



## Cardiology Research Program Area

### ***02098-A: Measurement of a Cardiac Muscle Development Protein to Enhance Diagnosis and Prognosis of Cardiomyopathy***

Principal Investigator: Dr. Mark A. Oyama, DVM; University of Pennsylvania

Total Grant Amount: \$12,028.00; Grant Period: 12/1/2013 - 11/30/2014

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a heart disease that causes fainting and heart failure in dogs. ARVC is particularly common in the Boxer breed of dogs. Examination of dogs with ARVC involves performing an electrocardiogram (ECG), x-rays, and ultrasound exam of the heart. These tests are used to help diagnosis ARVC and to assess the severity of the disease. BIN-1 is a cardiac muscle development protein that helps the heart contract properly. Studies in humans show that BIN-1 is detectable from blood samples, and that BIN-1 levels can be used to help determine the severity of ARVC-related heart disease. In addition, the amount of BIN-1 might be able to help predict whether there will be future abnormal heart rhythms that can cause fainting. Dr. Oyama proposes to measure the blood levels of BIN-1 in dogs with ARVC, to compare these amounts with levels in dogs with other non-ARVC forms of heart disease, and to see if BIN-1 can detect disease, provide additional information about the severity of disease, and predict future abnormal heart rhythms.

**Research Deliverable: Identification and validation of BIN-1 as a novel biological marker that can prognosticate severity and progression of cardiomyopathy**

### ***02046: Using a Novel Combination of Drugs to Treat Arrhythmia and Heart Failure in Dogs***

Principal Investigator: Dr. Janice McIntosh Bright, DVM, BSN; Colorado State University

Total Grant Amount: \$33,060.00; Grant Period: 1/1/2014 - 12/31/2015

Atrial fibrillation is a common heart rhythm abnormality (arrhythmia) in dogs. This arrhythmia affects all dog breeds and frequently coexists with heart failure causing worsening of disease and high mortality. Atrial fibrillation may be managed by administering drugs to slow heart rate or by restoring normal rhythm (cardioversion). Dr. Bright will evaluate dogs with naturally occurring atrial fibrillation and heart failure for their responsiveness to two drugs -- amiodarone, an antiarrhythmic agent, and ranolazine, a drug used in humans with coronary heart disease. She will determine whether ranolazine given with amiodarone prolongs normal rhythm compared to amiodarone alone and whether ranolazine also improves heart function. Results will validate combined ranolazine/amiodarone administration as an improved new treatment for atrial fibrillation in dogs with heart failure, extending their quality of life.

**Research Deliverable: Immediate clinical impact by adding a new drug into the pipeline to treat atrial fibrillation**



**01982: *Personalized Medicine: The Intersection of Genotype and Drug Responsiveness in the Treatment of Canine Pulmonary Hypertension***

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

Total Grant Amount: \$27,971.00; Grant Period: 1/1/2014 - 12/31/2015

Genetic background is thought to alter the way animals and humans respond to disease and drug therapy. The unique DNA signature of an individual is now recognized as a pivotal influence on disease outcome during treatment and has become the central concept propelling the study of pharmacogenomics and individualized medicine. Dr. Stern will apply this cutting-edge knowledge to pulmonary hypertension in dogs, a common disease with serious consequences including exercise intolerance, respiratory distress, and sudden death. Dr. Stern has identified a mutation in the gene phosphodiesterase 5A (PDE5A), the target of a drug called sildenafil, and believes this mutation may influence responsiveness of dogs to the drug. Dr. Stern will evaluate the responsiveness of dogs to sildenafil through pre- and post- echocardiogram, identification of biological markers of disease, and quality of life questionnaires. Differences between treatment responses will be compared to genotype. He aims to establish a diagnostic test that allows clinicians to make treatment recommendations on a personalized basis and tailor the therapeutic approach to treatment of pulmonary hypertension.

