RESEARCH PROGRESS REPORT SUMMARY

Grant 03106: Clinical Validation of Urinary miR-126 as a Marker of Immune Complex- Mediated Glomerulonephritis in Dogs

Principal Investigator: Mary Nabity, DVM, PhD

Research Institution: Texas A&M AgriLife Research

Grant Amount: $109,788.00

Start Date: 6/1/2023 **End Date:** 5/31/2025

Progress Report: End-Year 1

Report Due: 5/31/2024 **Report Received:** 6/4/2024

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Original Project Description:

Chronic kidney disease is a significant cause of illness and death in dogs and is often caused by glomerular diseases. A specific category of glomerular disease called immune-complex glomerulonephritis (ICGN) accounts for approximately 50% of dogs that have a kidney biopsy due to suspicion of glomerular disease. The treatment for ICGN compared with other glomerular diseases differs in that immunosuppressive therapy is typically recommended. however, such therapy can be harmful in dogs without an immune-mediated component to their disease. Currently, ICGN can only be diagnosed with evaluation of a kidney biopsy, as there are no available biomarkers that can accurately identify category of glomerular disease.

MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression. The researchers have recently obtained preliminary data supporting that urinary miR-126 can differentiate dogs with ICGN from dogs with two other common causes of glomerular disease. The goal of this study is to determine the clinical usefulness of urinary miR-126 to diagnosis ICGN in dogs. The research team will quantify miR-126 in a larger number of dogs that have a variety of glomerular diseases. They will also determine urinary miR-126 expression in dogs with non-renal diseases and with urine containing blood, inflammatory cells, and bacteria. The investigators hypothesize that miR-126 will be highly sensitive and specific for ICGN in dogs. Successful completion of this study would allow veterinarians to noninvasively diagnose and therefore more appropriately treat ICGN in those dogs that are not good candidates for a kidney biopsy.

Publications:

None at this time

None at this time

Presentations:

None at this time. The summer veterinary student helping with this project will present a poster and oral presentation at the end of the summer on the data that has been obtained by mid-July. We also plan to submit an abstract for the ACVP 2024 meeting if we can generate data for the majority of renal cases within the next month.

Report to Grant Sponsor from Investigator:

Immune-complex mediated glomerulonephritis (ICGN) is a common cause of glomerular disease in dogs. A diagnosis of ICGN often warrants specific treatment, which may prolong quality life. Currently, definitive diagnosis of ICGN relies on a kidney biopsy.

The goal of our project is to determine if urinary microRNA-126 (miR-126) expression levels could serve as a reliable non-invasive indicator for ICGN. Our first objective is to compare urinary miR-126 expression between healthy dogs and those with kidney diseases and between the different categories of glomerular diseases to determine the diagnostic sensitivity and specificity of urinary miR-126. Thus far, we have identified >90% of the samples needed for this objective, and we anticipate identification of the remaining samples (from uncommon glomerular disease categories) within the next four months.

Our second objective is to investigate non-renal factors influencing urinary miR-126 in dogs. Our focus is on common systemic diseases and lower urinary tract interferences (e.g., infection). By comparing miR-126 expression levels in these conditions with those found in dogs with ICGN, we will determine if co-morbidities in dogs with glomerular disease could interfere with urinary miR-126 interpretation. To identify and collect urine samples, we initiated collaborations with clinicians at Texas A&M University and Colorado State University, as well as the Gastrointestinal Laboratory. So far, we have collected 20-30% of the urine samples needed for this objective. However, obtaining these samples has been particularly challenging due to volume constraints and stringent inclusion criteria. We are brainstorming new ways to obtain the required samples more quickly.

We encountered several unexpected technical difficulties over the past 6 months. We are currently troubleshooting the equipment and software necessary to run the samples and need to ensure a successful trial run prior to using study samples. We anticipate our first sample run in the next 1-2 weeks.