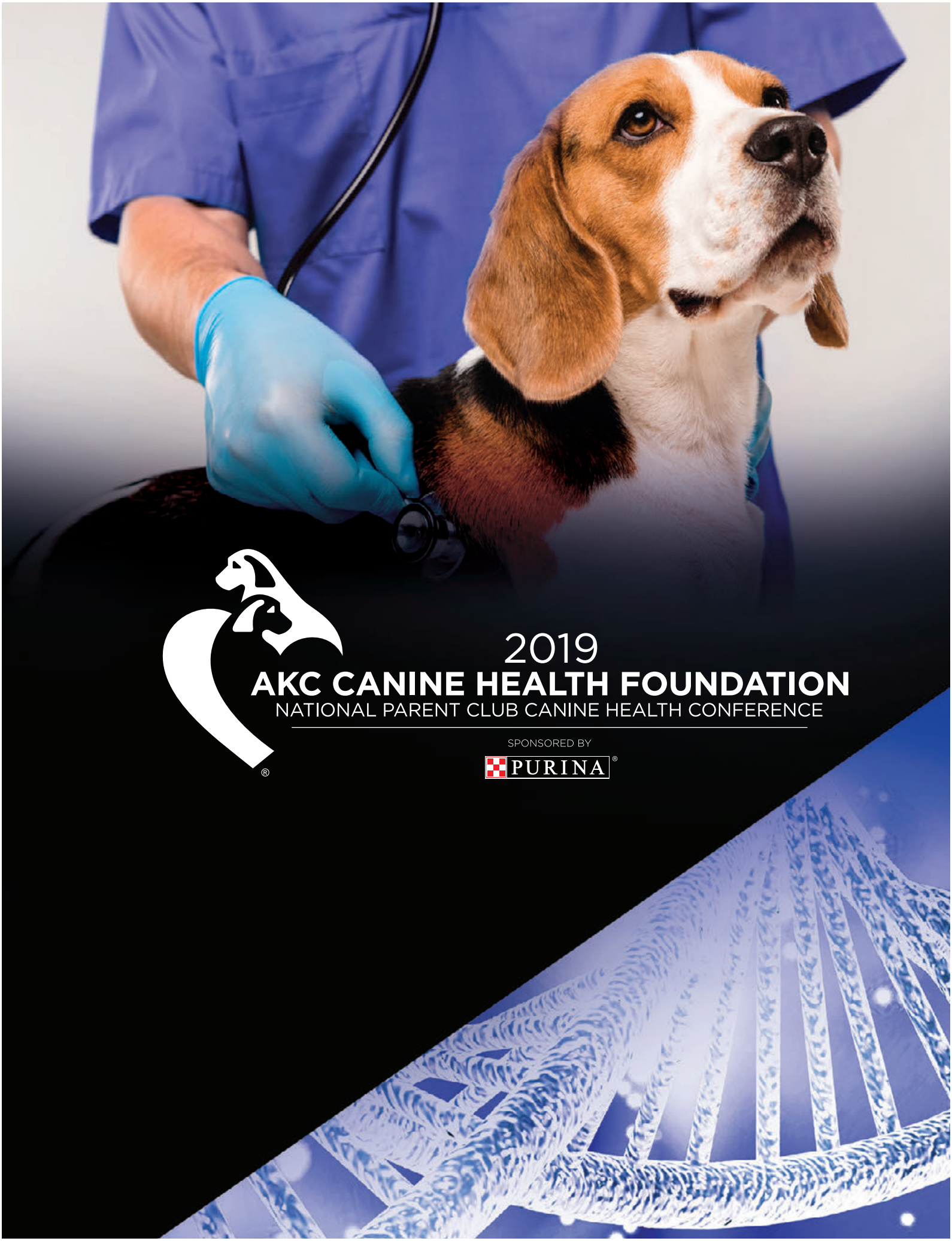

2019
AKC CANINE HEALTH FOUNDATION
NATIONAL PARENT CLUB CANINE HEALTH CONFERENCE

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Helps support dogs with anxious behaviors such as excessive vocalization, jumping, pacing, and spinning

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Helps dogs cope with external stressors like separation, unfamiliar visitors, novel sounds, or changes in routine and location

*Data was collected by Relevation Research via an online survey from August 15-19, 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 adult dogs, were household members most responsible for taking the dog(s) to a veterinarian, and had taken the dog(s) to a veterinarian in the past 12 months.

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Introduction

August 9, 2019

On behalf of the Board of Directors and Staff of the AKC Canine Health Foundation (CHF), I am pleased to welcome you to the 2019 National Parent Club Canine Health Conference, sponsored since 1997 by our partners at Nestlé Purina. Working closely with you since we last gathered in August 2017, we have collaborated to fund critical research to address the health needs of dogs. Together we continue to achieve our shared mission to prevent, treat and cure canine disease.

Advancing Canine Health through Research Programs Growth

In 2017 and 2018:

- Awarded $4.64 million for new research grants across 23 Research Program Areas
- Launched three new research initiatives in tick-borne disease, epilepsy, and hemangiosarcoma
- 2018 was the single largest year of Purina Parent Club Partnership Program earnings to date
- Our partners at the American Kennel Club (AKC) more than doubled their contribution to CHF-funded canine health research (largest contribution since 2008)
- Achieved the highest possible 4-Star Charity Navigator rating
- Thanks to YOU and our partners – CHF met $1.9 million in Matched Fund challenges

Highlights for 2019 (through June):

- 38 new grants have been awarded, totaling $2.5 million
- Over $10 million in currently active funding across 23 Research Program Areas
- Increased veterinary outreach & communications
- Launched new club, clinic and individual membership drives

One measure of the impact of a Foundation's work is the number of peer-reviewed scientific publications resulting from funded research that are then read and cited by others. CHF-funded researchers have published more than 760 scientific articles, which have been cited more than 26,000 times by other authors in peer-reviewed journals. CHF's funded research and your contributions to this research through donations of time, dollars and samples are resulting in substantial and measurable outcomes for the health of dogs and their people.

The AKC Canine Health Foundation is proud to partner with *your* Parent Club organizations, breed foundations and charitable trusts, all-breed clubs, and with Nestlé Purina, the AKC, Orthopedic Foundation for Animals (OFA), AKC Reunite, AKC Pet Partners, and Elanco Animal Health to drive more than $52 million in innovative research and educational programs for canine health. I want to also acknowledge the tireless efforts of the CHF Scientific Review Committee whose members volunteer their time year-round to ensure the quality and integrity of the research projects selected for funding; they are led by Dr. Mary Smith. While the needs are great, the opportunities are many.

As we look forward to the 25th anniversary of the AKC Canine Health Foundation in 2020, we thank you for being here to share ideas. We are grateful for your ongoing support of the AKC Canine Health Foundation, and most importantly for making a difference in the lives of dogs everywhere.

Diane Brown

Diane Brown, DVM, PhD, DACVP
Chief Executive Officer/Chief Scientific Officer

Nestlé Purina PetCare

North America

1 CHECKERBOARD SQUARE
ST. LOUIS, MO 63164, USA

August 9, 2019

On behalf of Purina, I welcome you to St. Louis – home of the North American headquarters for Nestlé Purina PetCare, the maker of *Purina Pro Plan*, the dog food fed to 95 of the top 100 all-breed show champions and 91 of the Top 100 sporting dogs. A team-spirited city, St. Louis is proud of its St. Louis Blues Stanley Cup champions and 11-time World Series champion St. Louis Cardinals. One block east of here is the landmark Gateway Arch, a reminder of our heritage as the gateway to the west and St. Louis' beginning in 1764 on the west bank of the Mississippi River. Likewise, Purina was founded 125 years ago by William H. Danforth, who chose the name Purina because it reflected his belief in the purity of quality products. In 1926, Purina began producing food for hunting dogs and working farm dogs that was sold through rural Purina feed dealers. Today, the values and beliefs of our founder still inspire all that we do. Integrity, creativity, expertise, and the drive to continually challenge ourselves to do better to create richer lives for pets and the people who love them are our mantra.

Aligning with the legacy of our founder, Purina became a corporate partner of the AKC Canine Health Foundation and sponsor of this National Parent Club Canine Health Conference in 1997. Our vision of helping to fund canine health research so dogs live long, healthy lives has been realized through the plethora of discoveries that have resulted from these scientific endeavors. In 2002, Purina began the PPCP (Purina Parent Club Partnership) Program to support canine health research, breed rescue and education efforts. Thanks to the enthusiastic participation of members of parent clubs, $8 million has been raised through the PPCP Program. A record donation of $473,829 from 2018 earnings went to your Donor Advised Funds at the AKC Canine Health Foundation, and a matching amount was distributed directly to parent clubs. Together, we are funding scientific research to prevent, treat and cure canine diseases.

At Purina, our nutritional innovations are rooted in scientific evidence and groundbreaking ideas focused on making life better for pets. A global team of over 500 expert scientists drive the delivery of excellent nutrition where even the most challenging health issues are effectively managed. An example is *Purina Pro Plan* Veterinary Supplements Calming Care, a probiotic supplement introduced in January 2019 that helps dogs displaying anxious behaviors cope with external stressors and maintain calm behavior. A revolutionary scientific breakthrough recently announced is a novel approach to managing cat allergens by safely neutralizing the major cat allergen, Fel d1, in hair and dander by incorporating an egg product containing anti-Fel d1 antibodies in a cat's diet. More than 10 years in development, this discovery will help the one in five people sensitized to cat allergens.

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In 2018, Purina provided more than $31 million in funding, *Purina* pet food and *Tidy Cats* litter to nonprofit organizations across the country. Pet passionate and devoted to ensuring all pets receive the best life possible, Purina comes to the forefront when natural disasters strike. Part of the 2018 donation included $60,000 and more than 60,000 pounds of *Purina* pet food and *Tidy Cats* litter to support victims of natural disasters across the U.S. Thus far, in 2019, Purina has donated $25,000 and 9,500 pounds of *Purina* pet food and *Tidy Cats* litter to support victims of tornadoes and flooding in the Midwest. Our

commitment to helping pets and people stay together is seen in our partnership with Red Rover through the Purina Purple Leash Project, in which $500,000 in grants will help make domestic violence shelters across the U.S. pet friendly so those escaping domestic abuse can safely keep their pets with them.

This is just a glimpse of the breadth of work Purina does to help pets and those who love them. If there is a takeaway, I hope that you can relate to our heartfelt, passionate belief that the world is better when pets and people are together. Importantly, we are glad you are here. We could not effectively get the word out about the scientific canine research being presented here without you. You are the conduit to your parent clubs, to dog breeders, and to show, sporting and performance competitors. Your voice will carry these messages far and wide. You are our partner, and we are glad to work with you to ensure pets have the best life possible.