**Research Deliverable: Use of genotype to determine responsiveness of a dog to a currently available drug to treat hypertension**

**01898-A: *Enhancing Diagnosis and Treatment of Cardiomyopathy through Identification of Biological Markers of Disease***

Principal Investigator: Dr. Suzanne M. Cunningham, DVM; Tufts University

Total Grant Amount: \$12,960.00; Grant Period: 2/1/2013 - 1/31/2015

Cardiomyopathy is a common heart disease associated with irregular heart rhythm (arrhythmia), cardiac dilation, or both. The recent discovery of a mutation in the striatin gene in dogs with cardiomyopathy allows us to identify carrier animals that are at increased risk for developing the disease. However, genetic tests are imperfect and genetic screening usually entails a combination of family history, genetic testing, Holter monitoring and echocardiographic findings. Dr. Cunningham hypothesizes that dogs with cardiomyopathy will have increased levels of a cardiac biomarker known as NT-proBNP and inflammatory markers when compared to healthy dogs, and that these changes will be more profound in dogs with cardiac dilation. The results of this study are anticipated to improve our understanding of cardiomyopathy in the dog, and to open exciting new avenues for screening and treatment of affected dogs.

**Research Deliverable: Identification and validation of NT-proBNP as a novel biological marker that can prognosticate severity and progression of cardiomyopathy**



### **01753: *Identification of Genetic Factors That Alter the Severity of Cardiomyopathy***

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

Total Grant Amount: \$73,343.00; Grant Period: 1/1/2013 - 12/31/2014

Arrhythmogenic right ventricular cardiomyopathy is a genetic-based heart disease in adult dogs that was recently found to be due to a deletion mutation in the striatin gene. Dogs with this genetic mutation can suffer from irregular heartbeat, loss of consciousness and sudden death. Dr. Meurs' lab has demonstrated that Boxer dogs with 2 copies of a genetic deletion (homozygous) are most likely to have the more severe form of the disease, however dogs with 1 copy of the mutation are more likely to have variable disease; some will become quite sick while others will remain free of clinical signs. The mechanism for the variability in clinical signs is unknown but is thought to be associated with the concurrent inheritance of other genetic factors. Dr. Meurs' research will determine if additional genetic factors exist, thus greatly improving our ability to use and interpret the genetic test for the striatin mutation.

**Research Deliverable: Further identification of genes beyond striatin that confer risk for development of cardiomyopathy in boxers**

### **01760: *Use of Gene Therapy to Treat Dilated Cardiomyopathy***

Principal Investigator: Dr. Margaret M. Sleeper, VMD; University of Pennsylvania

Total Grant Amount: \$146,774.00; Grant Period: 1/1/2013 - 12/31/2014

Dilated cardiomyopathy (DCM) is the second most common cause of heart disease in dogs, and medical management of the secondary signs is the only therapeutic option. The outcome for affected dogs depends on the stage of disease and the breed. Once diagnosed, dogs typically exhibit rapid and uniform progression to congestive heart failure (CHF), with most living less than 6 months. Previous research has shown that heart function is critically dependent upon calcium channel function. These gate-like channels found within the wall of cardiac muscle cells open and close, allowing calcium ions to flow into the cell. Calcium influx then regulates muscle contraction. Heart disease is strongly associated with malfunctioning calcium channels within cardiac cells. Gene transfer strategies to reduce calcium cycling abnormalities improve heart function in animal models as well as in human clinical trials. In this study, Dr. Sleeper will conduct a placebo-controlled, double blinded study to evaluate gene delivery approaches for treatment of Doberman Pinschers affected with DCM and CHF. If results show that the gene delivery slows progression of heart failure in Dobermans with DCM, the results will have significant ramifications for all dogs with heart disease, as calcium handling proteins are abnormally expressed in dogs with heart disease of varying causes.

