

Canine Health Foundation

Grant Sponsorship Summary Report Report

French Bulldog Club of America

4 January 2010

Spon Type	Commitment Date	Actual Payment Date	Amount
<u>French Bulldog Club of America</u>			
<u>00257</u>			
<i>Investigation of Predictors of Outcome for Canine Mast Cell Tumors</i>			
DAF	11/15/2004	5/31/2005	\$1,250.00
DAF	11/15/2004	5/4/2006	\$1,250.00
<i>Total 00257 (2 items)</i>			<hr/> \$2,500.00
<u>00593A</u>			
<i>Mapping Genes Associated with Canine Hemangiosarcoma</i>			
DAF	4/14/2008	6/18/2008	\$2,500.00
<i>Total 00593A (1 item)</i>			<hr/> \$2,500.00
<u>00615A-T</u>			
<i>Heritable and Sporadic Genetic Lesions in Canine Lymphoma</i>			
DAF	12/10/2005	5/4/2006	\$2,500.00
DAF	12/10/2005	5/30/2007	\$2,500.00
<i>Total 00615A-T (2 items)</i>			<hr/> \$5,000.00
<u>00615B</u>			
<i>Heritable and Sporadic Genetic Lesions in Canine Lymphoma</i>			
DAF	12/10/2005	5/4/2006	\$0.00
DAF	12/10/2005	5/30/2007	\$0.00
<i>Total 00615B (2 items)</i>			<hr/> \$0.00
<u>00632</u>			
<i>MicroRNAs and Canine Lymphoma</i>			
DAF	1/15/2006	5/4/2006	\$850.00
DAF	1/15/2006	5/30/2007	\$850.00
<i>Total 00632 (2 items)</i>			<hr/> \$1,700.00
<u>00759</u>			
<i>Investigation of Antigenic Causes of Vaccine-Associated Allergic Reactions in Dogs</i>			
DAF	11/19/2006	5/30/2007	\$1,000.00
<i>Total 00759 (1 item)</i>			<hr/> \$1,000.00

Spon Type	Commitment Date	Actual Payment Date	Amount
<u>00779</u>			
<i>Characterization of the Canine Y Chromosome: Identifying Genes that Cause Male Infertility</i>			
DAF	11/19/2006	5/30/2007	\$1,000.00
DAF	10/23/2009	11/19/2009	\$2,500.00
<i>Total 00779 (2 items)</i>			<hr/> \$3,500.00
<u>00821</u>			
<i>Phenotypic Characterization and Mapping Genes Associated with Canine Degenerative Myelopathy in the Boxer Dog</i>			
DAF	11/19/2006	5/30/2007	\$5,000.00
<i>Total 00821 (1 item)</i>			<hr/> \$5,000.00
<u>00885</u>			
<i>Center of Canine Cytotherapeutics</i>			
DAF	4/14/2008	6/18/2008	\$2,500.00
<i>Total 00885 (1 item)</i>			<hr/> \$2,500.00
<u>00910-A</u>			
<i>Epidermal Growth Factor Receptor and Cyclooxygenase-2 Cross-Talk in Canine Mammary Cancers</i>			
DAF	4/14/2008	6/18/2008	\$1,000.00
<i>Total 00910-A (1 item)</i>			<hr/> \$1,000.00
<u>00945</u>			
<i>Mucosal Gene Expression Profiles in Canine Inflammatory Bowel Disease</i>			
DAF	10/23/2009	11/19/2009	\$2,500.00
<i>Total 00945 (1 item)</i>			<hr/> \$2,500.00
<u>00970</u>			
<i>Tissue Regeneration Using Canine Mesenchymal Stem Cells: Effects of Donor Characteristics and ex vivo Expansion on Cell Pluripotency</i>			
DAF	10/23/2009	11/19/2009	\$2,500.00
<i>Total 00970 (1 item)</i>			<hr/> \$2,500.00
<u>01056-A</u>			
<i>Determine the Effect of Stenotic Nares on the Development of the Brachycephalic Syndrome in Brachycephalic Dogs</i>			
DAF	4/14/2008	6/18/2008	\$1,000.00
<i>Total 01056-A (1 item)</i>			<hr/> \$1,000.00

Spon Type	Commitment Date	Actual Payment Date	Amount
<u>01105</u>			
<i>Understanding the Dynamics of Canine Influenza Virus Transmission in Dog Populations and Intervention Strategies for Reducing Transmission</i>			
DAF	5/21/2009	6/24/2009	\$2,500.00
<i>Total 01105 (1 item)</i>			<hr/> \$2,500.00
<u>01131</u>			
<i>Genetic Background and the Angiogenic Phenotype in Cancer</i>			
DAF	5/21/2009		\$2,500.00
<i>Total 01131 (1 item)</i>			<hr/> \$2,500.00
<u>01139</u>			
<i>Immune Targeting of Canine Hemangiosarcoma Using a Canine Derived Single Chain Antibody Approach</i>			
DAF	10/1/2008	2/18/2009	\$1,000.00
DAF	5/21/2009	6/24/2009	\$2,500.00
<i>Total 01139 (2 items)</i>			<hr/> \$3,500.00
<u>01180-A</u>			
<i>The Prognostic Value of Various Cerebrospinal Fluid Biomarkers in Dogs with Acute Thoracolumbar Disk Herniation</i>			
DAF	10/23/2009	11/19/2009	\$2,000.00
<i>Total 01180-A (1 item)</i>			<hr/> \$2,000.00
<u>01188-A</u>			
<i>Capacity for Respiratory-Based Thermoregulation in Brachycephalic Breeds</i>			
DAF	5/21/2009	6/24/2009	\$1,000.00
<i>Total 01188-A (1 item)</i>			<hr/> \$1,000.00
<u>01240-A</u>			
<i>Development of a Diagnostic Method for Canine Atopic Dermatitis</i>			
DAF	5/21/2009	6/24/2009	\$1,000.00
<i>Total 01240-A (1 item)</i>			<hr/> \$1,000.00
<u>2209</u>			
<i>Galactokinase 1: A Candidate Gene for Juvenile Cataracts in Dogs</i>			
DAF		8/30/2003	\$1,500.00
<i>Total 2209 (1 item)</i>			<hr/> \$1,500.00

