



2017
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Genetic Predisposition to Infections: Avian Tuberculosis in Miniature Schnauzers

Urs Giger, Prof. Dr. med. vet., MS, FVH, Dipl. ACVIM & ECVIM
(Internal Medicine), Dipl. ECVCP (Clinical Pathology)



BIOGRAPHY

Dr. Giger received his veterinary degree from the University of Zürich, Switzerland, where he also pursued his doctoral thesis on the surgical repair of hip dysplasia, initial clinical training in small animal medicine and surgery and postgraduate research work. After moving to the United States, he completed a residency in small animal internal medicine at the University of Florida and then joined the faculty of the School of Veterinary Medicine at the University of Pennsylvania in Philadelphia where he has the endowed Charlotte Newton Sheppard Professor of Medicine chair. He has a secondary professorship in small animal internal medicine at the University of Zürich as well as professorship in hematology at the Medical School University of Pennsylvania. He is a diplomate of the American and European College of Veterinary Internal Medicine, as well as a diplomate of the European College of Clinical Pathology. He headed the Transfusion and Hematology Center and Pediatrics and Genetics Clinic, and is the director of the Metabolic Genetics and the DNA Genetic Disease Testing (PennGen) Laboratories. His clinical and research expertise and interests are in hereditary and hematologic disorders and are reflected in over 230 original research publications as well as many more reviews and scientific abstracts. He is also chairing the World Small Animal Veterinary Association (WSAVA) Hereditary Disease Committee. Among other awards, he was the recipient of a Transfusion Medicine Academic Award and Shannon Award from the National Institutes of Health, the 2002 WSAVA International Scientific Lifetime Achievement Award, the 2007 International Bourgelat Award from the BSAVA and the 2015 AVMA Excellence in Feline Research Award for outstanding clinical research in feline medicine. He is a frequently invited speaker at many national and international conferences.

Current CHF Grant – 2245-MOU: Genetic Predisposition to Avian Tuberculosis in Miniature Schnauzers and Basset Hounds

PRESENTATION ABSTRACT

Dogs with recurring or persistent, antimicrobial-unresponsive and unusual infections likely suffer from a hereditary(primary) immunodeficiency disorder. Immunodeficiencies represent a large heterogeneous group of dysfunctions of host immunity increasing the risk for infections. They can arise through disturbances in antigen-specific defense mechanisms mediated by lymphocytes, the nonspecific defense system (which includes phagocytes, plasma proteins, and physical barriers), or both. Many genetically determined immune defects have been described in the dog, whereas only a few are known in cats. While the clinical signs may be suggestive of a primary immunodeficiency, a definitive diagnosis often requires specific immune testing, in addition to routine laboratory tests. The molecular defects for several primary immunodeficiencies have been elucidated allowing for DNA screening. A few hereditary immunodeficiency disorders are prevalent within certain breeds of dogs, whereas others occur in isolated families/cases. Furthermore, because of the underlying immunodeficiency, the infections are poorly responsive to treatment and often recur; thus, therapeutic interventions are limited.

Diffuse Large B Cell Lymphoma (DLBCL) of Golden Retrievers Has a Unique DNA Methylation Signature That Yields Biomarkers of Disease

Jeffrey Bryan, DVM, PhD, DACVIM-Oncology

BIOGRAPHY

Dr. Jeffrey Bryan's research focuses on comparative examination of cancers in companion animals to better understand cancers in all species. Bryan is an associate professor of veterinary oncology and director of the Comparative Oncology and Epigenetics Laboratory. His particular areas of interest are targeted imaging and therapy and epigenetics of cancer. Targeted imaging and therapy agents take advantage of particular properties of cancer to deliver an imaging or therapy payload to tumors. Bryan is leading research projects studying an immunotherapy agent targeted to the low-oxygen environment of cancer, an herbal derivative that targets iron in tumors, and a nanoparticle chemotherapy targeted to the lymphatic drainage of cancer. The agents under evaluation are destined for use in both dogs and humans to treat lymphomas as well as solid tumors like sarcomas, head and neck cancer, and breast cancer. Each of these trials is designed to develop an approach that is less toxic and more effective than our current cancer treatments.



Dr. Bryan earned a Bachelor of Science degree in veterinary science from the University of California - Davis in 1991. He received his DVM. from the University of California - Davis in 1993. He then worked as an Associate Veterinarian from 1993-1995, and then served as Medical Director of the Irving Street Veterinary Hospital in San Francisco, CA from 1995-2002. Bryan then completed a medical oncology residency, a Masters of Biomedical Sciences, and a PhD in Pathobiology at the University of Missouri. He received certification by the American College of Veterinary Internal Medicine in Oncology 2005. He has been a research assistant professor at the University of Missouri and an assistant professor of Oncology at Washington State University prior to his current post at the University of Missouri.

Current CHF Grant – 1918-G: Discovery of Biomarkers to Detect Lymphoma Risk, Classify for Treatment, and Predict Outcome in Golden Retrievers

Current CHF Clinician-Scientist Fellowship – Mentee: Shirley Chu, DVM

PRESENTATION ABSTRACT

DNA methylation changes are the earliest and most persistent epigenetic mechanism to control gene expression. DNA hypermethylation changes can be reversed, often occur before genetic mutations, and can be more consistent and numerous than mutations in carcinogenesis. The aims of this study were to define the DNA methylation signature of Diffuse Large B Cell Lymphoma (DLBCL) that distinguishes it from normal lymphocytes to develop biomarkers of disease for diagnosis and risk prediction. DLBCL has distinct changes of the methylome from normal B lymphocytes. The methylome in DLBCL is a tumor landscape to be mined for novel early detection biomarkers, therapeutic drug targets and additional depth to our understanding of carcinogenesis.

