GRANT PROGRESS REPORT REVIEW

Grant: 01311: Genome-wide association mapping study of hypertrophic osteodystrophy in Irish Setters

Principal Investigator: Dr. Keith E. Murphy, PhD
Research Institution: Clemson University
Grant Amount: $74,237.00
Start Date: 1/1/2010  End Date: 6/30/2012

Progress Report: 24 month
Report Due: 12/31/2011  Report Received: 4/2/2012

Recommended for Approval:
(Content of this report is not confidential. A grant sponsor’s CHF Health Liaison may request the confidential scientific report submitted by the investigator by contacting the CHF office. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:
Background: Hypertrophic osteodystrophy (HOD) is a debilitating, metabolic bone disease that, in mild cases, can lead to deformation of mature bone, and in severe cases, can require euthanasia of affected dogs. At present, the cause of HOD is unknown. Most cases of HOD are observed shortly after vaccinations, the most often proposed causes are distemper virus infection, post-vaccination infection, bacterial infection, or other viral infections. The predominance of HOD in several breeds of dog suggests a heritable component of the disease. Due to the complex nature of the immune system and its many components, analysis of candidate genes would have to be exhaustive.

Objective: The researchers aim to identify genes involved in HOD with the whole genome association mapping using the canine single nucleotide polymorphism (SNP) chip. This resource will identify regions exhibiting linkage with HOD. Such regions will then be assessed for gene(s) involved in the disease.

Grant Objectives:
Objective 1: Sample collection and phenotype confirmation. Collect a total of 200 samples.

Objective 2: Probe SNP array for genome wide association.
Hypertrophic osteodystrophy (HOD) is an orthopedic disorder of unknown etiology in puppies of large breeds. The primary clinical signs include inflammation of long bones in the forelimbs, accompanied by fever, lethargy, and weight loss. This study aims to identify genomic regions associated with HOD in one breed at increased risk, the Irish Setter. To this end, we are using whole-genome data generated through a SNP-based association study and next-generation sequencing to produce a comprehensive genome survey of HOD-affected and healthy Irish Setters. A preliminary association study in a subset of our Irish Setter study population has been completed, and the remaining experiments are scheduled for completion. Three regions of interest were identified from the preliminary study; one candidate gene was sequenced and excluded in HOD. Data produced from this work suggest that HOD is not a trait with simple inheritance.

We initially wrote to collect blood samples from 200 Irish Setters: 100 affected and 100 unaffected. To date, we have received 43 affected and 58 unaffected Irish Setters, or approximately half of our anticipated numbers. The statistical analyses of SNP data from 100 dogs as opposed to 200 dogs may not be sufficient to detect any associations, given that HOD is genetically complex. Thus, we have proposed next-generation whole-genome sequence as a means to augment the SNP data to maximize the use of the dogs we currently have samples from and the budget we requested to complete the work. Plans for the remaining grant period include 1) genotyping additional Irish Setters with the Affymetrix SNP array and 2) generating whole-genome sequence for affected and unaffected Irish Setters.