

AKC Canine Health Foundation

2011 National Parent Club Canine Health Conference

August 12-14, 2011

Report submitted to:

The Rottweiler Health Foundation and The American Rottweiler Club

Dr. Tommy Caisango, RHF Representative for the Conference

History of Veterinary Medicine and Canine Research

Keynote Speaker: Donald F. Smith, DVM; Cornell University

Modern veterinary medicine in the U.S. had its original roots during the Civil War when over one million horses and mules were lost to starvation, disease, and trauma. Over time dogs became critical for future human success in comparative medicine in both physiology and pathology. Pets are important to human health in many ways. In 1960, research was based mostly on companion animals. Then in 1980, the biomedical aspect of canine health research became popular. The term, Zooeyia, was coined meaning the positive benefits animals give to humans (e.g., physical, emotional, and physiological).

It was not until the last two decades of the 20th century that major foundations, corporations, and individual donors began to devote substantial resources for companion animal research. However, veterinary medicine today is still a small profession with insufficient political influence to manifest robust financial support for companion animal research. The great tragedy of the 2010 federal health care bill is that animals and veterinary medicine remain estranged in the public policy arena from people and human medicine.

Dog Genetics and the Mammalian Mind

Mark Neff, PhD; Van Andel Research Institute

The 1990s were declared “The Decade of the Brain” by an act of congress. Although we learned a great deal about the physical properties of neurons and how neuronal networks are formed, there remain profound gaps in our understanding of how variations in these networks actually shape behavior. The lack of a basic understanding of the brain function has meant that patients suffering from mental illness and psychiatric disease continue to have unmet needs. Dogs also suffer from mental illness and psychiatric diseases. Such disorders are difficult to diagnosis and challenging to treat.

The domestic dog is unique in that breeds demonstrate inherited predispositions for temperaments, tendencies, and action patterns. We must be aware of our breed's behavioral genetics and instincts; helpful for lifespan and longevity. Working, Sporting, and Hound breeds should be used for what they were bred to do (e.g., sight hound, herding dog, retriever, etc.). Revealing the genes responsible for these traits will also shed light on rules governing the mammalian mind; which will be important for treating both human and canine patients suffering from complex disorders of the central nervous system.

Coping with Stress: Nutritional Approaches to Enhanced Immune Function

Arleigh Reynolds, DVM, PhD; Nestle Purina PetCare

It is well established that travel and competition result in an increased incidence of illness in professional human athletes. Changes in diet, environmental conditions, and exposure to novel pathogens may all play a role in this syndrome. The role of exercise varies with intensity and duration. Now in the study of canine stress, the research shows a similar comparison with that of human athletes.

Dogs exposed to high stress without proper nutrition can result in more injuries, increased diarrhea (IBD), kennel cough, poor response to training, and intestinal inflammation (colitis).

The studies looked at every day naturally occurring stressors such as exercise and travel on immune functions in dogs. The measured effects of nutrition on the immune system's response to these stressors were also considered. Studies examining the immune response to dietary supplementation with probiotics, egg and milk biologics, and antioxidants were also discussed as important to our dog's digestive tract. Such results have been shown in athletic, show, and pet dogs, alike.

Advances in Diagnosis and Treatment of Canine IBD

Albert Jergens, DVM, PhD; Iowa State University

Canine inflammatory bowel disease (IBD) denotes a heterogeneous group of idiopathic, chronic, relapsing inflammatory disorders of the gastrointestinal tract that are immunologically-mediated. While their exact etiologies remain unknown, research results suggest that interplay between genetic factors and enteric bacteria are crucial for disease development, owing to abnormal host responses directed against the commensal microbiota. Key clinical signs include vomiting, diarrhea and weight loss, and histopathologic lesions of inflammation may involve the stomach, small intestine, or colon.

Treatment of IBD involves both dietary and pharmacologic interventions as well as manipulation of the enteric microbiota through the use of antibiotics, prebiotics, and probiotics. Also the use of the Canine IBD Activity Index (CIBDAI) which uses a 0-3 point scale to measure: activity level, appetite, vomiting, stool consistency, stool frequency, and weight loss.

