifies histones, EZH2, has been found to play a role in some human lymphomas. However, this has been unexplored in canine lymphoma. Given the striking similarities between human and canine lymphoma, the objective of this work 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. The information obtained from this study will help guide the future development of this targeted inhibitor for use as a novel therapy to treat canine lymphoma.

02317

New

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

Principal Investigator: 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. Among these cases diffuse large B-cell lymphoma (DLBCL) is the most common subtype. Despite continued advances in veterinary medicine, 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 with CHOP. Patients with signatures predictive of poor response to conventional CHOP chemotherapy may benefit from more aggressive treatment at the outset to improve outcome.

Oncology - Osteosarcoma

01660

Identifying the Genes That Confer Risk for Osteosarcoma

Principal Investigator: Carlos E. Alvarez, PhD; The Research Institute at Nationwide Children's Hospital

Total Grant Amount: \$120,000

Grant Period: 1/1/2012- 12/31/2018

Project Abstract:

Osteosarcoma (OSA) is the most common cancer of the bone in both dogs and humans. A prime candidate for investigation of the genetic component of OSA is the Greyhound, which has the highest risk of OSA of any breed. However, despite significant effort, classical genetic approaches have not identified any Greyhound variant that accounts for most OSA cases in that breed. Dr. Alvarez proposes that Greyhound OSA variants have been directly or indirectly selected for in racing performance, consistent with the vastly elevated incidence in racing vs. show Greyhounds. If this is true and all racers carried an OSA mutation on both chromosomes, then this could not be detected using classical approaches (which require different genetic markers to distinguish cases v. controls). Here Dr. Alvarez proposes an innovative genetic approach that is impervious to the limitations described above, and enables genome-wide discovery of Greyhound variation with large effects on OSA risk. Such findings would lead to rapid development of therapies and clinical trials in dogs, and translation to human medicine.

02215

A Cancer Vaccine for Canine Osteosarcoma**Principal Investigator:** Rowan J. Milner, BVSc; University of Florida**Total Grant Amount:** \$80,974**Grant Period:** 1/1/2016- 12/31/2017**Project Abstract:**

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

Ophthalmology

02340

New

Clinical and Genetic Background of Progressive Retinal Atrophy in Miniature Schnauzers**Principal Investigator:** Hannes T. Lohi, PhD; Folkhälsan Institute of Genetics**Total Grant Amount:** \$46,224**Grant Period:** 12/1/2017- 11/30/2018**Project Abstract:**

Dogs may be affected with hereditary eye disorders, which cause severe vision impairment, and sometimes progress to complete blindness. One hereditary condition is progressive retinal atrophy (PRA), in which the light-sensing receptors in the retina are lost, leading to complete blindness. Currently there are no treatment options for this disease. The development of genetic testing would be an important breakthrough for veterinary medicine. The identification of a causative gene would also enable a study of the molecular background of the disease for improved treatment plans. The investigators have established a large pedigree and clinically-investigated sample cohort in Miniature Schnauzers with PRA to identify its genetic cause, and have already identified the chromosomal region suspected to harbor the causative gene. Through this study, they researchers hope to identify a PRA gene and mutation, leading to a genetic test for the eradication of this disorder from the Miniature Schnauzer breed.

02061

Emergence of Pigmentary Uveitis as a Potential Cause of Cataracts and Glaucoma**Principal Investigator:** Wendy M. Townsend, DVM, MS; Purdue University**Total Grant Amount:** \$74,070**Grant Period:** 1/1/2014- 12/31/2017**Project Abstract:**

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

02164-MOU

Determining the Genetic Contribution to Boxer Corneal Ulcers

Principal Investigator: Kathryn M. Meurs, DVM, PhD; North Carolina State University

Total Grant Amount: \$68,053

Grant Period: 1/1/2015- 12/31/2017

Project Abstract:

Spontaneous chronic corneal epithelial defects (SCCEDs) are chronic corneal ulcers that fail to undergo normal healing that are commonly observed 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 to heal the corneal ulcer 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 SCCED is an adult onset disease, many dogs are selected for breeding before they are diagnosed. A blood test that could identify affected animals before they are used for breeding would greatly decrease the prevalence of SCCEDs. In a previous study funded by the AKC-CHF Dr. Meurs and colleagues collected samples from adult boxers with and without SCCED and performed a genome wide association study. In the study proposed here they will perform whole genome sequencing (GWAS) on a subset of affected and unaffected dogs and use the data from the GWAS to focus in on important variants. They will then more closely evaluate variants of interest to determine the gene and ultimately the causative genetic mutation. They hope that the identification of a genetic cause for SCCEDs in the Boxer can be used to reduce the prevalence of this disease in this breed but also to provide information for other affected breeds.