How Flow Cytometry Expands Our Understanding of Canine Lymphoma

Anne Avery, VMD, PhD

BIOGRAPHY

Dr. Avery completed her PhD in Immunology at Cornell University in 1986. She then attended veterinary school at the University of Pennsylvania where she graduated in 1990. After an internship in small animal medicine, also at Penn, she did post-doctoral training at the Dana-Farber Cancer Institute in Boston, while continuing to practice as an emergency and relief vet. She moved to CSU's college of Veterinary Medicine in 1994 and is now an Associate Professor in the Department of Microbiology, Immunology and Pathology. Dr. Avery is the director of the Clinical Immunology Laboratory at CSU, which uses diagnostic testing to help clinicians diagnose lymphoma and leukemia in canine and feline patients, as well provide prognostic information for many of these cases. Her laboratory's research is directed at using canine and feline lymphoproliferative disorders as models for human disease, and for what they teach us about the biology and function of the immune system.



Current CHF Grant – 2316: Genetic Risk Factors for Canine T-zone Lymphoma

PRESENTATION ABSTRACT

Canine lymphoproliferative diseases include a very broad array of disorders ranging from clinically aggressive (acute leukemia) to indolent diseases with long survival times that may not require treatment (T zone lymphoma). The World Health Organization (WHO) classification system has been applied to canine lymphoproliferative diseases, and studies have demonstrated the value of this system for determining prognosis and more recently, for choosing treatment. A combination of histology/immunohistochemistry and flow cytometry can be used to classify many types of lymphoma into WHO categories, and can provide accurate prognostic information for owners and clinicians. In addition, the development of a large database of different forms of lymphoma has allowed us to identify striking breed-specific predilections which provide the basis for identifying genetic risk factors.

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Chemotherapy and Probiotics

Korinn Saker DVM, PhD, DACVN

BIOGRAPHY

Dr. Saker is currently an Associate Professor of Nutrition and Director of the Nutrition Program at North Carolina State University-College of Veterinary Medicine (NCSU-CVM). She received her MS in Animal Nutrition from Clemson University and her DVM from University of Georgia. Following 5 years in mixed animal general practice she completed a PhD in Nutrition and a Clinical Nutrition Residency at Virginia-Maryland Regional College of Veterinary Medicine. There she spent 12 years as a clinical nutritionist and research professor, before moving to NCSU to initiate a nutrition program at the veterinary school in Spring of 2007. She currently divides her time between clinical work, teaching, running a clinical nutrition training program, and pursuing her research interests in nutrition for health and disease.



PRESENTATION ABSTRACT

Dogs receiving chemotherapy drugs as a treatment for cancer can suffer from gastrointestinal discomfort, including severe diarrhea, lack of appetite, nausea and weight loss. These side effects may discourage the dog's owner from continuing chemotherapy or, if they are severe enough, may require the anticancer drug protocol to be altered in a way that minimizes its effectiveness. The investigators evaluated whether oral probiotic supplementation would prevent or minimize adverse gastrointestinal side effects associated with chemotherapy. Giving patients a natural, nondrug supplement, such as probiotics, may decrease the severity or frequency of gastrointestinal toxicity and inflammation, improve nutritional health and improve the overall quality of life for dogs undergoing chemotherapy. The results were extremely positive suggesting a benefit from oral probiotic supplementation in dogs receiving doxorubicin by mitigating the adverse manifestations of GI toxicity during this type of chemotherapy protocol.

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Bringing Genomic Data Back to The Clinic

Matthew Breen, PhD, CBIOL, FRSB

BIOGRAPHY

Dr. Matthew Breen's research focuses on genomics, genome mapping and the comparative aspects of canine cancer. Over the past decade Dr. Breen and his team have developed a series of genetic tools and applied these to investigate molecular changes in numerous canine cancers. These studies have resulted in the development of molecular assays to enhance diagnosis, early detection and prognosis. Several of these new genetic tests are either available for dog owners or soon will be. Taking a comparative approach, these studies are also advancing what we know about human cancers. Dr. Breen's research interests all include assessment of the genetics of performance in working dogs, and the use of genetic tools to combat illegal animal killing and trafficking through veterinary/wildlife forensics.



Dr. Breen is a Professor of Genomics and the Oscar J. Fletcher Distinguished Professor of Comparative Oncology Genetics in the Dept. of Molecular Biomedical Sciences at the NCSU College of Veterinary Medicine. He is also Associate Director of the NC State Forensic Science Institute, a member of the NCSU Comparative Medicine Institute (CMI) the NCSU Genetics Program in the College of Science, and the Cancer Genetics Program at the University of North Carolina's Lineberger Comprehensive Cancer Center. He serves on the steering committee of the Consortium for Canine Comparative Oncology (C3O), a strategic partnership between NC State College of Veterinary Medicine and the Duke Cancer Institute. Dr. Breen was a charter member, and serves on the Board of Directors, of the Canine Comparative Oncology and Genomics Consortium (CCOGC), a 501c3 not-for-profit organization established to promote the role of the dog in comparative biomedical research, and also serves on the board of directors of the Canines-N-Kids Foundation, a 501c3 committed to finding a cure to the devastating cancers that canines and children face in common. He is also a charter member of the Sea Lion Cancer Consortium (SLiCC) and a founder of Sentinel Biomedical, an NC State company established to bring advanced molecular cancer diagnostics to the broader canine community.

