



AMERICAN KENNEL CLUB
**CANINE HEALTH
FOUNDATION**
PREVENT TREAT & CURE

GRANT PROGRESS REPORT REVIEW

Grant: 00925: *Identification of Mutations Causing Hereditary Cerebellar Cortical Degeneration in American Staffordshire Terriers and Old English Sheepdogs*

Principal Investigator: Dr. Natasha J Olby, VetMB PhD

Research Institution: North Carolina State University

Grant Amount: \$64,800.00

Start Date: 4/1/2008 **End Date:** 3/31/2011

Progress Report: 30 month

Report Due: 9/30/2010 **Report Received:** 11/1/2010

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: American Staffordshire Terriers and Old English Sheepdogs suffer from similar, but likely distinct, hereditary neurodegenerative diseases of the cerebellum. In both breeds the disease is inherited in a recessive fashion and the underlying mutation has become widely dispersed in the population. The researchers have collected DNA from affected dogs and their relatives in both breeds and have genotyped them using markers spaced at regular intervals throughout the genome. They have used the resulting data to link a chromosomal region to the disease trait. The researchers have established linkage in both breeds of dog; the disease is linked to a different chromosomal region in each breed.

Objective: In this project the researchers will identify candidate genes for the disease in linked regions using published information on the canine genome. These genes will be sequenced to identify mutations. If there are no good candidate genes, they will saturate the linked regions with closely spaced markers, thus narrowing the target region to the extent that all genes contained within can be sequenced. Identifying the mutation in either of these breeds will be relevant for additional breeds of dog that have similar diseases such as the Scottish Terrier and Gordon Setter.

Grant Objectives:

Objective 1: Identify candidate genes in linked chromosomal regions

Objective 2: Perform high-density mapping of linked chromosomal regions

Objective 3: Sequence candidate genes

Publications:

- Olby NJ, Harris T, Mehta PM, Breen M, Thomas R, Myers R, Nielsen D. Linkage analysis in American Staffordshire Terriers with hereditary cerebellar cortical degeneration. *J Vet Intern Med* 2008;22:723-724

- Abitbol, M., Thibaud, J.-L., Olby, N.J., Hitte, C., Puech, J.-P., Maurer, M., Pilot-Storck, F., Hedan, B., Dreano, S.p., Brahimi, S., Delattre, D., Andre, C., Gray, F.o., Delisle, F.o., Caillaud, C., Bernex, F., Panthier, J.-J., Aubin-Houzelstein, G.v., Blot, S.p., Tiret, L., 2010, A canine Arylsulfatase G (ARSG) mutation leading to a sulfatase deficiency is associated with neuronal ceroid lipofuscinosis. *Proceedings of the National Academy of Sciences* 107, 14775-14780.

Report to Grant Sponsor from Investigator:

Report for Old English Sheepdog Club of America

Our work to date has confirmed that Cerebellar Abiotrophy in Old English Sheepdogs is linked to a region of a single chromosome using two different techniques (linkage and association), and so we are confident about this finding. However, the linked region is large, containing many genes. In order to narrow the region so that the causative mutation can be pinpointed, ideally we need to genotype a lot more affected individuals; over the summer we were able to genotype three new individuals, but this did not narrow the region for us. As an alternative, we propose to use some new technology to attempt to sequence all the genes in the region linked to the disease. In the past this would have been extremely time consuming and expensive, but developments in technology allow us to be able to attempt this sequencing in a more timely and cost efficient manner. Over the next year we will welcome any additional samples from affected dogs, will genotype them when possible (this has to be batched), and will focus on our attempt to sequence the entire region we have identified as linked to the disease.