



## RESEARCH PROGRESS REPORT SUMMARY

**Grant 02162-MOU:** Defining The Genetic Foundations of Chiari-Like Malformation and Syringomyelia as a Tool to Better Treat Neuropathic Pain in the Dog

**Principal Investigator:** Dr. Natasha J Olby, VetMB PhD

**Research Institution:** North Carolina State University

**Grant Amount:** \$37,530.00

**Start Date:** 1/1/2015

**End Date:** 12/31/2016

**Progress Report:** Mid-Year 2

**Report Due:** 6/30/2016

**Report Received:** 8/26/2016

**Recommended for Approval:** Approved

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*(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:

Chiari like malformations and syringomyelia (CM/SM) are a common problem in Cavalier King Charles Spaniels (CKCS) causing severe neuropathic pain. The morphometry of the skull has been examined in detail and the development of clinical signs and syringomyelia has been correlated to reduced caudal fossa to cranial cavity volume ratios and stenosis of the jugular foramen respectively. There is evidence this disorder is a complex hereditary trait, but attempts to identify genetic causes have been hampered by assigning an affected or normal phenotype. Use of quantitative data from magnetic resonance imaging (MRI) will allow us to perform a more appropriate genetic analysis of this important and common disease. Quantification of neuropathic pain is challenging and while owners of affected CKCS frequently complain that their pet is experiencing significant pain, a routine evaluation by palpation does not always correlate well to their history. Humans with CM report increased sensitivity to touch and temperature. During case phenotyping for the genetic study, we would like to investigate sensory thresholds in affected and normal CKCS to improve our ability to document and treat pain in these patients. This project will define the genetic etiology of this disease with the long-term aim of developing genetic tests for use by breeders, and will quantify the sensory dysfunction experienced by these dogs to facilitate objective therapeutic trials.

### Grant Objectives:



To identify chromosomal regions associated with Chiari-Like Malformation and Syringomyelia in Cavalier King Charles Spaniels with the long-term goal of developing genetic tests for use by breeders to reduce disease prevalence.

### **Publications:**

In preparation.

### **Report to Grant Sponsor from Investigator:**

As noted in previous reports, in this two-part project, we aim to quantify sensory thresholds to cold, heat and pressure, and to evaluate a novel pain map and questionnaire filled out by owners. We will compare our findings with the presence and severity of syringomyelia detected on MRI. We aimed to collect data on 50 dogs and at time of writing we have MRI data on 53 dogs and sensory threshold data on 47 dogs with 3 more dogs undergoing testing and MRI this week. We have tested the owner questionnaires and maps against each other for consistency, and we have quantified this owner generated data. We have compared the data generated to the presence and size of syringomyelia on MRI. The lateralization of signs reported by the owners correlates well the lateralization of the syrinx, but not to the presence of a syrinx. Indeed, we encountered both dogs that have clear clinical signs but no syrinx, and dogs with large syringes and no clinical signs.

In the other part of the project, we are collecting DNA on 192 dogs with MRIs to perform a genome wide association study in the next year of work. Progress on this aim has been slower than anticipated with 96 samples now banked on dogs with MRIs (enough to perform an initial genome wide association study). We would really appreciate any help that the breed society can give us to recruit additional samples.