Canine Degenerative Myelopathy: A Translational Medicine Approach to Amyotrophic Lateral Sclerosis – Lou Gehrig’s Disease

Joan Coates, DVM; University of Missouri, Columbia

This is a disease of the spinal cord. DM has been histopathologically documented in over eighteen breeds of dogs. The Rottweiler was not listed as one of the top eighteen. The breeds most commonly diagnosed are Pembroke Welsh Corgis, Boxer, Chesapeake Bay Retriever, German Shepherd Dog, and Rhodesian Ridgeback.

Canine degenerative myelopathy (DM) is an adult onset neurodegenerative disease that occurs in many breeds (see note above). The initial clinical signs are upper motor neuron asymmetric spastic weakness and general proprioceptive ataxia in the pelvic limbs, which subsequently progress to paraplegia. Dog owners often elect euthanasia within a year of diagnosis. When euthanasia is delayed, lower motor neuron signs emerge as ascending tetraparesis, flaccid paralysis, widespread muscle atrophy, difficulty swallowing, and inability to bark.

Currently, there are no effective treatments for ALS or DM. The only currently FDA-approved drug for therapy in ALS, riluzole, has shown marginal effects at slowing disease progression.

Recent Progress in Molecular Genetics of Cancer and Challenges Ahead

Jaime Modiano, VMD, PhD; University of Minnesota

Microscopic assessment of tissue samples is the first step in diagnosis. The cause is attributed to sporadic mutational events of heritable cancer. Although there is limited research due to cost, there is progress.

When a dog reaches the age of six, the risks of cancer increases. His study with Rottweilers looked at Canine Lymphoma (about 4%, not seen as heritable as other cancers, some get it quite young), Hemangiosarcoma (consider stem cell make-up, distinct cell intrinsic signature in tumor tissue), and Osteosarcoma (about 13%). With the last listed as being the most common. Treatment of amputation and chemo/radiation, a dog can live approximately eleven months; without treatment, approximately seven weeks.

The good news is in the last decade dramatic improvements have been seen in molecular genetic research of canine cancer. This includes new and improved diagnostic tests and approval of the first immune-based cancer therapy (ONCEPT, Merck canine melanoma vaccine) and the first targeted small molecule inhibitor (Palladia, Pfizer c-Kit inhibitor for treatment of mast cell tumors).

There has also been significant progress defining breed associated cancer susceptibility. The research has focused on defining the role that “breed” plays not only on the frequency of the tumor occurrence, but also on tumor behavior.

Comparative Cytogenetics of Cancer. Just how Human are our Dogs?

Matthew Breen, PhD; North Carolina State University

The application of genomics to canine biomedical research has resulted in significant advances, as we strive to enhance the health and welfare of our canine companions. Over the past several years, tumor tissues and blood samples have been recruited from hundreds of dogs with a variety of cancers. During that same time period, a series of sophisticated molecular cytogenetic reagents and resources were generated to complete the genomics “toolbox.”

Research has demonstrated the presence of numerous cytogenetic signatures associated with canine cancer subtypes and they are being used to offer a more sophisticated means of tumor diagnosis. Also research has begun to define genomic lesions that correlate with prognosis. For example, with canine lymphoma, research has developed a cytogenetic test that allows the prediction of how long a dog diagnosed with lymphoma will respond to doxorubicin based chemotherapy.

Finding such evidence in the dog will also lead to improved understanding of human cancers.

Canine-derived Antibody Fragments of Targeted Therapy of Cancer

Nicola Mason, BVetmed, PhD; University of Pennsylvania

Antibodies that target tumor cells or neutralize their growth factors have revolutionized treatment of many different human cancers. However, such targeted antibody therapy is not currently available in veterinary medicine. Humanized antibodies used to target human cancers cannot be used in dogs because they don't cross-react with dog tumor cells and they are rapidly destroyed by the dog.

In order to develop targeted antibody therapies for use in canines, a platform technology has been developed to generate libraries of canine-derived antibody fragments from white blood cells or lymphocytes of dogs with cancer.

Vascular Endothelial Growth Factor (VEGF) is considered to be one of the major factors that stimulate the growth of blood vessels in and around tumors, which is necessary for the survival of the tumor. Neutralization of VEGF has led to prolonged overall survival times in human patients with several different types of cancer including hemangiosarcoma. These canine-derived VEGF-specific antibody fragments represent the first targeted biological antibody therapy that may be employed in dogs to retard the growth of a number of different tumor types including canine hemangiosarcoma.

In addition, libraries generated from dogs with different tumor types such as osteosarcoma and lymphoma may contain novel antibody fragments that could be used to target these cancer types in the future.