Spon Type	Commitment Date	Actual Payment Date	Amount
<u>2234</u>			
<i>Basophil/Mast Cell Response to Lectins as a Predictor for Risk of Allergic Disease in Genetically Susceptible Dogs</i>			
DAF	7/23/2001	4/30/2002	\$1,600.00
<i>Total 2234 (1 item)</i>			<hr/> \$1,600.00
<u>2465</u>			
<i>Identification and Characterization of Genetic Mutations in Canine Mast Cell Tumors</i>			
DAF	9/22/2003	12/30/2003	\$2,500.00
<i>Total 2465 (1 item)</i>			<hr/> \$2,500.00
<u>336B</u>			
<i>Mapping of the Gene for Malignant Histiocytosis in the Bernese Mountain Dog</i>			
DAF	11/15/2004	10/31/2005	\$1,250.00
DAF	11/15/2004	5/30/2007	\$1,250.00
<i>Total 336B (2 items)</i>			<hr/> \$2,500.00
<u>415</u>			
<i>Anti-HLA-DR Antibody Therapy in Canine B-cell Lymphoma: Preliminary Clinical Evaluation</i>			
DAF	11/15/2004	5/31/2005	\$1,250.00
DAF	11/15/2004	5/4/2006	\$1,250.00
<i>Total 415 (2 items)</i>			<hr/> \$2,500.00
<u>678</u>			
<i>Generation and Analysis of Canine Bone Marrow Derived Mast Cells</i>			
DAF	5/9/2006	5/30/2007	\$4,000.00
<i>Total 678 (1 item)</i>			<hr/> \$4,000.00
<u>705-A</u>			
<i>Characterization of Fluorine-18-Fluorodeoxyglucose Uptake in Dogs with Cutaneous Mast Cell Tumor and Malignant Lymphoma</i>			
DAF	2/12/2006	10/31/2007	\$500.00
<i>Total 705-A (1 item)</i>			<hr/> \$500.00
<u>774</u>			
<i>Identifying a Gene for Atrial Fibrillation in Irish Wolfhounds</i>			
DAF	11/19/2006	5/30/2007	\$2,500.00
<i>Total 774 (1 item)</i>			<hr/> \$2,500.00

Spon Type	Commitment Date	Actual Payment Date	Amount
<i>Total French Bulldog Club of America (35 items)</i>			\$60,800.00
Grand Totals (35 items)			\$60,800.00

Canine Health Foundation

Grant Sponsorship - French Bulldog Club of America

4 January 2010

Grant Information

Sponsorship Information

French Bulldog Club of America

01240-A - Development of a Diagnostic Method for Canine Atopic Dermatitis

Grant Amount - \$11,880.00 Project Dates : 5/1/2009 - 4/30/2010

Abstract: Background: Atopic dermatitis, an autoimmune disease in which dogs develop hypersensitivity to environmental or food allergens, is a common and frustrating canine skin condition. There are few effective therapies and many dogs require prolonged administration of steroids or other immunosuppressive drugs. The only specific cure is skin testing and desensitization treatments over prolonged periods of time, managed by skilled veterinarians. Palliative treatments, including newer immunosuppressive drugs such as cyclosporine are only partially effective. It is now known that dogs with atopic dermatitis have specific immunological imbalances compared to normal dogs. A new vaccine has been developed that may correct the underlying immunological imbalance, and is showing encouraging results in ongoing clinical trials. Unfortunately, there is at present no convenient, cost-effective way of determining whether or not a particular dog has that immunological imbalance or whether the dog would likely respond to the new vaccine. Fortunately, research has shown that animals and humans with autoimmune disease have serum antibodies against their own T-cell receptors (TCR). This hyper-reactivity can be detected with simple blood tests. However, the tests must be specifically designed for each species (dog, human, etc).

Objective: This project aims to develop simple blood tests to detect whether or not a particular dog is hyper-reactive to its own immune cells, which is characteristic of atopic dermatitis. The researchers will also develop screening tests for dogs and use these tests to determine response to treatment.

01188-A - Capacity for Respiratory-Based Thermoregulation in Brachycephalic Breeds

Grant Amount - \$12,474.00 Project Dates : 1/1/2009 - 6/30/2010

Abstract: Background: Dogs can not sweat effectively to cool themselves, and thus have to rely on their breathing to rid themselves of excess body heat. When a dog needs to shed more body heat, it increases its breathing, often by panting. This is a relatively inefficient way of controlling body temperature, and may be even more inefficient in dogs with short, compressed faces such as Boxers, Pugs, and Bulldogs which have narrow airways and require increased effort to breathe. Recently airlines have begun restricting these types of dog breeds as cargo due to the suspicion that the breeds are too susceptible to high environmental temperatures that may be encountered during shipping, and are more likely to suffer from heat stroke or death during routine transport.

Objective: This project will determine whether these types of dogs are less capable of controlling their body temperature during heat stress compared to the average dog, and provide a method of testing individual dogs for the ability to effectively cool themselves during typical air transport.

DAF: \$1,000.00

Commitment Date:5/21/2009

Payment Date: 6/24/2009

DAF: \$1,000.00

Commitment Date:5/21/2009

Payment Date: 6/24/2009

Grant Information**Sponsorship Information**

01180-A - The Prognostic Value of Various Cerebrospinal Fluid Biomarkers in Dogs with Acute Thoracolumbar Disk Herniation

Grant Amount - \$12,960.00 Project Dates : 7/1/2008 - 12/31/2009

Abstract: Background: Intervertebral disk herniation is a relatively common condition seen predominantly in chondrodystrophoid dogs, such as the Dachshund, and can cause spinal cord injury resulting in paralysis. Dogs that present with this condition undergo a cerebrospinal fluid tap and imaging studies before surgical intervention and recovery.

