



## 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:** End-Year 3  
**Report Due:** 4/30/2022      **Report Received:** 4/27/2022

---

*(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 now completed recruitment and marker genotyping of Labrador Retriever dogs under this award. A final single nucleotide polymorphism (SNP) marker data set of 1,006 dogs has been assembled and filtered for data analysis, slightly exceeding what was promised under the award. We are now working on completing analysis of these data to estimate heritability of cruciate ligament rupture, determine the extent of the polygenicity of the disease, and develop a method for genetic testing for risk of cruciate ligament rupture. Heritability of cruciate ligament rupture in the Labrador Retriever is estimated to be 0.62. In our initial analysis, the accuracy of genetic testing for risk of cruciate ligament rupture is excellent and we expect to offer genetic testing to the public soon. We are extremely grateful for the outstanding engagement with this project by the community of Labrador Retriever owners and breeders that we work with.