RESEARCH PROGRESS REPORT SUMMARY

Grant 01760-T: Use of Gene Therapy to Treat Dilated Cardiomyopathy

Principal Investigator: Margaret Sleeper, VMD

Research Institution: University of Florida

Grant Amount: $146,774.00

Start Date: 9/1/2016 **End Date:** 12/31/2025

Progress Report: EY 9

Report Due: 2/29/2024 **Report Received:** 4/4/2024

(The content of this report is not confidential and may be used in communications with your organization.)

Original Project Description:

Dilated cardiomyopathy (DCM) is the second most common cause of heart disease in dogs, and medical management of the secondary signs is the only therapeutic option. The outcome for affected dogs depends on the stage of disease and the breed. Once diagnosed, dogs typically exhibit rapid and uniform progression to congestive heart failure (CHF), with most living less than 6 months. Previous research has shown that heart function is critically dependent upon calcium channel function. These gate-like channels found within the wall of cardiac muscle cells open and close, allowing calcium ions to flow into the cell. Calcium influx then regulates muscle contraction. Heart disease is strongly associated with malfunctioning calcium channels within cardiac cells. Gene transfer strategies to reduce calcium cycling abnormalities improve heart function in animal models as well as in human clinical trials. In this study, Dr. Sleeper will conduct a placebo-controlled, double blinded study to evaluate gene delivery approaches for treatment of Doberman Pinschers affected with DCM and CHF. If results show that the gene delivery slows progression of heart failure in Dobermans with DCM, the results will have significant ramifications for all dogs with heart disease, as calcium handling proteins are abnormally expressed in dogs with heart disease of varying causes.

Publications:

None to date.

Presentations:

Presentation at Canine Health Foundation Conference 2023 and an abstract was presented at the European College of Veterinary Internal Medicine Conference 2024.

Report to Grant Sponsor from Investigator:

We completed the proposed plan of treating 12 Dobermans with congestive heart failure secondary to dilated cardiomyopathy with therapeutic gene delivery. The therapy appears to provide a modest (measured in months) survival benefit for dogs destined to succumb to congestive heart failure, however there appears to be no benefit for dogs destined to succumb to a fatal arrhythmia. With the remaining funds we plan to treat 4 Dobermans in the occult stage of disease (significant systolic dysfunction without evidence of congestive heart failure). This population theoretically is more likely to benefit from the therapy because they have greater cardiac reserve than dogs with end stage disease.

The Principal Investigator was awarded a no-cost extension to complete the project through 12/31/2025.