Request for Chinese Crested Grant Support

01312: ***Association mapping study of Legg-Calve-Perthes Disease in the West Highland White Terrier, Yorkshire Terrier, and Miniature Pinscher***

Primary Investigator: Dr. Keith E. Murphy, PhD; Dr. Alison Starr, PhD
Institution: Clemson University

Total Grant Amount: $78,688.00 **Requested Sponsorship: $2,500**

Project Abstract:

Background: Legg-Calve-Perthes Disease (LCPD) is a debilitating developmental disease that affects small breeds of dog, particularly terrier breeds. The only outward indications of this condition are pain, lameness, and muscle atrophy of the hip joint. These signs are not exclusive to LCPD, and are often attributed to minor trauma during the early stages of disease. LCPD is primarily diagnosed by radiographic changes of the femoral head within the hip joint. Due to the developmental nature and the unknown etiology of the disease, LCPD is difficult to predict and prevent. No disease mapping strategies have been employed to date.

Objective: This study is using the Affymetrix canine single nucleotide polymorphism (SNP) chip to identify regions that are linked to LCPD in the West Highland White Terrier, Yorkshire Terrier, and Miniature Pinscher breeds.

01248: ***Whole Genome Association Analyses for Cryptorchidism in Dogs***

Primary Investigator: Dr. Max Rothschild, PhD
Institution: Iowa State University

Total Grant Amount: $74,104 **Requested Sponsorship: $2,500**

Project Abstract:

Background: Cryptorchidism, or retained testicles, is one of the common congenital problems in dogs. The testes of cryptorchids are more prone to testicular cancer and infertility. Therefore, cryptorchids and animals carrying genes for cryptorchidism should be eliminated from the breeding population. Some evidence exists to suggest that it appears to be a multigenic trait but single genes with large effects may exist. In earlier studies, the researchers utilized a candidate gene approach using 50 polymorphisms (called SNPs) in 22 candidate genes and found that collagen 2A1 (COL2A1) was significantly associated with cryptorchidism in Siberian Huskies.

Now, they need to use the whole genome association analysis which typically provides more comprehensive analyses of chromosomal regions associated with a particular trait. This will then allow them to confirm previous findings or suggest other contributing regions or genes.

Objective: The researchers will utilize a new tool called the canine SNP chip which allows them to genotype for over 200,000 genetic differences between affected and unaffected animals. All results will be published and available freely to all dog breeders and they also aim to develop a test to remove the defect from the population.

01262: ***Sequencing and Functional Analysis of the Canine Y Chromosome***

Primary Investigator: Dr. William J. Murphy, PhD
Institution: Texas A&M University

Total Grant Amount: $106,309.00 Requested Sponsorship: $2,500

Project Abstract:

Background: Studies of the human and mouse Y chromosomes have shown they contain many testis-specific genes that, when defective, cause infertility and sperm abnormalities. The causes of male infertility in dogs are not well known. Though a high quality draft genome sequence exists for the canine autosomes and X chromosome, virtually nothing is known about the canine Y chromosome and the genes it harbors.

Objective: The researchers will use an existing map of the canine Y chromosome to generate a comprehensive sequence of the chromosome, and explain the sequence for coding and non-coding potential using cDNAs selected from a large number of canine tissues. The identification of a comprehensive set of canine Y chromosome genes, their regulatory regions and noncoding RNAs will provide targets for development of molecular diagnostic tests that examine the influence of these genetic elements on canine male infertility as well as many other sexually dimorphic traits.

01272: ***Isolation and Characterization of Canine Induced Pluripotential Stem Cells (iPS)***

Primary Investigator: Dr. Jorge Piedrahita, PhD
Institution: North Carolina State University

Total Grant Amount: $82,610.00 **Requested Sponsorship: $2,500**

Project Abstract:

Background: Stem cells have tremendous promise to alleviate clinical conditions in dogs such as spinal cord damage, hematopoietic malignancies, and cardiac and hepatic disease. While a range of adult stem cells have been isolated and studied, most of these have a limited capacity to differentiate outside a living organism and inside a living organism. Recently, approaches have been developed to convert differentiated cells into cells resembling embryonic stem (ES) cells by the use of "reprogramming" factors. These cells referred to as induced pluripotential stem cells (iPS) have the ability, like ES cell, to differentiate into multiple tissue types. As virtually any cell can be converted to an iPS cell this means that it is now possible to isolate patient-derived stem cells.

Objective: The researchers will utilize this technology for the development of canine iPS. Briefly, adipocyte-derived mesenchymal cells and keratinocytes will be transformed with the required reprogramming factors and plated under a condition that allows development of iPS cells. Colonies will be selected, expanded, and studied for their ability to differentiate outside a living organism into multiple tissue types. The development of patient-specific pluripotential stem cells is a critical step toward the successful scientific application of this promising technology.

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

Primary Investigator: Dr. Susan Volk, VMD PhD
Institution: University of Pennsylvania - School of Veterinary Medicine

Total Grant Amount: $165,348.00 **Requested Sponsorship: $2,500**

Project 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.

Objective: This study 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.