RESEARCH PROGRESS REPORT SUMMARY

Grant 01753: Identification of Genetic Factors That Alter the Severity of Cardiomyopathy

Principal Investigator: Dr. Kathryn M Meurs, DVM, PhD

Research Institution: North Carolina State University

Grant Amount: $73,343.00

Start Date: 1/1/2013 **End Date:** 6/30/2016

Progress Report: FINAL

Report Due: 6/30/2016 **Report Received:** 10/31/2016

Recommended for Approval: Approved

(Content of this report is not confidential. A grant sponsor's CHF Health Liaison may request the confidential scientific report submitted by the investigator by contacting the CHF office. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:

Arrhythmic heart disease in the Boxer was first described in the 1980s as Boxer cardiomyopathy but is more commonly called Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC). Recent studies have confirmed that this is an adult onset, familial disease characterized by the presence of ventricular arrhythmias, syncope and sudden death, and is associated with a deletion mutation in the striatin gene in many boxer families. We have demonstrated that boxer dogs with 2 copies of the deletion (homozygous) are most likely to have the more severe form of the disease, however dogs with 1 copy of the mutation are more likely to have variable disease, some will become quite sick while others will remain free of clinical signs. The mechanism for the variability in clinical signs is unknown but is thought to be associated with the concurrent inheritance of other genetic factors. Understanding if these genetic factors exist and what they are will greatly improve the ability to use and interpret the genetic test for the striatin mutation.

Grant Objectives:

Objective 1: Identify 100, 7 year old boxer dogs that are positive heterozygous for the striatin mutation, 50 with less than 100 VPCs/24 hours (low disease expression) and 50 with at least 500 VPCs/ 24 hours (high disease expression)

Objective 2: Perform genome wide association on the 100 samples collected above to identify an association between genes located on specific chromosomal regions and the level of expression of disease

Publications:

None at this time.

Report to Grant Sponsor from Investigator:

At this point we have been able to identify that there are genetic differences between dogs with the mild form of ARVC and dogs with the severe form even though all of them have one copy of the striatin deletion. However, we are not yet sure if these genetic differences actually cause the difference in disease severity or a simply factors of these dogs coming from different lines and families. We are still completing analysis to determine if the variants we have identified so far are really cause and effect or simply observed with the disease. We hope to complete this analysis shortly.