Current CHF Grants – 2317: The Role of Complex Translocations Associated with TP53 Somatic Mutations for Aiding Prognosis of Canine Diffuse Large B-cell Lymphoma

1889-G: Innovations in Prevention, Diagnosis, and Treatment of Cancer - Golden's Lead the Way

PRESENTATION ABSTRACT

The application of genomics to canine biomedical research has resulted in significant advances as we strive to enhance the health and welfare of our companions. Over the past several years we have recruited tumor tissues and blood samples from thousands of dogs presenting with a variety of cancers, as well as their family members. During the same period we generated a series of sophisticated molecular reagents and resources that complete the genomics 'toolbox'. Collectively these tools provided a robust means to interrogate tumor specimens for organizational changes to the genome, which lead to identification of genome regions and genes associated with cancer. We have demonstrated the presence of numerous genetic signatures associated with canine cancer subtypes and are using these to develop more sophisticated means of cancer diagnosis and prognosis. These studies thus provide a path back to the

For example, we identified that 85% of dogs with a transitional cell carcinoma (TCC) have a specific mutation in their cancer cells. We have developed a highly sensitive test to detect these mutant bearing cells in a non-invasive/free catch urine sample from a dog. This test is now being used for 1) early detection of pre-clinical TCC, 2) to confirm diagnosis of TCC in dogs presenting with urinary tract ymptoms, and 3) to monitor the impact of treatment of TCC. In addition we have begun to define genetic lesions that correlate with prognosis. For example, in our work with canine lymphoma we have developed a genetic test that allows us to predict how long dogs diagnosed with lymphoma, at the time of diagnosis, will respond to doxorubicin based chemotherapy. We have also developed a test that can differentiate histiocytic malignancies from other round cell cancers, and a test that can identify the ~20% of dogs with osteosarcoma that have a high chance of survival beyond 18 months if treated with amputation and standard of care chemotherapy.

A brief overview of these studies will be presented.

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The Effects of an Omega-3 Fatty Acid-Rich Diet with Rehabilitation on Recovery, Activity, and Osteoarthritis in Dogs Following Tibial Plateau Leveling Osteotomy Surgery for Cranial Cruciate Ligament Disease

Wendy Baltzer DVM, PhD, DACVS

BIOGRAPHY

Dr. Baltzer graduated with a DVM from UC Davis in 1994. She received her PhD at Texas A&M University in 2003 and became board certified in the American College of Veterinary Surgery following her residency at Texas A&M in 2007. She received board certification as a Certified Canine Rehabilitation Practitioner by the University of Tennessee in 2012 and became a diplomate in the American College of Veterinary Sports Medicine and Rehabilitation-Canine in 2013. From 2005 to 2016, she was an associate professor of small animal surgery and sports medicine at the College of Veterinary Medicine at Oregon State University. She is currently an Associate Professor of small animal surgery at Massey University Institute of Veterinary, Animal and Biomedical Sciences in New Zealand. Her research, which includes over 45 publications, has investigated the effects of oxidant stress on agility exercise in dogs, ligament and tendon injury, augmentation of fracture repair with omentum and the management of osteoarthritis in small animals. She resides in Palmerston North, NZ with her husband, son and daughter, dog and cat.



PRESENTATION ABSTRACT

Can an omega-3 fatty acid rich diet improve recovery and activity of dogs after surgery for cranial cruciate ligament disease? Is rehabilitation of dogs following cruciate ligament surgery worth all the money and hassle? The answer is yes! In a double-blinded (owners and veterinarians were blinded), placebo-controlled clinical trial, which followed the recovery of dogs after cruciate ligament surgery for 6 months, dogs fed Purina® Pro Plan® Veterinary Diets JM Joint Mobility® had reduced lameness, reduced inflammation in the operated joint, and reduced progression of arthritis compared to dogs fed a commercial adult dog food. Owners saw less lameness when the dogs were trotting, running or making sharp turns in the dogs fed Purina JM™ diet. Rehabilitation also improved the dogs' recovery and slowed the development of arthritis. Dogs that had rehabilitation exercise with both home and underwater treadmill treatments were more physically active, even 3 months after treatment, than dogs that did not have postoperative therapy.

Providing a diet rich in omega-3 fatty acids and rehabilitating dogs after surgery for cruciate ligament rupture can have lasting beneficial effects helping dogs to return to a more active, healthy lifestyle.

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Canine Lyme Disease – Is the Clock Ticking?

Jason Stull, VMD, PhD, DACVPM

BIOGRAPHY

Dr. Jason Stull is an Assistant Professor at The Ohio State University, College of Veterinary Medicine. He holds a VMD from the University of Pennsylvania, Masters in Preventive Veterinary Medicine from the University of California at Davis, and PhD in veterinary infectious disease from the University of Guelph. He is a Diplomat of the American College of Veterinary Preventive Medicine. His research focuses on veterinary infectious disease epidemiology, promoting the human-animal bond and preventing and controlling zoonotic infectious diseases in veterinary care, households, and unique environments.



Current CHF Grants – 2284-A: Lyme Disease in Dogs: Prevalence, Clinical Illness, and Prognosis

2380-A: Estimating Prevalence and Identifying Risk Factors for Canine Leptospirosis in North America

PRESENTATION ABSTRACT

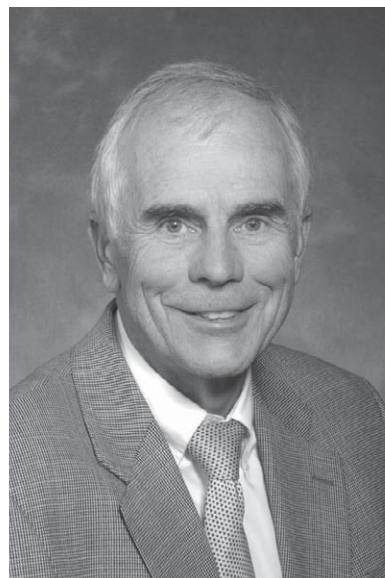
Lyme disease is a poorly understood condition in dogs. The range of *Borrelia*-infected ticks, responsible for transmitting Lyme disease, continues to expand in the US and Canada resulting in many infected dogs. Infected dogs rarely show signs of illness, however, Lyme disease can be severe (e.g., kidney disease). This talk will review our current knowledge of canine Lyme disease risk and forecasted emergence and recommendations for prevention and control. Preliminary results from a large on-going US and Canada study will be presented.