**Research Deliverable: Gene therapy holds promise for a potential cure of genetic-based cardiomyopathy**



## Gastrointestinal Disease Research Program Area

### **02002: *Defining the Genetic Basis of Inflammatory Bowel Disease***

Principal Investigator: Dr. Karin Allenspach, DVM PhD; Royal Veterinary College, University of London  
Total Grant Amount: \$119,268.00; Grant Period: 1/1/2014 - 12/31/2015

Inflammatory Bowel Disease (IBD) is a group of disorders in which the intestinal tract has become invaded with the dog's own white blood cells leading to inflammation. Over time, this inflammation causes the intestine to become less efficient at absorbing nutrients from digested food and weight loss, and vomiting or diarrhea often result. IBD can be controlled, but not cured. The cause of IBD is poorly understood, but it appears that genetics, diet, intestinal bacteria, and abnormalities of the dog's immune system all play a role. Dr. Allenspach has recently identified genetic markers known as SNPs (single nucleotide polymorphisms) which she believes contribute to disease susceptibility. Beyond genetics, this research group has mechanistic data showing one of the putative mutations contributes to the inflammation seen in the intestine of dogs with IBD. In order to find all underlying genetic factors that could contribute to disease, they propose to perform a genome-wide association study. This study will lead to the development of new diagnostic and therapeutic avenues for canine IBD as has already been the case in people with IBD.

**Research Deliverable: Development of new diagnostic and therapeutic options for canine IBD**

### **02050: *Defining the Genetic Susceptibility to Granulomatous Colitis, a Severe Form of Inflammatory Bowel Disease***

Principal Investigator: Dr. Kenneth W. Simpson, BVMS, PhD; Cornell University  
Total Grant Amount: \$187,730.00; Grant Period: 1/1/2014 - 12/31/2015

Granulomatous colitis is a severe inflammatory bowel disease (IBD), usually diagnosed in young dogs. Affected dogs present with hemorrhagic diarrhea, often progressing to weight loss and debilitation. Recent studies have identified invasive *Escherichia coli* (*E. coli*) bacteria within macrophages in the inflamed large intestine, and eradication of *E. coli* induces dramatic clinical and histologic improvement. Unfortunately, the emergence of antimicrobial resistance has greatly reduced our ability to treat this disease, and persistently affected dogs are frequently euthanized. The type of *E. coli* isolated from dogs with granulomatous colitis is very similar to adherent and invasive *E. coli* (AIEC) associated with IBD in people. This type of *E. coli* is considered opportunistic pathogens that can exploit genetic defects in bacterial killing in an IBD susceptible individual. Dr. Simpson suspects this is due to a heritable abnormality that confers susceptibility to invasion and persistence of *E. coli*. In preliminary studies his research group has identified a region of the canine genome that is associated with granulomatous colitis affected dogs. This region contains candidate genes associated with IBD in people and mouse models, and has been specifically linked to sensing and killing of *E. coli*. The purpose of this study is to identify the gene(s), causal variant(s) and cellular pathways involved in the development of granulomatous colitis. This would enable the development of screening tests to eradicate this disease, and advance understanding of the development of IBD in dogs and people.

**Research Deliverable: Identification of the genes responsible for the most severe form of IBD**



## Oncology Research Program Area

### **01426: *Personalized Medicine for the Treatment of Canine Mast Cell Tumors***

Principal Investigator: Dr. Douglas H Thamm, VMD; Colorado State University

Total Grant Amount: \$90,000.00; Grant Period: 1/1/2011 - 6/30/2014

While surgery remains the mainstay of treatment for canine mast cell tumors (MCT), surgery alone is not curative in some cases, and not possible in other cases. Medical therapy remains an important component of MCT therapy. New drugs that impair signaling through growth factor receptors known to "feed" the tumor are showing considerable promise for the treatment of canine MCT, and MCT with mutations in these growth factor receptors may make tumors more sensitive to certain drugs. Dr. Thamm's research group recently developed a rapid test, which can be performed on fine-needle aspirates, to determine whether MCT possess mutations in growth factor receptors. In this study they will determine if testing for the presence of a growth factor receptor mutation is a useful decision-making tool for the selection of the best possible medical therapy for dogs with MCT. This study will be the first step toward personalized medicine in the treatment of canine mast cell tumors.

