RESEARCH PROGRESS REPORT SUMMARY

Grant 02157-MOU: Genomics of Deafness in the Dalmatian

Principal Investigator: Claire Wade, PhD

Research Institution: University of Sydney

Grant Amount: $120,960.00

Start Date: 1/1/2015 **End Date:** 12/31/2018

Progress Report: End-Year 3

Report Due: 12/31/2017 **Report Received:** 2/15/2018

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Original Project Description:

Congenital deafness is a health issue that has higher prevalence in certain breeds, including the Dalmatian. Other studies in this breed have found the trait to be inherited in a complex rather than simple Mendelian manner. Using a large number of samples from animals that have been tested for hearing status, Dr. Wade will employ the latest genomic technologies and computational analyses to conduct this study. The ultimate goal is to identify mutations underlying the trait of congenital deafness in the Dalmatian breed and work towards a genetic testing solution for the Dalmatian breeding community.

Funding for the research is provided through the efforts and generosity of the Dalmatian Club of America Foundation. The AKC Canine Health Foundation supports the funding of this effort and will oversee administration of funds and scientific progress reports.

Publications:

Thesis: Ms Jennifer Liu (confidential)

Presentations:

We presented a poster on the project at the International conference on Canine and Feline genomics in Minnesota USA in July 2017.

Report to Grant Sponsor from Investigator:

Our original analysis assaying 170,000 genetic markers in 9 deaf and 24 bilateral hearing dogs identified five candidate regions that showed complete or near concordant association in our whole-genome sequenced (5 bilateral deaf and 2 hearing) Dalmatian samples. In the past year we obtained deep sequence from a 6th bilateral deaf animal to enable superior access to certain parts of the DNA that were not sequenced very well in the earlier technology.

Throughout the study we have continued to collect samples for breed risk analysis via our neurology clinic run by Dr Georgina Child. Throughout the course of the project we have obtained samples of 37 bilateral deaf, 55 unilateral and 164 hearing pups. These numbers are not representative of population risk frequencies as our sampling is biased to collection of samples of all phenotypes from litters that contain bilateral deaf or unilateral deaf puppies. The majority of the samples collected have been assayed using canine genotyping arrays.

Through 2017 we deeply investigated two of the most promising loci. These loci were chosen because they had been previously implicated in work by other research groups (chromosome 10 and chromosome 20). We believe that we have identified a protective haplotype for bilateral deafness at one of the original loci under investigation (the white markings locus on chromosome 20).

We are unprepared to release a test at this time as we are yet to ascertain the impact (if any) that this variant has on the external appearance of the dog. This question will be the subject of a student project to run throughout 2018. For this student project, we will invite dogs of known genotype to a judging critique by an Australian National Kennel Council judge licensed to judge Dalmatians and suggested by the Dalmatian club of NSW. The judge will not know the genotypes of the dogs. We will invite dogs from other breeders to participate in the critique and can hopefully DNA sample these dogs on the day. At the end of the assessments, we will compare the genotyped groups of dogs for their critique. Our null hypothesis is that the low-risk variant does not affect external appearance. If this is true, we will have greater confidence in releasing access to the test for the low risk variant.

It must be made very clear that deafness in this breed is unlikely to be caused by a single locus, and indeed there are some bilateral deaf dogs (4 of 29 tested thus far in our data) that have one copy of the low-risk variant but just one that has two low-risk genes.

Further, with our increasing sample sizes we have identified two new loci that warrant further investigation into the inheritance of this complex trait. That investigation will form the basis of a study to follow.