Objective: The researchers are performing additional tests (lactate, glucose, aspartate aminotransferase, creatine kinase, calcium, myelin basic protein, and protein tau) on the cerebrospinal fluid collected to determine whether elevation in any of these substances can be correlated with the severity of injury or the capability for the dog to walk again.

01139 - Immune Targeting of Canine Hemangiosarcoma Using a Canine Derived Single Chain Antibody Approach

Grant Amount - \$123,125.40 Project Dates : 1/1/2009 - 12/31/2010

Abstract: Background: Canine hemangiosarcoma is a common and highly aggressive tumor of blood vessels that is often fatal. At diagnosis most dogs have evidence of metastatic disease and despite chemotherapy, survival times rarely exceed 6 months. New approaches to the treatment of this disease are needed. The use of monoclonal antibodies and antibody fragments to directly target different tumors has shown promise in clinical trials in man.

Objective: This project aims to use a new canine synthetic antibody system to target the tumor and deliver cytotoxic agents directly to both primary and metastatic lesions. Using advanced molecular techniques, the researchers intend to review antibody responses that dogs with hemangiosarcoma may make against their own tumors and use these as a template to generate canine antibody fragments that specifically recognize tumor particles. Tumor-specific antibody fragments will be linked to an exotoxin and evaluated for their ability to kill canine hemangiosarcoma cells in vitro. This allows for the direct delivery of cytotoxic agents to the tumor, which decreases side effects and increases therapeutic value. This work aims to develop the first canine-derived, tumor-specific targeting approach for the treatment of HSA and to provide proof-of-principal for this approach that can then be used to therapeutically target many other tumor types in this species in vivo.

DAF: \$2,000.00

Commitment

Date:10/23/2009

Payment Date: 11/19/2009

DAF: \$1,000.00

Commitment Date:10/1/2008

Payment Date: 2/18/2009

Grant Information**01139 - Immune Targeting of Canine Hemangiosarcoma Using a Canine Derived Single Chain Antibody Approach**

Grant Amount - \$123,125.40 Project Dates : 1/1/2009 - 12/31/2010

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01131 - Genetic Background and the Angiogenic Phenotype in Cancer

Grant Amount - \$254,871.00 Project Dates : 1/1/2010 - 12/31/2012

Abstract: Background: Certain dog breeds are prone to develop certain types of cancer; yet, there has been little progress to define genes or other factors that account for this risk. The researchers' recent work on hemangiosarcoma is the first to clearly demonstrate that a dog's genetic background, defined by "breed," can influence the type of genes that show up as tumors. This means that certain breeds are diagnosed with specific cancers more frequently than others because of the behavior of tumors after they show up, and not simply because they show up more frequently. Specifically, this may apply to the observed tendency for hemangiosarcoma seen in Golden Retrievers, German Shepherd Dogs, and Portuguese Water Dogs. In addition, one-size-fits-all therapies may be not enough to effectively treat this disease.

Objective: This project will continue the researchers' observations on gene appearance profiles in hemangiosarcoma from Golden Retrievers to German Shepherd Dogs and Portuguese Water Dogs, and it also will define how new targeted therapies may effectively control the disease in these and other dog breeds.

Sponsorship InformationDAF: \$2,500.00
Commitment Date:5/21/2009
Payment Date: 6/24/2009DAF: \$2,500.00
Commitment Date:5/21/2009

Grant Information**01105 - Understanding the Dynamics of Canine Influenza Virus Transmission in Dog Populations and Intervention Strategies for Reducing Transmission**

Grant Amount - \$104,220.00 Project Dates : 1/1/2009 - 12/31/2010

Abstract: Background: Canine influenza is a newly emerging and highly contagious respiratory infection of dogs caused by a novel influenza A virus of the subtype H3N8. The canine influenza virus (CIV) has caused respiratory disease outbreaks in thousands of dogs housed at greyhound race tracks, boarding/training kennels, and shelter facilities across the U.S. Although most dogs recover, many develop a debilitating pneumonia that can be fatal. There is no information on whether dogs housed in different types of premises are more or less at risk for canine influenza.

Objective: For this study, the researchers are analyzing data from previous canine influenza outbreaks to determine if dog populations in different types of premises have different risk for canine influenza. Using the results from this analysis, they will develop a computer model to investigate parameters important to CIV transmission in dog populations at race tracks, boarding/training kennels, shelter facilities, and dog shows. The model will then be used to determine what intervention strategies (vaccination, quarantine, sanitation) are most effective in reducing or preventing virus transmission. The results of this study will provide valuable information to dog show organizers, and others responsible for the health of dogs in other settings, to guide development of policies for control and prevention of canine influenza.

01056-A - Determine the Effect of Stenotic Nares on the Development of the Brachycephalic Syndrome in Brachycephalic Dogs

Grant Amount - \$6,525.00 Project Dates : 1/1/2008 - 12/31/2009

Abstract: Background: The brachycephalic syndrome is most frequently characterized by stenotic nares, elongation of the soft palate, eversion of the laryngeal sacculles, and often results in difficulty breathing. It is not clear if stenotic nares play a causative role in the pathophysiology of the brachycephalic syndrome. Brachycephalic puppies have been acquired through the Veterinary Teaching Hospital of Michigan State University. Puppies were included/excluded from this study according to established criteria, then allotted to control (n=21) and surgery (n=25) groups. The degree of nasal stenosis was quantified and a brachycephalic score was recorded. Dogs were/will be examined at 1, 1 ½, 2, and 2 ½ years of age to quantify the severity of the brachycephalic syndrome.

