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:** 9/30/2016

Progress Report: Mid-Year 1

Report Due: 3/31/2015 **Report Received:** 3/30/2015

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:

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:

None at this time.

Report to Grant Sponsor from Investigator:

This study is investigating the genetics of Inflammatory Bowel Disease (IBD) in German Shepherd Dogs (GSD) from the UK and the USA by using a new technique called Genome---Wide Association Study. The results of this study will reveal important factors that contribute to the disease and that could in the future help to find novel treatment options. Owners and veterinarians of the cases and control dogs were contacted to ascertain that their group allocation is still correct. We have started extracting DNA from GSD with IBD and controls from the UK and are well underway to get the samples analyzed by Genome---Wide Association Study.

For the US part of the study, we are looking for help from owners and breeders of GSD. We will need DNA from GSD that have either been diagnosed with IBD at their vets or are healthy, over 8 years of age and have never had significant bouts of diarrhea in their lives. If you own a GSD that could fit one of these criteria, please get in touch with us to see if you could contribute to this important study by donating DNA from your dog.

Contact information: Atiyeh Peiravan, Department of Veterinary Clinical Sciences and Services Royal Veterinary College (RVC), University of London, Hawkshead Lane, North Mymms, AL9 7TA, UK. apeiravan@rvc.ac.uk.

Do you own a German Shepherd Dog?

You could help this research.

This study will investigate the genetics of Inflammatory Bowel Disease (IBD) in German Shepherd Dogs (GSD) from the UK and the USA by using a new technique called Genome-Wide Association Study. The results of this study will reveal important factors that contribute to the disease and that could in the future help to find novel treatment options.

How can you get involved?

We are interested in GSDs that:

A:

- Have been diagnosed with IBD on the basis of histopathology of the intestinal biopsies.
- Do not suffer from known or suspected immune-mediated diseases and/or inflammatory skin conditions.

OR

B:

- Are over 8 years of age.
- Do not have a current or previous history of diarrhoea more than 5 consecutive days, and/or chronic skin condition.

We would be grateful if you considered donating a residual blood or saliva sample of your dog to be used for extraction of DNA.

Royal Veterinary College
University of London

For further information and a sample collection kit please contact:
Atiyeh Peiravan , MSc,MMB, PhD scholar **Email:**apeiravan@rvc.ac.uk

The Clinical Investigation Centre
Royal Veterinary College,
Hawkshead Lane, North Mymms,
Hertfordshire AL9 7TA

Tel: +44 (0) 1707 666605
Fax: +44 (0) 1707 666223
Email: cic@rvc.ac.uk

Royal Veterinary College
University of London

Healthy Controls: German Shepherd Dog Questionnaire

The Royal Veterinary College is conducting a study into the genetic causes of chronic diarrhoea and inflammatory bowel disease in German Shepherds. As part of this study we are looking for samples from healthy GSDs to be used as controls in our study. We would be very grateful if you could take a few minutes to answer the following questions. We can assure you that this information will remain confidential.

Owner's name and surname: _____ **Dog's name:** _____

Dog's age: _____ **Dog's presenting complaint (if any):**
_____

Dog's current medications (type i.e. antibiotic, steroids, pain killer): _____

Dog's previous medical conditions: _____

Dog's diet (brand or meat source): _____

Has your pet ever suffered from one of the following: chronic (> 3 weeks' duration) diarrhoea, vomiting, inappetence, weight loss? _____

If yes, when was the last time? _____

Does your pet suffer from chronic skin problems (itchiness, recurrent ear infections)? _____

For each of the following criteria please give the score that applies to your pet for the last 12 weeks (circle the correct score)

Attitude/activity 0 (normal) 1 (slightly decreased) 2 (moderately decreased) 3 (severely decreased)

Appetite 0 (normal) 1 (slightly decreased) 2 (moderately decreased) 3 (severely decreased)

Vomiting 0 (normal) 1 (mild = 1x week) 2 (moderate = 2-3x week) 3 (severe = 3x week)

Stool consistency 0 (normal) 1 (slightly soft faeces or with fresh blood, mucus or both) 2 (very soft faeces) 3 (watery diarrhoea)

Stool frequency 0 (normal) 1 (slightly increased = 2-3x day) 2 (moderately increased = 4-5x day) 3 (severely increased = over 5x day)

Pruritus (Itchiness) 0 (no itchiness) 1 (occasional episodes of itchiness) 2 (regular episodes of itching, but stops when asleep) 3 (dog regularly wakes up because of itching)