



AKC Canine Health Foundation Awarded Grants

11/1/2018 - 1/31/2019

Blood Disorders

New

02637-A: Reducing Misdiagnosis of Immune-Mediated Hemolytic Anemia

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

Total Grant Amount: \$5,995; Grant Period: 2/1/2019 - 1/31/2020

Immune-mediated hemolytic anemia (IMHA) is a common life-threatening disease requiring intensive and expensive therapy. Veterinarians often diagnose IMHA using a saline agglutination test. This test aims to distinguish red cell aggregates induced by antibodies from non-immune-mediated red cell interactions. However, this test can produce up to 20% false positives, thus requiring an improved test. One reason for the high false positive rate may be the test's use of a 1:1 ratio of saline to blood, which may not be sufficient to break apart non-immune-mediated red cell interactions. This study will determine if increasing the ratio of saline to blood will reduce false positive results. The results could improve the diagnostic test and prevent misdiagnosis of IMHA and unnecessary immunosuppressive therapy.

Cardiology

New

02550: The role of *Bartonella* spp. exposure and cardiac genetic variation on the clinical expression of arrhythmogenic right ventricular cardiomyopathy in the Boxer dog

Principal Investigator: Edward Breitschwerdt, DVM and Kathryn Meurs, DVM, PhD; North Carolina State University

Total Grant Amount: \$63,105; Grant Period: 2/1/2019 - 1/31/2020

One Health

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. The investigators have identified a causative mutation in the cardiac Striatin gene that is highly associated with the development of Boxer ARVC, and 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 an individual dog which could include a role for chronic infections, as well as genetics, hormonal levels, or other external factors including diet or exercise. The range of disease manifestation of Bartonella infection in dogs is broad, but has been shown to infiltrate the heart muscle, and has also been identified in human



beings with ARVC. The investigators hypothesize that chronic *Bartonella spp.* infection may lead to the development of a more severe form of Boxer ARVC. Understanding the role of this, and other infectious diseases, in the severity of ARVC may greatly improve the ability to manage this common and sometimes fatal heart disease.

Dermatology and Allergic Disease

New

02653-A: Evaluation of the Serum and Cutaneous Levels of Chemokines in Atopic Dogs

Principal Investigator: Domenico Santoro, DVM; University of Florida

Total Grant Amount: \$14,967; Grant Period: 2/1/2019 - 1/31/2020

One Health

Atopic dermatitis (AD) is very common in dogs and children. AD is affected by complex and yet incompletely understood interactions between many factors such as environment, different types of white blood cells, and immunological factors. Chemokines are one of the factors that are used to modulate the immune system, leading to AD. Specific inflammatory chemokines were chosen for this study based on their relevance to AD from previously published studies in human and veterinary medicine. This study will evaluate the levels of these chemokines in blood, exosomes (a small pouch from cells that is used for communication between cells via blood), and skin of dogs with AD. In addition, the investigators will look for a correlation between the levels of these chemokines and severity of AD with a long-term goal to find a potential tool for monitoring and treating AD in dogs and humans.

Epilepsy Initiative

New

02561: Is gut dysbiosis associated with canine idiopathic epilepsy?

Principal Investigator: Karen Muñana, DVM; North Carolina State

Total Grant Amount: \$104,453; Grant Period: 2/1/2019 - 1/31/2022

Idiopathic epilepsy is the most common chronic nervous system disorder of dogs. Its cause is poorly understood, but is believed to involve genetic and environmental factors. Treatment with anti-seizure drugs remains the standard of care. However, approximately one-third of dogs fail to achieve satisfactory seizure control, highlighting the need to investigate factors that may influence disease course. An association between epilepsy and inflammatory gastrointestinal disease is well documented in humans, and several other nervous system disorders have been linked to alterations in gut microbial populations, with considerable attention focused on the bacteria *Helicobacter* and *Lactobacilli*. The aim of this study is to determine whether dogs with idiopathic epilepsy have shifts in the gastrointestinal environment that may influence disease course. The researchers hypothesize that dogs with idiopathic epilepsy have alterations in the gut microbial population—characterized by the presence of *Helicobacter*, a decrease in



Lactobacillus, and resulting inflammation—that are associated with epilepsy development and outcome. The investigators will collect and study paired fecal samples from untreated and phenobarbital treated epileptic dogs and including an unaffected dog from the same household. The occurrence of *Helicobacter* and *Lactobacillus* species will be analyzed using molecular genetic techniques and specific biomarkers of inflammation and evaluated for associations with disease onset and outcome. In exploring the association between the gut microbial population and canine epilepsy, this study has the potential to improve our understanding of epilepsy, and ultimately guide the development of more effective therapies for this disorder.