Objective: The overall goal is to answer the question: Will correction of stenotic nares in brachycephalic puppies prevent or improve development of the brachycephalic syndrome in the adult? The specific aim is to complete the necessary follow up evaluations to answer the question. Based on the findings to date, it appears that correction of stenotic nares in the brachycephalic puppy improves the brachycephalic syndrome in the adult. The researchers need to complete sufficient follow up surgeries and examinations to have sufficient statistical confidence in this result. They will then make recommendations about the appropriateness of correction of stenotic nares in the brachycephalic puppy which, if positive, will have a tremendous impact on the health and well-being of brachycephalic pets.

Sponsorship Information

DAF: \$2,500.00

Commitment Date:5/21/2009

Payment Date: 6/24/2009

DAF: \$1,000.00

Commitment Date:4/14/2008

Payment Date: 6/18/2008

Grant Information**Sponsorship Information**

00615A-T - Heritable and Sporadic Genetic Lesions in Canine Lymphoma

Grant Amount - \$77,066.00 Project Dates : 10/1/2007 - 3/31/2009

Abstract: It has been apparent for some time that certain dog breeds are prone to develop certain types of cancer. Specifically, studies completed between the late 1960's and the early 1980's defined relative risk of lymphoma for different dog breeds. Yet, there has been little progress since then to define factors that account for this risk. As part of ongoing programs supported by the AKC CHF in our laboratories, we showed recently that the breed-specific risk of lymphoma extends beyond the simple disease condition to a predisposition for specific forms of lymphoma. More importantly, we showed there are recurrent chromosomal abnormalities that segregate with specific forms of lymphoma and that are more common in Golden Retrievers than in other breeds, suggesting breed-specific profiles of genetic abnormalities will be found in canine lymphoma. To continue this work, we plan to use contemporary "array-based" technologies to identify genes that map to these regions and how they contribute to the disease. We anticipate that the results from this work will allow us to predict how heritable factors influence the occurrence of abnormalities in these genes, and will set the groundwork to identify specific genes associated with breed-dependent cancer risk.

DAF: \$2,500.00

Commitment

Date:12/10/2005

Payment Date: 5/30/2007

00615A-T - Heritable and Sporadic Genetic Lesions in Canine Lymphoma

Grant Amount - \$77,066.00 Project Dates : 10/1/2007 - 3/31/2009

Abstract: It has been apparent for some time that certain dog breeds are prone to develop certain types of cancer. Specifically, studies completed between the late 1960's and the early 1980's defined relative risk of lymphoma for different dog breeds. Yet, there has been little progress since then to define factors that account for this risk. As part of ongoing programs supported by the AKC CHF in our laboratories, we showed recently that the breed-specific risk of lymphoma extends beyond the simple disease condition to a predisposition for specific forms of lymphoma. More importantly, we showed there are recurrent chromosomal abnormalities that segregate with specific forms of lymphoma and that are more common in Golden Retrievers than in other breeds, suggesting breed-specific profiles of genetic abnormalities will be found in canine lymphoma. To continue this work, we plan to use contemporary "array-based" technologies to identify genes that map to these regions and how they contribute to the disease. We anticipate that the results from this work will allow us to predict how heritable factors influence the occurrence of abnormalities in these genes, and will set the groundwork to identify specific genes associated with breed-dependent cancer risk.

DAF: \$2,500.00

Commitment

Date:12/10/2005

Payment Date: 5/4/2006

00970 - Tissue Regeneration Using Canine Mesenchymal Stem Cells: Effects of Donor Characteristics and ex vivo Expansion on Cell Pluripotency

Grant Amount - \$165,348.00 Project Dates : 1/1/2008 - 12/31/2009

Abstract: Background: Special cells can be isolated from bone marrow (mesenchymal stem cells or MSCs) and used to produce different types of cells that form bone, muscle, cartilage or nervous tissue. These cells can be put back into the body in order to replace cells damaged by inherited diseases, trauma, or age associated conditions in order to restore function to a wide variety of tissues and organs. Clinical trial using MSCs in humans are currently underway and provide a basis for exciting new therapies for many of the most common ailments of dogs: heart failure, neurologic conditions, osteoarthritis, kidney and liver diseases and diabetes. A major hurdle in the development of rational stem cell therapy clinical trials in dogs is a general lack of understanding of basic properties of canine MSCs.

DAF: \$2,500.00

Commitment

Date:10/23/2009

Payment Date: 11/19/2009

Objective: This studies will define optimal donor characteristics, culture conditions, and safety for using these MSC to treat dogs. Understanding basic properties of these specialized cells from dogs will bring promising stem cell therapies closer to reality in veterinary medicine.

Grant Information**Sponsorship Information**

00945 - Mucosal Gene Expression Profiles in Canine Inflammatory Bowel Disease

Grant Amount - \$60,000.00 Project Dates : 6/1/2008 - 5/31/2010

Abstract: Background: Canine inflammatory bowel disease (IBD) is a chronic intestinal disorder likely resulting from the interaction between genes and environmental factors. While it is generally accepted that luminal bacteria play a critical role in provoking gut inflammation, genetic factors may also contribute to the bacterial-driven inflammatory response. Several susceptibility genes, such as NOD2/CARD15, have recently been identified in humans with IBD and provide a basis for the development of aberrant immune responses to bacteria in certain individuals. It is reasonable to hypothesize that susceptibility genes also affect clinical disease in dogs with IBD by negatively affecting the interaction with intestinal bacteria and/or their products. Genetic factors are thought to contribute to the pathogenesis of canine IBD as in humans. A role for luminal bacteria is suggested by observations that antibiotics reduce clinical signs, and by reports of increased bacterial numbers in intestinal biopsy specimens obtained from dogs with IBD. Given the recognized breed predispositions, genetic susceptibility to IBD is also likely, although studies are lacking.

