RESEARCH PROGRESS REPORT SUMMARY

Grant 03094-MOU: Identification of Gene Mutation Underlying Ocular Melanosis in Cairn Terriers

Principal Investigator:	Simon Petersen-Jones, DVM PhD
Research Institution:	Michigan State University
Grant Amount:	$51,941.52
Start Date: 11/1/2022	**End Date:** 4/30/2024
Progress Report:	FINAL
Report Due: 4/30/2024	**Report Received:** 4/26/2024

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Original Project Description:

Ocular Melanosis (OM) is an important cause of vision loss and pain in the Cairn Terrier breed. It is an inherited condition and there is a need for a genetic test to allow dog breeders the opportunity to eradicate the condition. The condition develops in both eyes and results from a proliferation of pigmented cells within the eye. The abnormal cells can block fluid drainage from the eye resulting in an increase pressure within the eye (glaucoma). This can occur from as early as seven years of age, but not all affected dogs will progress to develop glaucoma. This type of glaucoma is difficult to treat and save vision and prevent pain and loss of the eye. The investigators have collected DNA samples from a large number of affected dogs. Using these samples, they have identified the location of the disease-causing DNA change. Despite "mapping" the region of the genome likely to harbor the disease-causing DNA mutation has not yet been found. To develop a DNA-test for breeders and to allow us to understand the disease mechanism which may suggest some therapy approaches for affected dogs, this DNA mutation needs to be identified. The long-term aim is to provide genetic testing that allows breeders to eradicate the condition. To allow the research team to identify the DNA variation that causes Ocular Melanosis, the latest DNA sequencing technologies will be used to improve the sequence data for the dog genome. The hope is that this approach will help identify disease causing DNA variants that have previously remained elusive.

Funding for the research is provided through the generosity of the Foundation of the Cairn Terrier Club of America and the AKC Canine Health Foundation, which will oversee grant administration and scientific progress.

Publications:

Peter Z Schall, Paige A Winkler, Simon M Petersen-Jones, Vilma Yuzbasiyan-Gurkan, Jeffrey M Kidd, Genome-wide methylation patterns from canine nanopore assemblies, G3 Genes|Genomes|Genetics, Volume 13, Issue 11, November 2023, jkad203, https://doi.org/10.1093/g3journal/jkad203

Manuscript in preparation: Identification of region linked to ocular melanosis in Cairn terriers

We were successful in the de novo assembly Cairn terrier (unaffected and affected) genomes using Nanopore long-read data. This resolved assembly errors in the canine reference genomes. The unaffected Cairn terrier assembled genome is publicly available.

Presentations:

None at this time.

Report to Grant Sponsor from Investigator:

The overall aim of the proposal is to identify the DNA mutation that is responsible for ocular melanosis in Cairn Terriers. Objectives 1 and 2: New DNA sequencing technologies are being used on affected and unaffected Cairn Terrier DNA samples to aid in understanding and resolving the normal complexities of the dog genome. These new technologies and analysis methods will help establish a higher quality “normal” dog genome which can help us understand what is abnormal and disease-causing in the affected Cairn Terrier dogs. This work has led to a publication.

Objectives 3 and 4: Traditional whole genome sequencing was done on 10 affected Cairn Terriers; this type of sequencing is more affordable per sample (by cost and time to analyze). Ten samples (plus 11 samples from previous funding sources) have been analyzed using existing newly available canine reference genomes as well as our assemblies made from an unaffected and affected Cairn Terrier.

We have been able to considerably narrow down the chromosomal region to which the OM disease maps in Cairn Terriers although we have not as yet identified the causal mutation. We are continuing to analyze the region to enable us to identify the DNA change that leads to OM. As we have now narrowed the region we propose to develop and offer a linked-marker test which we will make available for Cairn Terrier owners and breeders after extensive verification. Availability of a marker-based test will allow breeders to selectively breed away from the OM disease phenotype and identify which younger dogs are at risk of developing the condition so that they can be monitored by a veterinary ophthalmologist.