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Bartonellosis: The Dog that Changed the Course of My Research, Career, and Life

Edward Breitschwerdt, DVM, DACVIM*

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



BIOGRAPHY

Dr. Edward B. Breitschwerdt is a professor of medicine and infectious diseases at North Carolina State University College of Veterinary Medicine. He is also an 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 North Carolina State University. He also co-directs the Vector Borne Diseases Diagnostic Laboratory and is the director of the NCSU-CVM Biosafety Level 3 Laboratory. A graduate of the University of Georgia, Breitschwerdt completed an internship and residency in Internal Medicine at the University of Missouri between 1974 and 1977. He has served as president of the Specialty of Internal Medicine and as chairperson of the ACVIM Board of Regents. He is a former associate editor for the Journal of Veterinary Internal Medicine and was a founding member of the ACVIM Foundation.

Breitschwerdt's clinical interests include infectious diseases, immunology, and nephrology. For over 30 years, his research has emphasized vector-transmitted, intracellular pathogens. Most recently, his research group has contributed to cutting-edge research in the areas of animal and human bartonellosis. In addition to authoring numerous book chapters and proceedings, Dr. Breitschwerdt's research group has published more than 350 manuscripts in peer-reviewed scientific journals. In 2012, he received the North Carolina State University Alumni Association Outstanding Research Award and in 2013, he received the Holladay Medal, the highest award bestowed on a faculty member at North Carolina State University. In 2017, Dr. Breitschwerdt received the American Association of Veterinary Medical Colleges Outstanding Research Award.

Current CHF Grant – 2287: Enhanced Testing for the Diagnosis of Bartonellosis in Dogs

PRESENTATION ABSTRACT

***Bartonella* species** are fastidious Gram-negative bacteria that are highly adapted to a mammalian reservoir host and within which the bacteria usually cause a long-lasting, intra-erythrocytic and endotheliotropic bloodstream infection. These facts are of particular importance to veterinarians, physicians, diagnosticians, public health officials, and pet owners as an increasing number of animals have been identified as reservoir hosts for zoonotic *Bartonella* species. Among numerous examples, *Bartonella henselae*, *Bartonella koehlerae* and *Bartonella clarridgeae* have co-evolved with cats, *Bartonella vinsonii* subsp. *berkhoffii* and *Bartonella rochalimae* have co-evolved with dogs and wild canines, and *Bartonella bovis* has co-evolved with cattle. Importantly, the list of reservoir-adapted *Bartonella* species, including a large number of recently identified bat and rodent species, continues to expand exponentially, as new *Bartonella* spp. and additional reservoir hosts are discovered throughout the world.

Bartonellosis is a zoonotic infectious disease of worldwide distribution, caused by an expanding number of recently discovered *Bartonella* spp. Of comparative medical importance, *Bartonella* spp. are transmitted

In 1993, I examined a 3 year-old Labrador retriever that had experienced a chronic, insidious and progressive illness during the preceding 9 months. Dr. Dorsey Kordick, then a Ph. D. student in my research laboratory, successfully isolated a *Bartonella* species from this dog, representing the first time this genus of bacteria was isolated from a dog anywhere in the world. Subsequently, in collaboration with bacteriologists at the Centers for Disease Control and Prevention, the newly isolated bacteria was defined as microbiologically unique and named ***Bartonella vinsonii subsp. berkhoffii***. To a substantial degree, this young retriever and this bacterial isolate served as the foundation for a research program that has generated an important and controversial body of medical evidence related to canine and human bartonellosis. Not only are dogs our best friends, but naturally-infected dogs continue to provide important comparative medical insights that have enhanced our understanding of human bartonellosis.

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Characterization of the Hematologic Response to Ehrlichia canis Infection

Anne Avery, VMD, PhD



BIOGRAPHY

Dr. Avery completed her PhD in Immunology at Cornell University in 1986. She then attended veterinary school at the University of Pennsylvania where she graduated in 1990. After an internship in small animal medicine, also at Penn, she did post-doctoral training at the Dana-Farber Cancer Institute in Boston, while continuing to practice as an emergency and relief vet. She moved to CSU's college of Veterinary Medicine in 1994 and is now an Associate Professor in the Department of Microbiology, Immunology and Pathology. Dr. Avery is the director of the Clinical Immunology Laboratory at CSU, which uses diagnostic testing to help clinicians diagnose lymphoma and leukemia in canine and feline patients, as well provide prognostic information for many of these cases. Her laboratory's research is directed at using canine and feline lymphoproliferative disorders as models for human disease, and for what they teach us about the biology and function of the immune system.

Current CHF Grant – 2295-A: The Role of Lymphocytes in Canine Monocytic Ehrlichiosis

PRESENTATION ABSTRACT

Ehrlichia canis is a rickettsia that infects canine monocytes and causes a variety of unique clinical and hematologic signs, including monoclonal gammopathy and clonal expansion of CD8 T cells. *E. canis* infection can be confounding in dogs with a clinical suspicion of T cell leukemia, because common diagnostic methods (flow cytometry and clonality) may not be able to distinguish between these entities. The goals of this study conducted at Ross University in St. Kitts, where *E. canis* is endemic, were to better define the nature of the hematologic response to naturally acquired *E. canis* infection. This data allows us to diagnose T cell leukemia in clinical situations where patients also have evidence of *E. canis* exposure.