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.

02336

Genetics of Primary Angle Closure Glaucoma in American Cocker Spaniels

Principal Investigator: Sara M. Thomasy, DVM, PhD; University of California, Davis

Total Grant Amount: \$40,000

Grant Period: 5/1/2017- 4/30/2018

Project Abstract:

Glaucoma is a leading cause of irreversible blindness and globe removal (enucleation) in dogs. Primary angle closure glaucoma (PACG) is the most common form of glaucoma in dogs whereby acute blockage of the iridocorneal angle leads to a rapid increase in intraocular pressure. Consequently, PACG is painful, demands immediate medical attention, and often causes incurable vision loss. The American Cocker Spaniel (ACS) has the highest reported prevalence of any canine breed for PACG. The investigators will study the genetics of PACG in the ACS to identify potential disease-causing loci and variants. Dogs will be extensively phenotyped as PACG cases or controls using advanced imaging equipment used to investigate glaucoma in human patients. Identification of genetic markers associated with PACG in ACSs will facilitate the development of a genetic test to inform breeding programs. Furthermore, identification of the molecular basis of PACG may help elucidate novel therapeutic or testing strategies in the management of this blinding disease that may be translatable to the human condition.

New

02403-MOU

Microphthalmia and Delayed Growth Syndrome in the Portuguese Water Dog

Principal Investigator: Margret L. Casal, DVM, PhD; University of Pennsylvania

Total Grant Amount: \$12,960

Grant Period: 11/1/2017- 10/31/2019

Project Abstract:

Microphthalmia and delayed growth syndrome (aka "puppy eye syndrome") has been reported by Portuguese Water Dog breeders dating as far back as 1986. However, there is no information in the scientific literature and the majority of data concerning this syndrome has been obtained from records of breeders, which have anecdotal reports of the disease and little, if any, medical diagnostics. Affected dogs present with microphthalmia of varying severity, other eye abnormalities, short stature and other findings. To date, the investigators have been able to collect DNA from 24 affected dogs. Males and females can be affected, although females predominate (about 70%). Preliminary pedigree studies suggest an autosomal recessive inheritance. Human literature reports numerous syndromes associated with microphthalmia, and many genes have been identified as having a causative role. The goals of this investigation are to better characterize the clinical syndrome seen in Portuguese Water Dogs, confirm a suspected mode of inheritance, obtain additional samples for investigation into the genetic mutation, and develop a mutation based, genetic test for breeders to eliminate this syndrome from the Portuguese Water Dog breed.

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

02332-A

New

Identification of Mutations for Primary Lens Luxation in Multiple Dog Breeds

Principal Investigator: Cathryn S. Mellersh, PhD; Animal Health Trust

Total Grant Amount: \$14,812

Grant Period: 5/1/2017- 4/30/2018

Project Abstract:

Primary lens luxation (PLL) is a painful inherited disease that affects many breeds of dog. A mutation in the gene ADAMTS17 has been identified that causes PLL in at least 20 breeds and DNA tests are available for these breeds. Different mutations in ADAMTS17 are also known to cause a different disease, primary open angle glaucoma (POAG), in a small number of additional breeds and POAG in two more breeds is known to be caused by mutations in the closely related gene ADAMTS10. POAG is characterized by increased pressure within the eye that is due to abnormalities deep within the part of the eye known as the ciliary cleft that disrupt the normal drainage of fluid within the eye. Although PLL and POAG are different diseases, they are both caused by abnormalities in the part of the eye known as the ciliary body or in nearby tissues. There are currently several breeds of dog that are affected by PLL but for which mutations are currently unknown. The investigators will investigate both ADAMTS10 and ADAMTS17 for novel mutations that explain PLL in five breeds of dog. The DNA sequence data can also be used to facilitate future studies of other inherited disorders in dogs, beyond the scope of this study.

