RESEARCH PROGRESS REPORT SUMMARY

Grant 02684-A: Evaluation of Serum Zonulin as a Non-invasive Biomarker and Therapeutic Target in Dogs with Chronic Canine Enteropathy

Principal Investigator: Jamie Kopper, DVM, PhD

Research Institution: Iowa State University

Grant Amount: $12,085

Start Date: 3/1/2020 **End Date:** 2/28/2021

Progress Report: FINAL

Report Due: 2/28/2021 **Report Received:** 2/23/2021

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Original Project Description:

Canine chronic enteropathy (CE) is the most common cause of gastrointestinal (GI) disease in dogs. The exact mechanisms causing CE are unknown, however, disruption of the inner lining of the GI tract is believed to play a significant role resulting in a "leaky" GI tract, leading to absorption of GI contents and overstimulation of the immune system. Unfortunately, treatment for CE currently requires life-long management such as food elimination diets which can be expensive and labor intensive for owners and/or require the use of medications which carry the risk for significant systemic side effects. Diagnosis and monitoring for disease relapse rely upon owner reported clinical signs and invasive diagnostic testing such as endoscopic intestinal biopsies. Thus, non-invasive diagnostics as well as specific treatments are needed. Zonulin, a protein found in animals and humans, plays an integral role in maintenance of intestinal barrier function. Humans and other animals with inflammatory bowel disease (IBD) have elevations in serum zonulin which can serve as a non-invasive biomarker for intestinal permeability or "leakiness" and disease severity as well as a therapeutic target. Zonulin has not been evaluated in dogs, therefore, the objective of this research is to determine if serum zonulin is elevated in dogs with CE.

Publications:

IN PREPARATION: Dinesh N, Slovak JE, Kogan CJ, Kopper JJ. Evaluation of serum zonulin in canine chronic enteropathies. 2021. In preparation for submission to the *Journal of Internal Medicine*. We anticipate to submit this manuscript by June 1 of 2021.

Presentations:

The following research abstract has been submitted to the American College of Veterinary Internal Medicine annual forum (pending acceptance) for presentation in 2021: Dinesh N, Slovak JE, Kogan CJ, Kopper JJ. Evaluation of serum zonulin in canine chronic enteropathies.

Report to Grant Sponsor from Investigator:

Canine chronic enteropathy (CE), is the most common cause of gastrointestinal (GI) disease in canine patients. The exact mechanisms leading to CE are unknown. Unfortunately, treatment for CE currently requires life-long management strategies (i.e. food elimination diets) which can be expensive and labor intensive for owners and/or require the use of medications which carry the risk for significant systemic side effects (i.e. steroids). Diagnosis and monitoring for disease relapse relies upon owner reported clinical signs and invasive diagnostic testing (i.e. endoscopic intestinal biopsies). Thus, non-invasive diagnostics as well as specific treatments are needed. Zonulin, a eukaryotic protein, plays an integral role maintenance of intestinal barrier function Humans and laboratory animals (i.e. mice, rats) with Inflammatory Bowel Disease (IBD) have elevations in serum zonulin which can serve as a non-invasive biomarker for intestinal permeability and disease severity. The objective of this project was to determine if serum zonulin was elevated in dogs with CE to determine if further investigations regarding zonulin for diagnostic and/or therapeutic potential were warranted in canine patients. Results from this study did not support the use of serum zonulin as a biomarker for canine CE. Based on the results of this study, there was no evidence of a difference between dogs with CE and control dogs ($P = 0.9746$). Although the results from this study were negative (i.e. we did not support our hypothesis that serum zonulin would be a biomarker for dogs with CE), they are important. These results indicate that although serum zonulin appears to serve as a biomarker in other species, it likely should not be further investigated in the dog as a biomarker or therapeutic target.