RESEARCH PROGRESS REPORT SUMMARY

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

Principal Investigator: Margaret Sleeper, BS, VMD

Research Institution: University of Florida

Grant Amount: $146,774

Start Date: 9/1/2016 **End Date:** 2/28/2022

Progress Report: End-Year 6

Report Due: 2/29/2020 **Report Received:** 4/7/2020

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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 at this time.

Presentations: None at this time.

Report to Grant Sponsor from Investigator:

To date, 12 dogs have been screened for enrollment in this study, five dogs have undergone treatment (enrolled), one dog had a fatal arrhythmia while waiting for vector antibody titer results to determine if she was an appropriate candidate to enroll and six dogs have had vector antibody titers too high to safely treat. Data collection is therefore underway and as more dogs are treated interim statistical analysis will be performed to evaluate benefit or negative impact of treatment. We continue to advertise the clinical trial by various methods.