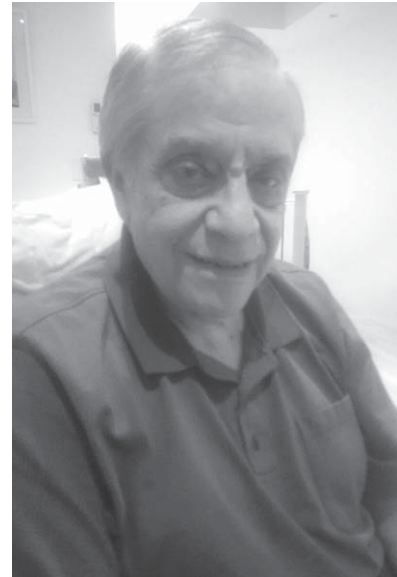
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Canine Cognition: A Neuropsychological Approach

Bill Milgram, PhD

BIOGRAPHY

After completing his undergraduate training at the University of California in 1964 in Psychology, Dr. Milgram went to the McGill University where he received a PhD in 1968 in Physiological Psychology, which is now more commonly known as behavioral neuroscience. Upon graduation, Dr. Milgram completed a two year postdoctoral stint at Princeton and subsequently joined the life science department at the University of Toronto at Scarborough, where he taught behavioral neuroscience from 1970 to 2009. In 1989, his research, which had focused exclusively on rodents, turned towards understanding cognition and aging in dogs and he has published over 100 refereed scientific articles pertaining to canine cognitive aging. In 2002, with a few of his graduate students, he started a company, CanCog technologies, that was focused on providing contracted research for pharmaceutical, nutraceutical and pet food companies to assist in developing products that targeted disorders associated with age, including cognitive decline. In 2009, Dr. Milgram retired from the university, but maintained an appointment at the Department of Pharmacology, and his main focus now centered on developing CanCog, which has morphed into a full-service contract research organization focused in general on developing interventions that improve the quality of life of companion animals. Dr. Milgram also serves on the board of directors of two biotechnology companies and provides consultative services to companies in the companion animal space.



PRESENTATION ABSTRACT

Cognition in dogs, as in humans, refers to mental experiences (thoughts) and cognitive level refers to mental capabilities. Both depend on processes that are not directly observable but are inferred from behavior. Our research has focused on characterizing cognition, understanding how cognition develops early in life, how it changes with advanced age and whether it can be modified with the use of drugs, nutritional supplements, or behavioral interventions. Our focus on the importance of the development of interventions differentiates our approach from a purely academic approach that seeks to understand comparative similarities and differences between canine and human cognition. We view cognition through a neuropsychological perspective, which assumes that cognition consists of a limited set of distinct cognitive domains, with each associated with distinct underlying neural structure. To this end, we have developed a battery of neuropsychological test protocols that targets each of these domains and we have used these tests to study the effects of age and various interventions on cognitive abilities. Our research has demonstrated that canine cognitive abilities decline in a domain specific manner. For example, episodic memory, which relates to the ability to learn complex tasks declines relatively in life, while working memory, which refers to short term recall and use of information remains relatively intact until later in age.

There are also notable individual differences in the effect of age on cognitive decline. Some dogs show surprisingly little change. Others develop a cognitive dysfunction syndrome (CDS), which becomes apparent because of obvious changes in the dog's everyday behaviors. Although behavioral changes associated with CDS are at least partially distinct from neuropsychological cognitive changes, we have

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Searching for Genetic Risk Factors for Canine Epilepsy in Whole Genome Sequences

Gary Johnson, DVM, PhD

BIOGRAPHY

Gary S. Johnson earned a BA degree in Chemistry at Augsburg College (Minneapolis MN), a PhD in Biochemistry at Kansas State University, and a DVM at the University of Minnesota. He also did postdoctoral studies with Dr. Y. C. Lee at Johns Hopkins University and with Dr. W.J. Dodds at the New York State Department of Health. He joined the faculty in the University College of Veterinary Medicine at the University of Missouri in 1980. For the first 10 years at the University of Missouri, Dr. Johnson's research focus was on the biochemistry of von Willebrand's disease and other bleeding disorders of dogs. Since then, his research goals have been to identify the molecular genetic causes for a variety of heritable canine diseases including epilepsy.



Current CHF Grant – 2257: Identification of Genetic Risk Factors for Canine Epilepsy

PRESENTATION ABSTRACT

Epilepsy is a neurological disorder characterized by recurrent seizures. I will present background information about epilepsy in the dog, describe various subtypes of canine epilepsy and how they relate to other episodic canine diseases, and summarize our current understanding of the disease mechanisms that underlie seizures. Also, I will provide conclusions about the effect of gender and age on the risk of developing epilepsy, based on information about the >2000 epileptic dogs that provided samples for our DNA repository. In addition, I will summarize past efforts by us and others to identify mutations responsible for canine epilepsy.

Next I will provide background information about the canine genome. I will go on to describe recent advances in genome sequencing and analysis as well as the limitations that currently prevent the routine clinical use of this technology. I will also point out some examples where we and others have used whole genome sequencing to identify the mutations responsible for a variety of heritable canine diseases.

Finally, I will give an updated progress report of our ongoing efforts to use whole genome sequencing to identify genetic risk factors for canine epilepsy. The initial funds for this investigation were provided by the AKC Canine Health Foundation. The two Specific Aims for this grant were (1) to identify genetic risk factors that are contributing to the development of epilepsy within individual breeds and (2) to identify genetic risk factors that are contributing to the development of epilepsy across breeds. Specific breeds were not specified in the initial grant application. Individual breeds have been chosen for study based on the availability of DNA from same-breed epileptic dogs that can serve to validate risk factor candidates. Recently, additional funds have been provided through a breed-specific "add-on" to the grant from the AKC Canine Health Foundation and directly from a Breed Club-associated Foundation. Thus, the investigation has been expanded to include an emphasis on finding epilepsy risk factors in Standard Schnauzers and Poodles.

Exploring the Role of the Gut Microbiome in Epilepsy

Karen Muñana, DVM, PhD, 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 80 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 research interest is canine epilepsy, with a focus on evaluating the effectiveness of novel anti-seizure therapies and understanding why some dogs respond poorly to treatment. Her research frequently involves clinical trials, in which a new treatment or diagnostic tool is evaluated on epileptic dogs from the community.

