RESEARCH PROGRESS REPORT SUMMARY

Grant 02403-MOU: Microphthalmia and Delayed Growth Syndrome in the Portuguese Water Dog

Principal Investigator: Margret Casal, DVM, PhD

Research Institution: University of Pennsylvania

Grant Amount: $12,960.00

Start Date: 11/1/2017 **End Date:** 10/31/2019

Progress Report: Mid-Year 2

Report Due: 4/30/2019 **Report Received:** 4/30/2019

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Original Project Description:

Microphthalmia and delayed growth syndrome (aka "puppy eye syndrome") has been reported by Portuguese Water Dog breeders dating as far back as 1986. However, there is no information in the scientific literature and the majority of data concerning this syndrome has been obtained from records of breeders, which have anecdotal reports of the disease and little, if any, medical diagnostics. Affected dogs present with microphthalmia of varying severity, other eye abnormalities, short stature and other findings. To date, the investigators have been able to collect DNA from 24 affected dogs. Males and females can be affected, although females predominate (about 70%). Preliminary pedigree studies suggest an autosomal recessive inheritance. Human literature reports numerous syndromes associated with microphthalmia, and many genes have been identified as having a causative role. The goals of this investigation are to better characterize the clinical syndrome seen in Portuguese Water Dogs, confirm a suspected mode of inheritance, obtain additional samples for investigation into the genetic mutation, and develop a mutation based, genetic test for breeders to eliminate this syndrome from the Portuguese Water Dog breed.

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

Publications:

None at this time, however one publication is in progress describing the ocular and systemic abnormalities associated with microphthalmia in the Portuguese Water Dog.

Presentations:

None at this time.

Report to Grant Sponsor from Investigator:

Study Objectives
The objective of this study is to A) clinicopathologically and molecularly characterize microphthalmia with delayed growth in the Portuguese Water Dog (POWD) and B) develop a DNA-based test to assist breeders with their breeding programs and avoid producing affected dogs.

Results
Objective A is over 95% complete. A draft of the paper describing the clinicopathological findings had been written but we found more data on affected puppies, which we are currently adding to the paper to be submitted by the end of May 2019. A paper was published about microphthalmia in POWDs recently by a group out of Cornell. However, this paper described only the ocular changes in affected dogs. With our publication, we will show that there are other abnormalities such as low platelet counts and stunted growth, which makes this a truly syndromic disorder. We have also included pedigree analyses showing the autosomal recessive mode of inheritance.

For Objective B, we received enough DNA samples from affected dogs and their relatives to perform an initial genome wide association study (GWAS). The DNA was aliquoted into plates for the GWAS and was sent to Illumina (Neogen) the end of November 2018. We received the results as expected in January 2019. We are absolutely thrilled with the results: A single, very significant peak was seen on the “Manhattan plot”, which allows us to locate not only the chromosome but the general area of that chromosome in which the gene must be located. Indeed, there is a gene in this area that, when mutated in mice and humans, causes a microphthalmia syndrome. We are currently in the process of sequencing this gene. If we do not find a disease-causing variant in this gene, we will sequence the entire genome of one affected dog and one normal POWD.