02243-A

Genomic Profiling of Canine Corneal Endothelial Dystrophy

Principal Investigator: 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. This results in corneal swelling, and secondary vision compromise and corneal ulceration. The only definitive treatment for CED is a corneal transplant. Unfortunately, corneal transplants are rarely performed in canine patients with CED due to the expense of the surgery and follow-up care, high risk of complications, and lack of appropriate donor tissue. Several dog breeds including Boston Terriers, German Shorthaired Pointers and German Wirehaired Pointers are seen more commonly for CED in comparison to other breeds. This observation suggests that this disease may have a genetic basis. A similar condition called Fuchs endothelial corneal dystrophy (FECD) occurs in humans and several genes associated with FECD have been identified. This project will investigate the genetics of CED in dogs, and will include thorough eye examinations and advanced ocular imaging as well as extraction of DNA from blood collected from dogs with CED and age-matched controls. The entire canine genome will be evaluated for an association with CED. This work will be used to identify the gene(s) responsible for this condition in these 3 breeds and to develop a genetic test for CED.

Kidney and Urological Disease

02152

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

Principal Investigator: Mary B. Nabity, DVM, PhD; Texas A&M AgriLife Research

Total Grant Amount: \$26,988

Grant Period: 1/1/2015- 12/31/2017

Project Abstract:

Chronic kidney disease (CKD) is a significant cause of illness and death in dogs and is often due to glomerular diseases. Dogs with glomerular disease often have poor outcomes with standard therapy, and specific treatment recommendations are difficult without performing a kidney biopsy to determine the type of glomerular disease present, since treatment and outcome among these diseases differs substantially. Even then, we lack an understanding of the mechanisms driving these diseases, limiting our ability to optimally treat these dogs. Therefore, tests to non-invasively diagnosis the type of glomerular disease would help veterinarians more appropriately treat these patients and provide insight into the mechanisms that cause the diseases. This could lead to better therapies that slow disease progression and improve quality and length of life in dogs with CKD. One area of emerging importance in CKD is the role of microRNAs (miRNAs) in disease pathogenesis and progression. miRNAs are small molecules that can regulate gene expression by up or down regulation of messenger RNA transcripts and proteins in target tissues. Many studies have found that increases or decreases in miRNAs can serve as biomarkers of diseases, including human CKD. They also contribute to the development of diseases. The goal of Dr. Nabity's study is to identify miRNAs in serum and urine of dogs that are specific for the three major causes of glomerular disease in this species. They also aim to identify miRNAs associated with disease progression for each of these diseases. Successful completion of these goals will support the translation of miRNAs into diagnostic tests and viable targets for future drug development.

02263-MOU

Characterization of Kidney Disease in Dalmatians

Principal Investigator: 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. Although one specific type of glomerular disease has been reported in the literature, 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 autopsy 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 could be performed on related dogs that 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 and 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.

02066

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

Principal Investigator: Mary B. Nabity, DVM, PhD; Texas A&M AgriLife Research

Total Grant Amount: \$108,243

Grant Period: 1/1/2014- 6/30/2018

Project Abstract:

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

01844

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

Principal Investigator: Shelly Vaden, DVM, PhD; North Carolina State University

Total Grant Amount: \$116,184

Grant Period: 1/1/2013- 12/31/2017

Project Abstract:

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

02267-A

An Epidemiological Study of *Brucella canis*

Principal Investigator: Tory V. Whitten, MPH; Minnesota Department of Health

Total Grant Amount: \$14,986

Grant Period: 11/1/2016- 12/31/2017

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 how common exposure to this disease is 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 at the Minnesota Veterinary Diagnostic Laboratory. An important outcome of this study will be to create prevention and control measures applicable to this important population of dogs.