Current CHF Grant – 2249-A: Studying the Role of the Gastrointestinal Tract in Canine Epilepsy

Current CHF Clinician-Scientist Fellowship – Mentee: Jeanie Lau, BVSc; Study of Steroid Responsive Meningitis-Arteritis (SRMA) in Dogs

PRESENTATION ABSTRACT

Epilepsy is the most common nervous system disorder of dogs, affecting up to 0.75% of the canine population. Approximately one-third of dogs with epilepsy fail to achieve adequate seizure control with anti-seizure medication, and are considered to have drug resistant epilepsy. These dogs are known to have increased disease complications and a shorter lifespan associated with poor seizure control, and account for much of the financial burden of epilepsy management.

Drug resistance in epilepsy is thought to involve both genetic and environmental factors, but the mechanisms that lead to drug resistance are poorly understood.

Within the past several years, there has been extensive research on the relationship between the gastrointestinal tract and nervous system. The term “microbiota-gut-brain axis” is used to describe the complex bidirectional signaling that occurs between the gastrointestinal tract and the nervous system, and emphasizes the newly recognized role of intestinal microbes in these interactions. This system is considered vital for maintaining health, and can influence an individual's susceptibility to disease. For example, alterations in the population of intestinal bacteria of the *Lactobacillus* group are thought to play a role in the development and progression of several neurological disorders, including anxiety/depression, autism, multiple sclerosis and Alzheimer's disease. *Lactobacillus* bacteria are capable of producing gamma-aminobutyric acid (GABA), one of the main chemicals used to transmit signals in the brain, and an increase in GABA levels in the gastrointestinal tract is associated with increased levels in the brain. Oral administration of *Lactobacillus* microbes has been demonstrated to have a beneficial therapeutic effect in experimental models of neurological disease, as well as in recent clinical trials on depression and anxiety disorders in humans.

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Epilepsy & Nutrition

Holger Volk, DVM, PhD, DECVN

BIOGRAPHY

Holger is the Head of Department of the Clinical Science and Services at the Royal Veterinary College, Professor of Veterinary Neurology and Neurosurgery and the Past-President of the European College of Veterinary Neurology. He graduated from the Veterinary School of Hanover in 2001, where he also did his PhD in Neuropharmacology studying basic mechanisms of drug-resistant epilepsy. He then completed his specialist clinical education doing an internship and a residency in Neurology and Neurosurgery at the RVC. Holger is internationally known for his work in the field of Chiari-like malformation/syringomyelia and epilepsy. Holger has been chairing the International Veterinary Epilepsy Task Force, which published recently seven consensus statements for canine and feline epilepsy and was a co-chair of the recent published ACVIM consensus statement about medical treatment of epilepsy. He has been a recipient of several Jim Bee educator excellent in teaching awards, the prestigious Bourgelat Award from BSAVA and the International Canine Health Award from the Kennel Club. He has published multiple books and book chapters, >170 articles, >100 conference abstracts, and is a frequent flyer on the international conference circuit.



Current CHF Grant – 2252: Investigating a Ketogenic Medium-Chain Triglyceride (MCT) Supplement for the Treatment of Drug-Resistant Canine Idiopathic Epilepsy and Its Behavioral Comorbidities

PRESENTATION ABSTRACT

Every practitioner and breeder has had the experience dealing with a dog with epilepsy. Most veterinary practitioners also have had the experience that despite an ever-increasing number of available antiepileptic drugs, the majority of dogs will continue to seizure and suffer from quality-of-life limiting side-effects. Epilepsy is not caused by one single disease, it can be caused by a plethora of disease processes. Recurrent seizures are the basis for the definition of epilepsy and seizures can be seen as the cardinal clinical signs. As epilepsy is a complex, multifactorial brain disease, new management strategies should reflect this and new more multimodal (holistic) approaches to epilepsy management are needed. The 'right mix' in epilepsy management usually needs to include antiepileptic drug(s) medication tailored to the individual case, a balanced and potentially specialized nutrition plan, a reduction of potential seizure triggers and stress factors, and a treatment plan for comorbidities. The role of nutrition in epilepsy management is currently heavily debated. Until recently there has been only anecdotal evidence that nutrition can influence seizure control. It has been known that salt content in a diet can influence pharmacokinetics of the antiepileptic drug potassium bromide. However, that nutrition could have a direct impact on epilepsy management has just recently been shown. A ketogenic diet based on medium chain triglycerides (MCT) has recently been shown to improve seizure control and reduce behavioral comorbidities in some dogs with idiopathic epilepsy when fed as an adjunct to antiepileptic drug treatment. Fourteen percent of dogs became seizure free when fed the MCT diet and 48% of dogs showed a 50% or greater reduction in seizure frequency. New management options are needed for epilepsy and nutrition might play one factor in its successful management.

Harmonization of Genetic Testing for Dogs

Brenda Bonnett, DVM, PhD

BIOGRAPHY

Brenda qualified as a veterinarian at the University of Guelph, in Canada. After several years in private practice, post-graduate training in Theriogenology and Epidemiology, and many years as a tenured Associate Professor at the Department of Population Medicine, Ontario Veterinary College, University of Guelph in Ontario, Canada, Brenda is currently a Consulting Epidemiologist and CEO of International Partnership for Dogs. She is an author of over 70 refereed publications and several book chapters. She 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), human–animal interactions and medical communication. Brenda has been involved in numerous pet welfare initiatives for various organizations.



Current CHF Grant – 2328-A: Harmonization of Genetic Testing for Dogs

PRESENTATION ABSTRACT

There is widespread consensus amongst the veterinary and research communities on the need for a collaborative, international effort to address challenges surrounding effective use of genetic health testing (GT) in dogs. There is currently no mandatory accreditation or standardization for GT for companion animals, putting the health of many individual dogs and their progeny at risk, frustrating veterinarians and consumers, and negatively impacting the reputation of GT, in general. There is a need not only for transparency of the overall quality of commercial entities, and of the specific tests/ products they are offering, but also for better information and counselling to support the global dog community, veterinarians and consumers.

