AKC CANINE HEALTH FOUNDATION

Discoveries

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

Summer 2019

The Microbiome-Gut-Brain Axis in Canine Epilepsy

By Sharon Albright, DVM, CCRT
Manager of Communications & Veterinary Outreach, AKC Canine Health Foundation

The adage "you are what you eat" may be more profound than we ever realized. A growing body of evidence shows a complex system of two-way communication between the gastrointestinal (GI) tract and neurologic system in humans and dogs. The link between GI health and diseases such as multiple sclerosis, autism, and epilepsy has been studied in humans. In fact, patients with celiac disease or inflammatory bowel disease have an increased risk of developing epilepsy. Since the community of microorganisms that live in the digestive tract – known as the gut microbiome – plays an important role in GI health, what impact does it have on neurologic disease? AKC Canine Health Foundation (CHF) funded researchers are exploring the role of this microbiome-gut-brain axis in canine epilepsy.

At North Carolina State University, Dr. Karen Muñana and her research team are investigating how alterations in the gut microbiome affect the development and severity of canine idiopathic epilepsy with funding from CHF grants 02249 and 02561. They are specifically studying *Lactobacillus* and *Helicobacter* bacteria. *Lactobacillus* is considered a "good bug." Some strains can produce the inhibitory neurotransmitter GABA, which decreases neuronal excitability throughout the nervous system. *Helicobacter* is a "bad bug" and a primary pathogenic factor for upper GI disease in humans. Alterations in the populations of these two microbes within the canine GI tract and the resulting inflammation may impact the course of canine epilepsy. A better understanding of this relationship may allow us to treat canine epilepsy by influencing the gut microbiome.

At the Royal Veterinary College, University of London, investigators are exploring whether the beneficial effects of the ketogenic diet seen in humans apply to canine epilepsy. This high fat, low carbohydrate diet alters the gut microbiome and has successfully decreased seizure

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CALENDAR OF EVENTS

WHERE TO FIND US

July 17-21
Houston World Series of Dog Shows, Houston, TX

August 9-11
AKC CHF 2019 National Parent Club Canine Health Conference, St. Louis, MO

August 27-29
AKC Detection Dog Conference, Durham, NC

September 1
Tarheel Labor Day Cluster, Raleigh, NC

September 28
Responsible Dog Ownership Day, Raleigh, NC

October 19-20
2019 Master National, Cheraw, SC

UPCOMING WEBINARS

Register at **akcchf.org/vetvine**.

July 18
What the Flu! Protecting Dogs and Communities from Canine Influenza Virus
Presented by: Jason Stull, VMD, MPVM, PhD, DACVPM

October 17
Canine Degenerative Myelopathy: From Gene Mutation Discovery to Clinical Trials
Presented by: Joan R. Coates, DVM, MS, DACVIM (Neurology)

Sign up to receive CHF's latest canine health research information at akcchf.org/registration.

The Microbiome-Gut-Brain Axis in Canine Epilepsy

continued

activity in children. Supplementation with medium-chain triglycerides (MCT), one component of the ketogenic diet, did result in decreased seizure frequency in a small population of dogs. With funding from CHF Grant 02252, investigators are assessing the effect of MCT supplementation on seizure frequency and severity in dogs. They are also investigating whether MCT supplementation influences the side effects of common anti-epileptic drugs, behavioral problems, and stress levels in affected dogs. Results will improve our understanding and use of MCT supplementation as a treatment for canine epilepsy.

CHF's Epilepsy Research Initiative focuses research funding on important topics such as the microbiome-gut-brain axis to develop more effective treatments for dogs with epilepsy. CHF and its donors remain committed to improving outcomes for dogs affected by idiopathic epilepsy, the most common medical neurologic disease in dogs. Learn more at akcchf.org/epilepsy.

Researching New Treatment Strategies for Canine Atopy

By Sharon Albright, DVM, CCRT – Manager of Communications & Veterinary Outreach, AKC Canine Health Foundation

Canine atopic dermatitis, or atopy, is a common and frustrating condition. It results from over-reaction of the immune system in response to a variety of commonplace and otherwise harmless substances in the environment - such as pollens, house dust mites, mold spores, and more. Clinical signs can occur seasonally or year-round and include scratching, chewing, licking, and rubbing affected areas of skin. The trauma from all this itching leads to hair loss, thickened or red skin, and recurrent skin and ear infections. Unfortunately, the disease cannot be cured, but must be managed with a combination of avoidance (when possible), medications, and allergen-specific immunotherapy. Canine atopy is a challenge because individual dogs respond differently to the various treatments and a dog's response to treatment may vary over time. To improve the clinical outcome for affected dogs, AKC Canine Health Foundation (CHF) and its donors are investing in research to identify new treatment targets for canine atopy.