With best wishes,

Patrick Mullen
Vice President, Professional Engagement Team
Nestlé Purina PetCare

Nestlé

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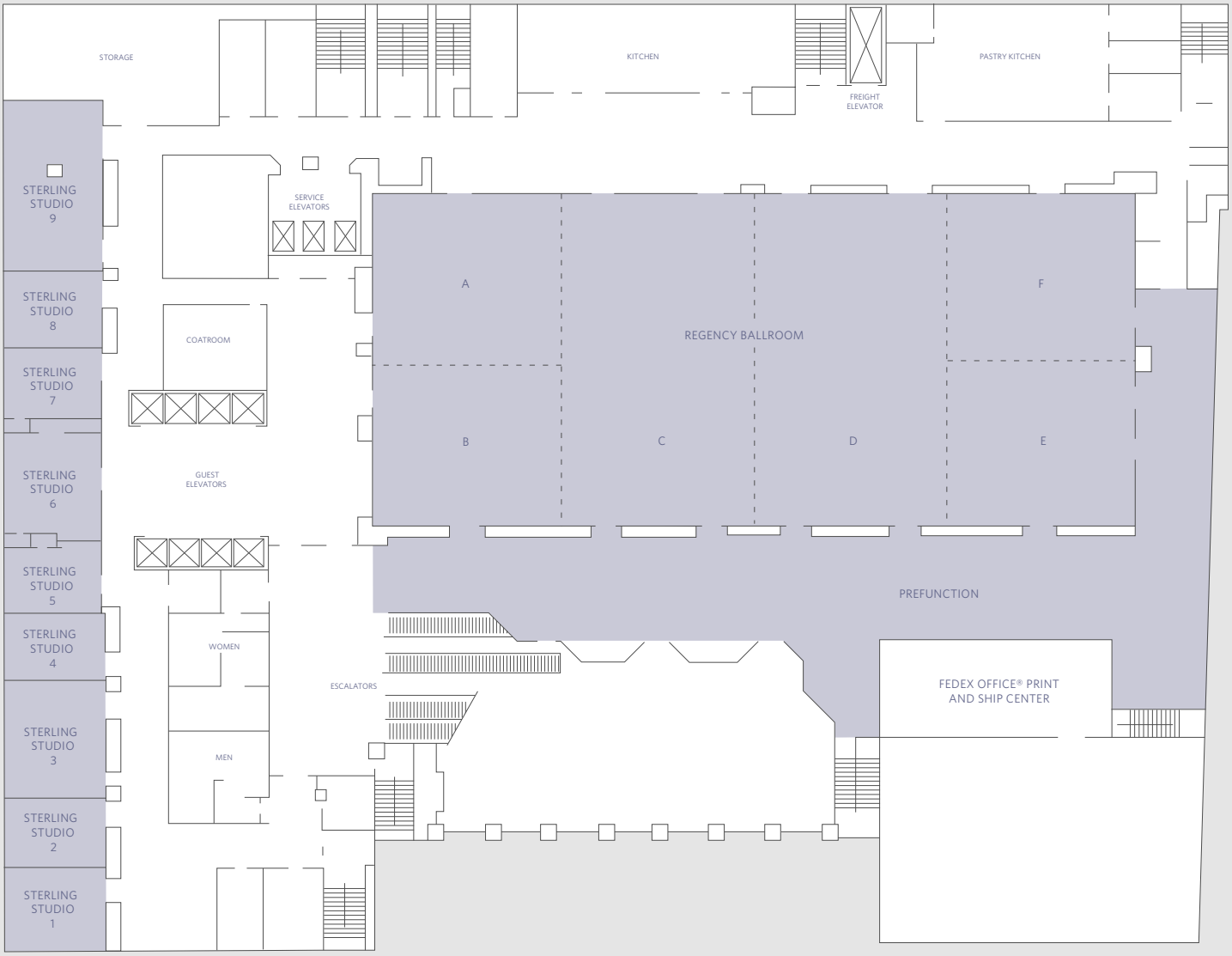

2019 National Parent Club Canine Health Conference

All sessions take place in Regency Ballroom ABC on the 2nd floor unless otherwise noted

Friday Afternoon, August 9th

1:30 PM	Conference Welcome Diane E. Brown, DVM, PhD, DACVP, Chief Executive Officer; AKC Canine Health Foundation Ann Viklund, Director - Conformation, Professional Engagement Team, Nestlé Purina PetCare
1:45 PM	New Approaches to Diagnosis and Therapy of Intestinal Microbiota Jan Suchodolski, DrMedVet, PhD, DACVM, AGAF
2:25 PM	Effects of Probiotics on the GI Microbiome and Immune System of Dogs and Cats Michael Lappin, DVM, PhD, DACVIM (SAIM)
3:05 PM	The Gut-Brain Axis and Those "Gut Feelings": Impact of BL999 (*Bifidobacterium longum*) on Anxious Dogs Ragen T.S. McGowan, PhD
3:45 PM	*Afternoon Break – Beverages/Snacks Provided*
4:00 PM	Food for Thought: Updates on Nutritional Considerations & Heart Disease Staging in Dogs Darcy Adin, DVM, DACVIM (Cardiology)
4:40 PM	An Update on Cannabidiol Research in Dogs Stephanie McGrath, DVM, MS, DACVIM (Neurology)
5:20 PM	Nutrition & Disease Panel Discussion Drs. Adin (MC), Lappin, McGowan, McGrath, Suchodolski
5:50 PM	*Conference Concludes for the Day*
8:00 PM	*Welcome Reception – Coffee, Dessert, and Cash Bar (Regency Ballroom AB Foyer)*

Saturday Morning, August 10th

7:30 AM	*Coffee, Tea and Light Breakfast Items Provided*
8:00 AM	The Canine Health Information Center Program – Status Update and Call to Action Eddie Dziuk, MBA
8:10 AM	Addison's Disease: A Research Update Steven Friedenberg, DVM, PhD, DACVECC
8:50 AM	Clinical Characteristics of Steroid Responsive Meningitis Arteritis in Dogs in North America Karen Muñana, DVM, MS, DACVIM (Neurology)
9:30 AM	A Case of Mistaken Identity: Autoimmunity & Endocrine Disorders (Keynote) Anita Oberbauer, PhD (2019 Asa Mays, DVM Award Recipient)
10:30 AM	*Morning Break – Beverages/Snacks Provided*
10:45 AM	Vector-borne Infections and Autoimmune Disease: What's the Link? Linda Kidd, DVM, PhD, DACVIM (SAIM)
11:15 AM	Autoimmunity & Disease Panel Discussion Drs. Friedenberg (MC), Kidd, Muñana, Oberbauer

Please, no recording or photography is allowed during the presentations.

Saturday Afternoon, August 10th

11:45 AM	*Lunch Break – Boxed Lunch Provided (Regency Ballroom DEF, 2nd floor)*
12:30 PM	*Afternoon Announcements*
12:35 PM	Emergence of Canine Leptospirosis: Coming Soon to a Puddle Near You? Jason Stull, VMD, MPVM, PhD, DACVPM
1:15 PM	The genus *Bartonella* and Vasoproliferative Cancers in Dogs and Humans Edward B. Breitschwerdt, DVM, DACVIM (SAIM)
1:55 PM	*Afternoon Break – Beverages/Snacks Provided*
2:10 PM	Advances in Immunotherapy for Canine Cancer Steven Dow, DVM, PhD, DACVIM (SAIM)
2:50 PM	Propranolol and Hemangiosarcoma: Can We Use an Old Drug to Learn New Tricks? Erin Dickerson, PhD
3:30 PM	Two Decades of Advances in Canine Hemangiosarcoma. The Light at the End of the Tunnel is Getting Brighter, and It's Not a Train! Jaime Modiano, VMD, PhD
4:10 PM	Infectious Disease & Canine Cancer Panel Discussion Drs. Breitschwerdt (MC), Dickerson, Dow, Modiano, Stull
4:45 PM	Approaches to Genetics & Breed Diversity Panel Discussion Drs. Oberbauer (MC), Bell, Clark, Friedenberg, Stern
5:30 PM	*Conference Concludes for the Day*
6:00 PM	*Cocktail Reception (Regency Ballroom DEF, 2nd floor)*
7:00 PM	*Dinner and 2019 Asa Mays, DVM Award Recipient Introduction (Regency Ballroom DEF, 2nd floor)*

Session sponsored by: Elanco

Sunday Morning, August 12th

7:30 AM	*Coffee, Tea and Light Breakfast Items Provided*
8:15 AM*	Breakout Session for Veterinary Students* (*Regency Ballroom EF, 2nd floor*) Eddie Dziuk, MBA; Orthopedic Foundation for Animals Mari-Beth O'Neill; American Kennel Club
8:15 AM	Harmonization of Genetic Testing for Dogs Brenda Bonnett, DVM, PhD
8:45 AM	Cardiac Disease of Purebred Dogs - Genetics & Beyond Joshua Stern, DVM, PhD, DACVIM (Cardiology)
9:30 AM	Understanding Dog Breeds as Populations Jerold S. Bell, DVM
10:15 AM	*Morning Break – Beverages Provided*
10:30 AM	Development and Utilization of a Genetic Risk Assessment for a Multifactorial Disease Leigh Anne Clark, PhD
11:15 AM	Genetics & Disease Panel Discussion Drs. Bell (MC), Bonnett, Clark, Oberbauer, Stern
12:20 PM	*Conference Conclusion*

Please, no recording or photography is allowed during the presentations.

Introducing the 2019 AKC Canine Health Foundation
Asa Mays, DVM Award Recipient for Excellence in Canine Health Research

Anita Oberbauer, PhD

Dr. Anita Oberbauer is a Professor of Animal Science and the Associate Dean in the College of Agricultural and Environmental Sciences at the University of California, Davis. Previously she chaired the Department of Animal Science for 8 years. She was at the forefront of incorporating companion animals into animal science curricula and has received Distinguished Teaching awards from the UC Davis Senate and the American Society of Animal Science Western Section, as well as Outstanding Mentor Awards. She was recently awarded the prestigious UC Davis Prize for Teaching and Scholarly Achievements. Her research program emphasizes cellular components regulating skeletal growth and body composition, and the genetic basis for health disorders in dogs and cattle. She has trained more than 30 PhD, MS and Visiting Scholars. Her research was recognized with the American Society of Animal Science Corbin Award in Companion Animal Biology. She is a director on the board of the OFA, provides numerous invited talks on canine genetics, and serves on federal grant review panels and journal editorial boards. She received her BS *summa cum laude* from UC Davis and her PhD in Animal Physiology from Cornell University followed by postdoctoral fellowships at Loma Linda University in perinatal biology and UCLA in biological chemistry.

Join us for the Award Presentation on Saturday, August 10
Cocktail Reception at 6:00 pm in foyer outside Regency Ballroom DEF, 2nd floor
Dinner at 7:00 pm in the Regency Ballroom DEF, 2nd floor

This biennial award is bestowed on an investigator who demonstrates meritorious advancements in furthering the AKC Canine Health Foundation's mission of identifying, characterizing, and treating canine disease and ailments. Dr. Asa Mays was a founding Board Member of the AKC Canine Health Foundation.