**Research Deliverable: Personalized treatment of canine mast cell tumors**

### **01843: *Further Investigation of the Genes Controlling Canine Leukemia to Properly Diagnose and Control the Disease***

Principal Investigator: Dr. Matthew Breen, PhD; North Carolina State University

Total Grant Amount: \$131,265.00; Grant Period: 1/1/2013 - 12/31/2014

Leukemia represents a range of cancers, most often classified according to the type of blood cell affected and the clinical progression. Leukemia may be chronic, progressing slowly for many years with minimal symptoms, or acute, with sudden onset and rapid progression of symptoms, often resulting in euthanasia. The true incidence of leukemia in dogs is unknown, but consensus opinion is that many cases remain undiagnosed. In previous studies Dr. Breen found that canine leukemia presents with characteristic chromosomal and genetic changes shared with those known in human leukemia. In humans these chromosomal and genetic aberrations have been linked to disease progression and response to therapeutics, and in turn, this information drives clinical management of the patient. In this multicenter study, Dr. Breen's group will use high-resolution genome-wide chromosomal evaluation to screen a large cohort of canine leukemia patients for the presence of recurrent chromosomal and genetic changes. This study will enhance our understanding of the pathogenesis of canine leukemia by identifying regions of the canine genome, and thus individual genes that may be critical for the control of these cancers. Additionally, this study will provide data that will impact our knowledge of the corresponding human disease.

**Research Deliverable: Development of cytogenetics as a diagnostic and prognostic tool for prevention and management of canine leukemia**



**01889-Ga: *Innovations in Prevention, Diagnosis, and Treatment of Cancer - Golden Lead the Way***

Principal Investigator: Dr. Jaime F Modiano, VMD PhD; University of Minnesota  
Total Grant Amount: \$360,933.00; Grant Period: 1/1/2014 - 12/31/2016

Lymphoma and hemangiosarcoma are major health problems in Golden Retrievers, causing both suffering and premature death. Through ongoing collaboration, Drs. Jaime Modiano, Matthew Breen, and Kerstin Lindblad-Toh have identified several regions of the genome that contain genetic heritable risk factors for lymphoma and hemangiosarcoma in Golden Retrievers. They have tumor-specific mutations that occur recurrently in both cancers, some of which are linked to duration of remission when treated with standard of care. Their results indicate that a few heritable genetic risk factors account for as much as 50% of the risk for these cancers. These findings offer the potential to develop tests and strategies for DNA tests that can predict risk for individual dogs, as well as to manage risk across the population as a whole. Indeed, both the inherited risk factors and tumor mutations point to pathways that have been implicated in the pathogenesis of lymphoma and hemangiosarcoma, and thus should inform the development of targeted therapies. In the current study, Drs. Modiano, Breen, and Lindblad-Toh will find the precise mutations for the heritable genetic risk factors and to validate markers (mutations) used to determine risk at the heritable loci in a larger independent population of Golden Retrievers from the United States and from Europe in order to develop robust risk prediction tools and an accompanying DNA test. Further, they will identify and characterize tumor mutations and study their relationship to the heritable risk factors, tumor pathogenetic mechanisms, and disease outcome.

**Research Deliverable: Identification of heritable risk factors for lymphoma and hemangiosarcoma in dogs**



## **Oncology - Hemangiosarcoma Research Program Area**

### ***01759: Disrupting the Differentiation of Cancer Stem Cells to Prevent the Spread of Hemangiosarcoma***

Principal Investigator: Dr. Jaime F Modiano, VMD PhD; University of Minnesota  
Total Grant Amount: \$233,914.00; Grant Period: 1/1/2013 - 12/31/2015