A recent publication from CHF-funded research (Santoro D, Archer L, Kelley K. (2019) A defective release of host defense peptides is present in canine atopic skin, Comparative Immunology, Microbiology and Infectious Diseases) showed that secretion of host defense peptides is defective in atopic skin. These molecules are part of the innate immune response and have anti-microbial activity. Atopic dogs may be prone to recurrent skin infections due to altered secretion and increased adhesion of these peptides. Further study of the biochemical and structural alterations in the host defense peptides of atopic dogs may provide new treatment targets and improving the skin's anti-microbial defenses may reduce the need for antibiotics.

Lokivetmab (Cytopoint®) is a relatively new treatment option for canine atopy. It is a monoclonal antibody that targets IL-31, an inflammatory molecule involved in causing an unpleasant itchy sensation. With funding from CHF Grant 02472-A, investigators are examining how lokivetmab modulates the expression of various genes in affected and unaffected skin of atopic dogs. Results may identify additional inflammatory molecules or pathways that can be targeted for therapy.

Investigators that received funding through CHF Grant 02651 are analyzing the epidermal lipid (fat) composition of the skin of healthy and atopic dogs. We know that canine and human atopic dermatitis is associated with changes in this epidermal lipid composition, but do not know if the changes occur before or after inflammation sets in. A better understanding of these epidermal lipid changes may lead to better diagnostic tests and provide a method to predict or monitor response to treatment in atopic dogs.

Finally, with funding from CHF Grant 02653-A, investigators are evaluating the correlation between disease severity and the levels of various signaling proteins in the blood, exosomes (pouches used for cell to cell communication), and skin of atopic dogs. The specific proteins being studied were chosen based on previous canine and human research and may provide a target for treatment or monitoring a dog's response to treatment.

CHF and its donors are dedicated to improving the diagnosis and treatment of canine atopic dermatitis. Since the molecular characteristics of canine and human atopy are similar, the knowledge gained may have One Health implications benefiting dogs and people. These innovative approaches to understanding atopy have the potential to greatly improve quality of life for affected dogs and their caregivers. Learn more at akcchf.org/derm.

A Calming Probiotic Impacts Dogs Displaying Anxious Behavior

By Barbara Fawver — Purina Manager of Pet Influential Communications

Efforts by Purina research scientists to understand how probiotics can positively affect dogs displaying anxious behavior has led to the introduction of *Purina Pro Plan* Veterinary Supplements Calming Care in January 2019. This probiotic supplement helps dogs cope with external stressors. The beneficial probiotic strain, *Bifidobacterium longum* (BL999), is shown to help dogs maintain calm behavior. One potential mechanism is via the microbiota-gut-brain axis, a bidirectional communication system between the gastrointestinal tract and the brain.

To better understand the impact of anxious behaviors, Purina recently conducted a survey of 826 U.S. dog owners whose dogs visited the veterinarian in the last 12 months.[1] The findings revealed that these behaviors can be quite common, with 62 percent of dog owners surveyed reporting that they have regularly seen anxious behaviors in their dog. Excessive barking, jumping, spinning, and pacing can be signs of anxious behavior in dogs. Other signs are panting when not hot, repeated yawning, lip licking or smacking, urinating or defecating, and even aggression.

> **"Short-term stress is a normal and healthy response to startling or novel stimuli, but chronic stress can be harmful because it can affect a dog's physical, mental and social health.**
>
> — Purina Research Scientist Ragen T.S. McGowan, PhD, animal behaviorist

To assess the impact of BL999 on dogs, Purina evaluated 24 Labrador Retrievers displaying anxious behaviors in a 15-week crossover study. By the end of the study, 90 percent of the dogs showed improvements in displaying anxious behaviors such as excessive barking, jumping, pacing and spinning. They also showed improvement in physiological factors such as positive cardiac activity during stressful events.

"From both a behavioral and physiological standpoint, BL999 had a calming effect on dogs," Dr. McGowan says. "We found that BL999 could serve as a useful tool in the development of management plans for dogs displaying anxious behaviors." Dr. McGowan will be presenting the findings of this research at the AKC Canine Health Foundation National Parent Club Canine Health Conference in August.

2019 AKC CANINE HEALTH FOUNDATION

Learn more about the AKC Canine Health Foundation National Parent Club Canine Health Conference at akcchf.org/npcchc.

