GRANT PROGRESS REPORT REVIEW

Grant: 00927: *Gene Discovery in Hereditary Cerebellar Abiotrophy of Scottish Terriers*

Principal Investigator: Dr. Natasha J Olby, VetMB PhD

Research Institution: North Carolina State University

Grant Amount: $54,810.00

Start Date: 1/1/2008 **End Date:** 12/31/2010

Progress Report: 30 month

Report Due: 6/30/2010 **Report Received:** 8/17/2010

Recommended for Approval: Approved

(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: A hereditary neurodegenerative disease called a cerebellar abiotrophy has emerged as a significant problem in the Scottish Terrier. The disease causes neuronal death in the cerebellum, resulting in progressive loss of coordination. Signs appear between three and 24 months of age and progress until the animal is incapacitated; currently there is no treatment. The disease is inherited in an autosomal recessive manner therefore carriers of the disease are normal. As a result, the abnormal gene has been spread within the Scottish Terrier breeding population.

Objective: The researchers have collected DNA samples from affected dogs and their relatives and will classify families of these affected dogs using a set of markers that span the canine genome at regular intervals. A connection study will be performed with the data to link a chromosomal region to the disease. Candidate genes in the linked regions will be sequenced to identify mutations. In the absence of candidate genes, linked regions will be saturated with closely spaced markers to narrow the region of interest, facilitating sequencing of genes in the area. Once the abnormal gene has been identified, a genetic test will be developed to identify carriers and affected dogs.

Grant Objectives:
Objective 1: Phenotype confirmation and DNA/RNA banking from families of affected Scottish terriers

Objective 2: Identification of chromosomal region(s) linked to cerebellar abiotrophy in Scottish terriers
Objective 3: Identification of candidate genes in linked chromosomal regions

Objective 4: Sequencing of candidate genes to identify the causative mutation

Publications:
- Urkasemsin, G., Linder, K.E., Bell, J.S., Lahunta, A.d., Olby, N.J., 2010, Hereditary Cerebellar Degeneration in Scottish Terriers. Journal of Veterinary Internal Medicine 24, 565-570.

Report to Grant Sponsor from Investigator:
In this project we aimed to better define the phenotype of Scottish Terriers with Cerebellar Degeneration, to bank DNA from as many affected and related normal dogs as possible and to perform a genome-wide screen to look for linkage of trait to a specific chromosomal region. If a linked region was identified, candidate genes in the region were to be investigated further.
Since our last report, we have genotyped additional dogs using the illumina SNP chip and we have identified a region that is significantly associated with the disease trait. We are now working on identifying and sequencing genes of interest in this region.
Thank you for the ongoing support you have shown us – we hope that we will ultimately identify the underlying mutation and develop a test for the disease.
Natasha Olby