Canine Oncology Clinical Trials

Douglas Thamm, VMD; Colorado State University

This presentation was about why clinical trials conducted on pet animals and the types of trials, not on any specific canine cancer trials.

Although there are many definitions of clinical trials, they are generally considered to be health-related research studies that follow a pre-defined protocol. These can include both interventional and observational types of studies. Interventional studies are those in which the research subjects are assigned by the investigator to a treatment or other intervention and their outcomes are measured. Observational studies are those in which subjects are observed and their outcomes are measured by investigators.

The purpose of canine oncology trials is to investigate new and hopefully better ways to diagnose, treat, and monitor cancer in dogs. Many naturally occurring cancers in pet animals closely resemble human cancer and provide meaningful systems of cancer research to benefit both species. Therapies are studied in dogs to provide important information about whether this form of treatment might be appropriate for testing in humans.

Five types of trials were discussed: Treatment trials, Prevention trials, Diagnostic trials, Screening trials, and Quality of Life trials; each of these supporting a different part of cancer research.

Some clinical trials that involve simple procedures such as blood collection or special handling of tissues to be removed from surgery may be appropriate for any dog with cancer. Participation in therapeutic trials with new drugs or treatments, especially early-phase trials, needs to be considered more carefully, as the effectiveness of these treatments is generally not as well known, and potential toxicity may not be as well established.

There are multiple websites that list ongoing clinical trials for pets with cancer. The most frequently updated and comprehensive is the site managed by the veterinary Cancer Society. <http://www.vetcancersociety.org/clinical-research.html>

Vitamin D and Cancer

Rondo Middleton, PhD; Nestle Purina PetCare

Since its discovery as a molecule necessary for proper calcium and phosphate metabolism, Vitamin D, and more specifically the hormonally active form, 1,25-dihydroxyvitamin D3 (calcitriol), has become known as an important player in many other biological systems. These areas include cancer, heart disease, autoimmune diseases, and skin disorders.

Research has shown that higher levels of Vitamin D in the blood are associated with reduced incidence and recurrence, and greater survival in various types of cancer. The expression of many genes encoding for enzymes involved in the metabolism of Vitamin D, as well as other proteins regulated by Vitamin D, are altered in cancer.

Antioxidant enzymes appear to interact with the identified differentially expressed genes and show beneficial modulation of key cancer processes.

Factors Influencing Development of New Veterinary Medicine Oncology Products

Karen Greenwood, BSc, Pfizer Animal Health, Director, Companion Animal Internal Medicine Unit

Her discussion included the medications: Palladia – for mast cell tumors and ONCEPT – the melanoma vaccine. She also discussed the use of people drugs for pet animals. Many of the human-approved drugs today are not suitable for pet animals. She discussed the serious side effects in dogs that would be tolerable in humans for cancer treatment.

The second half of her presentation was on other variables that affect the effectiveness of drug treatments. These included: dosage, regimen, side effects, drug safety, short-term v. long-term usage, tolerance, target pathways, and efficacy.

She also discussed the regulatory agencies: FDA (CVM), USDA, and EPA.

What We Know About the Inheritance of Dilated Cardiomyopathy, Arrhythmogenic, Right Ventricular Cardiomyopathy and Subaortic Stenosis in the Dog

Kathryn M Meurs, DVM, PhD; North Carolina State University

Cardiomyopathy is a primary muscle disease that has been shown to be inherited in the dog as well as several other species. There are two common forms: dilated and arrhythmogenic.

Dilated cardiomyopathy is characterized by heart muscle dysfunction and enlargement of the heart chamber, particularly the left. Affected dogs may die suddenly or develop congestive heart failure as characterized by coughing and shortness of breath. There is no cure. In human beings there are now 20 different genes that cause the development of this disease. It is likely that that there is 1 cause in dogs. An important aspect of all cardiomyopathies is that they are impacted by variable penetrance, meaning that not all dogs that have the genetic cause will show the same severity of disease, some will show severe clinical signs, while others will remain free of symptoms their whole life.

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is a heart muscle disease characterized by cardiac arrhythmias that result in fainting or sudden death. It is most commonly observed in Boxers. A deletion mutation has been identified. The mutation prevents the cells from holding together properly and this leads to fainting or sudden death.