Continuing Education

This program 272-37125 is approved by the AAVSB RACE to offer a total of 16.25 CE Credits (16.25 max) being available to any one veterinarian and/or veterinary technician. This RACE approval is for the subject matter category of Medical Program using the delivery method of Seminar/Lecture. This approval is valid in jurisdictions which recognize AAVSB RACE; however, participants are responsible for ascertaining each board's CE requirements. RACE does not "accredit" or "endorse" or "certify" any program or person, nor does RACE approval validate the content of the program.

Certificates of Attendance including RACE credits will be provided at the conference. Please contact chf@akcchf.org or 888-682-9696 if you have any questions.

Conference Evaluations

Please visit http://support.caninehealthfoundation.org/2019NPCCHC_Survey to complete the evaluation for this year's conference. Those who complete the survey within one week of the conference will be entered to win a FREE tribute brick on the Purina Walk of Champions / Path of Honor.

AKC Canine Health Foundation

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The Board and Staff of the AKC Canine Health Foundation would like to extend a special THANK YOU to the CHF Scientific Review Committee, chaired by Dr. Mary Smith, for their time, efforts, and expertise.

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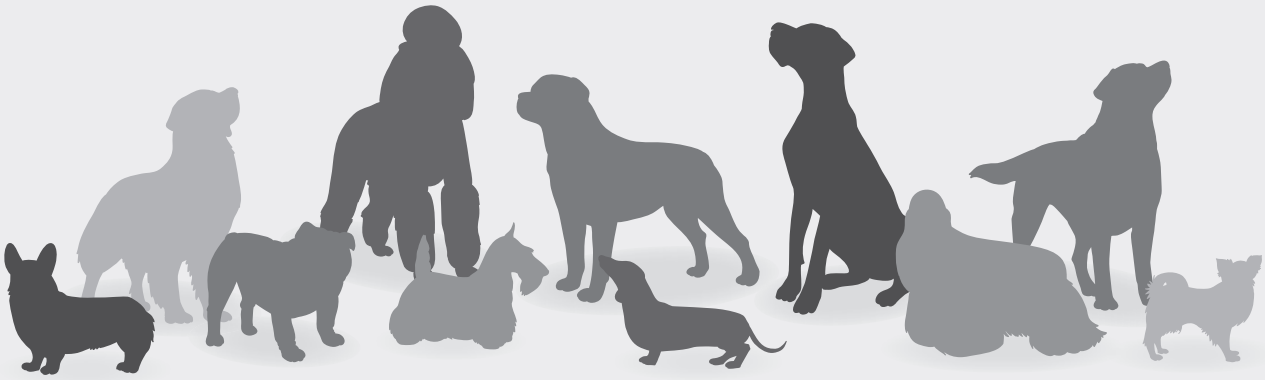

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Helps support dogs with anxious behaviors such as excessive vocalization, jumping, pacing, and spinning

- Helps dogs cope with external stressors like separation, unfamiliar visitors, novel sounds, or changes in routine and location
- Helps dogs maintain positive cardiac activity during stressful events
- Promotes a positive emotional state and healthy immune system in dogs

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Presentations

New Approaches to Diagnosis and Therapy of Intestinal Microbiota Dysbiosis

Jan S. Suchodolski, DrMedVet, PhD, DACVM, AGAF

BIOGRAPHY

Dr. Jan S. Suchodolski graduated with a veterinary degree from the University of Veterinary Medicine in Vienna, Austria in 1997. After working for several years in a small animal specialty clinic he returned to academia and received his Dr. med. vet. degree from the University of Vienna, Austria in recognition for his research on potential diagnostic markers for canine gastric disease. In 2005 Dr. Suchodolski received his PhD in Veterinary Microbiology from Texas A&M University for his work on molecular markers for the assessment of the intestinal microbiota. He is also board certified in immunology by the American College of Veterinary Microbiologists (ACVM). He currently serves as Associate Professor and Associate Director of the GI Lab at Texas A & M University.

PRESENTATION ABSTRACT

Intestinal microbiota (bacteria, fungi, archaea, protozoa, and viruses) are of fundamental importance in maintaining gut homeostasis. Various studies have reported changes in microbial communities in acute and chronic gastrointestinal diseases, which result in functional and immunological consequences for the host. The depletion of commensal groups and their respective immunoregulatory metabolites (e.g., indoles, and secondary bile acids) may impair the ability of the host to down-regulate the aberrant intestinal immune response, making dysbiosis an integral part of the pathogenesis of GI disease. Better characterization of dysbiosis and functional consequences may guide treatment decisions (e.g., antimicrobials vs. dietary modulation, use of probiotics, and/or immunosuppression). This talk will summarize recent work using wide screen microbiome and metabolome analysis to better define the differences in the pathophysiology of various acute and chronic GI disorders.

Notes:

Effects of Probiotics on the GI Microbiome and Immune System of Dogs and Cats

Dr. Michael Lappin, DVM, PhD, DACVIM (Small Animal Internal Medicine)

BIOGRAPHY

Dr. Michael Lappin graduated from Oklahoma State University and then completed an internship, internal medicine residency, and PhD program in Parasitology at the University of Georgia. Dr. Lappin is the Kenneth W. Smith Professor in Small Animal Clinical Veterinary Medicine at Colorado State University, is the director of the "Center for Companion Animal Studies" and he helps direct the shelter medicine program. He is the chair of the WSAVA One Health Committee. His principal areas of interest are prevention of infectious diseases, the upper respiratory disease complex, infectious causes of fever, infectious causes of diarrhea, and zoonoses. His research group has published over 300 primary papers or book chapters concerning small animal infectious diseases. Awards include the Norden Distinguished Teaching Award, NAVC Small Animal Speaker of the Year, the European Society of Feline Medicine International Award for Outstanding Contribution to Feline Medicine, the Winn Feline Research Award, the ACVIM Robert W. Kirk Award for Professional Excellence, the WSAVA Scientific Achievement Award, and the AVMA Clinical Research Award.

PRESENTATION ABSTRACT

Probiotics are live microorganisms that when administered in adequate amounts confer a beneficial health effect on the host. There have been many studies and reviews of the effects of probiotics on the health of humans, but fewer in small animals. Evidence supporting the use of probiotics is generally strongest for managing gastrointestinal syndromes such as acute or chronic diarrhea due to infectious diseases or inflammatory bowel disease. There is also some evidence that probiotics might be beneficial for mitigating antibiotic-associated vomiting or diarrhea. It is known that some probiotics help balance the endogenous microbiota and that some can inhibit replication of pathogenic bacteria. There is also evidence that some probiotics induce immune modulating effects with potential benefits for the management of inflammatory bowel disease, atopy, or infectious diseases with systemic involvement (e.g., feline herpesvirus-1; FHV-1). In this presentation, Dr. Lappin will use clinical cases as well as review the most important studies in dogs and cats that show evidence for a benefit to the use of probiotics.

Notes:

The Gut-Brain Axis and Those "Gut Feelings": Impact of BL999 (*Bifidobacterium longum*) on Anxious Dogs

Ragen T.S. McGowan, PhD

BIOGRAPHY

Dr. Ragen McGowan is a Research Scientist in Behavior and Welfare at Nestlé Purina. She joined Nestlé Purina in 2009. Her research has focused on a holistic approach, incorporating behavior, physiology and endocrinology to quantify affective states and temperament in dogs and cats. She aims to create products that cater to behavioral needs of pets and to better understand and quantify the human-animal bond from the pet's perspective. Dr. McGowan earned her BS in Zoology, BA in Foreign Language and Literature and PhD in Applied Ethology from Washington State University. Her PhD research focused on Contrafreeloading behavior, a phenomenon whereby animals choose to work for food even when the same food is freely available. Her other projects examined play behavior in piglets and children and means to reduce problem behaviors in laying hens. Prior to joining Nestlé Purina Dr. McGowan held a post-doctoral research position in the Section for Ethology and Animal Welfare at the Swedish University of Agricultural Sciences in Uppsala, Sweden; her research focused on the study of emotionality in dogs, and she explored new methodology to objectively evaluate positive emotions in animals. This included using Cognitive Bias and Contrast to measure emotional states in dogs and studying the 'Eureka Effect' (emotional reactions to learning) in dogs. In addition to her passion for animals Dr. McGowan is an avid dancer and an instructor of ballroom dance for many years. She is based in Saint Joseph, Missouri where she lives with her husband, two children and two dogs.

PRESENTATION ABSTRACT

Anxiety is a concern for owners who want to see their dogs live happy, comfortable lives. Chronic behavior issues can be detrimental to the pet-owner relationship and anxiety related behavior issues are among the top reasons pet dogs are relinquished to shelters. Nutritional solutions should be considered as part of a management plan for improving the well-being of anxious dogs. A broad overview of the impact of diet on behavior will be presented with recommendations for interventions showing promise for alleviating symptoms of anxiety. There is mounting evidence that manipulation of the gut microbiota can influence anxious behavior, specifically via the gut-brain axis. Thus, probiotic supplementation has potential to help alleviate symptoms of anxiety in dogs. Using a holistic approach incorporating both behavioral and physiological measures we demonstrate a positive impact of the probiotic BL999 on mediating anxious behavior and stress responses in anxiety-prone dogs. Dogs supplemented with BL999 showed significant improvement in day-to-day anxious behavior including reductions in barking ($P < 0.0001$), jumping ($P < 0.01$), spinning ($P < 0.05$) and pacing ($P < 0.05$). During formal anxiety tests dogs supplemented with BL999 showed increased exploratory behavior in a novel environment ($P<0.05$). Dogs also had reduced salivary cortisol concentrations in response to both exercise and anxiety inducing stimuli when supplemented with BL999 ($P < 0.001$). Considering cardiac activity, dogs showed a decrease in heart rate ($P < 0.001$) and an increase in heart rate variability (HF: $P < 0.03$; RMSSD: $P < 0.001$) indicating a more positive response to anxiety inducing stimuli when supplemented with BL999. From both a behavioral and physiological standpoint BL999 had an anxiolytic effect on anxious dogs and could serve as a tool in management plans to improve the well-being of dogs who suffer from anxiety.

Notes:

Food for Thought: Updates on Nutritional Considerations and Heart Disease Staging in Dogs

Darcy Adin, DVM, DACVIM (Cardiology)

BIOGRAPHY

Dr. Darcy Adin is a Clinical Associate Professor of Cardiology at the University of Florida, College of Veterinary Medicine. She received her DVM from Cornell University in 1996. She completed a rotating internship at VCA South Shore Animal Hospital in 1997 and a cardiology residency at the University of California, Davis in 1999, with ACVIM board certification in Cardiology in 2000. Dr. Adin has held positions in both academic and private specialty practice. Her clinical research focuses on the investigation of diuretic treatments and neurohormonal modulation of congestive heart failure. She has also been active in recent investigations of diet-associated dilated cardiomyopathy in dogs. Dr. Adin and her husband, Dr. Christopher Adin, have 3 children, a Soft-Coated Wheaten Terrier, a Cavalier King Charles Spaniel and a Thoroughbred horse. Outside of the office, she enjoys spending time with her family and gardening.