General Canine Health

New

02614-A: Validation of Fine Needle Aspiration as a Minimally Invasive Sampling Method for Gene Expression Quantification of Pharmacogenetic Targets

Principal Investigator: Jennifer Reinhart, DVM, PhD; University of Illinois

Total Grant Amount: \$5,940; Grant Period: 3/1/2019 - 2/29/2020

Gene expression is the process in which genes are activated and perform their action through the creation of proteins. Measuring gene expression in different organs improves our understanding of disease because it detects what has become dysregulated in the body. Gene expression is also important in pharmacogenetics: the study of how genetics influences the body's response to drugs. Drugs are most commonly metabolized in the liver, so measuring the expression of genes in the liver helps us understand how an individual animal's genetics determine the way they will handle a drug. Usually, measuring gene expression requires a biopsy sample, which is an invasive procedure requiring anesthesia. A different sampling technique, fine needle aspiration (FNA), is safer, less painful, and may be preferred over surgically-obtained samples if FNA can be demonstrated to yield consistent, accurate results. FNA samples have been used to examine liver gene expression before, but it has not been determined if results differ between locations within the organ. Despite its potential advantages as a diagnostic tool, the FNA technique must be shown to yield consistent results before it can be recommended for routine clinical use. Therefore, the purpose of this study is to determine whether gene expression in liver FNA samples is affected by sampling site. The investigators will compare the expression of three pharmacologically important genes between various locations within the canine liver. If validated, FNA would be a valuable, low-risk tool for evaluating gene expression with many applications in pharmacogenetics and the study of disease.

New

02593-A: Evaluation of the Transversus Abdominis Plane Block to Control Pain Associated with Abdominal Surgery in Dogs

Principal Investigator: Alonso Guedes, DVM, MS, PhD; University of Minnesota

Total Grant Amount: \$14,999; Grant Period: 3/1/2019 - 2/29/2020

Abdominal surgery is common in veterinary practice, and opioids are the mainstay of pain



management. Although effective painkillers, opioids are not free of adverse effects, and challenges stemming from the opioid epidemic in humans increased the urgency for developing alternative pain control strategies. In dogs, local nerve blocks are well-described for limb surgery, but comparatively little information exists for abdominal surgery. This study will determine whether surgical abdominal pain in dogs can be effectively and safely managed with a nerve block technique known as transversus abdominis plane (TAP) block; assessors will be blinded to treatment groups. The investigators will also examine whether a new long-acting form of the local anesthetic bupivacaine can provide long-lasting pain control for abdominal surgery. The results will advance canine health by providing evidence-based information of an alternative strategy to manage surgical abdominal pain in dogs.

Hepatic Disease

New

02644-A: Evaluation of gallbladder motility in dogs with hyperlipidemia

Principal Investigator: Stefanie DeMonaco, DVM, MS; Virginia-Maryland Regional College of Veterinary Medicine

Total Grant Amount: \$9,148; Grant Period: 2/1/2019 - 1/31/2021

Gallbladder (GB) diseases are frequently recognized in dogs as a significant cause of illness and potentially death. In particular, gallbladder mucoceles (GBM), the distention of the GB with mucus, can rupture and cause a critical condition that can quickly lead to death if not addressed immediately. Currently, the cause of GBM is unknown making treatment and preventative strategies difficult. Dogs with GBM have poor GB motility and often increased lipid levels, such as cholesterol and triglycerides. Impaired GB motility occurs in people and rodents with increased lipid levels suggesting that this may also occur in dogs, therefore, it is possible that increased lipid levels may lead to abnormal GB motility and eventually GBM formation in dogs. Breeds with inherited disorders resulting in increased lipid levels, such as Shetland Sheepdogs and Miniature Schnauzers, are the same breeds that have the highest risk for GBM formation. However, it has yet to be determined if increased lipid levels are associated with impaired GB motility in dogs. The investigators will utilize ultrasound to compare GB motility between healthy dogs and those with increased lipid levels in an attempt to ascertain an association between increased lipid levels and abnormal GB motility. If this is established, then diets and medications aimed to reduce lipid levels in conjunction with vigilant monitoring for the development of GB disease may prove beneficial to prevent or reduce disease severity and risk of death, particularly in predisposed breeds.

