Grant Number: *03113*
Principal Investigator: *Dr Andrew Lawrence Mason*
Date: *05 Jun 2026*

AKC Canine Health Foundation
Progress Report

CHF Grant Number	03113
Project Title	Investigation of candidate genetic variants for copper-associated hepatopathy in the Dalmatian
Institution	University of Alberta
Investigator(s)	Dr Andrew Lawrence Mason
Project Start Date	2/1/2023
Report Number	Requested Update
Current Date	05/June/2026

Non-Confidential, Lay language Progress Summary

Our familial study of CAH in the Dalmatian was designed to further our understanding of liver copper accumulation in the Dalmatian breed, and to ascertain if there was a clear genetic contribution to the disorder, for example, as in the Bedlington Terrier where a deletion in the COMMD1 gene is associated with copper toxicosis and demonstrates an autosomal recessive pattern of inheritance.

Although rare, the disorder can be particularly severe in the Dalmatian, with several Dalmatians in our study exhibiting very high levels of copper. The disorder can be fatal, particularly if not caught early and treated with a copper chelator, such as penicillamine. We have observed variability in the onset of symptoms normally associated with high liver copper. Some Dalmatians harbor high levels of liver copper and show little to no symptoms prior to the onset of an acute attack with liver failure, and others remain asymptomatic throughout their lives. This variability makes it difficult for owners and veterinarians to effectively maintain some Dalmatians in good health.

Our pedigree studies suggest incomplete penetrance for the CAH phenotype. Therefore, we performed comparisons of Dalmatians with high and low liver copper values from across several families. We have assessed genome sequence data derived from these interrelated Dalmatian CAH-affected family groups and identified two variants in *ATP7B* that may interfere with the function of the ATP7B protein. Each variant is limited to small family groups and neither explains copper accumulation in all the Dalmatians tested. One of these is a variant previously identified by researchers in the Netherland that is associated with CAH in the Labrador Retriever, shown to reduce ATP7B function and leads to copper accumulation. Commercial testing for this variant is already available. This variant is not associated with all Dalmatians with CAH in our study. Therefore, the contribution of this variant to CAH remains complex and difficult to interpret. In our follow-up assessment, the second CAH-associated *ATP7B* variant was identified in three additional families but has not been tested for its impact on ATP7B function. Our extensive global genome analyses did not reveal a single significant gene variant that explains CAH in the Dalmatian breed. While we have made some progress in identifying CAH-associated genetic variation in the Dalmatian, for several family groups, no credible CAH-associated variant has been identified to date. This might suggest the influence of several genetic variants that would require much larger sample sizes for the analysis.

Our study indicates that in the Dalmatian breed, CAH is more complex than the single-gene disorder observed in copper toxicosis in the Bedlington Terrier and might be more akin to the complex CAH seen in the Labrador Retriever, observed by other researchers, with several gene variants potentially at play. *ATP7B* gene variants may affect the function of the ATP7B copper pump and lead to hepatic copper accumulation in some Dalmatians. In the absence of clear gene-to-CAH findings, and the heightened awareness of CAH beyond specific breeds, the influence of environmental copper must also be considered, and it would be prudent for concerned owners to discuss lower copper diets with their veterinarian.

We appreciate the efforts of all breeders and owners who have responded to our requests throughout this study. For more information on our study, please contact Dr Georgina Macintyre (Dr Andrew Mason's group, University of Alberta, Edmonton).