Objective: The researchers are utilizing unique molecular biology tools to: (1) identify key genetic factors contributing to disease expression, (2) characterize gene expression profiles which may predict responsiveness to specific therapies, and (3) provide the framework upon which to facilitate identification of IBD susceptibility genes that predispose specific canine breeds to clinical disease.

DAF: \$2,500.00

Commitment

Date:10/23/2009

Payment Date: 11/19/2009

00910-A - Epidermal Growth Factor Receptor and Cyclooxygenase-2 Cross-Talk in Canine Mammary Cancers

Grant Amount - \$12,960.00 Project Dates : 8/1/2007 - 1/31/2009

Abstract: Mammary cancer is the most common neoplasm in female dogs, and malignant neoplasms account for 50 percent of all mammary cancers and thus it becomes a devastating in dogs. Currently, chemotherapeutic strategies are very limited in dogs. Prostaglandin E2 (PGE2), a hormone secreted by cancer tissues promotes tumor cell migration, invasion, metastasis, and angiogenesis (formation of new blood vessels), inhibition of tumor cell apoptosis (cell death), and inactivation of host anti-tumor immune cells. Cyclooxygenase-2 (COX-2) is the rate limiting enzyme regulates PGE2 production. Increased level of COX-2 is considered a hallmark of mammary neoplasia. Inhibition of COX-2 by non-steroidal anti-inflammatory drugs decreases the incidence of various cancers. Epidermal growth factor receptor (EGFR) regulates COX-2 expression and function. In the present study, cross-talk between EGFR and COX-2 in canine mammary cancers will be studied. Mammary tumor tissues collected from clinical patients and immortalized canine mammary carcinoma cells will be used as in vivo and in vitro models, respectively. The proposed project will determine EGFR/COX-2 pathway in canine mammary cancer and lead to discover novel chemotherapy for the treatment and/or prevention of mammary carcinoma in dogs.

DAF: \$1,000.00

Commitment Date:4/14/2008

Payment Date: 6/18/2008

00885 - Center of Canine Cytotherapeutics

Grant Amount - \$100,956.00 Project Dates : 1/1/2007 - 12/31/2008

Abstract: Stem cells are cells that have the ability to become many other cell types. In the proposed project, we will inject adult bone marrow stem cells into dogs with diseases that modern veterinary medicine lacks an effective cure. It is anticipated that the plastic stem cells will change into a form beneficial to the dog patient and improve the disease. Diseases that we will investigate for benefit from stem cells include dilated cardiomyopathy, degenerative myelopathy, inflammatory bowel disease and correction of inborn errors of metabolism. Modern veterinary medicine lacks effective cures for all of these diseases and we hope to develop methods for dealing with them.

DAF: \$2,500.00

Commitment Date:4/14/2008

Payment Date: 6/18/2008

Grant Information**Sponsorship Information**

00821 - Phenotypic Characterization and Mapping Genes Associated with Canine Degenerative Myelopathy in the Boxer Dog

Grant Amount - \$176,272.00 Project Dates : 4/1/2007 - 3/31/2010

Abstract: Background: Degenerative myelopathy (DM) is a degenerative spinal cord disease affecting several breeds of dogs in adulthood. Affected dogs show gradual rear leg weakness and eventual complete loss of mobility. A particularly high prevalence in certain breeds, such as Boxer, Cardigan and Pembroke Welsh Corgis and Rhodesian Ridgebacks, suggests a genetic link.

Objective: This study will first characterize DM in the Boxer to ensure that the disease is the same as has been identified in other breeds. Then, the researchers will identify the mutation responsible for DM and identify genes that contribute to the increased risk for DM in Boxers and other at-risk breeds of dogs. This mapping strategy will determine the location of DM mutation on the dog chromosome. They will then examine the genes at that chromosomal location to identify the DM mutation and develop a genetic test for predisposition to the disease. A DNA test will detect carriers of the mutation permitting wise breeding strategies to decrease the frequency of the disease in the breed. It will allow for definitive diagnosis of DM in affected dogs eliminating the need for expensive tests ruling out other conditions. The researchers expect this research to be applicable to several breeds presently affected by DM, and perhaps others in which the condition is not yet recognized.

DAF: \$5,000.00

Commitment

Date:11/19/2006

Payment Date: 5/30/2007

00779 - Characterization of the Canine Y Chromosome: Identifying Genes that Cause Male Infertility

Grant Amount - \$203,344.00 Project Dates : 7/1/2007 - 12/31/2009

Abstract: Background: Studies of the human and mouse Y chromosomes have shown that they contain many testis specific genes that, when defective, cause infertility and spermatogenesis defects. The causes of male infertility in dogs are not well known. The canine genome sequence has assisted in knowledge about X chromosome; however, virtually nothing is known about the canine Y chromosome and the genes it harbors.

Objective: This study will show in detail the gene content of the dog Y chromosome by sequencing from a cDNA selection library that is enriched for Y chromosome gene transcripts. This procedure will isolate the majority of canine Y chromosome genes and the DNA fragments they reside on, which will be mapped in the dog genome. The copy number and expression profile of these genes will be determined in a broad range of tissues to discern which genes have testis-specific expression patterns, and may therefore be good candidates for abnormal spermatogenesis. The identification of testes-specific Y chromosome genes will provide gene targets for future development of molecular diagnostic assays that examine the influence of these genes on canine male infertility.

DAF: \$2,500.00

Commitment

Date:10/23/2009

Payment Date: 11/19/2009

Grant Information**Sponsorship Information**

00779 - Characterization of the Canine Y Chromosome: Identifying Genes that Cause Male Infertility

Grant Amount - \$203,344.00 Project Dates : 7/1/2007 - 12/31/2009

Abstract: Background: Studies of the human and mouse Y chromosomes have shown that they contain many testis specific genes that, when defective, cause infertility and spermatogenesis defects. The causes of male infertility in dogs are not well known. The canine genome sequence has assisted in knowledge about X chromosome; however, virtually nothing is known about the canine Y chromosome and the genes it harbors.