Immunology and Infectious Disease

New

02647-A: Investigation of Cytokine Biomarkers for the Diagnosis of Canine Tuberculosis

Principal Investigator: Conor O'Halloran, BVSc; R(D)SVS and Roslin Institute, University of Edinburgh

Total Grant Amount: \$15,000; Grant Period: 3/1/2019 - 8/31/2019

One
Health

Tuberculosis (TB) is a global disease which affects both humans and animals. As our most commonly kept companion animals, domestic dogs can be the source or recipient of human TB infections. The pathogen *Mycobacterium (M.) bovis* is one of the organisms capable of causing TB in a very broad range of potential host animals in both the USA and the United Kingdom (UK), including many species of deer, cattle and camelids but also pet cats, dogs and humans. Data from the US Centers for Disease Control indicate that ~2% of human TB cases in the USA are *M. bovis* infections. Historically, canine TB cases have only been reported in small numbers of individual animals. Between 2016 and 2017 the investigators studied a prolonged outbreak of *M. bovis* TB in a kennel of dogs in the UK. Over half of the animals were positive for *M. bovis*, and all dogs with bacterial isolates had the same strain. The researchers will test these samples for markers of inflammation to improve the accuracy of diagnostic testing for the emergent infectious disease.

New

02633: Validation and Diagnostic Performance of a Novel Monoclonal Antibody based *Histoplasma* Urine Immunoassay in Dogs with Histoplasmosis

Principal Investigator: Andrew Hanzlicek, DVM, MS; Oklahoma State University

Total Grant Amount: \$17,088; Grant Period: 3/1/2019 - 2/29/2020

One
Health

Histoplasmosis is a severe disease caused by the fungus *Histoplasma capsulatum* that can be fatal to dogs. The fungus is found in soil and dust around the world and most commonly in the Midwestern, Southern, and Southeastern US. Dogs contract the disease when they inhale spores produced by the fungus in the environment. The most common method of diagnosis is by finding the fungal organism in tissue or body fluid samples. Unfortunately, collecting these samples can be invasive and is not always feasible, depending on the location of the infection and the severity of illness. A commercial urine test for diagnosis in dogs, cats, and humans to aid diagnosis, is of limited availability. The current cost of testing, especially when repeated, can be prohibitive for some pet-owners. There is a need for an affordable test that is more widely available for dogs. This study aims to develop and describe the performance of a non-invasive, in-house *Histoplasma* urine test for dogs to address this important disease.

Musculoskeletal Conditions and Disease

New

02610-A: The Role of Motilin Signaling in Canine Osteoarthritis

Principal Investigator: Li Zeng, PhD; Tufts University

Total Grant Amount: \$15,000; Grant Period: 3/1/2019 - 2/29/2020

One
Health

Osteoarthritis is a devastating disease characterized by joint pain and immobility and while it is highly prevalent in dogs, there is no optimal treatment for this disease. The goal of this study is to design strategies to prevent osteoarthritis progression and improve the quality of life for dogs. A central feature for osteoarthritis is the destruction of joint cartilage, a tissue that normally serves as a cushion between bones. Without this cushion, there is increased friction at the joint, causing mechanical stress and accelerating joint degeneration. One treatment strategy is to combat inflammation, because inflammation results in joint cartilage loss and is a key component in the pathogenesis of osteoarthritis. In preliminary studies, the investigators found that the hormone motilin has an anti-inflammatory activity that has not been previously reported. Their hypothesis is that motilin protects the canine joint against inflammation and improves the health of the cartilage in osteoarthritis. Outcomes of this research may benefit both dogs and humans suffering from osteoarthritis.

