



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

DISCOVERIES

issue 51 • winter 2015



MISSION:

The Foundation is dedicated to advancing the health of all dogs and their owners by funding sound scientific research and supporting the dissemination of health information to prevent, treat and cure canine disease.

ADVANCING THE MISSION

AKC Canine Health Foundation Marks 20th Anniversary!

February 21 marks the AKC Canine Health Foundation's 20th anniversary. We are kicking off a year-long celebration to mark this milestone, reflecting on our accomplishments, recognizing those who support us and charting our course for the future.

Since 1995, CHF has*:

- Funded \$33,747,865 in canine health research.
- Provided \$9,366,068 in educational services.
- Supported 797 grants.
- Partnered with 121 institutions.
- Awarded 16 Clinician-Scientist Fellowships for young, up-and-coming researchers.
- Impacted countless numbers of dogs and the people who love them.

Without your support, these milestones would not be possible.

The AKC Canine Health Foundation (CHF) is the leading organization exclusively funding canine health research. We're dedicated to helping all dogs live longer, healthier lives through research and education to prevent, treat and cure canine disease. Your support is helping redefine the practice of veterinary medicine, providing more accurate diagnoses and better treatments for the diseases that impact our dogs.

Learn more about how your continued support during our 20th anniversary celebration can make great things happen for the dogs you love today and the dogs you will love in the future! www.akcchf.org/anniversary 🐾

(*As of September 30, 2014)

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Save the Date!

**National Parent Club
Canine Health Conference**

**August 7-9, 2015
St. Louis, Missouri**

AKC Canine Health Foundation Recognizes Six Organizations as Distinguished Research Partners

The AKC Canine Health Foundation (CHF) honored six organizations as Distinguished Research Partners in canine health at its annual Canines & Cocktails event in Orlando, Florida, in December. The following six organizations, collectively, have donated more than \$3.3 million to CHF to help prevent, treat and cure canine disease over the course of the past 20 years.

- Orthopedic Foundation for Animals (OFA): \$330,875
- Irish Setter Club of America Foundation: \$131,100
- Newfoundland Club of America Charitable Trust: \$225,493
- Collie Health Foundation: \$337,059
- Golden Retriever Foundation: \$1,163,612
- American Boxer Charitable Foundation: \$1,180,130

"These clubs and organizations are making a lasting impact on canine health," said Dr. Shila Nordone, CHF's chief scientific officer. "Their donations to CHF are supporting research that addresses some of the most prominent health concerns for our dogs. We are tackling cancer, subvalvular aortic stenosis, hypothyroidism, degenerative myelopathy, epilepsy, bloat and cardiomyopathy. Together, we are working to provide better treatments and more accurate diagnoses for all dogs."

The Distinguished Research Partner awards help kick off the year-long 20th anniversary celebration of CHF. Susan Lilly, CHF's CEO, said, "We are deeply indebted to these organizations for their commitment to canine health, and we greatly value their partnership over the



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past 20 years. We look forward to continuing these partnerships and impacting the health of all dogs for years to come." 🐾

AKC Canine Health Foundation Presents Thomas A. Grabe with President's Award



The AKC Canine Health Foundation (CHF) announced Mr. Thomas A. Grabe, publisher of *The Canine Chronicle*, as the recipient of the 2014 President's Award. This award, given annually to a person or organization that has made an exceptional contribution to advancing canine health, is selected by the Foundation's chairman, currently Dr. A. Duane Butherus. Mr. Grabe was presented with the award during CHF's Canines & Cocktails event in December at the Rosen Centre Hotel in Orlando, Florida.

Mr. Grabe and *The Canine Chronicle* have underwritten the printing and distribution costs of CHF's annual calendar, "Champions for Canine Health," for the past seven years. *The Canine Chronicle* has also been the lead sponsor of the Canines & Cocktails event for the past four years. All told, through the support of Mr. Grabe and *The Canine Chronicle*, more than \$1 million has been raised to support canine health research.

"Canines & Cocktails is a great event where we celebrate all supporters of CHF and the difference their contributions make in advancing canine health research," said Dr. Butherus. "Tom and *The Canine Chronicle* have been long-time supporters of the Foundation. Their monetary and in-kind donations, as well as their ability to publicize CHF's work, are exceptional. We are grateful for their extraordinary commitment to help all dogs live longer, healthier lives." 🐾

Kudos – Winter 2015

(Donations received as of 11-24-14)

We salute **The Labrador Retriever Club, Inc.**, for their \$25,000 match-eligible contribution to support our reproduction research program area.

Many thanks to all our **2014 Canines & Cocktails Sponsors** who have helped to further our mission to fund canine health research!

A grand thank you to the **Laura J. Niles Foundation** for a remarkable match-eligible contribution of \$25,000 toward our behavior research program area helping to support our funded researcher, Dr. Brian Hare.

Hats off to **Ms. Cora N. Miller** for your commitment to helping dogs live longer, healthier lives!

We recognize the **Orthopedic Foundation for Animals** for their contribution of \$25,000 in support of five research studies within three different research program areas.

The American German Shepherd Dog Charitable Foundation expressed their generous support with a \$12,000 gift toward research in our reproduction, canine athlete and epilepsy program areas.

Our sincere gratitude to **Ms. Ellen Charles** for your generous contribution to CHF to help advance the health of all dogs!

More tails are wagging thanks to **Versatility In Poodles, Inc.**, for their sponsorship of our new hypothyroidism grant.

Kudos to **Mrs. Patte and Col. Nathan T. Titus** for your generous gift in support of our Epilepsy Initiative!

