

## **Labrador Retriever Muscular Dystrophy Research Program**

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For the past three years, we have been investigating the molecular basis of Autosomal Recessive Muscular Dystrophy (ARMD) in Labrador Retrievers. This project, which was begun by Dr. Kyle Braund, who has since retired, is now led by Dr. Bruce Smith. The project has been supported by grants from the AKC/CHF, Auburn University Sports Medicine Program, the Scott Ritchey Research Center, and private donations. The objectives of the program are to create a small breeding colony of carrier and affected dogs, that would allow the disease process to be studied, and to identify and sequence the gene thought to be responsible for the disease. Several affected and carrier dogs have been donated by concerned owners and breeders, and these have recently begun producing offspring. West Highland White Terrier are following these puppies from birth and attempting to identify clinical differences that will allow this disease to be more readily diagnosed in a clinical setting.

In addition, we have identified Calpain 3, a calcium activated cellular protease as a candidate gene for this disease. We have sequenced approximately 90% of the normal canine calpain gene. The remaining 10% has proven exceedingly difficult to sequence, however new technology in the laboratory is currently being applied to this remaining sequence. In addition, we have recently obtained high quality RNA from skeletal muscle of an affected dog and are beginning to sequence calpain from affected dogs. We hope to have this sequence completed within several months. When the sequence from the affected dogs is complete, we are able to compare it to normal dog sequence and determine if there is a mutation and where the mutation in the gene is located. This information will then be used to rapidly create a DNA based test for this disease that will hopefully be available within 6-9 months.

In our ongoing work with dogs with ARMD we have come in contact with Labrador Retrievers with two other muscle diseases. The first of these is x-linked Duchenne-like muscular dystrophy. The disease only affects male dogs, and in the litter we observed, had an extremely severe phenotype, with death occurring by 15 weeks. We are currently establishing a collaboration with one of the leading Duchenne Muscular Dystrophy laboratories to identify the mutation responsible for this disease, and are applying to the AKC for funding to pursue this project. The second disease is known by a number of different names including Malignant Hyperthermia, Exercise Induced Hyperthermia and Canine Stress Syndrome (CSS). This disease resembles both malignant hyperthermia in humans and porcine stress syndrome. We have obtained two dogs with this disease and are looking to obtain several additional dogs. Our initial goals are to study the inheritance pattern, identify appropriate clinical tests, and identify a candidate gene for future sequencing. This disease seems to be increasing in frequency and represents the next genetic threat to the Labrador Retriever breed beyond ARMD.