02512-A

Genome sequencing and antimicrobial susceptibilities of *Escherichia coli* isolated from clinical cases of canine pyometra

Principal Investigator: Erin E. Runcan, DVM; Ohio State University

Total Grant Amount: \$8,208

Grant Period: 12/1/2017- 11/30/2018

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 biofilm, a layer of polysaccharide that protects the organism from the host immune system as well as antibiotic agents, decreasing treatment efficacy. Current treatments for pyometra are costly, time-consuming, and not without risk to the bitch. The investigators postulate that biofilm production by *E. coli* within the uterine lining may be responsible for perpetuating the disease and making treatment difficult. In previous CHF-funded study, the investigators were able to prove that *E. coli* from clinical cases of canine pyometra is capable of producing biofilm both in the uterus and in laboratory settings. The purpose of this study is to characterize the presence of ten different genes associated with biofilm production and disease-contributing factors of *E. coli* organisms to determine if there is an association with those strains of *E. coli* that produce biofilm and certain disease factors found in other strains of *E. coli*. Disease factor genes and resistance patterns will be identified, and may serve as targets for new therapeutics directed at the disruption of biofilm in an effort to shorten the duration of treatment of pyometra.

New

02264-A

Role of *E. Coli* Biofilm in Canine Pyometra

Principal Investigator: Marco A. Coutinho da Silva, DVM, PhD; Ohio State University

Total Grant Amount: \$14,731

Grant Period: 5/1/2016- 12/31/2017

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. Current treatments for pyometra are costly, time-consuming, and not without risk to the bitch. 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 procured from collaborating private practitioners throughout the country 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.

Tick-Borne Disease Initiative

01780

Defining the Mechanism by Which Ticks Locate Dogs in Order to Better Prevent Disease Transmission

Principal Investigator: Emma Natalie Ivy Weeks, PhD; University of Florida

Total Grant Amount: \$104,867

Grant Period: 3/1/2013- 2/28/2018

Project Abstract:

The brown dog tick (BDT) is common across the U.S. and is the most widely distributed tick in the world. BDT's carry and transmit the pathogens that cause debilitating diseases such as canine *ehrlichiosis* and *babesiosis*. Prevention of these diseases is accomplished through tick control. BDT's can complete their entire life cycle indoors, making management difficult. Records of infestations are increasing and unpublished data indicates that a high level of pesticide resistance is present in domestic populations. Consequently once introduced, these ticks are particularly hard to eradicate and as one female tick may lay 5,000 eggs, the problem soon gets out-of-hand. Pesticide resistance leads to aggressive treatment regimes, which in turn, lead to increased exposure of humans and pets to chemical residues. Alternatives to pesticides are needed. Studies have shown that BDT's are attracted to dog odor, a blend of volatile chemicals used by ticks to find a blood meal. In this study, Dr. Weeks will identify the chemicals BDT's use to locate a dog. This will enable manipulation of tick behavior thereby facilitating management and reducing the need for extensive use of pesticides. Improved tick control without the need for increased environmental pesticide applications will improve the quality of life for dogs and their owners.

02292

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

Principal Investigator: Pedro Paul Diniz, DVM, PhD; Western University of Health Sciences

Total Grant Amount: \$60,717

Grant Period: 9/1/2016- 2/28/2018

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. Consequently, the current assays may suffer from "myopia": a self-fulfilling effect that prevents the detection of new or emerging organisms. Using an innovative approach, the investigators will employ next-generation sequencing (NGS) to overcome the limitations of current diagnostic technology. With NGS, the investigators can 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.

02287

Enhanced Testing for the Diagnosis of Bartonellosis in Dogs

Principal Investigator: Edward B. Breitschwerdt, DVM; North Carolina State University

Total Grant Amount: \$103,013

Grant Period: 8/1/2016- 7/31/2018

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. Dr. Breitschwerdt's laboratory demonstrated the first evidence for Bartonella infections in dogs in 1993. *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 worldwide 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.

02295-A

The Role of Lymphocytes in Canine Monocytic Ehrlichiosis

Principal Investigator: Mary Anna Thrall, DVM, MS; Ross University School of Veterinary Medicine

Total Grant Amount: \$15,000

Grant Period: 7/1/2016- 12/31/2017

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.