We appreciate the support from **Delaware County Kennel Club** for your contribution of \$3,500 to further our research to benefit our canine companions.

Sincere thanks to the **American Bloodhound Club** for their generous match-eligible donation of \$25,000 to support bloat research!

We are grateful for the support of **Randy and Pamela Foster** and their generous and long-standing commitment to epilepsy and cancer research.

Upcoming Events

Visit our Booth

Westminster Kennel Club Dog Show
February 10–11, Pier 94, New York, NY



**Our
Research.
Their
Love.
Your
Support.**

...help them stay **happy,
healthy & balanced.**
We're in this together.

For **10 tips** to keep your dog happy and healthy, visit www.akcchf.org/10tips

The AKC Canine Health Foundation is the leading organization exclusively funding canine health research. We're dedicated to helping all dogs live longer, healthier lives through research and education to prevent, treat and cure canine disease. Learn how your support can redefine the practice of veterinary medicine at www.akcchf.org.



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Brucellosis

In this interview, Dr. Matthew Krecic, a diagnostics specialist for Zoetis, discusses an important topic for all breeders — brucellosis. Dr. Krecic completed his DVM at Ohio State University, a master's degree in veterinary science from Mississippi State University and an MBA from the University of Florida, Warrington College of Business Administration. He is board-certified in small animal internal medicine through the American College of Veterinary Internal Medicine. Dr. Krecic served as a senior telemedicine veterinarian at IDEXX Laboratories before joining Zoetis in 2009, and he continues to practice small animal internal medicine in his spare time.

AKC CANINE HEALTH FOUNDATION (CHF): Let's start our conversation with some background on brucellosis: Can you tell us what causes the disease?

KRECIC: Bacteria cause brucellosis, specifically *Brucella canis* in dogs. Other species of *Brucella* bacteria exist and some of these other species (e.g., *Brucella abortus* and *Brucella suis*) have infected dogs, yet infection with *Brucella canis* is most common to dogs; dogs are the reservoir host for *Brucella canis* so it remains well-established within the dog population.

CHF: Do all the different species of *Brucella* infect dogs or is there some host specificity?

KRECIC: Yes, different species can infect dogs but host specificity predominates.

CHF: Is *Brucella canis* a danger to humans?

KRECIC: Yes, it is "zoonotic," meaning it can infect humans. Handling infected canine blood, semen or reproductive tissues can be a source of infection to humans. Humans are susceptible to infection with other *Brucella* species as a result of handling infected tissues from livestock.

CHF: How are the *Brucella* bacteria transmitted from dog to dog?

KRECIC: Transmission mainly occurs through natural breeding or artificial insemination (i.e., venereal) because the bacteria reside in the prostate gland and the epididymitis. Often, asymptomatic (or outwardly appearing well) infected males pass the infection through their semen to susceptible females. However, infection may also occur through a dog's contact with infected blood or reproductive tissues.

CHF: What are the clinical symptoms of disease?

KRECIC: Surprisingly, many dogs do not have any clinical signs, given the significance of the disease to reproductive success. For this reason, all dogs involved in a breeding program, again regardless of the absence of clinical signs, should be tested for the presence of brucellosis. Clinical signs, if they do develop, are vague and non-specific; there may be fever and anorexia. I am most familiar with diagnosing this infection when the bacterial infection resides within the bloodstream (i.e., sepsis), leading to infection of the intervertebral discs called discospondylitis.

CHF: Are there specific signs of disease in dogs or bitches?

KRECIC: Yes. For stud dogs, some will have epididymitis, scrotal enlargement (which can be painful) and scrotal dermatitis. For bitches, some will abort within late gestation without any other clinical signs.

CHF: Does fetal abortion always occur or can an infected bitch deliver a litter of puppies?

KRECIC: No, not always. Some bitches deliver weak puppies. Reportedly, some bitches that have had unsuccessful pregnancies may still deliver normally in the future. However, these bitches may still, in fact, be infected.

CHF: Does brucellosis affect a bitch's ability to go into heat, breed or conceive?

KRECIC: Strangely enough, brucellosis does not affect the estrous cycle, so going into heat and breeding are unaffected. Conception failure occasionally occurs.

CHF: Can *Brucella* be spread through shipped semen?

KRECIC: Absolutely. Fresh-chilled or even frozen semen can maintain viable *Brucella canis* and therefore cause infection in a female upon artificial insemination.





CHF: This brings us to testing: How can breeders determine if their dog has contracted brucellosis?

KRECIC: Several tests are available through veterinarians and commercial reference laboratories. These include rapid slide agglutination test (RSAT), agar gel immunodiffusion (AGID) and polymerase chain reaction (PCR). Culture of the bacteria is the gold standard test.

CHF: Can you explain what a rapid slide agglutination test, or RSAT, is and whether it is testing for the presence of the bacteria or the response of the dog's body to the presence of bacteria?

KRECIC: This actually confuses many people so I am glad you asked. This test identifies the presence of antibodies made to the bacteria, not the bacteria themselves. One drop of a dog's serum (blood collected, allowed to clot and the clear fluid remaining is the serum) containing antibodies specific for *Brucella canis* combined with Brucella antigen, a piece of the bacteria, supplied with the test, agglutinates or adheres to the antigen, causing clumping that your veterinarian sees.

CHF: How sensitive is the RSAT and how long does it take to get test results back?

KRECIC: It is quite sensitive. The advantage of this test is veterinarians can have in-hospital results within two minutes.

CHF: If a dog has antibodies specific for Brucella, does that mean they have the infection?

