RESEARCH PROGRESS REPORT SUMMARY

Grant 02624: Embracing Polygenicity of Common Complex Disease in Dogs: Genome-wide Association of Cruciate Ligament Rupture

Principal Investigator: Peter Muir, BVSc, PhD

Research Institution: University of Wisconsin, Madison

Grant Amount: $154,116

Start Date: 5/1/2019 **End Date:** 10/31/2022

Progress Report: Mid-Year 3

Report Due: 10/31/2021 **Report Received:** 10/25/2021

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

Original Project Description:

Cruciate ligament rupture (CR) is a common disabling, degenerative condition of the knee. It places a large financial burden on the American public. Inflammation of the stifle and fraying of cruciate ligament fibers, particularly in the cranial cruciate ligament, eventually leads to ligament rupture with associated stifle instability in affected dogs. CR is a moderately heritable, complex disease with genetic and environmental risk. CR is common in certain breeds, such as the Labrador Retriever, and rare in other breeds. There is a critical gap in knowledge regarding the genetic contribution to CR, as the number of genes influencing disease risk has never been studied in detail. Our main goal is to comprehensively analyze the genetic features of the disease across the genome and use this knowledge to develop a genetic test for CR disease risk using genomic prediction. We aim to robustly estimate heritability, analyze the genetic architecture of CR, and advance genetic testing using genomic prediction in the Labrador Retriever, the most common purebred dog breed. The rationale for this work is that detailed knowledge of the genetic features of CR will advance development of a genetic test for CR risk using genomic prediction. This work will fundamentally advance knowledge of the genetic architecture of CR, a very common canine disease. Consequently, such knowledge will provide an invaluable guide to future research into other canine complex diseases. CR genetic testing would enable early identification of at-risk dogs for precision medical care, and selective breeding to reduce the disease burden.

Publications: None at this time.

Presentations: None at this time.

Report to Grant Sponsor from Investigator:

We have met our Labrador Retriever recruitment for this study over the past year months. We will continue to complete DNA isolation and marker genotyping of the remaining dogs needed for the study as long as the genotyping service remains open under the Covid-19 pandemic. Public engagement with the project continues to be good. Over the next 6 months, we will focus on finalizing the marker data set for the study for which we do not yet have SNP genotypes. We will then undertake the computing needed to robustly estimate the heritability of cruciate ligament rupture in the Labrador Retriever and further advance prediction of risk of disease using the genomic marker data. Our final data set is expected to include more than 1,000 Labrador Retriever dogs as promised under the award. We are extremely grateful for the outstanding engagement with this project by the community of Labrador Retriever owners and breeders that we work with.