GRANT PROGRESS REPORT SUMMARY

Grant: 01602: *Longitudinal Study Investigating the Progression and Pathogenesis of Atypical Hyperadrenocorticism in Scottish Terriers*

Principal Investigator: Dr. Kurt Zimmerman, DVM PhD

Research Institution: Virginia-Maryland Regional College of Veterinary Medicine

Grant Amount: $66,226.00

Start Date: 1/1/2012 **End Date:** 12/31/2013

Progress Report: Mid-Year 2

Report Due: 6/30/2013 **Report Received:** 6/28/2013

Recommended for Approval: Approved

(Content of this report is not confidential. A grant sponsor's CHF Health Liaison may request the confidential scientific report submitted by the investigator by contacting the CHF office. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:

Increased serum alkaline phosphatase (ALP) activity is common in Scottish Terriers. Findings in our preliminary work indicate that this increased ALP activity is attributable to hyperadrenocorticism (HAC). HAC is a chronic debilitating disorder in dogs and contributes to the development of negative health and behavior outcomes including diabetes mellitus, obesity, musculoskeletal weakness, immune system dysfunction, and inappropriate urination. However, what is unclear is why these affected Scottish Terriers demonstrate laboratory evidence of HAC at an early age and why it appears to be driven by a less common mechanism than seen in other breeds. Specifically in Scottish Terriers, HAC appears to be due to excessive amounts of noncortisol steroids (atypical form of HAC). These findings have prompted our research group to speculate that there might be a unique underlying cause for HAC in this breed. With this question in mind, we propose to examine this disorder from three different perspectives, over a two year time period, using traditional laboratory, functional, and genetic tests. Specifically we propose to: 1) determine if the severity of the disorder increases over time; 2) determine if the disorder is due to a functional problem of the brain or adrenal gland itself; and 3) determine if there is a problem with the receptors or message pathways which signal for steroid production in the adrenal gland. It is hoped these efforts will help us understanding why Scottish Terriers are predisposed to developing atypical HAC and how best to treat and screen for this disorder.

Grant Objectives:

1) Determine if the clinical severity of HAC in ST is clinically progressive by monitoring serial clinical/laboratory data

2) Determine if HAC in these dogs is pituitary or adrenal in origin by assessing ACTH and adrenal steroid profiles following dexamethasone suppression tests

3) Determine if glucocorticoid receptor/signaling or steroidogenesis pathway mRNA expression is different between ST with HAC, and normal ST and with unrelated breeds with HAC

4) Determine if a specific genetic glucocorticoid receptor or steroidogenesis pathway mutation is responsible for HAC in ST.

Publications:

None at this time.

Report to Grant Sponsor from Investigator:

Our initial round of testing is complete and data analysis is well underway. Currently after screening of all candidate dogs we have 8 Scotties terriers with atypical hyperadrenocorticism, 6 other breeds with hyperadrenocorticism and 7 normal other breed dogs participating in this study. The second round of routine laboratory and adrenal challenge testing will occur in December 2013 and January 2014.