Objective: This study will show in detail the gene content of the dog Y chromosome by sequencing from a cDNA selection library that is enriched for Y chromosome gene transcripts. This procedure will isolate the majority of canine Y chromosome genes and the DNA fragments they reside on, which will be mapped in the dog genome. The copy number and expression profile of these genes will be determined in a broad range of tissues to discern which genes have testis-specific expression patterns, and may therefore be good candidates for abnormal spermatogenesis. The identification of testes-specific Y chromosome genes will provide gene targets for future development of molecular diagnostic assays that examine the influence of these genes on canine male infertility.

DAF: \$1,000.00

Commitment

Date:11/19/2006

Payment Date: 5/30/2007

774 - Identifying a Gene for Atrial Fibrillation in Irish Wolfhounds

Grant Amount - \$0.00 Project Dates : 1/1/2007 - 12/31/2008

Abstract: The overall goal of our work is to identify the gene that causes canine genetic cardiomyopathy. Rapid progress in the canine genome project, i.e., obtaining the DNA sequence, has made gene mapping possible. We will study a large family of Irish Wolfhounds with heart disease, that usually involves both atrial fibrillation (AF) and dilated cardiomyopathy (DCM). We have identified a region on canine chromosome 23 that causes AF/DCM in the Irish Wolfhounds. We propose to screen candidate genes in the linked area for mutations to identify the gene causing this devastating heart disease in the Irish Wolfhounds. Once a mutation has been found a genetic test will be developed to aid carrier detection.

DAF: \$2,500.00

Commitment

Date:11/19/2006

Payment Date: 5/30/2007

00759 - Investigation of Antigenic Causes of Vaccine-Associated Allergic Reactions in Dogs

Grant Amount - \$31,631.12 Project Dates : 1/1/2007 - 12/31/2008

Abstract: Allergic reactions are the most common adverse event associated with vaccination in dogs. Recent research has demonstrated that small dogs in general, and several specific breeds, are at higher risk for these reactions. Laboratory studies have shown that normal dogs make antibodies against many vaccine components, even though they may not show an allergic reaction immediately following vaccination. Although the specific cause of allergic reactions in dogs remains unknown, vaccine components residual from the manufacturing process have been incriminated. Using serum from dogs of high-risk breeds, this study will compare antibody concentrations in dogs demonstrating allergic reactions versus antibody concentrations in dogs of the same breed that don't have reactions. From this study, vaccine components that stimulate allergic reactions will be identified, prompting vaccine manufacturers and/or the USDA (as regulating agency) to remove or reduce these substances and improve the safety of canine vaccines.

DAF: \$1,000.00

Commitment

Date:11/19/2006

Payment Date: 5/30/2007

Grant Information**00615B - Heritable and Sporadic Genetic Lesions in Canine Lymphoma**

Grant Amount - \$149,369.00 Project Dates : 8/1/2008 - 7/31/2010

Abstract: Background: Certain dog breeds are prone to develop certain types of cancer. Between the late 1960's and the early 1980's researchers related the risk of lymphoma for different dog breeds. Yet, there has been little progress since then to define factors that account for this risk. As part of ongoing programs supported by the AKC CHF, the researchers recently showed that the breed-specific risk of lymphoma extends beyond the simple disease condition to a tendency for specific forms of lymphoma. More importantly, the researchers showed there are frequent chromosomal abnormalities that separate with specific forms of lymphoma and that are more common in Golden Retrievers than in other breeds. This suggests breed-specific profiles of genetic abnormalities will be found in canine lymphoma.

Objective: To continue this work, the researchers are using contemporary "array-based" technologies to identify genes that map to these regions and how they contribute to the disease. The researchers anticipate that the results from this work will allow them to predict how genetic factors influence the occurrence of abnormalities in these genes, and will set the groundwork to identify specific genes associated with breed-dependent cancer risk.

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705-A - Characterization of Fluorine-18-Fluorodeoxyglucose Uptake in Dogs with Cutaneous Mast Cell Tumor and Malignant Lymphoma

Grant Amount - \$12,922.00 Project Dates : 1/1/2006 - 12/31/2006

Abstract: "The University of Tennessee's College of Veterinary Medicine (UTCVM) has a unique opportunity for collaboration with the Cancer Imaging and Tracer Development Research Program (CITDRP) at the University of Tennessee Medical Center. The UTCVM has established a strong collaboration with the CITDRP for the benefit of human and veterinary patients. We will use PET imaging to study cutaneous mast cell tumors (MCT) and canine lymphoma (LSA) in dogs. Whole-body PET scanning is uniquely suited for staging with evaluation of the skin, lymph nodes, spleen and liver for early signs of metastatic spread. All of these sites can be imaged in one non-invasive procedure, using uptake of the 18F-labeled glucose analog 2-deoxy-D-glucose (18FDG), to identify sites of metastasis. The proposed pilot study will evaluate the uptake of 18FDG in 30 tumor-bearing dogs (15 with MCT, 15 with LSA) using PET. All dogs will have their cancer diagnosed and staged using standard imaging techniques and results will be compared with whole-body PET results."