Hemangiosarcoma is a rapidly fatal disease. The lifetime risk is alarmingly high for some breeds like Golden Retrievers (~20% will die of this disease) and Portuguese Water Dogs (~15% will die of this disease). The risk of hemangiosarcoma is not limited to just these breeds but is considered a research priority for 40 different breed Parent Clubs. Despite considerable efforts to find effective treatments, the outcome for dogs with hemangiosarcoma has changed very little over the past 30 years. Recent evidence suggests hemangiosarcoma conforms to the "cancer stem cell" model, where a defined subset of cells is responsible for initiating and maintaining the tumor. These cells are resistant to conventional therapies and are very adaptable, being able to survive in a variety of tissues in the body. For this project, Dr. Modiano proposes to reduce the malignant potential of hemangiosarcoma stem cells by forcing them to terminally differentiate into cells which can no longer self-renew. He further proposes that by disrupting their ability to self-renew he will enhance the sensitivity of these cells to conventional and targeted therapies and improve the outcomes of dogs with this disease.

**Research Deliverable: Development of a novel treatment to target cancer stem cells and halt metastasis in hemangiosarcoma**

### ***02081-A: Integrating Cutting Edge Science with Scientific Training to Defeat Hemangiosarcoma***

Principal Investigator: Dr. Jaime F Modiano, VMD PhD; University of Minnesota  
Total Grant Amount: \$12,960.00; Grant Period: 8/1/2013 - 7/31/2014

Canine hemangiosarcoma (HSA) is an intractable disease with no warning signs and no effective treatments. Contemporary research is overturning long-held, yet incorrect assumptions about its origins and biological behavior. One approach to accelerate progress is to bring young, talented scientists with no deep-held biases into the field and allow them to evaluate data with a fresh perspective. This project is designed to nurture one such young scientist under the joint mentorship of a stellar post-doc and a tech, and a senior established investigator. Ms. Ashley Rodriguez, a 10th grader at the Potomac School in McLean, VA, helped to conceive this project. She formulated the hypothesis that sphingosine-1 phosphate receptors (S1PR) contribute to the progression of HSA. She arranged for this collaboration to test her hypothesis in Dr. Modiano's lab, where she will train through an intensive summer experience. Thereafter, she will continue working at the Potomac School under the guidance of Dr. Cohen, her science teacher, while Dr. Modiano complements her efforts at the U of M. She will not only acquire experimental skills, but also meet other scientists in the field and learn the art of scientific writing and reporting. The involvement of a senior team of scientists will ensure that the mentoring goals are completed and accompanied by scientific innovation. At the end of the project, we expect Ms. Rodriguez's ambition to become a veterinary scientist to be further solidified and to have data to support projects that can translate S1PR modulation into improved outcomes for dogs with HSA.

**Research Deliverable: Unique combination of student training and cutting edge science to identify a novel drug target for canine hemangiosarcoma**



## Ophthalmology Research Program Area

### **02057: *Identification of the Genetic Cause of Corneal Ulcers***

Principal Investigator: Dr. Keith W Montgomery, DVM; North Carolina State University

Total Grant Amount: \$27,201.00; Grant Period: 1/1/2014 - 12/31/2015

Spontaneous chronic corneal epithelial defects, or indolent ulcers, describe an eye disorder characterized by chronic corneal ulcers that fail to undergo normal healing. The predilection for Boxers suggests that indolent ulcers are inherited in this breed. Affected dogs develop spontaneous corneal ulcers that are often exceptionally painful and persist for weeks to months. Most dogs require surgical therapy to heal the corneal ulcer and experience corneal scarring as a result. Although indolent ulcers can be effectively treated, some dogs develop additional episodes of corneal ulcers during their lifetime. The impact on the quality of life for dogs during episodes of ulceration has led to increased interest in disease prevention. However, since indolent ulcers are an adult onset disease, many dogs are selected for breeding before they are diagnosed. A blood test that could identify affected animals before they are used for breeding would greatly decrease the prevalence of indolent ulcers. Dr. Montgomery will use a genome wide association approach to identify an association of a genetic region to indolent ulcers. They will then more closely evaluate the chromosomal region of interest to determine the gene and ultimately the causative genetic mutation. They believe that the identification of a genetic cause for indolent ulcers can be used to reduce the prevalence of this disease in multiple affected breeds.