PRESENTATION ABSTRACT

Dilated Cardiomyopathy (DCM) has a genetic basis for many dogs; however, nutrition can play a role in the development of DCM, as well as in the progression and control of congestive heart failure (CHF). Recent discussions surrounding the relationship between dietary intake and heart disease has led to increased awareness of the importance of obtaining a full dietary history in animals that are presented for heart disease. Although investigators are actively studying this issue, many questions remain unanswered at this time. Resources are available to aid in nutritional management of dogs with heart disease and to assist ongoing investigations.

In the absence of a reversible cause of heart disease, most dogs with CHF secondary to genetically based DCM or degenerative mitral valve disease will eventually succumb to their disease. Quality of life, therefore, is very important for these dogs and depends on appropriate management of CHF signs. End stage CHF is characterized by poor diuretic response and recurrent or refractory congestion, but an exact definition is elusive. Correct identification of these patients is essential to be able to guide specific therapies to restore diuresis and maintain a good quality of life. We studied indicators of diuresis and renin-angiotensin-aldosterone system (RAAS) activation in dogs grouped by ACVIM Heart Disease Stage, and found differences between groups for serum electrolyte profiles and RAAS activation. These clinical markers may be useful to identify dogs with diuretic resistance and could lead to specific medication therapies to restore diuresis in dogs with end stage CHF.

CURRENT CHF GRANTS

- 02436: Predicting Disease Stage and Diuretic Responsiveness in Dogs with Acquired Heart Disease

Notes:

An Update on Cannabidiol Research in Dogs

Stephanie McGrath, DVM, MS, DACVIM (Neurology)

BIOGRAPHY

Dr. Stephanie McGrath is an assistant professor in the Neurology Department at Colorado State University's College of Veterinary Medicine. She went to Michigan State University for veterinary school and completed an internship at Red Bank Veterinary Hospital. Dr. McGrath did her neurology residency at Colorado State University (CSU) and has been a faculty member there since 2012. She is interested in treating seizure disorders and inflammatory brain diseases, as well as a variety of spinal cord disorders. Dr. McGrath is currently conducting research in the use of cannabidiol in veterinary medicine and infectious etiologies and treatment options for canine inflammatory brain diseases.

PRESENTATION ABSTRACT

Cannabis-based therapies have been used for centuries for various medicinal purposes. They have recently gained publicity as an effective medication for use in human medicine and, as such, awareness is increasing among veterinarians and pet owners. However, side effects, pharmacokinetics and efficacy in dogs is not known. At CSU, we have successfully performed a safety and pharmacokinetic study to assess the measurability and tolerability of cannabidiol (CBD) in healthy dogs. The results of this study showed that cannabidiol seemed to be well tolerated in dogs and exposure was dose-proportional. These results provided a framework for our clinical trials in canine epilepsy. The objective of our current epilepsy clinical trial is to compare the effect of cannabidiol with a placebo on seizure frequency in dogs with naturally occurring epilepsy. If this study can demonstrate that dogs attain sufficient blood exposure with oral dosing and that CBD is effective in decreasing seizure frequency, it has the potential to improve the quality of life of this population of dogs, as well as decrease the rate of euthanasia. This presentation will address the study design and results of the safety/PK study, the challenges of performing the first cannabis clinical trials in dogs, and an update on the clinical trials and future directives.

CURRENT CHF GRANTS

- 02323: Efficacy of Cannabidiol (CBD) for the Treatment of Canine Epilepsy

Notes:

The Canine Health Information Center (CHIC) Program – Status Update and Call To Action

Eddie Dziuk, MBA

BIOGRAPHY

Eddie Dziuk has been actively involved in the sport of purebred dogs for over forty years. He obtained his first Beagle in 1977 and finished its championship as a junior owner handler and has never been without the breed since. He has bred or owned more than 75 Beagle champions, including 5 National BOB Winners, and 11 BIS Winners. In addition to Beagles, Eddie has also bred Miniature Pinschers and Norfolk Terriers, and has bred and owned BIS and National Specialty Winners in both these breeds. Eddie began judging in 2009, and is licensed for the Hound Group, a handful of additional breeds, and junior showmanship. He is the VP and show chair for the Columbia MO Kennel Club, the founder and president of the Gateway Hound Club, and is the AKC Delegate for the National Beagle Club. Professionally, Eddie holds a BS in Economics, an MBA from the University of Missouri, and is currently pursuing a second Master's in Data Science & Analytics at the University of Missouri. For the last 18 years, he has been the Chief Operating Officer of the Orthopedic Foundation for Animals (OFA) where he has the unique opportunity to combine his business and management experience with his love of dogs and passion and interest in canine health. One of his principle achievements at the OFA has been the successful launch and ongoing impact of the CHIC program. In all his activities, he is a fulltime advocate for the purebred dog and canine health & welfare, promoting responsible dog ownership and breeding practices.

PRESENTATION ABSTRACT

The Canine Health Information Center Program (CHIC), co-sponsored by OFA and AKC CHF, was first implemented in 2001 with 8 pilot breeds. The goal of the program is to provide a consolidated source for canine health test results, and recognize those dogs tested in accordance with a breed specific health testing protocol as established by the breed's parent club. Over 180 breeds now participate in the program, and over 130,000 dogs have earned their CHIC numbers. The NPCCHC conference is an appropriate venue to remind clubs that their requirements are fluid, and should be periodically reviewed and updated.

Another key element of the CHIC program is the CHIC DNA Repository. The CHIC DNA Repository stores canine DNA samples via blood or buccal swabs for future health research efforts. The bank has over 27,000 samples representing many different breeds. More than 3,000 samples have been distributed to a variety of research institutions all over the world. While all samples may be of potential use, the majority of the bank's samples represent young healthy dogs at the time of the sample collection. However, the most valuable samples are from affected dogs. The NPCCHC is the perfect opportunity to enlist clubs to periodically remind their members to update the bank with any health updates of significance that may increase the value of the sample and the likelihood of its use.

Notes:

Addison's Disease: A Research Update

Steven Friedenberg, DVM, PhD, DACVECC

BIOGRAPHY

Dr. Steven Friedenberg is an Assistant Professor in the Department of Veterinary Clinical Sciences at the University of Minnesota, where he has been since 2016. At the University of Minnesota, he is a core member of the Canine Genetics Laboratory and a member of the renowned Center for Immunology. He holds a BS in chemistry from Yale University, and graduated from veterinary school at Cornell University. He completed a rotating internship in Small Animal Medicine & Surgery and a residency in Emergency & Critical Care medicine at The Ohio State University. After finishing his residency program, he completed a PhD in genetics at North Carolina State University. He currently studies inherited autoimmune disorders in dogs, with a particular interest in both Addison's disease and immune-mediated hemolytic anemia. Through his research, he works closely with breed clubs, including the Poodle Club of America, the Portuguese Water Dog Foundation, the English Cocker Spaniel Club of America, and the Clumber Spaniel Club of America.

PRESENTATION ABSTRACT

Addison's disease is an autoimmune endocrine disorder in which the body attacks and destroys the outer layer of the adrenal gland, called the adrenal cortex. Dogs with Addison's disease are at high risk of developing a potentially deadly adrenal crisis characterized by shock, vomiting, and life-threatening electrolyte abnormalities. Treatment for Addison's disease is manageable but requires frequent monitoring and lifelong hormone supplementation. The disease is believed to be inherited in several dog breeds, including Standard Poodles, Portuguese Water Dogs, and Cocker Spaniels.

In this presentation, Dr. Friedenberg will discuss the latest research into the causes of Addison's disease. He will also share specific insights into the underlying genetics and immunology of the disease. Finally, recent publications, ongoing studies, and the latest research into what might trigger the onset of this challenging autoimmune disease will be highlighted.

CURRENT CHF GRANTS

- 02428: Identifying the Disease-Defining Autoantibodies in Canine Addison's Disease
- 02348: Whole Blood Transcriptome Profiling of Dogs with Immune-Mediated Hemolytic Anemia (IMHA)
- 02531 *(Co-investigator):* Identification of Genetic Risk Allele(s) Associated with the Development of Tricuspid Valve Dysplasia in the Labrador Retriever

Notes:

Clinical Characteristics of Steroid Responsive Meningitis-Arteritis in Dogs in North America

Karen Muñana, DVM, MS, DACVIM (Neurology)

BIOGRAPHY

Dr. Karen Muñana received her undergraduate degree from the University of California at Berkeley and attended veterinary school at the University of California at Davis. She went on to complete a rotating internship in small animal medicine and surgery at Kansas State University and a residency training program in neurology and neurosurgery at Colorado State University. She joined the faculty of North Carolina State University College of Veterinary Medicine in 1994, where she currently holds the rank of Professor of Neurology. She is a diplomate of the American College of Veterinary Internal Medicine, subspecialty of Neurology. Dr. Muñana has authored over 100 papers and book chapters on topics pertaining to veterinary neurology and has been an invited speaker at national and international veterinary meetings. Dr. Muñana's primary research interest is canine epilepsy, with a focus on the use of clinical trials to evaluate the effectiveness of novel anti-seizure therapies and understand why some dogs respond poorly to treatment. She also performs research on inflammatory neurological disorders of dogs.

PRESENTATION ABSTRACT

Steroid responsive meningitis-arteritis (SRMA) is a common inflammatory disease of the nervous system of dogs characterized by involvement of the meninges (the membranes that cover the brain and spinal cord) and associated blood vessels. The cause of SRMA is not fully understood, but is believed to be immune mediated in origin. The disorder typically affects dogs 6-18 months of age. Any breed can develop the disease, although a predisposition has previously been reported in Beagles, Bernese Mountain Dogs, Border Collies, Boxers, English Springer Spaniels, Russell Terriers, Nova Scotia Duck Tolling Retrievers, Weimaraners, and Whippets. The classical, or acute, form of SRMA presents with sudden onset of fever, neck pain and lethargy. Diagnosis is based on the presence of increased numbers of neutrophils, a type of white blood cell, in the cerebrospinal fluid of affected dogs, and exclusion of any underlying infectious cause. SRMA is treated with corticosteroids, and most dogs respond well with a resolution of clinical signs. However, relapses are common as treatment is tapered or discontinued. The majority of research on SRMA has originated from Europe, and potential geographical differences in the disease have not been explored. We recently completed a study that aimed to characterize SRMA in a population of dogs in North America; we investigated whether breed differences exist in disease course and treatment response, and evaluated caregivers' perception of SRMA on quality of life. Medical records from 61 dogs presenting to NC State Veterinary Hospital between 2003-2017 (n=32) or identified in an AKC Canine Health Foundation survey (n=29) were reviewed. Caregivers of dogs included in the study completed an online survey to evaluate the impact of SRMA on the dog's quality of life. Findings from the study will be presented.

CURRENT CHF GRANT – 02561: Is Gut Dysbiosis Associated with Canine Idiopathic Epilepsy?