KRECIC: Yes, if antibodies specific for Brucella are present, the dog has the infection, even without clinical signs.

CHF: Is the infection treatable with antibiotics?

KRECIC: Veterinarians prescribe antibiotics but their success at resolving the infection is doubtful because the bacteria like to hide within the dog's cells, and antibiotics are only moderately able to penetrate cells to clear all of the bacteria. Therefore, relapses of infection are common after stopping antibiotics.

Rather, the body's own defenses through cell-mediated immunity are often better to clear bacteria that are within cells.

Infected stud dogs should be removed from the breeding program and neutered to reduce the risk of infection to humans (i.e., their owners, trainers, handlers, etc).

Infected bitches could seemingly "recover" and deliver normal litters in the future; however, they may still, in fact, harbor the bacteria despite this. Therefore, transmission to her offspring in utero is probable.

CHF: If a breeder suspects brucellosis in their kennel, who should they call?

KRECIC: Please contact your veterinarian, who will properly guide your course of action.

CHF: Are there kennel management practices that can prevent brucellosis?

KRECIC: Prevention of any infection is so much easier than managing the consequences of infection. Brucellosis is a perfect example; simply prescribing and administering an antibiotic often does not resolve the infection, and no vaccine is available. Preemptive testing is therefore best.

Have your veterinarian test all dogs within your breeding program for brucellosis prior to every breeding and/or every six months, which is an ideal time for your veterinarian to also examine your dogs completely to ensure health, hopefully successful breeding and healthy litters. The RSAT test is a fast, easy and economical way to screen these dogs and hopefully prevent brucellosis from affecting your kennels.

CHF: Dr. Krecic, thank you so much for explaining brucellosis to our listeners and updating us on testing and prevention. The mission of CHF is to fund research that will improve the health of dogs. In your opinion, what is our greatest gap in knowledge with respect to brucellosis, and what sort of research do you think is necessary to close this gap?

KRECIC: The greatest knowledge gap is a way to stimulate the body's own defenses through cell-mediated immunity to effectively clear *Brucella canis* within cells.

This article was adapted from a podcast in our Zoetis-sponsored series on reproductive health, and is an abbreviated version of the interview. To read the full transcript or listen to this and other podcasts in this series, please visit www.akcchf.org/podcasts. 🐾

Who Will Fill in the Missing Pieces of our Greatest Scientific Puzzles?

Have you ever completed a puzzle only to find one piece is missing? Scientific discoveries are like pieces of a jigsaw puzzle. They appear unshapely when viewed in isolation. Possible connections to other pieces (discoveries) jut out in many directions. At first, no clear connections can be seen. Slowly, though, when joined together, the pieces bring order, creating links, sharing connections, bridging knowledge and deepening our view of a particular disease.

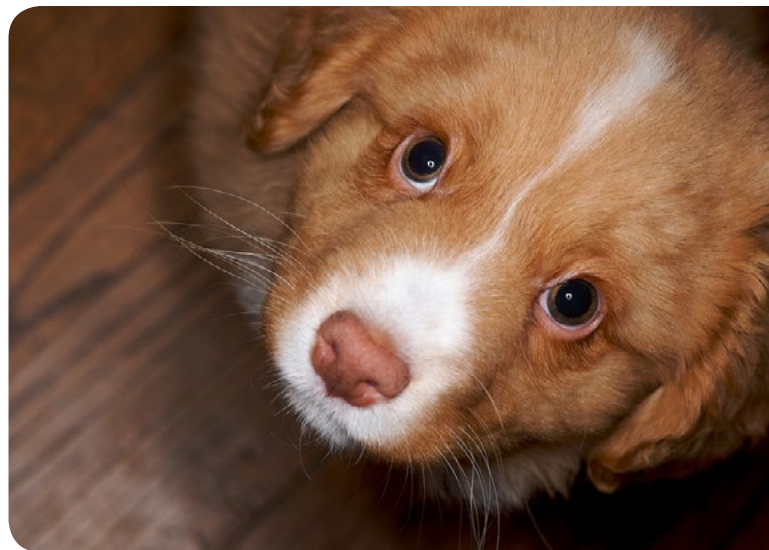
At its most basic level, science is about finding the missing pieces, and the people who fill the gaps are our funded researchers. In this difficult time of fiscal constraint for research funding, the AKC Canine Health Foundation's Clinician-Scientist Fellowship Program is committed to nurturing our up-and-coming leaders in the field of canine health who are working to find the missing pieces of the puzzle. These leaders not only build on the scientific knowledge that has been gained by others in the field, but they also work closely with CHF donors and breed clubs to help all dogs live longer, healthier lives.

The Nova Scotia Duck Tolling Retriever Club (USA) is committed to moving science forward. The club recently initiated the support of a CHF Clinician-Scientist Fellow to work with Dr. Danika Bannish of the University of California, Davis. Under the guidance of Dr. Bannish, Emily Brown – a DVM PhD student in the Veterinary Scientist Training Program (VSTP) at the University of California, Davis School of Veterinary Medicine – will conduct research on the genetics behind adult onset of Addison's disease.

"Addison's disease occurs at a higher rate in our breed than in the general dog population, and so we are genuinely interested in any research that might help determine a genetic predisposition or cause to Addison's," said Sue Dorschied, club president. "Having this information would help Toller breeders make more informed decisions, and has the potential to significantly reduce Addison's in Tollers."

For CHF Fellows, commitment from our supporters can make an enormous difference in their research.

