GRANT PROGRESS REPORT SUMMARY

Grant: 01615: *Identification of Idiopathic Epilepsy Genes in Australian Shepherds*

Principal Investigator: Dr. Ned E. Patterson, DVM PhD

Research Institution: University of Minnesota

Grant Amount: $106,289.00

Start Date: 1/1/2012 **End Date:** 12/31/2013

Progress Report: End-Year 1

Report Due: 12/31/2012 **Report Received:** 12/31/2012

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:

In 2010--2011 we performed a Genome Wide Association Scan (GWAS) with genetic markers for Idiopathic Epilepsy (IE) in 19 affected and 21 unaffected Australian shepherd (AS) dogs, and found a chromosomal region with a statistically significant association. This indicates that there is very likely to be a nearby genetic mutation related to epilepsy in Aussies. Another chromosomal region is close to achieving significant association. In this ongoing study, we plan to sequence the small chromosomal area in the area of significance to identify the gene that is causing or contributing to IE in Aussies, as well as perform an additional GWAS on 48 more affected and 48 more unaffected Aussies. The additional GWAS is needed to see if there is more than one gene contributing to the development of IE in AS. Once we identify a confirmed mutation we will then develop a DNA based genetic test. An IE genetic test would greatly assist breeding programs to identify affected puppies before they are sold by breeders and aid veterinarians in diagnosis and possibly treatment of affected dogs. It could also lead to the eventual elimination of this disease from the AS breed through selective breeding. In addition, once we identify one or more IE gene(s) in AS we will test to see if these mutation(s) affect other dog breeds with a high incidence of IE.

Grant Objectives:

Objective 1. Perform a GWAS in more Australian shepherds to determine if there are additional contributing loci.

Objective 2. Utilize positional DNA sequencing of the identified locus to find a contributing mutation.

Publications:

None at this time.

Report to Grant Sponsor from Investigator:

Genetic marker data from 88 Australian Shepherds (44 cases and 44controls) total has now been analyzed with standard genetic association statistical analysis. This includes 25 new cases and 23 new controls during this grant period. So far there are two different chromosomes that potentially contain an associated epilepsy gene or genes. In the past 6 months we have performed many additional new statistical analyses on the data. We have identified a confirmed a new third potential area in the last 6 months, and the area previously identified on chromosome 1 was not confirmed in the new analysis. These confirmed areas are on dog chromosomes 16,19 and 26.

We are continuing with additional in depth analysis, and working on finding the most likely genes in each area of each these 3 chromosomes that may be related to contributing to epilepsy, and we plan to find additional markers near the genes. Currently we are in the middle of sequencing two candidate genes from these three identified areas. We are now also planning to obtain up to 24 new case and 24 new controls, from our collaborators in the USA and/or Europe, for additional genetic marker analysis if sufficient funds remain in the budget. In addition we plan to utilize next generation DNA sequencing to sequence portions of these 3 chromosomal areas in the next 6-9 months, if needed, in our search for genetic mutations contributing to epilepsy in Australian Shepherds.