02383

Identifying Cellular Mechanisms of Inflammation During Canine Tick-Borne Diseases

Principal Investigator: Christine A. Petersen, DVM, PhD; University of Iowa

Total Grant Amount: \$207,526

Grant Period: 9/1/2017- 8/31/2019

Project Abstract:

Tick-borne diseases are found in all 50 states of the United States and are the most common vector-borne disease diagnosed in people in the US. The predominant disease is Lyme disease, caused by *Borrelia burgdorferi* and related species (*sensu lato*). Other important canine tick-borne diseases include those caused by *Anaplasma platys*, *Anaplasma phagocytophilum* (*Anaplasmosis*), *Babesia canis*, *Babesia conradae* and *Babesia gibsonii* (*Babesiosis*), and *Ehrlichia canis*, *Ehrlichia chaffinensis* and *Ehrlichia ewingii* (*Ehrlichiosis*). Many of these diseases also affect people. Dogs can serve as sentinel species for human disease and there are many areas where the immune responses and disease outcomes are very similar in people and dogs, meaning that important lessons can be learned by sharing information between human and animal health (One Health). The researchers will further investigate the dog's immune system to determine which immune cells are responsible for the cure or creation of canine tick-borne disease. Through understanding which cells are responsible for causing disease, the goal is to then specifically target the molecules they produce using immunotherapy or immune modulation to improve treatment of tick-borne diseases in all dogs.

New

02284-A

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

Principal Investigator: 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. In people, Lyme is the most common tick-transmitted disease in the US, with over 25,000 cases in 2014. 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 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. During this period the investigators will 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. These findings are likely to extend to better understanding of canine and human Lyme disease, and improve health outcomes. Collectively, this work 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.

CHF Clinician-Scientist Fellowship Program



The AKC Canine Health Foundation Clinician-Scientist Fellowship Program supports young scientists. Through this effort our 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,
- 2) Who will conduct research in line with CHF's mission to advance the health of all dogs,
- 3) Who will conduct research that will abide by CHF policies, including our Humane Use of Animals Policy.

2018 CHF Clinician-Scientist Fellows



Kathryn Dalton, VMD, MPH; Johns Hopkins Bloomberg School of Public Health
Mentor: Meghan Davis, DVM, MPH, PhD

Dr. Dalton received her VMD from the University of Pennsylvania. Dr. Dalton's work focuses on how microbial communities are transmitted among animals, humans and the environment, relating microbial community profiles to human and canine health outcomes.



Shelby Gasson, DVM; Texas A&M University
Mentor: W. Brian Saunders, DVM, PhD, Diplomate ACVS

Dr. Gasson received her DVM from Texas A&M University. She is this year's AKC Canine Health Foundation GCHP Hill Country's Let's Get Ready To Rumble "Rumble" Clinician-Scientist Fellow (akcchf.org/rumble). Dr. Gasson's work focuses on the development of tissue engineering constructs for treatment of osteochondral defects. Dr. Gasson will be evaluating growth and differentiation of canine mesenchymal stem cells on different tissue scaffolds.



Mariah Gentry, DVM; University of Pennsylvania
Mentor: Margret L. Casal, DVM, PhD, Diplomate ECAR

Dr. Gentry received her DVM from Cornell University. Dr. Gentry's work focuses on the heritability of renal dysplasia in Cairn Terriers and aims to develop a DNA-based marker test so the disorder can be diagnosed at an early age. The findings of this work would allow for more informed breeding decisions as well as make lifestyle changes earlier to prolong the lives of dogs with this disorder.



Sita Withers, BVSc(Hons); University of California, Davis
Mentor: Robert B. Rebhun, DVM, PhD, Diplomate ACVIM (Oncology)

Dr. Withers received her BVSc(Hons) from Melbourne University, Werribee. Dr. Withers' research aims to build a better understanding of how naturally occurring canine cancers can contribute to the study of immunotherapeutics in dogs as well as people. Her research is focused on the immune microenvironment in canine osteosarcoma both in the primary and metastatic sites.

AKC/AKC CHF/TF 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.



Carla Barstow, DVM; Auburn University (CHF Grant 02282-E)
Residency Coordinator: Robyn R. Wilborn, DVM, MS; 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.



Tessa Fiamengo, DVM; Ohio State University (CHF Grant 02294-E)
Residency Coordinator: Marco A. Coutinho da Silva, DVM, PhD; 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.



Victor Stora, DVM; University of Pennsylvania (CHF Grant 02283-E)
Residency Coordinator: Margret L. Casal, DVM, PhD; 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.



Karen Von Dollen, DVM; North Carolina State University (CHF Grant 02281-E)
Residency Coordinator: Scott Bailey, DVM, MS; 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.