The impact of the CHF Clinician-Scientist Fellowship Program goes far beyond training and science; it creates lasting respect and collaboration between researchers and clubs. Dr. Eva Furrow, DVM, PhD (class of 2014 Fellow), found the breed clubs she worked with fully invested partners in uncovering the complex



genetic conditions found in dogs. "They have a great amount of knowledge on aspects of disease that cannot always be gained through reading scientific literature, such as whether they are observing a condition sporadically in a dog, only in certain lineages or when particular diets are fed. This can be incredibly helpful in selecting the best approach to study genetic risk factors for a disease," said Dr. Furrow.

Dr. Furrow goes on to say, "The Fellowship contributed to my realization that it is invaluable to have ongoing communications with breed clubs. Early in the process of formulating research projects, they guided me in how to prioritize the diseases selected for research to best benefit the breed. Later in the research process, when results were available, they helped find the best way to communicate the results to the public so they are not misinterpreted and are appropriately applied to the management of diseases."

Receiving a CHF Clinician Scientist Fellowship makes a significant impact on the up-and-coming researchers in the field of canine health.

Dr. Lance Visser DVM, MS, DACVIM (class of 2013 Fellow), was recognized this past summer as a 2014 ACVIM Resident Research Award Winner by the American College of Veterinary Internal Medicine (ACVIM). The ACVIM Research Award is presented annually and recognizes 10 active researchers who are on the cutting-edge of veterinary medicine.

Dr. Visser presented on "Echocardiographic Assessment of Right Ventricular Systolic Function Following a Single Dose of Pimobendan Versus Atenolol in Conscious Healthy Dogs: A Prospective, Blinded, Randomized, Crossover Study." This is the same research he focused on through his CHF Clinician-Scientist Fellowship.

"Receiving the CHF Clinician-Scientist Fellowship played a significant role in inspiring me to pursue a career as a clinician-scientist in academia. I've recently started my professional career as an assistant professor of clinical cardiology at the University of California, Davis. I hope to continue to perform clinical-based research very similar to the award-winning research we were able to perform thanks to the generous support of the AKC Canine Health Foundation Clinician-Scientist Fellowship," said Dr. Visser.

Sue Dorschied echoes the benefits of working with up-and-coming researchers in the field of canine health. "Our club recognizes that funding for canine health research is increasingly difficult to obtain. We also realize that only a small percentage of veterinary students show interest and have enthusiasm for pursuing a career in canine health research. For these reasons, we believe it is important to support promising, up-and-coming students and key thought leaders in the area of canine health."

Breed clubs, donors like you, CHF-funded researchers and our dogs are all pieces of the canine health puzzle. The interconnectedness of each of these "pieces" enables the puzzle to take shape. Collectively, we help bring ideas together, and in the process, clear a path forward – toward better treatments and possible cures for the dogs we love. 🐾

AKC Canine Health Foundation Announces 2015 Clinician-Scientist Fellows

The AKC Canine Health Foundation is pleased to announce the 2015 Class of Clinician-Scientist Fellows. Six promising post-docs and students were selected by their colleges of veterinary medicine and will receive support from CHF for their training and research efforts. Established in 2013, the AKC Canine Health Foundation Clinician-Scientist Fellowship Program seeks to encourage and support the next generation of canine health researchers in order to sustain future advancements in canine and human health.

"We are excited to see the impact of this program grow so quickly, and to see our donors start to share in the enthusiasm for supporting our next generation of veterinary clinician-scientists," said Dr. Shila Nordone, CHF chief scientific officer. "As emerging key opinion leaders in veterinary medicine, their relationships with our donors and their understanding of the value of collaboration is critical to helping us solve our greatest health concerns faster."

The 2015 AKC Canine Health Foundation Clinician-Scientist Fellows:

Dr. Steven Friedenberg, DVM, MS, MBA North Carolina State University

Dr. Steven Friedenberg is a PhD student in the laboratory of Dr. Kate Meurs at North Carolina State University College of Veterinary Medicine. The focus of his research is understanding the genetic causes of autoimmune diseases in dogs. Autoimmune diseases occur when the body attacks a part of itself – like joints, blood cells or the pancreas – causing common diseases like rheumatoid arthritis or type I diabetes. Most of the time, we don't know why this happens, but the causes are likely a mix of both genes and the environment. Because dogs share a common environment with humans and have the same types of naturally occurring autoimmune diseases, they offer an excellent opportunity to learn about these debilitating diseases. The two diseases Dr. Friedenberg is currently studying are Addison's disease and immune-mediated hemolytic anemia (IMHA). Addison's disease is an endocrine disorder where the body attacks its own adrenal glands. The adrenal glands make important hormones that help humans and dogs cope with stress and control electrolyte balance. Similarly, IMHA is a blood disorder where the body attacks its own red blood cells – cells that are critical for carrying oxygen throughout the body. This disease is very common in breeds such as Cocker Spaniels and English Springer Spaniels, but is also seen in Labrador Retrievers, Shih Tzus and other breeds. Current therapies for IMHA involve suppressing the immune system, which can cause additional complications. Dr. Friedenberg will take advantage of major advances in DNA sequencing to uncover the gene mutations that cause Addison's disease and IMHA. By finding the mutations, he believes we can work to decrease the incidence of the disease.



Dr. Hyun Ji Noh, MS, PhD Broad Institute of MIT and Harvard

Dr. Noh obtained her master's degree in pharmacology in 2008 and her PhD in computational biology from Oxford University in 2012. She is currently a postdoctoral fellow in the laboratory of Kerstin Lindblad-Toh at the Broad Institute, focusing on study comparative genetics.



