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:	End-Year 3
Report Due: 2/28/2021	**Report Received:** 2/25/2021

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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 mid 2021. We plan on publishing our findings from this study specifically once we have finalized our experiments for Aims 1 and 2.

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Page 1 of 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.

I have presented very preliminary findings from this study at the AKC-CHF National Parent Club Canine Health Conference in August 2019, a VetVine seminar in November 2019, at a webinar for the Western Australia Labradoodle Club of America in October 2020, at an Embark canine health conference in February 2021, and at a webinar for the Twin Cities Portuguese Water Dog Club in February 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 2.5 years of this project we have collected all the samples required from Standard Poodles and Portuguese Water Dogs, and most of the samples required for English Cocker Spaniels. We are continuing to actively recruit newly diagnosed dogs across all three breeds through many online channels.

Over the past 1.5 years, we have these samples to detect the presence of autoantibodies in newly diagnosed dogs using a technique called two-dimensional Western blotting. Our findings show that there are autoantibodies that are consistently present against adrenocortical proteins in dogs with a new diagnosis of Addison's disease. We have also shown that the specific proteins targeted by these autoantibodies may be different by breed or by dog.

Currently, we are focused on the next phase of our work which is to identify which specific proteins are targeted by these autoantibodies. We are genetically engineering three candidate proteins in our laboratory at present. Once we have made and isolated these proteins, we will test the serum from affected and unaffected dogs for reactivity against these proteins. We hope that these tests of reactivity will help us determine the predominant target of autoantibodies in canine Addison's disease for each breed. This will then set us on a path to developing a robust immunologic test to predict which dogs are at highest risk of developing the disease.

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Page 2 of 2