Impact of Funding: Selected 2017 Scientific Publication Outcomes of Research

Accuracy of 3 Tesla Magnetic Resonance Imaging Using Detection of Fiber Loss and a Visual Analog Scale for Diagnosing Partial and Complete Cranial Cruciate Ligament Ruptures in Dogs

Fazio, Constance G., Peter Muir, Susan L. Schaefer, and Kenneth R. Waller. 2017. *Veterinary Radiology & Ultrasound* (May 2016):1–15. (www.ncbi.nlm.nih.gov/pubmed/29094513).

Utility of MRI for Characterizing Articular Cartilage Pathology in Dogs with Medial Coronoid Process Disease

Franklin, S. P., E. E. Burke, and S. P. Holmes. 2017. *Front Vet Sci* 4:25. (<https://www.ncbi.nlm.nih.gov/pubmed/28286752>).

Templated, Macroporous PEG-DA Hydrogels and Their Potential Utility as Tissue Engineering Scaffolds

Gacasan, Erica G., Rebecca M. Sehnert, Daniel A. Ehrhardt, and Melissa A. Grunlan. 2017. *Macromolecular Materials and Engineering* 302(5):1600512. (doi.wiley.com/10.1002/mame.201600512).

Prevalence and Mode of Inheritance of the Dal Blood Group in Dogs in North America

Goulet, S. et al. 2017. *J Vet Intern Med* 31(3):751–58. (<https://www.ncbi.nlm.nih.gov/pubmed/28391649>).

Evaluation of a Scoring System Based on Conformation Factors to Predict Cranial Cruciate Ligament Disease in Labrador Retrievers

Griffon, Dominique J. et al. 2017. *Veterinary Surgery* 46(2):206–12. (www.ncbi.nlm.nih.gov/pubmed/28029702).

Expression of Phosphorylated KIT in Canine Mast Cell Tumor

Halsey, C. H. C. et al. 2017. *Vet Pathol* 54(3):387–94. (www.ncbi.nlm.nih.gov/pubmed/28129097).

Evolutionary Dynamics of Pathoadaptation Revealed by Three Independent Acquisitions of the VirB/D4 Type IV Secretion System in Bartonella

Harms, A. et al. 2017. *Genome Biol Evol* 9(3):761–76. (<https://www.ncbi.nlm.nih.gov/pubmed/28338931>).

Semen Evaluation and Fertility Assessment in a Purebred Dog Breeding Facility

Hesser, A. et al. 2017. *Theriogenology* 87:115–23. (<https://www.ncbi.nlm.nih.gov/pubmed/27658745>).

Establishment of a Patient-Derived Xenograft of Canine Enteropathy-Associated T-Cell Lymphoma, Large Cell Type

Im, K. S. et al. 2017. *Journal of Comparative Pathology* 156(1):37–41. (www.ncbi.nlm.nih.gov/pubmed/28011041).

The Association of Specific Constituents of the Fecal Microbiota with Immune-Mediated Brain Disease in Dogs

Jeffery, Nick D. et al. 2017. *PLoS ONE* 12(1):1–14. (www.ncbi.nlm.nih.gov/pubmed/28125651).

Prevalence of Vector-Borne Pathogens in Southern California Dogs With Clinical and Laboratory Abnormalities Consistent With Immune-Mediated Disease

Kidd, L. et al. 2017. *J Vet Intern Med*. (<https://www.ncbi.nlm.nih.gov/pubmed/28558145>).

Homozygous PPT1 Splice Donor Mutation in a Cane Corso Dog With Neuronal Ceroid Lipofuscinosis

Kolicheski, A. et al. 2017. *J Vet Intern Med* 31(1):149–57. (<https://www.ncbi.nlm.nih.gov/pubmed/28008682>).

ADAM23 Is a Common Risk Gene for Canine Idiopathic Epilepsy

Koskinen, L. L. et al. 2017. *BMC Genet* 18(1):8. (<https://www.ncbi.nlm.nih.gov/pubmed/28143391>).

Individual Differences in Cooperative Communicative Skills Are More Similar between Dogs and Humans than Chimpanzees

MacLean, Evan L., Esther Herrmann, Sunil Suchindran, and Brian Hare. 2017. *Animal Behaviour* 126:41–51. (<http://dx.doi.org/10.1016/j.anbehav.2017.01.005>).