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CHF Clinician–Scientist Fellows Announced... *(continued)*

She is devoted to studying psychiatric disorders such as obsessive-compulsive disorder (OCD) in the dog. Dr. Noh has already published her first paper on canine OCD and has been speaking on the value and promise of canine genetics at international meetings worldwide. Dr. Noh's project is to understand the genetic risk factors that make certain breeds, such as Doberman Pinschers, susceptible to obsessive-compulsive disorder. Canine OCD patients, like humans, show time-consuming repetitive behaviors that only partially respond to drug therapy. Using DNA from Doberman Pinschers with and without OCD, she identified 119 candidate genes responsible for OCD. The best gene candidates are all involved in nerve synapsis formation and function, and the mutations are usually in regulatory sequences near the genes and not in the protein-coding sequence itself. She is now continuing to examine these same mutations in dog and human populations, and using dog cell lines to understand exactly which mutations cause the disease and how they disrupt normal brain function. Canine OCD is a severe and heartbreaking mental disease, and Dr. Noh's goal is to find appropriate drug targets to lead to new treatments in dogs, and hopefully also in humans.

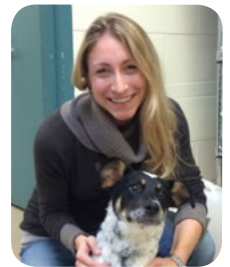
Dr. Alana Redfern–Allen, DVM Iowa State University

Dr. Redfern–Allen is currently working on a combined internal medicine residency and MSc program at Iowa State University. She has a strong interest in clinical research, particularly One Health–focused research activities that aim to improve the health of humans and animals alike. Working under the guidance of Dr. Al Jergens, Dr. Redfern–Allen's research focus will be diabetes mellitus, a common endocrine disease of dogs and humans. In humans, it has been shown that imbalances in gastrointestinal bacteria are associated with diabetes mellitus, and can contribute to high blood-sugar concentrations by antagonizing the effects of insulin. The short-term aims of her study are to compare the fecal microbiota in healthy dogs with those in diabetic patients to see if significant differences exist in microbial composition between dog groups. Additionally, Dr. Redfern–Allen will evaluate the potential efficacy of probiotics in modulating gut microbial populations to a more favorable composition that improves the effectiveness of administered insulin.



Dr. Christine Sibigroth, DVM University of Missouri

Dr. Sibigroth is working on a combined neurology/neurosurgery residency and PhD in the interdisciplinary neuroscience program with Dr. Joan Coates as her major advisor. She has a sincere enthusiasm for research and a passion for study of canine degenerative myelopathy (DM) and neuroscience. Canine DM is an adult-onset, progressive neurodegenerative disease in dogs that shares many characteristics with inherited amyotrophic lateral sclerosis (ALS) in humans. ALS triggers a deterioration of the nerves that connect the brain to the muscles, leading to stiffness, slowing of movement, loss of muscle tissue and weakness. Dogs with DM initially develop incoordination and progressive weakness of their rear legs resulting in paralysis within one year of onset of signs.



The immune system, specifically microglia, the primary immune cells of the central nervous system (CNS), has been implicated in ALS disease progression. Dr. Sibigroth's hypothesis is that the normal communication between motor neurons and microglia is similarly disrupted in canine DM, inducing a behavioral change in microglia cells. Microglia may transition from a neuroprotective to neurotoxic behavior, leading to progressive motor neuron damage and dysfunction. Owners of dogs with DM tend to have their pets euthanized at different stages of disease severity, and examination of the donated tissues from these dogs will provide an effective way to study the various stages of DM progression. Her work will provide valuable insight into the role of microglia within canine DM disease progression, and could identify key areas for the development of microglia-specific therapeutic targets that could slow or halt further disease progression.

Dr. Amelia Sinkin, VMD University of Georgia

Dr. Sinkin is a cardiology resident working under Dr. Amanda Coleman, DVM, DACVIM (cardiology). The focus of her research is myxomatous mitral valve disease (MMVD), a condition that affects an estimated 2–4.9 million dogs in the United States and leads to the development of congestive heart failure in approximately 15% of affected animals. The pathogenic role of renin-angiotensin-aldosterone system (RAAS) stimulation in the development and maintenance of MMVD is well-accepted. Consequently,



pharmacologic RAAS blockade, most frequently attempted through the use of angiotensin-converting enzyme inhibitors (ACEi), is considered standard-of-care for the treatment of patients with congestive heart failure, and administration of these drugs is associated with improvement in both clinical signs and survival time in patients. While the clinical benefit of ACE inhibition is clear, an unexpected and undesirable phenomenon known as aldosterone “breakthrough” (ABT) can occur in some dogs, impeding effective treatment. Addition of an aldosterone receptor blocker to standard congestive heart failure therapy may improve patient outcomes; however, the evidence-based use of this drug in dogs has yet to be fully defined. The major objective of Dr. Sinkin’s study will be to compare the incidence of ABT in client-owned dogs with advanced MMVD treated with an ACEi (enalapril) or an angiotensin receptor blocker (telmisartan). She hypothesizes that treatment with telmisartan will be associated with a significantly lower incidence of ABT than will treatment with enalapril. The results of this study will provide veterinarians with objective information to guide the way in which they approach RAAS blockade in clinical patients.