1. Revelation Research Online Survey (Aug. 15 to 19, 2018). A total of 826 nationally representative dog owners qualified and completed the survey. Qualified participants were men and women age 18 and older, owned one or more dogs (age 13 months or older), were household members most responsible for taking dog(s) to a veterinarian, and had taken the dog(s) to a veterinarian in the past 12 months.

Theriogenology Residency Program

The AKC/AKC CHF/TF Theriogenology Residency Program, started in 2014, is a collaboration between the American Kennel Club (AKC), the AKC Canine Health Foundation (AKC CHF), and the Theriogenology Foundation (TF) to increase the number of trained practitioners in companion animal theriogenology and clinical genetics. 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. Learn more about this grant program at akcchf.org/therio.

Jamie M. Douglas, DVM, MS (CHF Grant 02538-E)
Residency Coordinator: Robyn Wilborn, DVM, MS, DACT
Auburn University
Grant Period: 7/1/2019 — 6/30/2022

Dr. Jamie M. Douglas is the newest recipient of a residency grant through this program. She received her DVM from Michigan State University College of Veterinary Medicine in 2014 and her master's degree in animal science (focus: reproduction) from Southern Illinois University Carbondale's College of Agricultural Sciences in 2015. She is the proud owner of two Boston Terriers and one mixed breed dog.

MISSION: *The mission of the American Kennel Club Canine Health Foundation, Inc. is to advance the health of all dogs and their owners by funding scientific research and supporting the dissemination of health information to prevent, treat and cure canine disease.*

Researcher Spotlight

Karen Muñana, DVM, MS, DACVIM (Neurology)

Dr. Karen Muñana is a professor of neurology and head of the Companion Animal Epilepsy Laboratory at North Carolina State University College of Veterinary Medicine. She is a board-certified veterinary neurologist who was drawn into canine epilepsy research by the dedicated owners of epileptic dogs that were driven to participate in clinical research and advance the understanding of canine epilepsy, even if the benefit would not be realized for many years. Her research focus is understanding the causes of refractory (poorly controlled) epilepsy and the development of more effective treatments for dogs with seizures, as well as studies into the potential causes, diagnosis, and treatment of inflammatory brain disease in dogs and cats.

Dr. Muñana is grateful for the funding provided through CHF's Epilepsy Research Initiative because it focuses on research to benefit epileptic dogs and allows her to educate students and staff on the importance of this research. Thanks to recent genetic advances, human drug discoveries that can be applied to veterinary patients, and increased opportunities for collaboration through the American College of Veterinary Internal Medicine and International Veterinary Epilepsy Task Force, Dr. Muñana is hopeful that our understanding and management of canine epilepsy will continue to improve.

Recent CHF-Awarded Grant Highlights

Grant 02661: Investigation into Diet-Associated Dilated Cardiomyopathy in Dogs

Principal Investigators: Darcy B. Adin, DVM, MS; University of Florida and Lisa Freeman, DVM, PhD; Tufts University

A multi-institutional team of veterinary cardiologists and nutritionists will prospectively screen a large population of apparently healthy dogs for dilated cardiomyopathy and compare important cardiac disease measures, including ultrasound of the heart, blood biomarker and taurine concentrations, and the frequency of DCM in dogs eating boutique, exotic ingredient, or grain-free diets versus other diets. Results will inform the extent and cause of the recent increase in diet-related dilated cardiomyopathy in dogs.

Grant 02632: Canine Chagas Disease: Characterizing Cardiac Disease and Developing Screening Recommendations for Asymptomatic Dogs Seropositive for *Trypanosoma cruzi*

Principal Investigator: Ashley B. Saunders, DVM; Texas A&M AgriLife Research

Investigators are evaluating asymptomatic dogs with a positive Chagas test to characterize the presence of heart disease in dogs infected with this important parasite. Learn more from CHF's fact sheet available at **akcchf.org/tophealthconcerns.**

Grant 02597: Molecular Epidemiology of Methicillin-resistant *Staphylococcus pseudintermedius* in the United States

Principal Investigator: Stephen A. Kania, PhD; University of Tennessee

Building on previous research, investigators are identifying the clinically predominant strains of Methicillin-resistant *Staphylococcus pseudintermedius* in dogs and sequencing their genomes to develop next generation treatments for these important, emerging bacterial infections.

See our full research grants portfolio at akcchf.org/research**.**

How You Can Help

Double Your Donation!

In 2019, The American Kennel Club will match donations from new and lapsed* donors to the AKC Canine Health Foundation up to $400,000 and donations to CHF's Canine Cancer Research Initiative up to $250,000 with an equal donation to CHF for canine health research. Double your impact and support canine health research today at akcchf.org/match.

** last donation prior to 1/1/18*

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