Sponsorship Information

DAF: \$0.00

Commitment

Date:12/10/2005

Payment Date: 5/30/2007

DAF: \$0.00

Commitment

Date:12/10/2005

Payment Date: 5/4/2006

DAF: \$500.00

Commitment Date:2/12/2006

Payment Date: 10/31/2007

Grant Information**678 - Generation and Analysis of Canine Bone Marrow Derived Mast Cells**

Grant Amount - \$56,345.62 Project Dates : 4/1/2006 - 3/31/2007

Abstract: Disorders of mast cells, particularly mast cell tumors (MCTs), are common in dogs and there is now evidence that many of these exhibit breed specific tendencies, suggesting underlying genetic causes. This is particularly important for MCTs in which certain breeds (e.g., Pugs) develop benign disease while others (e.g., Chinese Shar-Pei) develop malignant disease. In comparison to humans and mice, very little is known about the biology of normal canine mast cells. Such knowledge is critical for understanding how mast cell disorders develop. In other species, large numbers of mast cells can be generated from purified bone marrow cells (termed BMMCs) and these are used to study normal mast cell biology. We have recently been successful in generating canine BMMCs from canine bone marrow. The purpose of this proposal is to fine tune the process of canine BMMC generation and to study the functional properties of mast cells in detail. These studies will supply important new information regarding the biology of normal canine mast cells and provide a platform for future work investigating the genetic basis of mast cell disease in dogs.

00632 - MicroRNAs and Canine Lymphoma

Grant Amount - \$98,766.00 Project Dates : 10/1/2005 - 3/31/2010

Abstract: Lymphoma is one of the most common cancers in the dog. The current classifications of lymphoma do not explain or predict its changing clinical behavior. Much of the progress in diagnosis, prognosis, and treatment of lymphoma and other cancers in people has been the result of advances in "genomics." Recently the canine genome has been sequenced, providing the opportunity to apply new genomic approaches to better understand and treat cancer in the dog. MicroRNAs (miRNA) are small non-protein coding molecules that have been linked in humans as having an important role in cancer and a variety of other diseases. In this study, the researchers will identify miRNAs using bioinformatic methods. The researchers will then use miRNA microarrays to study normal canine tissues and canine lymphoma biopsies. These results (miRNA expression profiles) will be linked with previous diagnosis and clinical restrictions. The goals of this study are to identify canine miRNAs and their normal patterns of expression and to determine if specific subtypes of lymphoma are characterized by unique miRNA expression profiles, if specific miRNAs have predictive importance, and to identify potential goals for future investigation and therapies. This study will also generate new tools for future miRNA investigation in the dog.

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Sponsorship Information

DAF: \$4,000.00

Commitment Date:5/9/2006

Payment Date: 5/30/2007

DAF: \$850.00

Commitment Date:1/15/2006

Payment Date: 5/4/2006

DAF: \$850.00

Commitment Date:1/15/2006

Payment Date: 5/30/2007

Grant Information**00593A - Mapping Genes Associated with Canine Hemangiosarcoma**

Grant Amount - \$141,266.59 Project Dates : 4/1/2006 - 9/30/2008

Abstract: Hemangiosarcoma (HSA), a malignant tumor of blood vessels, is a significant health concern in dogs, with a reported incidence of up to two percent of all tumors. HSA can affect all dogs, but a particularly high disease incidence has been reported in certain breeds, such as Golden Retriever (15 percent), German Shepherd Dog (10 percent), and Labrador Retriever. The higher incidence in these particular breeds suggests that genetic risk factors exist. We aim to identify the genetic risk factors associated with canine HSA in Golden Retrievers. These same risk factors are likely present in other breeds as well. We will collect DNA samples from healthy and affected dogs. We will use a newly developed powerful analytical method in order to search for small differences in the patterns of DNA. Subsequently, DNA patterns will be compared with other related breeds and it will be possible to identify a small region of the DNA that is associated with the disease and should lead to the identification of genes predisposing to HSA. When an associated region has been identified, carrier testing can be performed and breeding programs can be improved. Ultimately, understanding of the disease biology will lead to better treatment of HSA.

415 - Anti-HLA-DR Antibody Therapy in Canine B-cell Lymphoma: Preliminary Clinical Evaluation

Grant Amount - \$32,970.00 Project Dates : 10/1/2004 - 9/30/2005

Abstract: Canine lymphoma is a frequently occurring, temporarily controllable form of cancer that is similar to high-grade non-Hodgkin's lymphoma in people. The best conventional chemotherapy results in rapid improvement, but ultimately relapse and progression occur. Adjustment of current chemotherapy protocols is unlikely to result in substantial gains in survival due to development of multiple mechanisms of drug resistance occurring during treatment. Therefore, new strategies that have demonstrated efficacy in humans are worth developing for dogs. An antibody that recognizes cancer cells and stimulates the patient's immune system to eliminate the cancer is an example of such a strategy. We have determined that an antibody made against human lymphocytes cross-reacts with canine lymphoma and causes cell death. This antibody has been confirmed to be safe in normal dogs. We propose to optimize the administration of this antibody in dogs that have already failed chemotherapy for lymphoma. We will evaluate the safety and potential efficacy of this antibody as a prelude to more extensive testing in dogs with lymphoma. This antibody also recognizes cells from dogs with malignant histiocytosis and may be useful for management of this disorder as well.

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Sponsorship Information

DAF: \$2,500.00

Commitment Date:4/14/2008

Payment Date: 6/18/2008

DAF: \$1,250.00

Commitment

Date:11/15/2004

Payment Date: 5/4/2006

DAF: \$1,250.00

Commitment

Date:11/15/2004

Payment Date: 5/31/2005

Grant Information**Sponsorship Information**

336B - Mapping of the Gene for Malignant Histiocytosis in the Bernese Mountain Dog

Grant Amount - \$145,300.00 Project Dates : 4/1/2005 - 3/31/2007

Abstract: We are interested in finding the genes that predispose the Bernese Mountain Dog (BMD) to malignant histiocytosis (MH) for three reasons. First, we are interested in improving the health of this increasingly popular breed, which is severely affected by this deadly disease. Finding the underlying disease gene will lead to the development of genetic tests that can ultimately generate improvements in breeding programs. Second, once we know the underlying cause of MH we can begin to work toward targeted therapies that improve both life, quality and duration for affected dogs. Finally, we are interested in the genetics of similar disorders affecting humans. We propose two complementary strategies: 1) Family based linkage analysis to track the disease gene in a large BMD family affected with MH; and 2) An association-based linkage study encompassing a minimum of 119 affected and at least 100 unaffected control dogs. Both approaches can be expected to highlight regions of the genome where a gene of interest may lie. In summary, these approaches will allow us to eliminate false positive results, increase statistical power for fine linkage mapping, and provide a large resource for mutation screening.