Ms. Emily Brown, DVM / PhD Candidate
University of California, Davis

The Nova Scotia Duck Tolling Retriever Club of America, with matching funds from the UC Davis Center for Companion Animal Health (CAHA) is funding Emily Brown, a combined DVM/PhD student in the laboratory of Dr. Danika Bannasch, to conduct research investigating the genetic etiology of Addison’s disease in the Nova Scotia Duck Tolling Retriever (NSDTR). Addison’s disease is an endocrine disorder resulting from lack of hormone production by the adrenal gland and can occur in a dog of any breed at any age. Although relatively uncommon in the general dog population, certain breeds including the Nova Scotia Duck Tolling Retriever have been found to have a genetic predisposition. Previous research on Addison’s disease in the NSDTR has shown a wide distribution of age at Addison’s disease onset, suggesting two main categories of Addison’s disease in the breed: a juvenile-onset form occurring in dogs under 12 months of age and an adult-onset form occurring on average at 4.6 years of age. An associated locus has been identified for the juvenile-onset form of the disease using genome-wide association analysis; however, no locus has been identified as associated with the adult-onset form of the disease in the breed. Over the course of her PhD, Ms. Brown hopes to elucidate the genetic



cause of adult-onset Addison’s disease in the breed, providing both tools for clinicians in diagnosis and for breeders in producing healthier dogs.

Ms. Brown is a previous recipient of a veterinary student travel grant from the Orthopedic Foundation for Animals and attended the 2013 AKC Canine Health Foundation National Parent Club Canine Health Conference in St. Louis, Missouri. Through attending this meeting, she was able to interact with breeders and other veterinary scientists united in the goal of improving purebred canine health. Attendance at this meeting motivated Ms. Brown to focus her PhD on genetic health issues affecting purebred dogs. Upon completion of her DVM/PhD degrees, Brown plans to pursue a residency in theriogenology and eventually an academic position at a veterinary school. She hopes that through her combined knowledge of veterinary medicine and genetics, she will be able to assist breeders in improving canine health, as well as be an active participant in the translation of basic science research to veterinary medicine. 🐾

Special Thanks!

Thank you to the following clubs and individuals for supporting the next generation of leaders in canine health.

- Mr. Jeffrey Pepper
- American German Shepherd Dog Charitable Foundation, Inc.
- American Miniature Schnauzer Club, Inc.
- Nova Scotia Duck Tolling Retriever Club (USA)

New Grants

New research grants are detailed here. For more information about any of these studies, including ways to provide financial support/sponsorship, visit www.akcchf.org.

Cardiology Research Program Area

02163: Is Hypothyroidism a Contributor to Progression of Arrhythmogenic Right Ventricular Cardiomyopathy?

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

Total Grant Amount: \$50,857

Memorandum of Understanding grant with the American Boxer Charitable Foundation

Grant Period: 1/1/2015 – 12/31/2016

Project Abstract: Arrhythmogenic right ventricular cardiomyopathy (ARVC) in the Boxer dog is an adult-onset, familial disease characterized by the presence

Story continued on page 10

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. Dr. Meurs will investigate whether hypothyroidism complicates ARVC and plays a role in disease progression, including 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.

02147: Use of MicroRNA Profiles in the Serum of Dogs for Early Diagnosis of Mitral Valve Disease and Dilated Cardiomyopathy

Principal Investigator: Dr. Gerhard Wess, PhD; Ludwig-Maximilians-Universitaet Muenchen
Corporate Collaborative grant with Zoetis, Inc.

Total Grant Amount: \$24,850

Grant Period: 2/1/15 – 1/31/16

Project Abstract: Myxomatous mitral valve degeneration (MVD) is a common cardiac disease in dogs, especially in small breeds less than 40 pounds. While diagnosis of MVD is commonly accomplished using echocardiography, blood-based biological markers of MVD that could diagnose the earliest stage of disease would greatly improve patient care. Dr. Wess believes microRNAs may provide early diagnostic and prognostic tools for MVD. MicroRNAs are small molecules that are naturally produced by all cells and are known to regulate many cellular reactions. They

can be detected in every body fluid, even in samples stored for years, since they are very stable. This project aims to find MicroRNAs in the serum of dogs that could be used as specific diagnostic markers for mitral valve disease. To corroborate the specificity, a group of dogs with a different heart disease, dilated cardiomyopathy, will also be included.

02160: Identification of Genetic Variants Associated with Myxomatous Mitral Valve Degeneration in the Whippet Dog Through Whole-Genome Sequencing

Principal Investigator: Dr. Joshua A. Stern, DVM, PhD; University of California, Davis

Memorandum of Understanding grant with the Whippet Health Foundation & the American Whippet Club

Total Grant Amount: \$23,188

Grant Period: 2/1/15 – 1/31/16

Project Abstract: Myxomatous mitral valve degeneration (MVD) is one of the most common heart diseases in dogs. MVD leads to structural heart changes and congestive heart failure, making this disease one of high morbidity and mortality. The Whippet breed is overrepresented in cases of MVD and pedigree analysis suggests this to be an inherited condition in this breed. Longitudinal clinical investigations into Whippet dog MVD reveals that Whippets frequently suffer from this common disease and may be affected at a significantly younger age than the general dog population.



Dr. Stern's proposed study will complete the next phase of his ongoing genetic studies of MVD in Whippets and utilize prospective cardiac screenings already completed at the Whippet National Specialty and stored affected and unaffected DNA samples. Genome-wide association studies performed by the investigators have already provided chromosomal regions of interest most likely to contain disease-

associated variants within genes or microRNAs. DNA samples will be used to complete whole genome sequencing and identify variants of interest that segregate with disease.

Identification of the molecular basis of MVD may help elucidate novel therapeutic or testing strategies in the treatment and management of this condition.