Combining RPL27 with OAZ1 or RPL8 as Universal Normalizers of Gene Expression in Canine Endometrial Studies

Mair, Georg, Hermann Unger, and Cordula Gabriel. 2017. 1(September):23–34. *International Journal of Veterinary Science and Technology* (<http://www.scireslit.com/Veterinary/IJVST-ID15.pdf>).

XX Disorder of Sex Development Is Associated with an Insertion on Chromosome 9 and Downregulation of RSP01 in Dogs (Canis Lupus Familiaris)

Meyers-Wallen, Vicki N. et al. 2017. edited by C. Englert. *PLOS ONE* 12(10):e0186331. (www.ncbi.nlm.nih.gov/pubmed/29053721).

Integrating Evolutionary and Regulatory Information with a Multispecies Approach Implicates Genes and Pathways in Obsessive-Compulsive Disorder

Noh, Hyun Ji et al. 2017. *Nature Communications* 8(1). (www.ncbi.nlm.nih.gov/pubmed/29042551).

Radiographic and Magnetic Resonance Imaging Predicts Severity of Cruciate Ligament Fiber Damage and Synovitis in Dogs with Cranial Cruciate Ligament Rupture

Sample, S. J. et al. 2017. *PLoS One* 12(6):e0178086. (<https://www.ncbi.nlm.nih.gov/pubmed/28575001>).

Prevalence and Diagnostic Characteristics of Non-Clinical Mitral Regurgitation Murmurs in North American Whippets

Stepien, R. L. 2017. *J Vet Cardiol.* (www.ncbi.nlm.nih.gov/pubmed/28666945).

Further Characterization of Computed Tomographic and Clinical Features for Staging and Prognosis of Idiopathic Pulmonary Fibrosis in West Highland White Terriers

Thierry, F. et al. 2017. *Vet Radiol Ultrasound.* (<https://www.ncbi.nlm.nih.gov/pubmed/28335088>).

An Epigenetic Aging Clock for Dogs and Wolves

Thompson, Michael J., Bridgett von Holdt, Steve Horvath, and Matteo Pellegrini. 2017. *Aging* 9(3):1055–68. (www.ncbi.nlm.nih.gov/pubmed/28373601).

Cerebrospinal Fluid Levels of Phosphorylated Neurofilament Heavy as a Diagnostic Marker of Canine Degenerative Myelopathy

Toedebusch, C. M. et al. 2017. *Journal of Veterinary Internal Medicine* 31(2):513–20. (<https://www.ncbi.nlm.nih.gov/pubmed/28186658>).

Investigating the Adult Ixodid Tick Populations and Their Associated Anaplasma, Ehrlichia, and Rickettsia Bacteria at a Rocky Mountain Spotted Fever Hotspot in Western Tennessee

Trout Fryxell, R. T. et al. 2017. *Vector Borne Zoonotic Dis.* (<https://www.ncbi.nlm.nih.gov/pubmed/28598270>).

Genetics of Hereditary Ataxia in Scottish Terriers

Urkasemsin, G. et al. 2017. *Journal of Veterinary Internal Medicine* 31(4):1132–39. (www.ncbi.nlm.nih.gov/pubmed/28556454).

Thirteen Novel Canine Dog Leukocyte Antigen-88 Alleles Identified by Sequence-Based Typing

Venkataraman, G. M. et al. 2017. *Hla* 90(3):165–70. (www.ncbi.nlm.nih.gov/pubmed/28677267).

Clonal Complexes and Antimicrobial Susceptibility Profiles of Staphylococcus Pseudintermedius Isolates from Dogs in the United States

Videla, Ricardo et al. 2017. *Microbial Drug Resistance* 0(0):mdr.2016.0250. (www.ncbi.nlm.nih.gov/pubmed/28504897).

Generalized Myoclonic Epilepsy with Photosensitivity in Juvenile Dogs Caused by a Defective DIRAS Family GTPase 1

Wielander, Franziska et al. 2017. *Proceedings of the National Academy of Sciences* 114(10):2669–74. (www.ncbi.nlm.nih.gov/pubmed/28223533).

Biologic Variability of Cardiac Troponin I in Healthy Dogs and Dogs with Different Stages of Myxomatous Mitral Valve Disease Using Standard and High-Sensitivity Immunoassays

Winter, R. L. et al. 2017. *Vet Clin Pathol.* (<https://www.ncbi.nlm.nih.gov/pubmed/28449360>).

