RESEARCH PROGRESS REPORT SUMMARY

Grant 03279: Understanding the Immune Landscape of Canine Myxomatous Mitral Valve Disease and the Role of Inflammation in Disease Pathogenesis

Principal Investigator: Vicky Yang, DVM, PhD. DACVIM

Research Institution: Tufts University

Grant Amount: $137,135.00

Start Date: 9/1/2024 **End Date:** 11/30/2026

Progress Report: Mid-Year 2

Report Due: 5/31/2026

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

Original Project Description:

Canine myxomatous mitral valve disease (MMVD) is the most common acquired heart disease and the most frequent cause of heart failure in dogs, resulting in difficulty breathing and eventual death. This is an aging-related disease affecting many older dogs, especially small breed dogs such as the Cavalier King Charles Spaniel and Dachshund. Once in heart failure, the median survival time for dogs with MMVD is only approximately 11 months. The lack of medical therapies to slow the age-related progression of MMVD results from a limited understanding of what causes the disease and why the changes in the heart valve continue to worsen with time. In the human equivalent of this heart valve disease, there is evidence that inflammation may be involved and preliminary data indicates an increased number of immune cells found in the diseased valve leaflets. Understanding which particular type of immune cells are involved in MMVD may provide important insights into why these immune cells are there and their contribution to disease progression. Furthermore, an improved understanding of the exact inflammatory process involved in MMVD may help design a treatment for MMVD.

Researchers plan to use advanced sequencing technology, single cell (scRNA-seq) combined with RNAScope, to provide a detailed description of the immune cell types and their location in the valves. They will also test the effects of immune cell signaling on valve cells and determine if the immune cells contribute to the valve changes in disease. Data generated from this proposal will improve understanding of the interaction between immune cells and valvular cells during disease progression.

Publications:

Distribution of Iba1+ Macrophages and Papillary Muscle Fibrosis in Dogs with Myxomatous Mitral Valve Disease", accepted for publication by Journal of Veterinary Cardiology, pre-print now available online.

LeRoy EN, Williams AA, Skor MO, Lyons CE, Martinot AJ, Yang VK. Distribution of ionized calcium-binding adaptor molecule 1-positive macrophages and papillary muscle fibrosis in dogs with myxomatous mitral valve disease. J Vet Cardiol. 2025 Nov 3:S1760-2734(25)00114-6. doi: 10.1016/j.jvc.2025.10.007. Epub ahead of print. PMID: 41350143.

Presentations: N/A

Report to Grant Sponsor from Investigator:

The goal of this project is to better understand all of the cell types in the mitral valve from dogs affected by myxomatous mitral valve disease, comparing them to normal valves. 24 samples have already been processed and analyzed, 18 samples from diseased valves and 6 from normal valves. Dr. Batorsky (bioinformaticist on the project) is performing the data analysis and comparison for these samples with the analysis protocol she has established. Preliminary analysis shows that the type of cells in the disease valves are different from normal valves, including macrophages, immune cells involved in inflammation. We created different types of macrophages (some pro- and some anti-inflammatory) in the laboratory in attempt to recreate the type found in the myxomatous valves. Using the macrophage cell type that most resembles those found in the diseased valves, we further investigated their unique genetic signals. We found one genetic signal that may have functional consequences in promoting the myxomatous pathology. We are currently validating this finding with additional experiments.