General Canine Health Research Program Area

02103-A: Development of an Effective Canine Periodontal Disease Vaccine

Principal Investigator: Dr. Paola Massari, PhD; Boston Medical Center

Total Grant Amount: \$12,960

Grant Period: 11/1/2014 – 10/31/2015

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

02161-A: Supporting the Evidence-Based Use of Antibiotic Gels after Extensive Dental Plaque Removal in Dogs

Principal Investigator: Dr. Django Martel, DVM; Animal Medical Center

Total Grant Amount: \$12,156

Grant Period: 11/1/2014 – 10/31/2015

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

Neurology Research Program Area

02157: Genomics of Deafness in the Dalmatian

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

Total Grant Amount: \$120,960

Memorandum of Understanding grant with the Dalmatian Club of America Foundation

Grant Period: 1/1/2015 – 12/31/2016

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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 toward a genetic testing solution for the Dalmatian breeding community.

02162: Defining the Genetic Foundations of Chiari-Like Malformation and Syringomyelia as a Tool to Better Treat Neuropathic Pain in the Dog

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

Total Grant Amount: \$37,530

Memorandum of Understanding grant with the American Cavalier King Charles Spaniel Club Charitable Trust

Grant Period: 1/1/2015 – 12/31/2015

Project Abstract: Chiari-like malformations and syringomyelia (CM/SM) are common problems 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 neurologists to perform a more appropriate genetic analysis of this important and common disease. Further, 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.

02165: Identification of Biomarkers and Therapeutic Targets for Canine Degenerative Myelopathy: The Search for a Cure

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

Total Grant Amount: \$154,077

Memorandum of Understanding grant with the American Boxer Charitable Foundation

Grant Period: 1/1/2015 – 12/31/2016

Project Abstract: Degenerative myelopathy (DM) is an adult-onset disease of the spinal cord causing progressive weakness and paralysis of the hind limbs and eventually all limbs. Mutations in an enzyme that converts superoxide to water and hydrogen peroxide, superoxide dismutase 1 (SOD1), have been linked



to DM and amyotrophic lateral sclerosis (ALS – Lou Gehrig's disease). DM is associated with degenerative loss of axons, which transmit signals from the brain and spinal cord to their targets (muscle). Currently no diagnostic test exists that would allow for repeated measurements with minimal invasiveness. Dr. Coates

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.

Ophthalmology Research Program Area

02145-A: Prevention of Glaucoma and Goniodysgenesis Through Genetic Profiling of Disease

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

Total Grant Amount: \$12,960

Grant Period: 11/1/2014 – 10/31/2015

Project Abstract: Primary glaucoma is a painful and blinding disease associated with high pressure inside the eye. Glaucoma affects over 40 breeds of dogs worldwide, at least 1500 dogs in the UK each year, and in the USA, as many as 15,000 dogs per year could be affected. Treatment is usually unsuccessful and most affected dogs ultimately require removal of their eyes on welfare grounds. The most common

form of canine glaucoma is primary angle closure glaucoma (PACG), which is known to be significantly associated with goniodysgenesis, an abnormality affecting the drainage angle of the eye. PACG and goniodysgenesis are prevalent in several breeds, and goniodysgenesis has been demonstrated to be highly heritable. Not all dogs with goniodysgenesis develop glaucoma, indicating that more than one mutation is probably involved. This complex inheritance and the progressive nature of goniodysgenesis mean that breeding strategies based on eye examinations alone probably won't be sufficient to eliminate the disease. Goniodysgenesis and PACG affect Welsh Springer Spaniels (WSS) in both Europe and the USA, and are of considerable concern to breeders on both continents.

Dr. Mellersh and colleagues have collected DNA from WSSs with goniodysgenesis, PACG and with healthy eyes and now aim to compare the DNA from these three cohorts of dogs to identify region(s) of the DNA that harbor mutations responsible for goniodysgenesis and PACG. This is an essential first step toward their ultimate aim, which is to identify causal genetic mutations and develop DNA tests for multiple breeds that will enable disease prevalence to be effectively reduced.

02164: Determining the Genetic Contribution to Boxer Corneal Ulcers

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

Total Grant Amount: \$68,053

Memorandum of Understanding grant with the American Boxer Charitable Foundation

Grant Period: 1/1/2015 – 12/31/2015

Project Abstract: Spontaneous chronic corneal epithelial defects (SCCEDs) are chronic corneal ulcers that fail to undergo normal healing, 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. In a previous study funded by the AKC-CHF, Dr. Meurs and colleagues collected samples from adult Boxers with and without SCCEDs, 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.



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Renal Disease Research Program Area

02110-A: Investigating the Effects of an Infusion of Fenoldopam on Kidney Function to Improve Outcomes of Acute Kidney Injury Patients

Principal Investigator: Dr. Jonathan D. Foster, VMD; University of Pennsylvania

Total Grant Amount: \$11,493.36

Grant Period: 11/1/2014 – 10/31/2015

Project Abstract: Acute kidney injury (AKI) is a devastating disease in canine patients. AKI represents a spectrum of disease characterized by a rapid loss of kidney function, resulting in impaired kidney filtration of metabolic waste products. Regardless of the inciting injury, the resulting kidney dysfunction causes increased serum kidney values and often decreased urine production. The resulting retention of metabolic waste products causes the clinical illness of AKI. Decreased urine production (oliguria) or complete cessation of urine production (anuria) may indicate a more severe kidney injury and are associated with increased mortality. Patients with decreased urine production are more difficult to manage when hospitalized and have higher morbidity than patients with normal urine output. Therapeutic intervention with diuretics has historically been performed in an attempt to induce urine production and thus facilitate the filtration and excretion of metabolic wastes. Unfortunately, these therapies are often ineffective and are not without risk of unwanted side effects. Fenoldopam (a selective dopamine DA-1 receptor agonist that induces renal vasodilation) has recently been shown to increase urine production in people with minimal side effects. Little is known regarding the effect of the drug on kidney filtration and whether there is potential for its use in dogs. The purpose of this study is to determine the effect of fenoldopam on kidney filtration by measuring glomerular filtration rate during fenoldopam administration. If fenoldopam increases filtration rate, it may in turn facilitate removal of metabolic waste products, potentially leading to improved outcome in patients with AKI and decreased urine production.