New

02646-A: Effect of Hyperthermia on Skeletal Muscle Energy Efficiency

Principal Investigator: Michael Davis, DVM, PhD; Oklahoma State University

Total Grant Amount: \$14,831; Grant Period: 3/1/2019 - 2/29/2020

Working dogs are at risk for heat exhaustion and heat stroke due to the large amount of body heat they produce and the difficulties inherent in a dog's ability to dissipate heat. Preliminary data suggest that dogs that lack adequate fitness are at particular risk for hyperthermia due to inefficiency in their ability to burn cellular fuel to power their muscles. The investigators aim to confirm this observation and identify the mechanisms by which fitness improves energy efficiency in a dog's muscles, improving their well-being by allowing them to work harder in hot environments without overheating. Confirming the importance of physical conditioning of working dogs to avoid heat injury, will provide dog handlers, trainers, and veterinarians with an important tool to emphasize fitness training of working dogs.

Neurology

New

02575-MOU: Genetic Basis of Exercise-Induced Collapse in Border Collie Related Breeds

Principal Investigator: James Mickelson, PhD; University of Minnesota

Total Grant Amount: \$56,456; Grant Period: 1/1/2019 - 12/31/2019



An episodic nervous system disorder triggered by strenuous exercise, termed Border Collie collapse (BCC), exists in Border Collies, mixes, and related breeds, including Australian Shepherds, Kelpies, Bearded Collies, Shetland Sheepdogs, and Whippets. BCC is recognized throughout the world and is observed in dogs used for working stock, participating in agility and fly-ball competitions, or repeatedly retrieving a ball. Based on work with breed associations, field trial groups, and at competitions, the investigators estimate 5 - 10% prevalence of BCC in working Border Collies, and a somewhat lower frequency in Australian Shepherds. The research team has characterized the clinical and physiological signs of BCC to enable accurate phenotyping and the inclusion and exclusion of cases and control dogs from both breed. This study's hypothesis is that BCC is a moderately heritable polygenic disorder, and the objectives are to define its underlying genetic architecture, heritability, and potentially genomic loci, through computational analyses of dense whole-genome DNA marker genotyping data. Knowledge of the fraction of the BCC phenotype determined by genetics, as opposed to environment and genotype x environment interaction, and whether major gene mutations are likely to exist, will inform veterinarians and working/stock dog communities of the true nature of this condition. Future research strategies would be the acquisition and genotyping of validation cohorts, and the identification of a panel of markers to predict risk in susceptible Border Collies, Australian Shepherds, related breeds, and their crosses.

This research is co-funded through the collaborative efforts of the Border Collie Society of America and AKC Canine Health Foundation.

Ophthalmology

New

02608-A: Identification of Genetic Risk Factors for Primary Closed Angle Glaucoma and Pectinate Ligament Abnormality in the Basset Hound

Principal Investigator: Cathryn Mellersh, PhD; Animal Health Trust
Total Grant Amount: \$14,750; Grant Period: 3/1/2019 - 2/28/2021

Primary glaucoma is a painful and blinding disease associated with abnormally high intraocular pressure. Treatment in dogs is usually unsuccessful, and most affected dogs ultimately require removal of their eyes. The most common form of canine primary glaucoma is primary closed angle glaucoma (PCAG) which is significantly associated with pectinate ligament abnormality (PLA), also referred to as pectinate ligament dysplasia (PLD), an abnormality affecting the drainage angle of the eye. PCAG and PLA are prevalent in several breeds, and PLA is highly heritable. Not all dogs with PLA develop glaucoma, however, indicating that the inheritance of PCAG is complex. This complex inheritance and the progressive nature of PLA mean that breeding strategies based on ophthalmic examinations alone are unlikely to be sufficient to eliminate the disease. PCAG and PLA appear to be prevalent in the Basset Hound (BH) both in Europe and the USA. Two genetic regions have been identified in the BH which are strongly associated with PCAG



but not with PLA in European and USA BH dogs. This study will sequence the genomes of European and USA BH dogs with PCAG and PLA to identify variants that segregate with PCAG (and not PLA). Follow-up on PCAG candidate variants in large cohorts of European and USA BH will be performed to confirm association with disease in the breed. The ultimate aim is to develop DNA tests for PCAG in the BH that will reduce disease prevalence when used in parallel with breed-specific guidance for breeders while simultaneously allowing for breeding of BH with PLA that are not at risk of PCAG.

