

02297-MOU: Understanding the Genetics of Hepatic Copper Toxicosis in the Dalmatian

Grant Status: **Closed**

Grant Amount: \$107,668

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March 1, 2017 - August 31, 2022

Sponsor(s): Dalmatian Club of America, Dalmatian Club of America Foundation

Breed(s): Dalmatian

Research Program Area: Hepatic Disease

ABSTRACT

Copper toxicosis, leading to early death from liver disease, was first described in Bedlington Terriers in 1975, with similar diseases described in other dog breeds including the Labrador Retriever, West Highland White Terrier, Skye Terrier, and Doberman Pinscher. Genes have been linked to copper toxicosis in the Bedlington Terrier and the Labrador Retriever, but the genes differ by breed. In most breeds the genes are not known. Copper toxicosis was considered rare in the Dalmatian but may be more common than previously believed. Symptomatic dogs may be misdiagnosed as having other liver diseases, never appropriately diagnosed or only diagnosed with copper overload at a terminal stage. The investigators aim to identify the faulty gene(s) in Dalmatians using an advanced whole genome sequencing strategy to obtain the genome sequences of carefully selected members of an affected Dalmatian pedigree. Identification of the problem gene is the first step towards genetic testing and to improved breeding practices necessary to eradicate hepatic copper toxicosis from the Dalmatian breed. Gene identification will help raise awareness of copper toxicosis in the Dalmatian breed, lead to more rapid diagnosis of the condition, and support the search for the most effective therapy.

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

ADDITIONAL FUNDING – JANUARY 2022

In January 2022 DCAF approved additional funding for the first study to analyze data from two rounds of sequencing on 16 dogs (13 Dalmatians and 3 Bedlington Terriers). Using their DNA collections, the research team checked candidate gene variants from the whole genome sequencing data of additional copper toxicosis-affected dogs. The data is comprised of relatives to affected and healthy controls.

FINAL SUMMARY OF PHASE I RESEARCH

The final summary report for the study MOU reported the following:

- 1) established familial connections for all Copper Associated Hepatopathy affected Dalmatians recruited to the study
- 2) generated whole genome sequence information for 13 Dalmatian genomes and
- 3) successfully identified CAH-associated variants that may affect liver function. Some variants are within genes and others are in adjacent regions. They are tracking some variants across the pedigrees to find the culprit gene, or genes. The Dalmatian genome sequence information that was generated in this process is of immense value not only to the pursuit of CAH, but to other disorders that impact the health of the Dalmatian and other dog breeds.