



RESEARCH PROGRESS REPORT SUMMARY

Grant 02338: The Genetics of Bloat in German Shepherd Dogs: The Roles of Immune System Genes and the Gut Microbiome

Principal Investigator: Michael Harkey, PhD
Research Institution: Fred Hutchinson Cancer Research Center
Grant Amount: \$152,270
Start Date: 6/1/2017 **End Date:** 11/30/2019
Progress Report: End-Year 2

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Original Project Description:

While gastric dilatation volvulus (GDV), or bloat, is a serious problem for many large canine breeds, little is known about the causes of this deadly disease. The most significant factors may be genetic, since certain breeds are more susceptible than others, and strong familial predispositions are seen within breeds. The investigators have recently shown a significant association of three immune genes with bloat in Great Danes. For each of the three genes, one allele (variant) is found at unusually high frequency in dogs that have been treated for bloat, and the presence of any one of these "risk" alleles triples the chance that the dog will experience bloat at some time in its life. The research team also showed that the bacterial population living in the gut (the gut microbiome) is altered in dogs with bloat, and in dogs that carry these "risk" alleles, which may predispose these dogs to bloat. It is not known if other breeds show this same association of genetics and microbiome with bloat. The team will investigate whether bloat in German Shepherd Dogs is associated with the same risk alleles and the same microbiome profiles as were seen in Great Danes. The results of this work could lead to genetic tests for at-risk dogs, as well as dietary or probiotic therapies to prevent bloat.

Publications: Not at this time.

Presentations: Not at this time.



Report to Grant Sponsor from Investigator:

We have proposed that genetic tendency to bloat may be caused largely by certain “risk” variants of genes of the immune system. These genes are responsible for distinguishing foreign cells from “self”, and as such, regulate which bacterial species in the gut will survive and which will be targeted for destruction. So these genes regulate the so-called “gut microbiome”. We hypothesized that dogs with a particular set of immune gene variants will maintain an unhealthy microbiome that predisposes them to bloat. Our recent research has supported this hypothesis in Great Danes.

The purpose of the proposed research is to expand the genetic and microbiome analysis of bloat to German Shepherds. We proposed to repeat the genetic and microbiome analysis, described for Great Danes, in this group of German Shepherds. Our first goal was to sequence the 3 immune genes, DLA88, DRB1, and TLR5, and determine if any variants associate with bloat. We then planned to analyze the gut microbiome profiles of the same dogs to look for changes in the bacterial population that correlate with bloat.

Summary of Genetic Analysis:

With 100% of the genetic data now in, it is clear that German Shepherds exhibit different genetic markers for bloat than do Great Danes. Even so, the genetic markers in Shepherds and Danes share certain characteristics that we believe, will lead to more universal genetic tests for bloat risk across breeds, and help us understand more clearly the root causes of this condition. The distribution of DLA88 and DRB1 variants is very different in German Shepherds and Great Danes. As a result, a genetic “risk” variant for bloat in one breed may not be a risk variant in the other. It may not even exist in other breeds. However, specific mutations, of these genes are associated with bloat in both breeds, regardless of the formal variant designation. Further testing of other breeds will be needed to determine whether or not these mutations could be exploited as universal genetic markers of bloat among domestic dogs. The high risk variant of the TLR5 gene in Great Danes, does not exist in German Shepherds. This correlates with the 7-8 fold lower overall risk of bloat in German Shepherds.

Microbiome Analysis:

While the raw data has been generated from the gut microbiome, the complex analysis of the statistical relationships between bacterial species and bloat in German Shepherds has not yet been completed. So far, we have not found the same bloat-associated changes in the microbiomes of German Shepherds that we found previously in Great Danes.