



## RESEARCH PROGRESS REPORT SUMMARY

**Grant 02176-A:**  
*Intralymphatic  
Immunotherapy  
for the Treatment  
of Canine Atopic  
Dermatitis*

**Principal Investigator:**  
Dr. Andrea Lam, DVM

**Research Institution:**  
Tufts University

**Grant Amount:**  
\$12,113.82

**Start Date:** 7/1/2015  
**End Date:** 1/31/2017

**Progress Report:**  
Mid-Year 2

**Report Due:** 1/31/2017  
**Report Received:**  
1/17/2017

*(The content of this  
report is not confidential  
and may be used in  
communications with  
your organization.)*

### Original Project Description:

Atopic dermatitis (AD) is a genetically predisposed inflammatory skin condition affecting approximately 10% of dogs globally and is probably the most prevalent skin disease in all canines. Affected dogs manifest with itchy skin and ears and secondary infections. Clinical features are associated with IgE antibodies produced against indoor/outdoor environmental allergens. Breeds such as Boxers, Terriers, Retrievers, and Bulldogs are predisposed.

Current treatment options include antihistamines, corticosteroids, cyclosporine, oclacitinib, and allergen-specific immunotherapy (ASIT), as well as adjunctive topical and antimicrobial therapy. Antihistamines are effective in about 25% of dogs. Corticosteroids are extremely efficacious; however, side effects are common, thus long-term use is strongly discouraged. Cyclosporine is effective in many dogs with few serious adverse effects, but cost can be a limitation in large breed dogs. Oclacitinib has been shown to have good efficacy, but long-term side effects have not been studied. ASIT appears as the only treatment that is able to induce a clinical cure. However, the percentage of atopic dogs that respond to this treatment is only 60-70% and in many, the response is only partial.

It has been proposed that efficacy of subcutaneous ASIT is limited by the ability of the skin to stimulate the immune system. This study proposes to test an alternative route of administration using ASIT for this important skin condition. The investigator will test if direct administration of allergens into a peripheral lymph node may be more effective in stimulating an immunologic reaction, and thereby increasing the response rate, and potentially the cure rate, for canine atopic dermatitis.

### Publications:

None at this time.

### Report to Grant Sponsor from Investigator:

We have completed enrollment in the intralymphatic immunotherapy as a treatment for canine atopic dermatitis study.

The first enrolled patient has recently completed the 12-month review with excellent results. The owner has reported a complete lack of observed clinical signs for the first time since the dog developed atopic dermatitis. The second enrolled patient has unfortunately continued to struggle with relapsing infection. The third enrolled patient withdrew from the study following the first injection due to relapsing pneumonia (non-related). The final two patients are early in the post-treatment phase, thus it is too soon to tell how they will do long term.

No adverse reactions have been reported thus far and no complications have been associated with the simple protocol. With time, this may prove to be a novel and much more effective way to not only manage atopic dermatitis in our veterinary patients, but possibly provide a chance for cure.

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## 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

*(The content of this report is not confidential and may be used in communications with your organization.)*

**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, SCL22A5, 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.



## RESEARCH PROGRESS REPORT SUMMARY

### Grant 01609:

*Use of Probiotic to Reduce the Symptoms of Inflammatory Bowel Disease*

### Principal Investigator:

Dr. Albert E. Jergens,  
DVM, PhD

### Research Institution:

Iowa State University

### Grant Amount:

\$97,416.00

### Start Date: 1/1/2012

End Date: 6/30/2017

### Progress Report:

End-Year 5

### Report Due: 12/31/2016

### Report Received:

11/13/2016

### 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:

Idiopathic inflammatory bowel disease (IBD) is a common cause of chronic gastrointestinal disease in dogs. Accumulating evidence in human IBD and animal models suggests that imbalances in composition of the intestinal microbiota contribute to the pathogenesis of chronic intestinal inflammation. Recent studies have also shown that dogs with IBD have distinctly different duodenal microbial communities compared to healthy dogs. Current treatments for IBD include the administration of nonspecific anti-inflammatory drugs which may confer serious side effects and do not address the underlying basis for disease, namely, altered microbial composition. Use of probiotics (viable, non-pathogenic bacteria that exert health benefits beyond basic nutrition) offers an attractive, physiologic, and non-toxic alternative to shift the balance to protective species and treat IBD. The aim of the proposed study is to investigate the clinical, microbiologic, and anti-inflammatory effects of probiotic VSL#3 in the treatment of canine IBD. We hypothesize that VSL#3 used as an adjunct to standard therapy (i.e., elimination diet and prednisone) will induce a beneficial alteration of enteric bacteria leading to induction and maintenance of remission in dogs with IBD. A randomized, controlled clinical trial of 8 weeks duration will assess the efficacy of standard therapy + probiotic versus standard therapy alone. There is a need for additional data to be generated to provide proof of efficacy in probiotic therapy before these agents can be applied to widespread clinical use. These studies will also provide highly relevant insight into the anti-inflammatory effects of probiotics for treatment of human and canine IBD.

### Grant Objectives:

To determine the clinical, microbiologic, and anti-inflammatory affects of probiotic VSL #3 in the treatment of canine IBD.

### Publications:

- Otoni, R. Atilmann, M. Garcia-Sancho, et al. Serologic and fecal markers in prediction of acute disease course in canine chronic enteropathies. *J Vet Intern Med* 2012; 26:768-769.
- Slovak et al. Inter- and intra-observer assessment in the endoscopic assessment of canine inflammatory bowel disease. *J Vet Intern Med* 2013; 27:699.

### Report to Grant Sponsor from Investigator:

Thanks to the CHF for funding this project once again. Data to date demonstrates that dogs with diabetes have predictable microbial imbalances which result in changes in their metabolic function contributing to poor clinical response to exogenous insulin administration. Of interest, the bacterial metabolites which are altered include both primary and secondary bile acids, similar to disturbances in bacterial metabolism seen in humans with diabetes.

Summarizing, we have addressed our primary hypothesis as to whether dogs with DM have dysbiosis of their fecal microbiota – yes they do. Secondly, we provide new and innovative data on the role(s) of altered bile acid metabolism resulting from intestinal dysbiosis which favors the development of downstream insulin resistance.

What remains is to enroll additional dogs beyond the 3 to date for determination of the role of supplemental probiotics in modulating microbial imbalances and insulin sensitivity in dogs with spontaneous DM.