



RESEARCH PROGRESS REPORT SUMMARY

Grant 01937-B: Evaluating the Complex Genetic Basis of Bloat

Principal Investigator: Dr. Claire Rebecca Sharp, BVMS

Research Institution: Tufts University

Grant Amount: \$251,097.00

Start Date: 1/1/2014 **End Date:** 12/31/2015

Progress Report: End-Year 1

Report Due: 12/31/2014 **Report Received:** 1/6/2015

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:

Gastric dilatation and volvulus (GDV), or bloat, is a common condition in large and giant breed dogs with an unacceptably high morbidity and mortality rate. Due to the importance of GDV in many dog breeds, several large previous studies have investigated risk factors for the development of GDV. It is known that there is no single cause for GDV, rather its occurrence is multifactorial, with both genetic and environmental factors contributing. We propose to further investigate how these risk factors cause GDV through the application of genomic and molecular methods. We will do this by analyzing samples from purebred dogs with GDV and comparing them to dogs of similar age and breed that have not developed GDV. Part of the proposal herein is to perform a genome wide association study (GWAS) to identify differences in the genetic makeup of dogs with GDV, and see which genes are turned on and off in GDV (epigenomics). We also want to see if dogs with GDV have different types or amounts of proteins, hormones and other molecules in their blood and tissues (transcriptomics, proteomics and metabolomics). We hypothesize that only when we put all of this information together (genomic, epigenomic, transcriptomic, proteomic and metabolomic) will we truly understand what causes GDV. The ultimate aim of understanding what causes GDV is to allow us to best intervene to prevent the disease from occurring.



Grant Objectives:

1. To establish a biobank (a repository of biological samples with associated data) for use in this and future GDV research.
2. To identify susceptibility genes for GDV through a discovery genome-wide association study in German shepherd dogs and a validation study in other purebred dogs with GDV.
3. To perform gene expression profiling (transcriptomics) in blood and target cells/tissues (PBMCs, gastric smooth muscle and gastric ligaments), and compare gene expression between dogs with GDV and control dogs.
4. To identify epigenetic modifications associated with differential gene expression in GDV, specifically evaluating DNA methylation and histone modification.
5. To perform proteomics using Millipore multiplex assays for evaluation of key cytokines and gastrointestinal hormones for comparison between dogs with GDV and control dogs.
6. To characterize the metabolome in dogs with GDV.

Publications:

We currently do not have any publications in print as a result of this research, however we have presented one poster at the Meriel-NIH National Veterinary Scholars Symposium in August 2014 (abstract included in Mid-year report), and have just recently published numerous manuscripts regarding GDV.

Two of the investigators (Sharp CR and Rozanski EA), were co-guest-editors of a special issue of the journal Topics in Companion Animal Medicine to cover the topic of Gastric dilatation and volvulus in dogs. This will was published in September 2014. Dr. Jerry Bell (Co-I) has written one of the manuscripts for this publication regarding genetic predispositions to bloat. Drs. Sharp and Rozanski have also written a review article to contribute to this special issue. Additionally, Dr. Laura Nelson (recipient of the other AKC-CHF Bloat Initiative grant) also contributed a manuscript to this special issue.

Although these publications are not presenting study data, the investigators were invited to contribute due to our funding in the field of GDV research. The AKC-CHF funding through the Bloat Initiative was acknowledged.

Report to Grant Sponsor from Investigator:

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Currently we are in the early stages of this project, and our work is predominantly involving information gathering about GDV history of dogs of at risk breeds that have already had their DNA banked, and collecting samples of DNA from dogs that have had GDV (as well as from control dogs that have not had GDV). The investigators have established strong collaborations with breed clubs, and received overwhelming support from dog owners and veterinarians around the country which is allowing us maximize the numbers of dogs included.