RECENT CHF SRMA GRANT – 2017 Clinician-Scientist Fellowship – North Carolina State University

Notes:

A Case of Mistaken Identity: Autoimmunity & Endocrine Disorders

Anita Oberbauer, PhD*

*Keynote address given by this year's AKC Canine Health Foundation Asa Mays,DVM Awardee for Excellence in Canine Health Research

BIOGRAPHY

Dr. Anita Oberbauer is a Professor of Animal Science and the Associate Dean in the College of Agricultural and Environmental Sciences at the University of California, Davis. Previously she chaired the Department of Animal Science for 8 years. She was at the forefront of incorporating companion animals into animal science curricula and has received Distinguished Teaching awards from the UC Davis Senate and the American Society of Animal Science Western Section, as well as Outstanding Mentor Awards. She was recently awarded the prestigious UC Davis Prize for Teaching and Scholarly Achievements. Her research program emphasizes cellular components regulating skeletal growth and body composition, and the genetic basis for health disorders in dogs and cattle. She has trained more than 30 PhD, MS and Visiting Scholars. Her research was recognized with the American Society of Animal Science Corbin Award in Companion Animal Biology. She is a director on the board of the OFA, provides numerous invited talks on canine genetics, and serves on federal grant review panels and journal editorial boards. She received her BS *summa cum laude* from UC Davis and her Ph.D. in Animal Physiology from Cornell University followed by postdoctoral fellowships at Loma Linda University in perinatal biology and UCLA in biological chemistry.

PRESENTATION ABSTRACT

When the health of dogs is evaluated from patient records, the most frequent conditions are predominantly linked to the environment and include otitis externa, periodontal disease, anal sac impaction, overgrown nails, etc. Endocrine disorders, although relatively low prevalence in purebred and mixed breed dogs (e.g., 1.8 to 3.7%), can have devastating, lifelong consequences and may be caused by both environmental and genetic inputs. Hypothyroidism, hypoadrenocorticism, and diabetes mellitus are three of the five most prevalent endocrine disorders in the dog and purportedly caused by an autoimmune attack of the endocrine tissue wherein the individual's immune system is dysregulated and mounts an attack against its own healthy tissues. This results in gradual destruction of the endocrine function of the organs. For many autoimmune diseases in dogs, disease occurrence depends on a combination of genetic and environmental factors, including neutering. Though the role of environmental factors is not yet fully understood, discovery of the genetic components involved in disease susceptibility may help predict disease risk. In humans, autoimmunity is associated with altered immune-related genes that result in defective regulation of the immune system; the strongest associations for many human autoimmune diseases involve the major histocompatibility complex (MHC) class II genes. Genetic variants within the dog leukocyte antigen (DLA) genes, the dog MHC counterpart, have also been associated with autoimmune conditions. Three MHC class II genes are of particular importance in the dog and are designated DLA-DRB1, DLA-DQA1 and DLA-DQB1. Certain combinations, or haplotypes, across these genes are associated with susceptibility to autoimmune disease of endocrine organs. Haplotype susceptibility signatures that are shared across breeds appear to combine with other genes to confer risk

for specific endocrine disease as well as other common autoimmune conditions. Research in the field aims to identify genetic signatures to inform breeding decisions.

CURRENT CHF GRANT – 02488: Addison's Disease and Symmetrical Lupoid Onychodystrophy in Bearded Collies Provide Common Ground for Identifying Susceptibility Loci Underlying Canine Autoimmune Disorders

Notes:

Vector-borne Infections and Autoimmune Disease: What's the Link?

Linda Kidd, DVM, PhD, DACVIM (Small Animal Internal Medicine)

BIOGRAPHY

Dr. Linda Kidd received her DVM from the University of Wisconsin-Madison's School of Veterinary Medicine (UW-SVM). After several years in private small animal practice, she returned to the UW-SVM for specialty training in Small Animal Internal Medicine. She achieved board certification by the American College of Veterinary Internal Medicine, and stayed on as a Clinical Instructor of Small Animal Internal Medicine until December of 2002. Dr. Kidd then pursued research training at the Intracellular Pathogens Research Laboratory at North Carolina State University's College of Veterinary Medicine, under the mentorship of Dr. Ed Breitschwerdt, where she obtained a PhD in Immunology with a minor in Molecular Biology with research centered on the molecular characterization of Spotted Fever Rickettsiosis in dogs. She completed a postdoctoral fellowship at The Scripps Research Institute in a thrombosis and hemostasis laboratory under the direction of Dr. Nigel Mackman. Currently, Dr. Kidd is an Associate Professor of Small Animal Internal Medicine at Western University of Health Sciences, College of Veterinary Medicine. Dr. Kidd's clinical and research interests include vector borne disease, the role of undetected infection in immune-mediated diseases, mechanisms of thrombosis in dogs with immune mediated hemolytic anemia, and clinical reasoning. She has collaborative clinical research projects investigating the pathophysiology of immune mediated hemolytic anemia and vector borne disease with internal medicine specialty practices in Southern California, North Carolina State University and The University of North Carolina at Chapel Hill. She is the recipient of the Pfizer Award for Teaching Excellence and the Monica Menard award for Pathobiological Research and recently served as Co-Chair of the American College of Veterinary Medicine's Consensus Panel on the Diagnosis of Immune-mediated Hemolytic Anemia in Dogs and Cats.

PRESENTATION ABSTRACT

To understand immune-mediated disease it is important to understand immune-mediated health. To be immune to a pathogen is to maintain homeostasis in the face of a threat. Previously, it was thought that the role of the immune system was to recognize, target and eliminate what is foreign while preserving what is self. Indeed, virulent microorganisms are overt "foreign" threats that the immune system recognizes and eliminates. However, numerous microbes, like those that make up the microbiome, are helpful rather than harmful. In addition, for cells like red blood cells (RBCs), the immune system must target self-antigens in a controlled manner to remove senescent cells. Therefore, immunity is not targeting what is foreign and preserving self, but rather targeting what is harmful and preserving what is healthy. When the complex homeostatic balance in immune function is disrupted, immune-mediated disease results. Numerous immunoregulatory mechanisms prevent self-attack by the immune system. Genetic, epigenetic, and environmental factors play a role in immune dysregulation and disease development. Infections are important environmental factors that may trigger immune-mediated disease. This includes true autoimmunity where the immune response inappropriately targets self-antigen, and less specific damage that occurs as a result of the immune response.

Vector-borne infections are commonly associated with immune-mediated disease in dogs. Anti-RBC and anti-platelet antibodies are common in dogs infected with certain vector-borne disease agents. Anti-nuclear antibodies and anti-neutrophil cytoplasmic antibodies also occur. Furthermore, clinical and laboratory abnormalities caused by vector-borne diseases are essentially identical to those associated with idiopathic immune-mediated diseases such as immune-mediated hemolytic anemia, immune-mediated thrombocytopenia or immune complex glomerulonephritis. In this session, we will review evidence for the association of vector-borne disease with select immune-mediated diseases in the dog, along with the results of recent studies that help determine optimal vector-borne disease screening protocols for dogs with suspected immune-mediated disease.

RECENTLY COMPLETED CHF GRANT – 02285-A: Thrombocytopenia and Occult Vector-Borne Disease in Greyhound Dogs: Implications for Clinical Cases and Blood Donors

Notes:

Emergence of Canine Leptospirosis: Coming Soon to a Puddle Near You?

Jason Stull, VMD, MPVM, PhD, DACVPM

BIOGRAPHY

Dr. Jason Stull is an Assistant Professor at The Atlantic Veterinary College in Prince Edward Island, Canada and The Ohio State University, College of Veterinary Medicine in the US. He holds a veterinary degree from the University of Pennsylvania, Master's degree in Preventive Veterinary Medicine from the University of California at Davis, and PhD in veterinary infectious disease from the University of Guelph. Over the past 15 years, he had been involved in controlling and preventing veterinary infectious diseases. His research focuses on veterinary infectious disease epidemiology, with an emphasis on preventing canine leptospirosis and canine Lyme disease.

PRESENTATION ABSTRACT

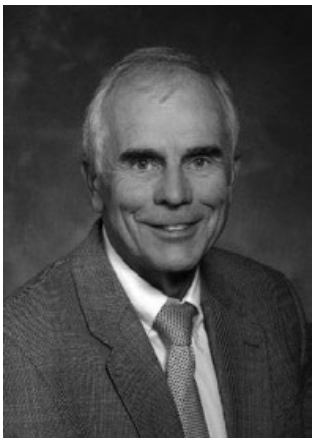
Over recent years, leptospirosis has received increased attention regarding its emergence and spread in dogs throughout North America. Dogs infected with the disease-causing bacterium can show a wide spectrum of signs, creating diagnostic challenges for owners and veterinarians. Many infected dogs experience severe, life-threating disease for which urgent care is required. Owners and others in-contact with infected dogs can likewise be infected with severe health consequences. This talk will review current knowledge of canine leptospirosis in North America. Highlights from recent research by the author into the epidemiology of this disease in the United States and Canada will be provided.

CURRENT CHF GRANTS

- 02284-A: Lyme Disease in Dogs: Prevalence, Clinical Illness, and Prognosis
- 02380-A: Estimating Prevalence and Identifying Risk Factors for Canine Leptospirosis in North America
- 02532-A: Canine Influenza: Occurrence, Spatial and Temporal Trends and Identifying Modifiable Factors to Reduce Transmission at Events in the United States

Notes:

The genus *Bartonella* and Vasoproliferative Cancers in Dogs and Humans



Edward B. Breitschwerdt, DVM, DACVIM (Small Animal Internal Medicine)

BIOGRAPHY

Dr. Edward Breitschwerdt is professor of medicine and infectious diseases and the Melanie S. Steele Distinguished Professor of Medicine at North Carolina State University (NCSU) College of Veterinary Medicine. He is also adjunct professor of medicine at Duke University Medical Center, and a Diplomate, American College of Veterinary Internal Medicine (ACVIM). Dr. Breitschwerdt directs the Intracellular Pathogens Research Laboratory in the Comparative Medicine Institute at NCSU, and co-directs the Vector Borne Diseases Diagnostic Laboratory and is the director of the NCSU-CVM Biosafety Level 3 Laboratory. A DVM graduate of the University of Georgia, Breitschwerdt completed an internship and residency in Internal Medicine at the University of Missouri. He has served as president of the Specialty of Internal Medicine and as chairperson of the ACVIM Board of Regents. He was a founding member of the ACVIM Foundation. Breitschwerdt's clinical interests include infectious diseases, immunology, and nephrology. His research has emphasized vector-transmitted, intracellular pathogens, and his research group has contributed to research in the areas of animal and human bartonellosis, authored numerous book chapters and proceedings, and published more than 350 manuscripts in peer-reviewed scientific journals. His awards include the NCSU Alumni Association Outstanding Research Award, the Holladay Medal, the highest award bestowed on a faculty member at NCSU, the American Association of Veterinary Medical Colleges Outstanding Research Award and the AKC Canine Health Foundation Asa Mays,DVM Excellence in Research Award.