**Research Deliverable: Identification of the genes responsible for corneal ulcers in boxers**



## Reproductive Conditions and Disease Research Program Area

### **01840: *Health Implications of Early Spay/Neuter on Canine Health***

Principal Investigator: Dr. Benjamin L Hart, DVM, PhD; University of California, Davis  
Total Grant Amount: \$146,589.00; Grant Period: 2/1/2014 - 1/31/2016

Most dogs in the United States are spayed or neutered, and the default recommendation has been to perform these elective surgeries prior to physical maturity. However, recent data suggest that early spay and neuter may adversely impact the health and well-being of dogs. In preliminary studies funded by CHF, Dr. Ben Hart of the UC Davis College of Veterinary Medicine found that early spay or neuter, prior to 12 months of age, was related to a significant increase in risk in five diseases of concern: hip dysplasia; cranial cruciate ligament tear; lymphosarcoma; hemangiosarcoma; and mast cell tumor.

CHF has now funded the second phase of Dr. Hart's research in which he will expand his work to consider breed differences in vulnerability to joint disorders and risks of various cancers after early or late spay/neuter. Breeds considered will include: Labrador Retrievers, German Shepherd Dogs, and Dachshunds. Rottweilers, Chihuahuas, Standard Poodles, and Miniature Poodles will be included if resources and patient data are available. The expectation is that by inclusion of multiple breeds in phase II Dr. Hart will be able to develop a generalized understanding of the impact of early spay and neuter on disease risk in dogs. This in turn will enable veterinarians and breeders to make data-driven recommendations regarding timing of spay/neuter procedures to reduce the risk of development of multiple devastating diseases.

**Research Deliverable: Determination of the role of early spay/neuter in the long term health and well-being of dogs, with emphasis on cancer and orthopedic disease risk**



## Regenerative Medicine

Regenerative medicine is a rapidly developing field with the potential to transform the treatment of canine disease. The ability to repair damaged tissue and treat diseases once believed to be incurable may soon be a reality. However, there are concerns that some techniques are being used prematurely. Due to the lower regulatory barriers in veterinary medicine, regenerative medicine techniques are currently used in general and specialty hospitals. These techniques vary widely and the evidence that they work is anecdotal at best. The AKC Canine Health Foundation has made the evidence-based practice of regenerative medicine a major focus within our research portfolio. Through an ongoing commitment to fund research studies that will inform the veterinary community in the use of safe and effective regenerative medicine techniques, we intend to protect dog owners and support veterinarians with innovative technology that will consistently improve outcomes for dogs.

Currently, our research focus includes the identification of tissue-engineered products that are used to:

- Induce bone and connective tissue growth
- Replace damaged knee cartilage
- Repair damaged spinal cord tissue
- Regenerate smooth muscle to enhance bladder control
- Ensure that regenerative medicine techniques do not exacerbate the development of cancer in susceptible dogs



## **Regenerative Medicine in Musculoskeletal Conditions and Disease Research Program Area**

### ***02078: Development of a Regenerative Medicine Technique to Treat Cartilage Disorders in Dogs***

Principal Investigator: Dr. William Brian Saunders, DVM, PhD; Texas A&M AgriLife Research  
Total Grant Amount: \$120,872.00; Grant Period: 1/1/2014 - 12/31/2015