The International Partnership for Dogs (IPFD), an independent, multi-stakeholder organization, has been recognized as the appropriate body to create and oversee an online resource to: catalog information from commercial test providers (CTPs) on measures of quality; host expert reviews of genetic tests; coordinate a program for standardized testing; assemble resources for genetic counselling and education; and provide the foundation for future developments. The basis of this program is the voluntary participation from CTPs and multi-stakeholder collaboration. The initiative, the Harmonization of Genetic Testing for Dogs (HGTD) parallels resources developed for human genetic testing (e.g. Eurogentest). As almost all genetics experts have an affiliation with a CTP, the HGTD resource will utilize panels of qualified experts to provide collective expert opinion. The online platform of the IPFD (DogWellNet.com), demonstrated here, can be continually expanded to accommodate a growing catalog of CTPs, expert reviews, and resources.

Research in GT and genomics and the subsequent development of tests continues at a rapid pace. Issues of quality and the complexities of application of tests – for different scenarios and for different breeds – has not received adequate attention. Many breeders, breed clubs, their veterinarians and advisors are overwhelmed by the challenges of integrating scientific developments into sound breeding decisions. The lack of transparent information on the quality of CTPs and tests; the confusion and frustration of

consumers and the financial and personal costs to them; is a crisis in the making.

The IPFD Harmonization of Genetic Testing for Dogs is a major step towards improving access to information, and encouraging and standardizing best practices for GT. This resource will aid international kennel clubs, breed clubs, breeding advisors, veterinarians and the end-user to make informed decisions regarding laboratories and testing for the health and welfare of their dogs. This, in turn, will lead to better translation of research developments to practical and effective applications.

Acknowledgements:

This initiative is backed by national kennel clubs and other partners of the IPFD; the AKC Canine Health Foundation; the Orthopedic Foundation for Animals; Leadership Sponsor CTPs; and others.

Notes:

This image shows a blank sheet of white paper with horizontal ruling lines. The lines are evenly spaced and extend across the width of the page. There are no margins, text, or other markings on the paper.

Semen Evaluation, Quality, and Effects of Aging

Stuart Meyers, DVM, PhD, DACT

BIOGRAPHY

Dr. Stuart Meyers is a Theriogenologist specializing in male fertility with more than 60 publications in this area. He obtained his BS and DVM degrees from Michigan State University, his MS degree in Animal Science from Oregon State University, and his PhD from the University of California, Davis in Comparative Pathology. He is board-certified in Theriogenology having completed a residency at Texas A&M University. He is a member of the faculty at UC Davis and teaches reproduction and anatomy in the School of Veterinary Medicine. Additionally, Dr. Meyers has experience in veterinary mixed and equine practice. His laboratory has studied sperm cryopreservation in horses, dogs, and fish as well as embryo biology in horses and nonhuman primates.



Current CHF Grant – 2192-A: Advanced Semen Analysis in Labrador Retrievers

PRESENTATION ABSTRACT

Semen quality in dogs has not been assessed in a longitudinal study that includes endpoints of female fertility and pregnancy. While use of artificial insemination with chilled semen is increasingly used in canine reproduction, the resultant level of predictability and odds of fertile matings for dogs is still not fully understood. This research provides, for the first time, comprehensive semen evaluation in a large population of dogs in which fertility has been tracked. Duplicate ejaculates were obtained from 39 Labrador retriever males of the Guide Dogs for the Blind (San Rafael, CA) breeding program. Sperm endpoints were determined in fresh semen and extended chilled semen at 48hr post-collection. Evaluation included total and progressive motility, average path velocity, morphology, membrane lipid peroxidation, presence of sperm reactive oxygen species, sperm chromatin structure, and mitochondrial DNA copy number. Male age ranged from 1 to 10 years, and were grouped as young (Y; 1 to 3 years, n=21), middle-aged (M; 4 to 6 years, n=13), and senior (S; 7 years or greater, n=5) for analysis. The effects of age and sperm state (fresh vs. chilled) on the above sperm endpoints were determined using a linear mixed effects model. Semen endpoint values for all parameters were established for this group of fertile males. Progressive motility was only lower in the senior male chilled samples compared to all other groups, fresh and chilled ($P<0.05$). Velocity decreased with increasing age and was lower overall in chilled samples ($P<0.05$). Percent morphologically normal sperm was lower in senior dogs compared to the other age groups ($P<0.05$). The presence of reactive oxygen species was lower in chilled samples compared to fresh ($P<0.05$). No differences were seen in total motility, membrane lipid peroxidation, mitochondrial DNA copy number, with regard to conception rate, or average litter size between age groups or between fresh and chilled samples. We observed no effects from semen quality on fertility or fecundity regardless of age, despite the differences found in semen quality. The use of advanced laboratory tests to evaluate sperm parameters beyond the standard motility, morphology, and concentration will open investigation to more specific and sensitive fertility tests in canine reproduction.

An Update on Canine Brucellosis: A Call for Interdisciplinary Action

Angela Arenas, DVM, PhD, DACVP

BIOGRAPHY

Dr. Arenas is a board Certified Veterinary Anatomic Pathologist with more than fifteen years of research experience with Select Agents, with a strong emphasis on brucellosis. Over the past years, the research in her laboratory has been focused on the development of improved vaccines for animals and humans. More recently, her research efforts have been also directed towards the development of Improved Diagnostic Tools for canine brucellosis. Dr. Arenas has a strong interest in “Global One Health” that is supported by continued and on-going international collaborations with countries where brucellosis is endemic including Sub Saharan Africa and Latin America. Her research and training programs are currently being funded by multiple Federal and Private organizations including the AKC Canine Health Foundation, NIH, NIH Fogarty, USDA-NIFA, DHS, USDA FAS among others.