02152: Translation of MicroRNA into an Early Diagnostic Test for Chronic Kidney Disease

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

Total Grant Amount: \$26,988

Corporate collaborative grant with Zoetis, Inc.

Grant Period: 1/1/2015 – 6/30/2016

Project Abstract: Chronic kidney disease (CKD) is a significant cause of illness and death in dogs, and is often due to glomerular diseases. Dogs with glomerular disease often have poor outcomes with standard therapy, and specific treatment recommendations are difficult without performing

a kidney biopsy to determine the type of glomerular disease present, since treatment and outcome among these diseases differ substantially. Even then, we lack an understanding of the mechanisms driving these diseases, limiting our ability to optimally treat these dogs. Therefore, tests to non-invasively 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.

Reproductive Conditions & Disease Research Program Area

02136-A: Development of a Low-Cost, Non-Invasive Test to Determine Whether Females Have Been Spayed

Principal Investigator: Dr. Margaret V. Root Kustritz, DVM, PhD; University of Minnesota

Total Grant Amount: \$6,031.80

Grant Period: 11/1/2014 – 10/31/2015

Project Abstract: Dogs rescued from shelters often come without medical records or detailed medical histories, and while it is fairly straightforward for rescue groups to get dogs vaccinated and tested for heartworms, it is much harder for breed club groups to determine whether a female has been spayed. A non-invasive, low-cost test to evaluate the presence or absence of ovaries could significantly reduce the need for costly, invasive procedures that become a barrier to breed club rescue efforts. Data suggest concentrations of insulin-like growth factor 1 (IGF-1), a component of the biochemical pathway controlling secretion and actions of insulin, is implicated in multiple aspects of growth and development, including development and function of the ovaries. Dr. Kustritz hypothesizes that IGF-1 in blood may be significantly lower in spayed than in unsplayed female dogs, and that measurement

of IGF-1 could be used to differentiate spayed from unsayed dogs. Through evaluation of IGF-1 concentrations in serum of 40 spayed and 40 intact dogs, Dr. Kustritz will determine whether IGF-1 can be developed into a diagnostic test for ovariectomy.

Blood Disorders Research Program Area

02148-A: The Prevalence of a Novel Canine Blood Type and Its Mode of Inheritance in Doberman Pinschers.

Principal Investigator: Dr. Marie-Claude Blais, DVM; University of Montreal

Total Grant Amount: \$12,376.80

Grant Period: 2/1/15 – 11/30/15



Project Abstract: Blood transfusions have become an integral part of advanced veterinary medicine. As in humans, several blood groups have been identified in dogs. A dog negative for a given blood group can produce antibodies following exposure to that specific blood group, which could lead to life-threatening hemolytic transfusion reactions with subsequent transfusions. Recently, Dr. Blais and colleagues identified a new canine blood type, named Dal, in an anemic Dalmatian patient. The Dal blood type can be associated with the production of

anti-Dal antibodies, which may result in ineffective transfusions and hemolytic transfusion reactions. The frequency of the Dal blood type reported was 100% (55/55) in non-Dalmatian dogs and 81% in Dalmatians (five out of 26 Dalmatians were Dal-negative). The high frequency of the Dal blood type creates particular challenges: 1) Dal-negative anemic dogs will most likely be sensitized via their first blood transfusion and produce anti-Dal antibodies, and 2) if further blood transfusions are required in those patients, compatible Dal-negative blood may be very difficult to find. This problematic scenario was seen in two recent cases of anemic Doberman Pinschers, which led to preliminary blood testing in the breed. Approximately a third of Doberman Pinschers tested to date in Canada are Dal-negative.

The purpose of this study is to establish the prevalence of the Dal-negative blood type in Doberman Pinschers and in Dalmatians and its mode of inheritance. The secondary objective is to identify Dal-negative healthy blood donors in order to offer readily available compatible blood to Dal-negative anemic patients. 🐾

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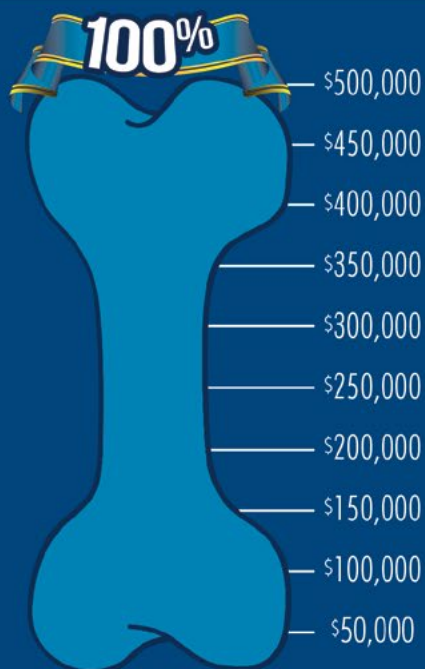
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