Osteochondrosis is a common and debilitating disease affecting large, athletic dogs. Osteochondrosis is caused by abnormal endochondral ossification, the process by which growth plate cartilage adjacent to joint surfaces transitions from cartilage to bone. The result is excessively thickened cartilage that partially or completely separates from surrounding bone. Cartilage separation exposes the joint to underlying bone and creates a large loose body, termed a joint mouse, within the joint. Surgical or medical treatment results vary widely based on the affected joint, size of the osteochondrosis defect, and intended purpose for each dog. Treatment options for osteochondrosis have remained essentially unchanged for decades. Tissue engineering represents a promising treatment alternative for dogs suffering from OC. Dr. Saunders believes the key to successful tissue engineering involves generation of regenerative osteochondral plugs, or ROPs. ROPs are tri-layered cylindrical plugs composed of hydrogels seeded with adult mesenchymal stem cells (MSCs). Each ROP layer is composed of materials that closely mimic specific zones of the joint and adjacent bone. ROP layers are bioactive, directing encapsulated MSCs to differentiate into specific tissues to more efficiently restore normal joint anatomy. Dr. Saunders will optimize the materials used to generate ROP layers and will determine if MSCs from tissue lining the joint (synovium) or inner cavity of bones (bone marrow) more effectively reconstruct native cartilage, transitional tissue, or bone. This work represents an important advance in canine regenerative medicine and is highly applicable to dogs with osteochondrosis or other common joint ailments such as osteoarthritis.

**Research Deliverable: Development of Tissue Engineering techniques to regenerate osteochondral plugs for treatment of common joint ailments such as arthritis**



## **Regenerative Medicine in Musculoskeletal Conditions and Disease Research Program Area**

### **01762: *Use of Plasma-Derived Growth Factors to Heal Cruciate Rupture***

Principal Investigator: Dr. Peter Muir, BVSc, PhD; University of Wisconsin, Madison  
Total Grant Amount: \$160,246.00; Grant Period: 1/1/2013 - 12/31/2014

Cruciate rupture (CR) is a common degenerative condition of the canine knee (stifle). This economically important condition causes 20% of lameness in dogs and is disabling. Each knee contains two cruciate ligaments (cranial and caudal) that are located within the joint and stabilize the knee. Degeneration, fraying and progressive fiber rupture commonly affects both ligaments, but particularly the cranial or anterior cruciate ligament (ACL). Current surgical treatments stabilize the knee but do not directly treat the damaged or ruptured ligament. The main goal of Dr. Muir's research is to develop a safe and effective therapy that will prevent progressive tearing of ligament fibers, enable ligament healing, and block arthritis progression in affected dogs. To accomplish this goal, his research group will study a new regenerative medicine treatment using growth factors derived from a type of white blood cell, the platelet, concentrated from the patient's own blood. They will determine whether this treatment can promote cruciate healing and reduce progressive ligament rupture in dogs with early CR and clinically stable knees. Overall, this work promises improved outcomes for all dogs affected by CR disease.

**Research Deliverable: Evidence-based practice of regenerative medicine using Platelet Rich Plasma to treat Cranial Cruciate Ligament Disease**

## **Regenerative Medicine in Renal Disease Research Program Area**

### **01844: *Treatment of Urinary Incontinence with Multipotent Muscle Cells: A Regenerative Medicine Approach to a Common Canine Health Problem***

Principal Investigator: Dr. Shelly Vaden, DVM PhD; North Carolina State University  
Total Grant Amount: \$116,184.24; Grant Period: 1/1/2013 - 12/31/2014

Urinary incontinence affects more than 20% of spayed female dogs, with medium and large breeds more commonly affected. In the majority of the cases urinary incontinence is caused by dysfunction of the muscles controlling the urethral sphincter. This results in uncontrolled loss of urine and can lead to serious bladder and kidney infections, in addition to irritation and/or ulceration of the skin in contact with the urine. Treatment can include hormone therapy, drugs designed to strengthen the muscle tone of the urethral sphincter, collagen injections, or surgery. Recently, Dr. Vaden's lab has reported that injection of muscle progenitor cells into damaged urethral sphincters can restore normal function in dogs. The purpose of this project is to extend those observations and examine the usefulness of cultured muscle cells for the restoration of function of the urethral sphincter in dogs with naturally occurring urinary incontinence. The effects of the procedure will be determined by owner reported continence scoring, as well as urodynamic testing that will provide an objective measurement for how well the bladder, sphincters, and urethra are storing and releasing urine.

**Research Deliverable: Use of stem cell therapy to treat canine incontinence**