Current CHF Grant – 2275-A: Development of a Brucellosis Vaccine for Dogs

PRESENTATION ABSTRACT

Canine infection by *Brucella* spp. constitutes a serious problem for dog breeders and pet owners, leading not only to huge economic cost associated with reproductive loss, but is also considered a public health concern because of its zoonotic potential. New evidence suggests the emergence or reemergence of canine brucellosis in the US. The increase in canine brucellosis cases is a direct result of the persistence of this organism in the host, the low dose required for infection, lack of protective vaccines and the difficulty in diagnosing infected animals. A comprehensive review of the current status of the disease, the mechanism of infection, pathogenesis, zoonotic potential, preventive measures that can be adopted in managing the disease as well as the current advancements towards the development of new vaccines and diagnostics tests will be discussed.

Notes:

Canine Pyometra

Marco Coutinho da Silva, DVM, PhD, DACT

BIOGRAPHY

Dr. Marco da Silva was born in Sao Paulo, Brazil, and obtained his DVM from Sao Paulo State University in 1999. He then attended Colorado State University where he obtained his MS and PhD degrees in Reproductive Physiology studying the interactions between sperm, oocyte and oviduct. While at Colorado State University, he also worked as a clinician in the oocyte transfer program at the Equine Reproduction Laboratory. He became a Diplomate of the American College of Theriogenologists in 2003. From 2006 to 2009, Dr. da Silva was a faculty in the College of Veterinary Medicine at Cornell University. In the summer of 2009, Dr. da Silva joined the faculty at The Ohio State University in the Theriogenology and Reproductive Medicine Service, with the objective of developing a comprehensive assisted-reproduction program. His research has been focused in understanding several aspects of mammalian fertilization, including oocyte maturation, sperm physiology, and embryo development.



Current CHF Grant – 2264-A: Role of E. Coli Biofilm in Canine Pyometra

2294-E: 2016 Theriogenology Residency – Resident: Tessa Fiamengo, DVM

PRESENTATION ABSTRACT

Pyometra is a potentially life-threatening infection of the canine uterus. The incidence of occurrence has been reported to be 9-15.2% with aged, nulliparous bitches most at risk. This presentation will discuss the reasons why dogs are susceptible to developing pyometra, as well as address treatment options and prognosis for life and reproduction. Often the therapy suggested for pyometra is spaying the female. However, some genetically valuable females can be successfully treated using a combination of prostaglandins, dopamine agonists, antibiotics, and supportive care. Currently available treatment protocols are costly, time-consuming, and not without risk themselves, often limited to healthy breeding bitches without evidence of renal compromise. At the end of this lecture, participants should have sufficient information to make the best decision for the health of their dogs in the event they ever develop pyometra.

Notes:

Epilepsy & Nutrition

Rowena Packer, PhD

BIOGRAPHY

Dr. Rowena Packer is a BBSRC Future Leader Research Fellow at the Royal Veterinary College (RVC), University of London. Her main research interest is canine inherited disease, with a primary focus on canine epilepsy. Her research explores the impact of epilepsy on dog behavior and cognition, improving the treatment of epilepsy including nutritional management, the relationship between stress and epilepsy, and the impact of epilepsy on carers. Dr. Packer holds a PhD from the RVC, and a first-class BSc in Animal Behavior and Welfare from the University of Bristol. In 2016 she was awarded the UFAW Young Animal Welfare Scientist of the Year award.



Dr. Packer is a co-Investigator with Dr. Holger Volk on CHF Grant 2252, and will be presenting this lecture, stepping in at the last minute as a speaker and panelist for the Conference while Dr. Volk is on paternity watch.

Dr. Holger Volk's Current CHF Grant – 2252: Investigating a Ketogenic Medium-Chain Triglyceride (MCT) Supplement for the Treatment of Drug-Resistant Canine Idiopathic Epilepsy and Its Behavioral Comorbidities

PRESENTATION ABSTRACT

Every practitioner and breeder has had the experience dealing with a dog with epilepsy. Most veterinary practitioners also have had the experience that despite an ever-increasing number of available antiepileptic drugs, the majority of dogs will continue to seizure and suffer from quality-of-life limiting side-effects. Epilepsy is not caused by one single disease, it can be caused by a plethora of disease processes. Recurrent seizures are the basis for the definition of epilepsy and seizures can be seen as the cardinal clinical signs. As epilepsy is a complex, multifactorial brain disease, new management strategies should reflect this and new more multimodal (holistic) approaches to epilepsy management are needed. The 'right mix' in epilepsy management usually needs to include antiepileptic drug(s) medication tailored to the individual case, a balanced and potentially specialized nutrition plan, a reduction of potential seizure triggers and stress factors, and a treatment plan for comorbidities. The role of nutrition in epilepsy management is currently heavily debated. Until recently there has been only anecdotal evidence that nutrition can influence seizure control. It has been known that salt content in a diet can influence pharmacokinetics of the antiepileptic drug potassium bromide. However, that nutrition could have a direct impact on epilepsy management has just recently been shown. A ketogenic diet based on medium chain triglycerides (MCT) has recently been shown to improve seizure control and reduce behavioral comorbidities in some dogs with idiopathic epilepsy when fed as an adjunct to antiepileptic drug treatment. Fourteen percent of dogs became seizure free when fed the MCT diet and 48% of dogs showed a 50% or greater reduction in seizure frequency. New management options are needed for epilepsy and nutrition might play one factor in its successful management.

Thank you to our co-host,
the Nestlé Purina PetCare Company, and to sponsors
of the Veterinary Student Scholarship program, the Orthopedic
Foundation for Animals and the American Kennel Club.

And a very special thank you to all of the individuals,
clubs, and foundations that have helped make
this conference thrive.



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