DAF: \$1,250.00

Commitment

Date:11/15/2004

Payment Date: 10/31/2005

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DAF: \$1,250.00

Commitment

Date:11/15/2004

Payment Date: 5/30/2007

00257 - Investigation of Predictors of Outcome for Canine Mast Cell Tumors

Grant Amount - \$45,696.59 Project Dates : 4/1/2005 - 9/30/2008

Abstract: Mast cell tumors are common and high grade tumors are often deadly in dogs. Treatment for aggressive MCT often fails, in part due to imprecise prediction of aggressiveness when surgical biopsy samples are examined. This project aims to improve the accuracy of prediction by determining the importance of several cellular proteins in relation to the ability of the malignant mast cells (MC) to invade tissue and to metastasize to lymph nodes and to distant organs. We will examine biopsy specimens from previous and current cases of MCT for expression of proteins that have critical functions in adhesion between cells and their environment, in signaling for cell proliferation, and for metastatic capability. Responses of the affected dogs to surgical, radiation and chemotherapies will be compared to protein marker expressions, to try to identify proteins that are associated with aggressiveness. This information can then be used for selection of appropriate therapy. We propose to collect fresh tumor tissue from both aggressive and relatively non-aggressive MCTs and to culture them for use in experiments detailing differences between aggressive and non-aggressive MCT. Cell lines derived from canine MCT also will be useful in future investigations into the basic physiology of canine MC and for use in preclinical testing of drug therapies for MCT.

DAF: \$1,250.00

Commitment

Date:11/15/2004

Payment Date: 5/31/2005

Grant Information**Sponsorship Information**

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DAF: \$1,250.00

Commitment

Date:11/15/2004

Payment Date: 5/4/2006

2465 - Identification and Characterization of Genetic Mutations in Canine Mast Cell Tumors

Grant Amount - \$57,212.50 Project Dates : 4/1/2003 - 3/31/2005

Abstract: The most common malignant tumor in dogs is the mast cell tumor (MCT, a form of skin cancer), occurring with an incidence of close to 20 percent in the canine population. MCTs range from relatively benign to extremely aggressive, leading to tumor spread and eventual death. Particular breeds of dog are at risk for the development of this tumor, indicating a role for genetic factors. We have previously identified mutations in the gene c-kit in 30-50 percent of dog MCTs. c-Kit plays a critical role in regulating the growth and function of normal mast cells, and as the mutations we discovered cause uncontrolled function of c-kit, it is likely they influence MCT development in dogs. This proposal will establish a prospective tumor registry of dog MCTs to be used for investigation of the true incidence of c-kit mutations within specific dog breeds. Moreover, the studies outlined in this grant will identify additional genetic mutations present in dog MCTs that can be used for the development of new targeted therapeutics. In summary, this work will provide a much more detailed understanding of dog MCTs, thereby building a framework for the development of new therapies and strategies for disease prevention.

DAF: \$2,500.00

Commitment Date:9/22/2003

Payment Date: 12/30/2003

2234 - Basophil/Mast Cell Response to Lectins as a Predictor for Risk of Allergic Disease in Genetically Susceptible Dogs

Grant Amount - \$89,069.54 Project Dates : 3/8/2002 - 3/31/2005

Abstract: Atopic dermatitis or skin allergies is a chronic debilitating disease that is widely distributed among the breeds of dogs. This inherited disease is listed as a high research priority for the following breeds: Bichon Frise, Boston Terrier, Bull Terrier, Cairn Terrier, Dalmatian, Vizsla, Welsh Terrier and West Highland White Terrier. The skin mast cell and circulating basophil are the cells mainly responsible for itching and skin damage seen in atopic dermatitis. This laboratory has just recently discovered that mast cells from atopic dogs release significantly more of the inflammatory mediator, tumor necrosis factor alpha (TNF- α), than normal dog mast cells when stimulated with lectins that bind glycoproteins on the surface of mast cells. If there is an inherited difference in how surface glycoproteins signal release of TNF- α , then knowledge of the molecular basis for this difference will lead to being able to identify dogs that will have a higher risk of developing atopic dermatitis. To accomplish this, atopic and nonatopic dogs will be compared with regard to the identity and quantity of the cell surface glycoproteins on basophils that are responsible for signaling immediate TNF- α release stimulated by lectins.

DAF: \$1,600.00

Commitment Date:7/23/2001

Payment Date: 4/30/2002

Grant Information**2209 - Galactokinase 1: A Candidate Gene for Juvenile Cataracts in Dogs**

Grant Amount - \$20,946.00 Project Dates : 5/7/2002 - 6/30/2003

Abstract: Juvenile cataracts occur in a number of breeds and in many cases appear to be inherited as an autosomal recessive trait. This means that it is impossible to eliminate carrier animals solely through removal of affected animals from the breeding population. Due to similarities between patterns of cataract formation in some dog breeds and humans with galactokinase deficiency, we feel that one or more mutations in Galactokinase1 (GALK1) may be responsible for juvenile cataracts in certain dog breeds.

We are requesting funding to complete the sequencing of the GALK1 exons (coding regions) in the dog. We will then sequence the eight exons in four breeds of dogs affected with juvenile cataracts. This will be a preliminary study to determine if a mutation in this gene may exist in the Boston Terrier, Australian Terrier, Siberian Husky or Brittany. Regardless of the outcome in these breeds, the ability to sequence the exons of this gene could lead to rapid development of a DNA-based test for carrier animals in other breeds.

Sponsorship Information

DAF: \$1,500.00

Payment Date: 8/30/2003

Grand Totals (35 items)