RESEARCH PROGRESS REPORT SUMMARY

Grant 02428: Identifying the Disease-Defining Autoantibodies in Canine Addison's Disease

Principal Investigator:	Steven Friedenberg, DVM, PhD
Research Institution:	University of Minnesota
Grant Amount:	$181,864
Start Date: 3/1/2018	**End Date:** 2/28/2022
Progress Report:	Mid-Year 3
Report Due: 8/31/2020	**Report Received:** 8/5/2020

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

Original Project Description:

Addison's disease is a common and life-threatening disorder in dogs in which the body's immune system destroys the outer layer of the adrenal glands. The adrenal glands produce hormones that are critical for energy metabolism, immune system function, intestinal health, and kidney function. Symptoms of Addison's disease can mimic other conditions, and as a result, many dogs remain undiagnosed for years. About one-third of dogs with Addison's disease are diagnosed only after suffering an acute adrenal crisis, which can cause a wide range of complications that require emergency stabilization and hospitalization. Today, there is no way to predict which dogs will develop Addison's disease before they become sick. If such a test were available, veterinarians would be able to evaluate high-risk dogs before they show signs, helping to prevent disease-related complications and potentially enabling earlier treatment. In this study, the investigator will use a novel approach combining gene and protein sequencing to identify the antibodies that target the adrenal glands in Standard Poodles, Portuguese Water Dogs, and English Cocker Spaniels with Addison's disease. These antibodies are produced by the immune system before the onset of clinical signs. The ability to identify these antibodies would therefore provide a test for early diagnosis. This research will contribute to progress in developing an important clinical test for Addison's disease that can help improve the lives of the many dogs at high risk of developing this life-threatening condition.

Publications:

None at this time. However, we are actively working on a review paper on the use of autoantibody testing in veterinary medicine which we plan to submit to JVIM by the end of 2020. We plan on

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Page 1 of 2

publishing our findings from this study specifically once we have finalized our experiments for Aims 1 and 2.

Presentations:

Presentations were given at the Poodle and English Cocker Spaniel national specialty shows to promote sample collection as part of this research project.

We had originally planned to present an abstract at the American Association of Immunologists annual meeting in May 2020, however this was cancelled due to Covid-19 so the abstract was only published in written form. We will likely submit an abstract related to this work for the same meeting in May 2021; we may also submit an abstract for ACVIM in 2021.

Report to Grant Sponsor from Investigator:

The goal of this project is to identify autoantibodies that are present in the blood of dogs who are newly diagnosed with Addison's disease in three breeds: Standard Poodles, Portuguese Water Dogs, and English Cocker Spaniels. To accomplish these goals, we have been focusing on (1) collecting blood samples from dogs across all three target breeds, and (2) employing methods that allow us to detect these autoantibodies.

In terms of collecting blood samples, during the first two years of this project we have collected all the samples required from Standard Poodles and Portuguese Water Dogs. Currently, we are focusing our efforts on increasing the number of newly diagnosed English Cocker Spaniels we have enrolled in the study. We are also continuing to actively recruit newly diagnosed dogs across all three breeds through many online resources.

Over the past year, we have started to use these samples to detect the presence of autoantibodies in newly diagnosed dogs. Given some of our early results, we focused our early efforts on a type of experiment called a Western blot. To date, we have performed over 20 Western blots per breed to test for anti-adrenocortical autoantibodies in all three dog breeds. These results strongly suggest that there are autoantibodies that are consistently present against one of several adrenal proteins in newly diagnosed dogs. This is an exciting finding!

Currently, we are focusing our efforts on narrowing which adrenal protein(s) are the most likely target of these autoantibodies. Once we have done this, we will proceed to the next phase of our work, which is to synthesize the relevant adrenal protein(s) in cell culture and test individual dogs for the presence of anti-adrenocortical autoantibodies. Our work has been impacted by Covid-related lab shutdowns for the past four months. This has delayed our progress; however, our laboratory is now open and we are resuming our efforts as quickly as we can, despite ongoing restrictions on the amount of time we can spend in the lab.

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Page 2 of 2