PRESENTATION ABSTRACT

Bartonella species are highly fastidious, vector borne, zoonotic bacteria that cause persistent intraerythrocytic bacteremia and endotheliotropic infection in reservoir and incidental hosts. Three *Bartonella* spp., *B. bacilliformis*, *B. henselae*, and *B. quintana* were known to induce proliferation of endothelial cells *in vitro*, and each species has been associated with vasoproliferative tumors in human patients. We documented that the canine adapted *Bartonella* sp., *B. vinsonii subsp. berkhoffii* induces activation of hypoxia inducible factor-1, resulting in production of vascular endothelial growth factor, thereby providing mechanistic evidence as to how these bacteria could contribute to the development of vasoproliferative lesions in dogs and humans. Hemangiosarcoma (HSA) accounts for the majority of canine malignant splenic tumors and occurs most often in several of the most popular large breeds including Boxers, German Shepherds, and Golden Retrievers. A less common site of HSA localization is the heart (cardiac HSA). Risk factors for cardiac and splenic HSA remain unclear, confounding development of preventative strategies. Previously, we reported a high prevalence of *Bartonella* spp. in dogs with HSA from North Carolina, suggesting a potential role in the initiation and/or progression of this cancer. *Bartonella* species exist worldwide and are transmitted by blood-sucking arthropods (e.g. ticks, fleas). Their presence in splenic tissue could potentially be explained by the fact that the spleen is primarily responsible for removal of blood-borne parasites from the systemic circulation. In our current AKC Canine Health Foundation funded research, we are comparing the prevalence of *Bartonella* DNA in tumor and blood samples from both splenic and cardiac HSA cases. We will also determine the prevalence of *Bartonella* within and between distant geographical locations in the US. Ultimately, demonstration of a

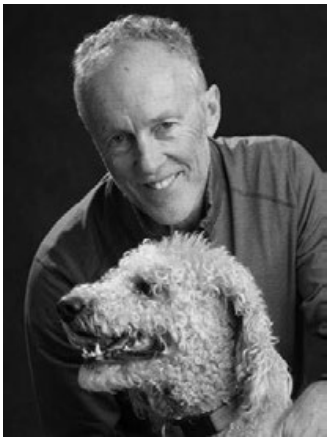
robust association between *Bartonella* infection and the development of HSA may lead to new opportunities for improved diagnosis, treatment and prevention of this devastating cancer.

CURRENT CHF GRANTS

- 02287: Enhanced Testing for the Diagnosis of Bartonellosis in Dogs
- 02519: Prevalence of *Bartonella spp*. Infection in Dogs with Cardiac and Splenic Hemangiosarcomas Within and Between Geographic Locations
- 02550: The Role of *Bartonella spp*. Exposure and Cardiac Genetic Variation on the Clinical Expression of Arrhythmogenic Right Ventricular Cardiomyopathy in the Boxer Dog

Notes:

Advances in Cancer Immunotherapy



Steven Dow, DVM, PhD, DACVIM (Small Animal Internal Medicine)

BIOGRAPHY

Dr. Steve Dow received his undergraduate degree at the University of Virginia, followed by his DVM training at the University of Georgia. This was followed by an internship at Angell Memorial Animal Hospital in Boston, and then residency and board certification in small animal internal medicine at Colorado State University (CSU). He then went on to complete a PhD program in comparative pathology in the laboratory of Dr. Ed Hoover at CSU, where he studied the immunopathogenesis of FIV infection. Dr. Dow then completed a post-doctoral fellowship in the laboratory of Dr. Terry Potter at National Jewish Hospital in Denver, where he investigated cancer immunotherapies and T cell responses. Following an instructorship at National Jewish Hospital, Dr. Dow joined the faculty at CSU in the Department of Clinical Sciences, where he works as a small animal internal medicine faculty member. Dr. Dow also directs several active research programs, including a program in cancer immunotherapy at the Flint Animal Cancer Center, as well as programs in infectious disease immunotherapy and stem cell therapy in the Translational Medicine Institute at CSU. For recreation, he enjoys many outdoor activities, especially cycling, with his wife Dr. Robyn Elmslie and their children, as well as their multiple dogs and a cat.

PRESENTATION ABSTRACT

Recent advances in cancer immunotherapy are dramatically transforming the human oncology field, and these advances are beginning to be felt in the veterinary oncology field as well. This presentation will provide a concise review of where the immunotherapy advances have been made, an explanation for how these therapies work mechanistically, and how these therapies can be most readily applied clinically. Specific topics to be covered include immunotherapies based on activation of the host innate immune response, immune therapies designed to alter the immune suppressive tumor microenvironment, checkpoint molecule targeted immunotherapies, and cancer vaccines. Examples of how these immunotherapies are being employed clinically will also be presented and discussed.

CURRENT CHF GRANT – 02487: OX40 Checkpoint Molecule Targeted Antibodies for Cancer Immunotherapy in Dogs

Notes:

Propranolol and Hemangiosarcoma: Can We Use an Old Drug to Learn New Tricks?

Erin Dickerson, PhD

BIOGRAPHY

Dr. Erin Dickerson received her BS in biochemistry from the University of California-Davis in 1989, and completed her PhD in biochemistry from the University of Wisconsin-Madison in 1997. She then completed her post-doctoral training and spent time as research scientist at the School of Veterinary Medicine in Madison, where she developed novel targeted drug approaches to treat cancer. In 2005, she became an Associate Scientist at the Ovarian Cancer Institute, Georgia Institute of Technology in Atlanta Georgia. Here she worked with several groups to develop targeted nanoparticles as vehicles to deliver drugs to cancer cells. In 2009, Dr. Dickerson joined the faculty at the University of Minnesota and is now an Associate Professor at the College of Veterinary Medicine and the Masonic Cancer Center. Dr. Dickerson's research focuses on the development of drug resistance by cancer cells, and the creation of new strategies to overcome this problem in cancer patients. She has spent the past decade developing a research program devoted to studying canine hemangiosarcoma, developing new approaches for treatment, and using it as a model for human disease.

PRESENTATION ABSTRACT

Propranolol is a beta-adrenergic receptor antagonist, or beta blocker, commonly used to treat heart disease. It is also a promising new agent for the treatment of human angiosarcoma, where its use has increased overall patient survival when combined with chemotherapy. While preliminary results showing that the addition of propranolol to chemotherapy protocols for the treatment of canine hemangiosarcoma are encouraging, the mechanism of action of propranolol on these tumors remains largely unknown. We have undertaken several studies to understand how propranolol inhibits tumor growth and whether it enhances the effects of chemotherapy. As a single agent, propranolol appears to exert its effects via beta adrenergic receptor-independent mechanisms by disrupting intracellular vesicular transport and blocking essential metabolic pathways needed for tumor cell survival. Propranolol also blocks the ability of the tumor cells to take up nutrients from the tumor microenvironment, further limiting access to vital metabolites needed for tumor growth. When combined with the chemotherapy drug, doxorubicin, propranolol enhances the effects of the chemotherapy agent by increasing drug concentrations within tumor cells. The results from these studies are guiding the translation of propranolol into clinical practice and informing future studies with other beta blocker and chemotherapy combinations.

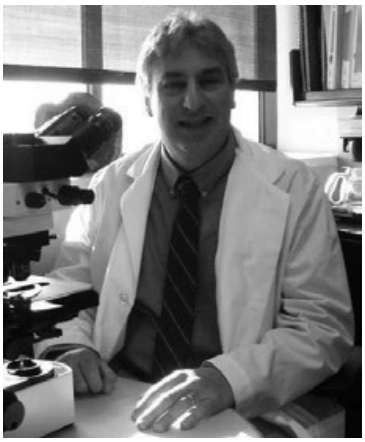
CURRENT CHF GRANTS

- 02534: Clinical Trial for Evaluation of Propranolol and Doxorubicin in the Treatment of Canine Hemangiosarcoma
- 02234-MOU *(Co-investigator):* A Novel Approach for Prevention of Canine Hemangiosarcoma

Notes:

Two Decades of Advances in Canine Hemangiosarcoma. The Light at the End of the Tunnel is Getting Brighter, and It's Not a Train!

Jaime F. Modiano, VMD, PhD



BIOGRAPHY

Dr. Jaime Modiano completed his veterinary training and PhD in Immunology through the Veterinary Medical Scientist Training Program at the University of Pennsylvania, followed by a residency in Veterinary Clinical Pathology at Colorado State University and a post-doctoral fellowship at the National Jewish Center for Immunology and Respiratory Medicine. He served on the faculty of Texas A&M University and the University of Colorado Health Sciences Center before joining the University of Minnesota. Dr. Modiano holds the Alvin and June Perlman Endowed Chair of Animal Oncology and is the Director of the Animal Cancer Care and Research Program of the College of Veterinary Medicine and the Masonic Cancer Center at the University of Minnesota. Dr. Modiano served as Director of Cancer Immunology and Immunotherapy for the Donald Monk Cancer Research Foundation. He is the Managing Partner for Veterinary Research Associates, LLC, and he was a founder of ApopLogic Pharmaceuticals, Inc, and of Half Moon Bay Biotechnology, LLC. Through his laboratory research, Dr. Modiano seeks to understand how and why cancer happens and to translate basic research into clinical applications that improve the health and wellbeing of companion animals and humans. His research has been supported by federal and private sources without interruption for 25 years. He has co-authored more than 500 scientific papers, abstracts, presentations, and book chapters focused on immunology, cancer biology and genetics, and therapeutic innovations for cancer.

PRESENTATION ABSTRACT

Our understanding of hemangiosarcoma has evolved significantly over the past 20 years of study. We now believe that hemangiosarcomas (HSA) arise from cells related to bone marrow nurse cells that support formation of blood cells and blood vessels. The signaling pathways that govern HSA cell behavior promote many of the biological processes associated with the disease, including disorganized growth, motility, invasion, and recruitment of inflammatory cells. However, the therapeutic opportunities for compounds that block these signals are limited because none of these factors are essential for tumor survival once the cells have organized into a malignant tissue. We have characterized three distinct molecular subtypes of HSA based on their transcriptional programs. We have also identified unexpected clonal relationships and patterns of metastasis in HSA, suggesting that multiple tumors might have independent origins, although the tumor microenvironment might also influence the evolution of each tumor.

While breed predilections are reported for this disease, HSA can happen in any dog of any breed and any age. Mutations that contribute to these tumors are indistinguishable among dogs of different breeds, and breed of origin similarly does not influence the biological behavior of the tumors or the response to treatment. We have spent considerable effort on developing new approaches to manage HSA. Our recent emphasis, exemplified by the Shine On study is to develop tests that provide a diagnosis early enough in the process of disease, when treatments might be most effective, and pairing these tests with rationally designed therapies, in essence creating a path for canine precision medicine. Our ultimate goal is that treatment becomes prevention, delaying or eliminating the probability that the cancer cells will ever form

a tumor. This presentation will summarize our past two decades of work in HSA, culminating with an update on data from the ongoing Shine On study.

