RESEARCH PROGRESS REPORT SUMMARY

Grant 02945-MOU: Understanding the Genetic Basis of Addison's Disease in Portuguese Water Dogs

Principal Investigator: Steven Friedenberg, DVM, PhD

Research Institution: University of Minnesota

Grant Amount: $207,381.00

Start Date: 5/1/2021 **End Date:** 4/30/2024

Progress Report: End-Year 2

Report Due: 4/30/2023 **Report Received:** 4/1/2023

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

Original Project Description:

Addison's disease (AD) is a common, life-threatening disorder in dogs characterized by the immune-mediated destruction of portions of the adrenal gland. This damage prevents the adrenal gland from synthesizing hormones that are necessary for normal cell metabolism, kidney function, and maintenance of the immune system. Dogs with AD are also highly predisposed to succumbing to a life-threatening adrenal crisis. AD is most common in Portuguese Water Dogs (PWDs), which have a 29-fold greater risk of developing the disease compared to other dog breeds, indicating a strong genetic component. To date, no genetic variants have been associated with AD in PWDs. This lack of knowledge has prevented the development of a genetic test that would allow for prediction of a dog's disease risk and the development of informed breeding practices related to AD. In this study, investigators will use state-of-the-art scientific tools to understand the genetic basis of AD in PWDs. The data generated here will provide the foundation for the development of a genetic test for AD in PWDs, enabling early diagnosis and treatment, as well as maintenance of genetic diversity within the breed while helping to decrease disease incidence.

Funding for the research is provided through the collaborative efforts and generosity of the Portuguese Water Dog Foundation, Inc. The AKC Canine Health Foundation supports the funding of this effort and will oversee grant administration and scientific progress.

Publications:

None at this time.

Presentations:

Dr. Friedenberg gave a 50-minute talk at the Portuguese Water Dog National Specialty on September 29, 2021 in Norfolk, VA. This talk discussed the pathophysiology of Addison's disease, Dr. Friedenberg's research strategy for the funded grant, as well as some preliminary data. There was significant audience engagement via Q&A throughout the talk.

Dr. Friedenberg also participated in a Q&A webinar through the CARE website on September 18, 2021. While this webinar was not solely related to this study, he did discuss it and encourage qualifying dogs to enroll in the study.

We gave a webinar on Addison's disease and our research to a seminar sponsored by the PWDF/PWDCA on 3/28/2023. The seminar was recorded and can be viewed at this link: https://www.pwdfoundation.org/project/understanding-the-genetic-basis-of-addisons-disease-in-pwds/

Report to Grant Sponsor from Investigator:

Over the first two years of this study, we have focused primarily on sample collection and running an initial set of genetics experiments. We collected samples mostly through PWD-related channels working directly with our collaborators in the PWDF/PWDCA. We also attended the PWD National Specialty in September 2021 and August 2022 to promote the study and collect samples, and we established a collaboration with Dr. Anita Oberbauer at UC Davis to share samples that she had already collected. To date, we have in hand 131 samples from affected PWDs and 167 samples from unaffected PWDs. Only a subset of these samples (41 affected, 43 unaffected) will qualify for our initial genotyping efforts based upon relatedness and DNA quality, but we are glad to have made such quick progress with sample collection thus far. We plan to continue our outreach efforts to try to reach our goal of 100 affected and 100 unaffected unrelated samples.

In addition to collecting DNA and cortisol samples from affected/unaffected dogs, we recently received back our first set of sequencing data for an initial genome-wide association study (28 affected PWDs and 35 unaffected PWDs). We did not find any significant hits, but this is expected as our enrollment number for unrelated dogs is still low. We are in the process of actively collecting samples from Europe to gain more dogs and also minimize relatedness to our existing population. We plan to submit another set of dogs for sequencing in the next several months once we have received additional unrelated samples.

We also performed an initial analysis of the variations in a set of genes called the major histocompatibility complex genes. These genes are very important in the immune system. We found

one “version” of this gene set that appears to be associated with Addison’s disease in PWDs. WE will continue to verify this finding as we enroll more dogs in the study.

We look forward to continued fruitful collaborators with the PWDF and PWDCA on this work.