



RESEARCH PROGRESS REPORT SUMMARY

Grant 02002: Defining the Genetic Basis of Inflammatory Bowel Disease

Principal Investigator: Dr. Karin Allenspach, DVM PhD

Research Institution: Royal Veterinary College, University of London

Grant Amount: \$119,268.00

Start Date: 10/1/2014 **End Date:** 9/30/2017

Progress Report: End-year 2

Report Due: 9/30/2016 **Report Received:** 9/16/2016

Recommended for Approval: Yes

(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:

Inflammatory Bowel Disease (IBD) is a group of disorders in which the intestinal tract has become invaded with the dog's own white blood cells leading to inflammation. Over time, this inflammation causes the intestine to become less efficient at absorbing nutrients from digested food and weight loss, and vomiting or diarrhea often result. IBD can be controlled, but not cured. The cause of IBD is poorly understood, but it appears that genetics, diet, intestinal bacteria and abnormalities of the dog's immune system all play a role. German shepherd dogs (GSD) are particularly susceptible to IBD and it is believed that this is due to their genetic make-up. We have recently found genetic markers known as SNPs (single nucleotide polymorphisms) in the GSD genome, which contribute to this susceptibility. Furthermore, for one of these mutations, we were able to prove that the mutated protein is hyper-responsive to its natural ligand, which contributes to the inflammation seen in the intestine of GSD and other breeds of dogs with IBD. However, as in people and animal models, it is likely that other genetic factors contribute to the development of this disease in GSD. In order to find all underlying genetic factors that could contribute to disease, we propose to perform a genome-wide association study. This could lead to the exploration of new diagnostic and therapeutic avenues for canine IBD as has already been the case in people with IBD.



Grant Objectives:

The objectives of the present study are to identify single nucleotide polymorphisms (SNPs), which may confer genetic susceptibility or resistance to IBD using a genome-wide association study (GWAS).

Publications:

Manuscript in preparation.

Report to Grant Sponsor from Investigator:

This study was investigating the genetics of Inflammatory Bowel Disease (IBD) in German Shepherd Dogs (GSD) from the UK using a Genome-Wide Association Study approach. The results of this study have revealed important genetic factors that contribute to the disease and that could in the future help to find novel treatment options or markers for IBD. In total we found 17 candidate genes. Twelve of these genes, two on chromosome 7 and ten on chromosome 11 (see Table) are involved in inflammatory or immune response pathways and also have been previously reported to be associated with human IBD.

Table: 17 genes identified using Genome Wide Association, 12 of which (two on Ch7 and ten on Ch11) have been shown to be associated with human IBD.

<i>Chromosome</i>	<i>Gene</i>
<i>Ch7</i>	<i>PTPRC, C1orf53</i>
<i>Ch11</i>	<i>IL3, IL4, IL5, CSF2, IL13, SLC22A4, SLC22A5, IRF1, ACSL6, PDLIM4</i>

These exciting results have identified previously unknown candidate genes that are involved in the pathogenesis of IBD in GSD. This knowledge will form the basis of further studies to identify the mutations in these genes contributing to the disease and will help identifying novel clinical markers and treatment options for IBD in dogs.