CURRENT CHF GRANTS

- 02655-E: 2019 Clinician-Scientist Fellowship - University of Minnesota
- 02234-MOU: A Novel Approach for Prevention of Canine Hemangiosarcoma

Notes:

Harmonization of Genetic Testing and Breed-Specific Resources

Brenda Bonnett, DVM, PhD

BIOGRAPHY

Dr. Brenda Bonnett qualified as a veterinarian at the University of Guelph, in Canada. After many years as a tenured Associate Professor at the Department of Population Medicine, Ontario Veterinary College, University of Guelph, she is now a Consulting Epidemiologist and CEO of the non-profit International Partnership for Dogs (IPFD). The IPFD Harmonization of Genetic Testing in Dogs is an international initiative to support quality, robust genetic testing on the IPFD platform DogWellNet.com involving many stakeholder organizations for dog health and welfare. Brenda is a frequent speaker at local, national and international venues to breeders, show judges, veterinarians, researchers and others. Her research projects in Europe and North America have involved numerous species and disciplines, including, e.g., theriogenology, population-based research using secondary data sources (most notably a large companion animal veterinary insurance database in Sweden), breed-specific health risks, human–animal interactions and medical communication. As Lead Scientist at Morris Animal Foundation (2010) she assisted in development of the (now titled) Golden Retriever Lifetime Study.

PRESENTATION ABSTRACT

How do breed clubs keep up with new developments in genetic testing, evaluate/prioritize recommendations, determine which test providers (labs) are best? And then – how do they also consider all conditions of importance in the breed – beyond those with a genetic test? These complexities challenge breed clubs. The International Partnership for Dogs (IPFD) is developing tools and resources to provide practical support to the dog breeding community and enhance collaboration across researchers, veterinarians, and breed and kennel clubs. This presentation will describe the latest developments and new projects for 2019. The IPFD, with our Partners (national kennel clubs, animal industries, veterinary, academic, welfare and other organizations), including the AKC Canine Health Foundation, has developed a practical and effective tool, the Harmonization of Genetic Testing for Dogs (HGTD); which is firstly a database of genetic test providers (GTPs) who are voluntarily sharing details about their 'quality'. This transparency allows for critical evaluation of tests and test-providers. The HGTD contains information on ¨300 tests, from 30 major GTPs for 400+ breeds. The HGTD is on DogWellNet.com together with an increasing body of information to support genetic counseling. Further developments planned for 2019 include: a) the Expert Panel program to provide collective advice on issues/controversies of genetic testing from internationally renowned experts; b) the Health Strategies Database for Dogs (HSDD) including all conditions for which testing is recommended by, e.g. kennel clubs or breed clubs, and searchable by source, breed, condition, country. Outputs will be tailored to the end-user, e.g. to support breed clubs, veterinary-client communication, or individual consumers. With these resources, IPFD plans to launch a proposed program to create comprehensive breed-specific packages that describe the health picture for breeds both nationally and internationally, including breed-specific recommendations for health testing.

CURRENT CHF GRANT – 02328-A: Harmonization of Genetic Testing for Dogs

Notes:

Cardiac Disease of Purebred Dogs - Genetics & Beyond

Joshua A. Stern, DVM, PhD, DACVIM (Cardiology)

BIOGRAPHY

Dr. Joshua Stern is an associate professor of cardiology at the University of California, Davis. He is the Small Animal Clinic Director for the Veterinary Medical Teaching Hospital at UC Davis and is a member of the Center for Companion Animal Health. His clinical interests include mechanisms of arrhythmia, inherited heart disease and medical management of cardiac disease. Dr. Stern is an active researcher in veterinary cardiology, canine & feline genetics and pharmacogenomics. He operates a cardiac genetics laboratory that trains graduate students in addition to cardiology residents. Dr. Stern has authored more than 70 publications and frequently lectures internationally on the topics of veterinary cardiology and genetics. He is an associate editor for the Journal of Veterinary Cardiology and a Small Animal Advisory Board Member for the Morris Animal Foundation. He is a graduate of The Ohio State University College of Veterinary Medicine where he also completed a small animal rotating internship. Dr. Stern completed his cardiology residency through North Carolina State University and earned his PhD through research and graduate studies with the Washington State University Veterinary Cardiac Genetics Laboratory.

PRESENTATION ABSTRACT

This presentation will focus on common cardiac disease in purebred dogs. The incidence of congenital cardiac disease and cardiomyopathy is high within purebred dog populations. Much of this may be owed to genetics and some have indeed been proven and provided breed enthusiasts with a tool to reduce the incidence of disease. Others have been more elusive and may represent complex patterns of inheritance or document the intersection of genetics and environment. Late-breaking updates on our team's research into inherited heart disease in dogs will be discussed.

CURRENT CHF GRANTS

- 02327-MOU: Identification of Genetic Markers for Familial Subvalvular Aortic Stenosis in Bullmastiffs
- 02388-MOU: Genetic Markers for Familial Subvalvular Aortic Stenosis in Newfoundlands
- 02520-MOU: Identification of Genetic Markers for Familial Subvalvular Aortic Stenosis in Rottweilers
- 02521-MOU: Identification of Genetic Markers for Familial Subvalvular Aortic Stenosis in Golden Retrievers
- 02424: Identification of Genetic Variants Associated with Pulmonary Valve Stenosis in Bulldogs through Whole-Genome Sequencing

Notes:

Understanding Dog Breeds as Populations

Jerold S. Bell, DVM

BIOGRAPHY

Dr. Jerold S. Bell is Adjunct Professor of Genetics at the Cummings School of Veterinary Medicine at Tufts University. He was trained in genetics and genetic counseling at Michigan State University and University of Missouri and received his DVM from Cornell University. Dr. Bell is Chairman of the Hereditary Diseases Committee of the World Small Animal Veterinary Medical Association, on the Board of Directors of the OFA, and the AKC Canine Health & Welfare Advisory Panel. He is author of "Veterinary Medical Guide to Dog & Cat Breeds". Dr. Bell practices small animal medicine at Freshwater Veterinary Hospital in Enfield, CT. Dr. Bell and his wife Candice breed and show Gordon Setters in conformation, hunt test, obedience, and dock diving.

PRESENTATION ABSTRACT

Dog breeds are like different ethnic populations of people. All people on earth are humans (*Homo sapiens*), but we are not all closely related. Ethnic populations originally arose due to geographic isolation. There are some mutated genes (and hereditary diseases) that are shared by different ethnic populations. These mutations occurred a long time ago in distant ancestors that preceded population migrations and the separation of ethnic populations. In some ethnic populations certain common genetic diseases occur at a higher frequency (like high blood pressure and diabetes).

The same thing occurs in purebred dog populations. Dog breed populations are like early isolated human populations. The most common genetic diseases that are seen by veterinarians every day in practice are due to ancient liability genes that originated in ancestors that preceded the separation of breeds. They occur in both purebred and mixed breed dogs. These include allergies, hip dysplasia, heart disease, cruciate ligament disease, slipping kneecaps, cataracts, hereditary cancers and others. Breed-specific genetic disorders are due to more recent mutations. For many genetic disorders genetic tests are available to identify carriers. For others, genetic screening will differentiate normal from affected dogs.

People decide which dogs get bred, and which get bred to each other. This is the difference between artificial selection and natural selection. If artificial selection does not select for health, then there can be no expectation of genetic health. If artificial selection selects for breed characteristics or linked traits that impair health, then breed-related disease is the natural outcome. Dog breeding is all about selection. The selection against disease-causing genes is the only way to reduce the transmission of genetic disease. If all breeders include pre-breeding genetic screening in mate selection, then America's dogs will be healthier. All dogs deserve to live healthy lives.

UNDERSTANDING BREEDS AS POPULATIONS

Jerold S. Bell DVM jerold.bell@tufts.edu
Cummings School of Veterinary Medicine at Tufts University

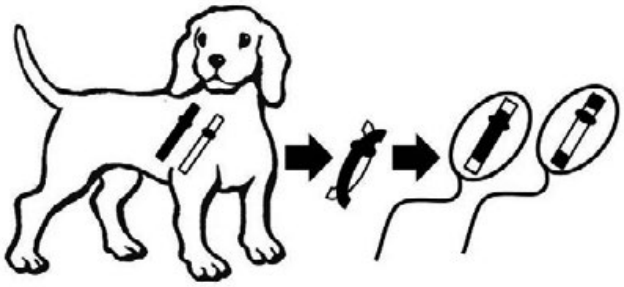
Dog breeds are like different ethnic populations of people. All people on earth are humans (Homo sapiens), but we are not all closely related. Ethnic populations originally arose due to geographic isolation. There are some mutated genes (and hereditary diseases) that are shared by different ethnic populations. These mutations occurred a long time ago in distant ancestors that preceded population migrations and the separation of ethnic populations. In some ethnic populations certain common genetic diseases occur at a higher frequency (like high blood pressure and diabetes). Some ethnic populations are prone to certain genetic diseases that are seen very rarely in other populations.

The same thing occurs in purebred dog populations. Dog breed populations are like early isolated human populations. The most common genetic diseases that are seen by veterinarians every day in practice are due to ancient liability genes that originated in ancestors that preceded the separation of breeds. They occur in both purebred and mixed breed dogs. These include allergies, hip dysplasia, heart disease, cruciate ligament disease, slipping kneecaps, cataracts, hereditary cancers and others. Breed-specific genetic disorders are due to more recent mutations. For many genetic disorders, validated genetic tests are available to identify carriers. For others, genetic screening and medical history differentiate normal from affected dogs.

BREED FORMATION & CHROMOSOMAL INHERITANCE

Breeds were formed by selecting for a working, behavioral and/or conformational standard. Dogs that did not adhere to a standard or were unhealthy were discarded. Those that did adhere were used for breeding. As only a small number of dogs are used to produce the next generation, rapid change can occur in the breed's genetic background. Dogs that embody and produce health and quality were considered superior to the standard and their offspring were used more frequently. Their genes were retained and propagated in the breed gene pool. Dogs that produced offspring that were unhealthy or inferior to a standard were not used. Their influence and that of their ancestors was diminished.

Dogs have 39 pairs of chromosomes – one in each pair from its sire and one from its dam. Dogs used for breeding supply one chromosome from each pair to every offspring. Due to chromosomal crossovers during meiosis producing sperm or eggs, each chromosome can include a mixture of chromosomal segments from its two parents. When genes are selected, the chromosomal segment (haplotype block) containing the gene is inherited along with many other "linked" genes in the segment. Selection for positive traits will cause the inheritance of a chromosomal segment from the parent(s) containing causative genes. Selection against deleterious traits or diseases will cause the loss of a chromosomal segment containing causative genes. As meiotic crossovers occur producing sperm and eggs through the generations, the size of the chromosomal segment containing genes under positive and negative selection can get smaller.



Chromosomal crossover during meiosis forming sperm or eggs can mix maternal and paternal segments on each chromosome.

As ancestors and dogs who pass on positive traits to the breed are linebred on (appearing in both the sire and dam's sides of the pedigree) this can cause haplotype blocks to pair up - causing runs of

homozygosity (ROH). Even without close linebreeding, selection for positive traits will increase their homozygosity having originated from distant ancestors. Breed-defining genes would be expected to be collected in runs of homozygosity due to selection over time.