New

02590-A: Histologic characterization of Golden Retriever Pigmentary Uveitis

Principal Investigator: Wendy Townsend, DVM, MS; Purdue University
Total Grant Amount: \$11,793; Grant Period: 2/1/2019 - 1/31/2020

Pigmentary uveitis affects an estimated 10% of senior Golden Retrievers and often results in blindness due to cataracts and glaucoma. There are no current methods to prevent or reverse the disease. Clinically, a known risk factor for the development of glaucoma in dogs affected by pigmentary uveitis is the presence of an undefined, amorphous material in the eye. On histologic examination of affected eyes, the amorphous material has been noted within uveal cysts, surrounding uveal cysts, coating the lens, and free floating in the anterior chamber. The material blocks fluid flow within the eye resulting in glaucoma. Limited analysis has shown the material is unusual with features of both collagen and an acid. This amorphous material is considered to play a significant role in the pathology of pigmentary uveitis and associated glaucoma, but little is known about its chemical composition, structure, or tissue of origin. The objectives of this study are: 1) determine if all Golden Retrievers with pigmentary uveitis have this amorphous material within their eyes, or if only a specific subset; 2) define the chemical composition of the amorphous material; and 3) determine the ocular tissue producing the material. This information may play an important role to help develop preventative or therapeutic measures for pigmentary uveitis and define phenotype(s) for genetic studies.

New

02569-MOU: Development of a Polygenic Risk Model for Pigmentary Uveitis in Golden Retrievers

Principal Investigator: Wendy Townsend, DVM, MS; Purdue University
Total Grant Amount: \$89,855; Grant Period: 3/1/2019 - 2/28/2021

Pigmentary uveitis (PU) affects 10% of senior Golden Retrievers and often results in blindness due to cataracts and glaucoma. There are no current methods to prevent or reverse the disease. The best options to maintain vision are early detection through annual ophthalmic examinations and early initiation of topical anti-inflammatory therapy. The disease does not develop until eight years of age or older, thus, affected dogs may have already been bred before their PU status is known. Using previous AKC CHF funding, the investigators have established a bank of Golden Retriever DNA and, in an initial genetic analysis, determined that PU involves not just one but multiple genes. The research problem remains to identify involved genes and risk alleles that are associated with PU. The objective of this study is to identify these genes and alleles using



genome-wide association studies and whole genome sequencing of severely affected dogs in conjunction with analysis of RNA expression within the iris and ciliary body of affected dogs. Identification of the involved genes and risk alleles will allow for creation of a genetic risk score to quantify an individual's genetic risk for developing PU, allowing identification of high-risk individuals and intervention prior to the onset of clinical signs. In addition, breeders will have the necessary knowledge to decrease the prevalence of PU.

This research is co-funded through the collaborative efforts of the Golden Retriever Foundation and AKC Canine Health Foundation.

New

Tick-Borne Disease Initiative

One Health

02553: Targeted next generation sequencing panel for comprehensive testing of vector-borne pathogens

Principal Investigator: Rebecca Wilkes, DVM, PhD; Purdue University

Total Grant Amount: \$103,245; Grant Period: 2/1/2019 - 1/31/2021

Diagnosing vector-borne disease (VBD) in dogs can be difficult for a number of reasons. First, there are many different disease-causing agents that can be transmitted from ticks/fleas, and the clinical signs caused by these agents in dogs can overlap. Additionally, because ticks/fleas can harbor more than one agent at a time, multiple pathogens may be passed to a dog with a single vector bite, resulting in co-infections. VBD infections can initially present with non-specific signs, such as fever, lethargy, vomiting, diarrhea, and/or respiratory signs. Severe cases can be associated with neurologic signs. These signs can be a diagnostic conundrum. While initial blood work can be helpful and suggest VBD, it does not determine the infecting agent. This study will develop a comprehensive next generation sequencing panel to detect and identify major VBD agents known to cause disease in dogs and to aid in diagnosis of active infections. Additionally, through parallel sequencing with this method, this panel will incorporate testing for additional infectious diseases that may cause GI, respiratory, or neurologic signs in dogs. The comprehensive nature of this sequencing panel should be a useful tool for surveillance of infectious diseases in the canine population for rapid identification of VBD in dogs and protection of pet owners from such zoonotic diseases.