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:	Mid-Year 3	
Report Due:	3/31/2017	**Report Received:** 3/30/2017

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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. Dr. Allenspach has recently identified genetic markers known as SNPs (single nucleotide polymorphisms) which she believes contribute to disease susceptibility. Beyond genetics, this research group has mechanistic data showing one of the putative mutations contributes to the inflammation seen in the intestine of dogs with IBD. In order to find all underlying genetic factors that could contribute to disease, they propose to perform a genome-wide association study. This study will lead to the development 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 and the USA by using a Genome-Wide Association Study approach. The results of this study have revealed important factors that contribute to the disease and that could in the future help to find novel treatment options. In total we found 17 candidate genes. Twelve 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 using Genome Wide Association, 12 of which (two on Ch7 and ten on Ch11) have been shown to be associated with human IBD.

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

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.