Deleterious (primarily recessive) mutated genes can accumulate in the background of the breed gene pool. These accumulate primarily because they are not expressed in the heterozygous (carrier) state. Deleterious genes can increase in frequency if linked to positively selected genes, or through genetic drift. An increasing frequency of breed-related disease will be due to homozygosity of deleterious recessive or additive liability genes. Individual liability genes can cause embryonic death (thus resulting in smaller litter size or infertility), increased neonatal death, or breed-specific genetic disease. This is due to the expression of specific deleterious genes and not a general result of increased homozygosity.

If disease liability genes are linked in haplotype blocks to positively selected genes, then dogs that demonstrate the positive traits and do not carry the disease-liability genes should be selected for breeding. These dogs can occur due to phenocopies (selected traits due to other genetic causes), or due to meiotic chromosomal crossovers that break the linkage between the positive and disease-liability genes. If the positive and deleterious genes cannot be separated due to tight linkage (adjacent genes or even multiple effects of the same gene) then this is not a healthy breed standard. The standard may need to be changed, achieved through other selected genes or possibly through crossbreeding.

As breeds develop and reproduce to a standard, their genetic difference from other breeds increases. Runs of homozygosity for breed-defining traits and quality genes is a positive development, even though it results in a loss of genetic diversity from genes that do not reproduce a standard or maintain health. The genetic diversity between breeds is large. This is why pure breeds can be separated by their DNA signatures. Breed subgroups (conformation versus working or breed populations on different continents) can also be differentiated based on their DNA. This can provide an important source of breed genetic variation if needed. The genetic diversity within the breed should be small, so that the breed reproduces itself to a healthy standard. This is the “big picture” of genetic diversity in dog breeds.

The fine detail of genetic diversity within a breed concerns maintaining a healthy phenotype and reproductive ability. Dogs from the breadth of the gene pool should be used for breeding as long as they represent health and quality. Restricted genetic diversity is not an issue in pure breeds, unless there is no alternative direction to go for health and quality.

DIFFERENCES BETWEEN BREEDS AND SPECIES

The force of species evolution is natural selection - the ability to thrive and reproduce within the species’ environment. Artificial selection that could be detrimental to species survival is not an issue in the wild. Genetic isolation can create subspecies (often with multiple isolation events) and can cause random genetic changes due to genetic drift.

Endangered species can share several population parameters with breeds. Their population size is usually small, and they have a closed population. In many instances, there is a limited foundation base (founder genome equivalent). Endangered species can experience decreased fertility and ability to thrive due to both genetic and environmental variation.

Genetic disease in endangered species occurs primarily through genetic drift. This is the random accumulation of disease liability genes in the absence of selection. As carriers of recessive and additive disease liability genes are healthy, they are not selected against and their genes are propagated in the

offspring. Who reproduces in the population is random, and if carriers reproduce, the liability genes are passed on. When recessive disease liability genes pair up, or when additive genes combine to cross a threshold, clinical disease results.

Species survival plans (SSPs) were developed by population geneticists working with rare and endangered species who have a limited number of available breedable individuals. With the assumption that avoidance of homozygosity of deleterious recessive genes provides for the healthiest and robust offspring, SSPs are designed to mate the most unrelated individuals together (through pedigree or molecular genetic markers). This hopefully limits the expression of recessive disease-causing genes. SSPs also work to maintain the breadth of genetic diversity (evaluating the rareness or commonness of genetic background) in the species population. The only individual selection in SSP systems is to not breed unhealthy animals. However, if an unhealthy animal represents a unique genetic background it could still be used in matings to maintain genetic diversity. The goal of an SSP is successful reproduction with the production of healthy, live offspring representing the diverse background of the species.

Purebred breeding requires constant (artificial) selection for positive traits including health, and against negative traits and disorders. Without constant selection for specific breeding goals and their associated genes, the health and quality of the offspring will decline. The ability of selective pressure to create change in the population is limited by the amount of variation that is present for the selected trait in the breed. Selecting for heterozygosity as a goal and mating the least related parents together, erases the differences between dogs in the breed that are required for selection. This limits the ability to apply selective pressure for improvement. As a breeder selects for more goals in any mating, the amount of selective pressure for each individual goal diminishes. I.e., it is easier and more productive to select for one to three goals at one time than for eight or nine goals. Any selective pressure (selection goal) that is not specifically directed toward health and quality will diminish the selective pressure for both.

SSP breeding systems are not appropriate for pure breeds. Only outbreeding for the most heterozygous dogs randomizes the positive and deleterious genes in the gene pool. Breed-specific genetic disorders are caused by liability genes that are already dispersed in the breed's gene pool. Outbreeding will not decrease the frequency of these genes in the population. The clinical occurrence and frequency of such disorders will not diminish based on outbreeding versus linebreeding. The disorder will just appear randomly in offspring from different matings. Outbreeding and linebreeding are tools, not goals. There are specific reasons for using either in planned matings.

IMPROVING BREED POPULATION HEALTH THROUGH HEALTH CONSCIOUS BREEDING

Purebred dog breeds were developed through artificial selection when dedicated breeders judiciously purged dogs and their genes from the breed gene pools if they were unhealthy or did not perform to a standard. Somewhere along the way, the responsibility to select for health and produce healthy offspring disappeared from dog breeding. Today, people just breed dogs and expect healthy offspring.

People decide which dogs get bred, and which get bred to each other. This is the difference between natural selection and artificial selection. If artificial selection does not select for health, then there can be no expectation of genetic health. If artificial selection selects for breed characteristics that impair health, then breed-related disease is the natural outcome. Dog breeding is all about selection.

In the planning of any proposed mating, the selection of healthy parents is paramount to the health of the offspring. A pre-breeding health examination includes phenotypic examination of the major organ systems for; musculoskeletal, cardiac, ophthalmologic, gastrointestinal, pulmonary, dermatologic and

behavioral abnormalities. Medical history should be examined for episodic inherited disease that cannot be identified on examination; i.e., allergies, seizures, bloat, bladder stones, cruciate ligament disease, etc. Dogs demonstrating hereditary disease should be selected against for breeding.

Pure breeds can also have breed-specific genetic disease due to more recent mutations. For many of these there are breed-validated genetic tests that can identify causative or disease liability genes, or genetic screening to identify affected dogs. The OFA Canine Health Information Center (www.ofa.org) and the AKC Bred With H.E.A.R.T. program (http://www.akc.org/breeder-programs/akc-bred-with-heart-program/) both have breed-specific genetic testing requirements that have been determined by the parent breed club. All prospective breeding dogs should undergo a veterinary pre-breeding health assessment that covers screening and medical history evaluation for all common and breed-related genetic disorders. **If all breeders include pre-breeding genetic screening in mate selection, then America's dogs will be healthier.**

The advent of multiplex genetic panel testing (Mars Wisdom Health, Embark, etc.) provides genetic test results for over 180 canine traits and disorders. Unfortunately, most of the disease liability genes tested for in these panels are breed specific. **Unless the gene(s) have been validated to cause clinical disease in other breeds or mixed breeds, the test result may not have any significance in your dog.** In addition, the panel tests utilize SNPs (single nucleotide changes) instead of testing for a mutation, so false positive and negative results can occur. **Breeding decisions regarding breed-validated liability genes should be based on direct mutation and not SNP testing.**

Typical genetic counseling recommendations utilize the breeding of quality carriers to non-carrier dogs and replacing the carrier parent with a quality non-carrier offspring. In this way breeding lines (and breed genetic diversity) are not abandoned and testable disease liability genes can be lost in one generation. If a valid genetic test is not available then selection should be based on genetic screening and open health databases that identify relative risk of carrying disease liability genes.

Health conscious breeders are fulfilling their ethical responsibilities to produce healthier dogs. If a breeder is not willing or able to provide official health screening results for the parents of litters, then BUYER BEWARE! There will be no expectation of genetic health in the puppies. Without evidence of pre-breeding genetic screening, health guarantees that provide for a replacement of a family member once the emotional bonds have been made are worthless. It is only a piece of paper written to excuse a breeder from performing their ethical responsibility of pre-breeding health screening.

There are many conversations concerning issues with dog breeding in America. Many people prefer the predictable characteristics of purebred dogs. The "Adopt, Don't Shop" movement promotes rescuing a dog from a shelter instead of buying from a breeder. The fact is that there isn't even a fraction of rescue dogs available to provide canine companionship to America's families. This has created the "bred for rescue" industry. Dogs will continue to be bred so that they can be our faithful companions. **If any purebred or mixed-breed mating is being planned, health-conscious breeding through pre-breeding health examination, genetic screening and genetic testing should be performed.** If the public demands health-conscious breeding then the issue of genetic disease in dogs will change.

"All dogs deserve to live healthy lives."
Quote from William J. Feeney, Chairman of the AKC Board of Directors.

Notes:

Development and Utilization of a Genetic Risk Assessment for a Multifactorial Disease

Leigh Anne Clark, PhD

BIOGRAPHY

Dr. Leigh Anne Clark earned her doctoral degree in 2004 from Texas A&M University, studying the genetic basis of canine exocrine pancreatic insufficiency. She continued at Texas A&M as a Research Assistant Professor, investigating the genetics of merle coat patterning and the autoimmune disease, dermatomyositis. In 2009, she moved her laboratory to Clemson University where she is an Associate Professor of Genetics and Biochemistry. Her current research concerns congenital idiopathic megaesophagus, dermatomyositis, dental abnormalities, and epilepsy.

PRESENTATION ABSTRACT

Dermatomyositis (DMS) is an autoimmune disease of the skin and muscle that primarily affects Collies and Shetland Sheepdogs. DMS has a complex inheritance pattern and a variable age of onset that usually follows an environmental trigger. These factors have made it impossible to breed away from the disease without a genetic test. We genotyped three major histocompatibility complex (MHC) genes, performed a genome-wide association study, and generated next generation sequencing data to identify genetic risk factors. We uncovered genetic variations of the MHC (chromosome 12), *PAN2* (chromosome 10), and *MAP3K7CL* (chromosome 31) that are strongly associated with DMS. Of the 27 possible ways in which alleles at these three loci can be inherited, nine combinations confer moderate to high risk for developing DMS and explain 93% of cases. The pattern of disease probability illustrates an interaction between genes, as well as an inverse correlation between age of onset and number of risk alleles. Environmental triggers and other minor loci also play a role in pathogenesis. Although breeds unaffected by DMS possess the risk alleles, Collies and Shetland Sheepdogs have uniquely high frequencies, likely a consequence of selection for desirable traits. Breeding strategies are, therefore, not focused on eliminating the highly frequent risk alleles, but rather on selecting breeding pairs that will produce puppies with low-risk genotypes.

CURRENT CHF GRANTS

- 02654-E: 2019 Clinician-Scientist Fellowship - Clemson University
- 02263-MOU (*Co-investigator*): Characterization of Kidney Disease in Dalmatians

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