Subvalvular Aortic Stenosis is one of the most common heart birth defects in the dog. It is known to be inherited in the Newfoundland, Rottweiler, and Golden Retriever. Affected dogs can live comfortably with the mild form of the disease, but severely affected dogs have an average life span of 2 years.

September 11 – Ten Years later for the Search and Rescue Dogs

Cynthia M Otto, DVM, PhD.; University of Pennsylvania

September 11, 2001 was an unprecedented day in the history of the United States. In response to the terrorist attacks in New York, Washington D.C., and the downed plane in Pennsylvania, hundreds of search and rescue dog-teams were deployed.

During their service, the health and well-being of these dogs were monitored. Remarkably, the dogs coped with the adverse conditions with minimal morbidity. The most commonly reported problems were cuts and scrapes, most of which were minor. Problems related to the intensive work included fatigue, weight loss, and dehydration. Interestingly, respiratory problems were rare.

Coming up on the 10 year anniversary, 73% of the deployed dogs have died. Of the dogs that have died, the median age at death was 12.2 years in deployed dogs, whereas in the controls it was 11.7 years. In both groups cancer was common and confirmed in 40% of deployed dogs and 45% in control dogs.

The legacy of 9/11 has been an increased awareness of the important role that these dogs play and the need for continued research in behavior, genetics, and sports medicine to enhance their capacity and safety. Because of this, Penn Vet Working Dog Center has been established at the University of Pennsylvania.

Breakout Sessions ----

Canine Nutrition and the Sporting and Working Dog

Arleigh Reynolds, DVM, PhD; Nestle Purina PetCare

He discussed the importance of considering the source your pet animal gets calcium. He recommended supplementation in the source of bone meal. He also discussed antibiotics. He said research has shown the overuse of antibiotics in pet animals. By doing this it changes the dog's GI flora (not always in a good way), adding bacteria. That is why there has been an increase in Giardia in pet animals. He recommended treating the pet animal's GI tract with probiotics.

He also discussed looking carefully at the pet animal's CBC results. An increase in WBCs usually shows that a systemic problem exists in the dog. If it is localized, he does not recommend treating with antibiotics.

Research Advantages of the Purebred Dog

Matthew Breen, PhD; North Carolina State University

The very things that make dogs so different from other species also make them ideal genetic research subjects. The dog has a wider range of body morphologies than any other species, living or extinct. Specific combinations of physical traits are what define pure breeds. Different breeds exhibit highly specialized behaviors shaped through their long association with humans to suit a wide range of purposes and it is due to their DNA. The AKC Canine Health Foundation (CHF) has played a significant role in funding many studies, as well as those of researchers exploring different aspects of behavioral genetics in dogs. If something works in one species the same developmental or metabolic function often causes a similar outcome in other species.

Because dogs exhibit so much physical and behavioral variety, the more that is known about how the actions of genes shape the ways dogs look and act has the potential to lead to better understanding of the genetic influences on the appearance and behavior of other types of mammals. Most genetic diseases found in dogs are analogous to similar diseases in people. Perhaps one of the most important is cancer; both dogs and humans are cancer-prone. All cancers are due to gene mutations or rearrangements of chromosomes. The interactions between mutant or misplaced genes and normal genes make cells multiply abnormally, leading to tumors and other types of cancer. A researcher can easily assemble and study a large multi-generational family of purebred dogs.

Genetic Tests: How to Interpret Results and Incorporate Them into Your Breeding Program

Jerold S. Bell, DVM; Tufts Cummings School of Veterinary Medicine

His discussion was based on genetics tests and how they vary on what they are able to identify and how they should be used in managing genetic disease.

He focused his attention on phenotypic tests, linked-marker based tests, and direct mutation based tests. Most direct genes identify a mutation that is causative for a genetic disorder. However, some genetic tests identify a mutation that causes an increased susceptibility of genetic disease. These susceptibility alleles can be part of polygenic/complexity inherited traits, or the cause of incomplete penetrance of assumed simple Mendelian traits.

He stated that we need to be knowledgeable about what genetic tests are available and in which individuals they should be run. For example, dogs from breeds with an incidence of von Willebrand disease should be tested early in life. He also stated we need to understand the temporal periods when genetic testing will be most accurate and allow for intervention. For most breed-specific genetic diseases, we know how to either prevent their occurrence or at least lessen the possibility of producing offspring with genetic disease.