Biologic Variability of N-Terminal pro-Brain Natriuretic Peptide in Healthy Dogs and Dogs with Myxomatous Mitral Valve Disease

Winter, R. L., A. B. Saunders, S. G. Gordon, J. S. Buch, and M. W. Miller. 2017. *J Vet Cardiol* 19(2):124–31. (<https://www.ncbi.nlm.nih.gov/pubmed/28111138>).

Comparative Genomics of Canine Hemoglobin Genes Reveals Primacy of Beta Subunit Delta in Adult Carnivores

Zaldívar-López, Sara et al. 2017. *BMC Genomics* 18(1):141. (www.ncbi.nlm.nih.gov/pubmed/28178945).

Intraoperative Optical Coherence Tomography for Soft Tissue Sarcoma Differentiation and Margin Identification

Mesa, Kelly J. et al. 2017. *Lasers in Surgery and Medicine* 49(3):240–48. (www.ncbi.nlm.nih.gov/pubmed/28319274).



RESEARCH SPONSORSHIP AGREEMENT

Please complete the form below. Indicate the name of the sponsoring party as you wish to be recognized. All research grants are supported through a Research Program Area. Please see CHF website for additional information on Research Program Areas. Research Sponsors of \$2,500 or more will receive:

-  Updates and final progress reports for all grants within the Program Area
-  Recognition on our website and publications

Name of Sponsoring Party: _____

Check here if the Sponsor wishes to remain anonymous.

Sponsoring Party Contact Email: _____

Contact Role: _____

Name of Grant and/or Research Program Area: _____

*All research grants are supported through a Research Program Area.

Donor Advised Fund Contribution \$ _____

Cash Contribution \$ _____

TOTAL CONTRIBUTION \$ _____

Printed Name

Title

Signature

Date



Return Completed Form and Donation to:

AKC Canine Health Foundation
P.O. Box 900061
Raleigh, NC 27675-9061
Fax: 919-334-4011
Email: chfgrants@akcchf.org



Research Program Areas and Sponsorship

All research grants are supported through a Research Program Area. This allows CHF to create depth in our capacity to fund research in areas of importance to our donors, expand our grant portfolio in a substantial way, and focus on funding research in areas of importance to your breed and organization. Sponsorship benefits include:

-  Updates and final progress reports for all grants within the Program Area
-  Recognition on our website and publications

By sponsoring a grant within a Research Program Area, your contribution will go towards research in the specific area of your designation and allow for even more studies to be funded in the future. Our Research Program Areas are as follows:

Behavior	Lung and Respiratory Disease
Blood Disease	Musculoskeletal Conditions and Disease
Canine Athlete Initiative	Neurology
Cardiology	Oncology
Dermatology and Allergic Disease	Oncology - Hemangiosarcoma
Endocrinology	Oncology - Lymphoma
Epilepsy	Oncology - Osteosarcoma
Gastrointestinal Disease and Bloat	Ophthalmology
General Canine Health	Kidney and Urological Disease
Hepatic Disease	Reproductive Conditions and Disease
Immunology and Infectious Disease	Tick-Borne Disease
Educational Grants: Clinician-Scientist Fellowship	

**To view all active grants within these Research Program Areas, please visit www.akcchf.org/researchportfolio or contact CHF at 888-682-9696 or chf@akcchf.org.*

Please know that your contribution for research will have a significant impact on canine health. Your support will create a greater understanding of canine diseases that will impact the health of dogs for generations to come.

Thank you for helping us to further our mission to help all dogs live longer, healthier lives.



DOUBLE THE IMPACT — OF YOUR — GIFT



Act Now!

**Support the
Canine Health Foundation**

For information on how to participate
in the American Kennel Club
Match Challenge visit:

www.akcchf.org/match



AMERICAN KENNEL CLUB
**CANINE HEALTH
FOUNDATION**
PREVENT TREAT & CURE®

The AKC Canine Health Foundation (CHF) supports research that will improve the health and lives of all dogs across their entire lifetime by focusing on all aspects of their physical, mental, and social well-being.



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



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

akcchf.org
888.682.9696
PO Box 900061
Raleigh, NC 27675-9061



AKCcaninehealthfoundation

