



RESEARCH PROGRESS REPORT SUMMARY

Grant 02052: Defining the Mechanism of Severe, Life-Threatening Bleeding Disorders in Dogs

Principal Investigator: Dr. Dana N. LeVine, DVM, PhD

Research Institution: Iowa State University

Grant Amount: \$51,297.00

Start Date: 2/1/2014

End Date: 1/31/2015

Progress Report: Mid-Year 1

Report Due: 7/30/2014

Report Received: 8/16/2014

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:

Immune thrombocytopenia (ITP) is a common bleeding disorder in dogs. It occurs when the immune system destroys the body's own platelets, blood cells that prevent hemorrhage. The resulting lack of platelets in some dogs causes mild bruising and in others causes severe, life-threatening hemorrhage.

Veterinarians do not understand what triggers ITP and cannot predict its severity. Consequently, all ITP patients are treated with potent medications that suppress the entire immune system. Many dogs experience treatment side-effects including excessive thirst and urination, ulcers, weight gain, and recurrent infections. For some dogs, the side-effects, rather than ITP, prove fatal.

Our first aim investigates the specific causes of ITP. We will identify an ITP disease profile by measuring immune cells and proteins that may be involved platelet destruction. We will also look for genes associated with the disease in Old English Sheepdogs and Cocker Spaniels, since these breeds are especially prone to ITP. These tests will suggest the specific immune and genetic causes of ITP, so targeted drugs can be developed that suppress just these mechanisms, not the whole immune system.



Our second aim is designed to find laboratory markers that predict bleeding severity. Using these markers, veterinarians will be able to reserve aggressive treatment for only those dogs at risk for significant blood loss.

Together, these aims will benefit ITP patients through individualized therapy that matches treatment intensity with disease severity. Discovery of the immune and genetic causes of ITP will not only improve disease treatment, but ultimately help to prevent it.

Grant Objectives:

1. To investigate the specific causes of immune thrombocytopenia (ITP).
2. To find laboratory markers that predict bleeding severity.

Publications:

None at this time.

Report to Grant Sponsor from Investigator:

Our project aims to investigate the specific causes of ITP by identifying an ITP disease profile by measuring immune cells and proteins that may be involved platelet destruction. We also plan to look for genes associated with the disease in Old English Sheepdogs (OES) and Cocker Spaniels (CS), since these breeds are especially prone to ITP.

In this initial study period we have established the infrastructure for a two-pronged attack on canine ITP:

1. Targeted evaluation of breeds at risk: OES and Cocker spaniels

Through the efforts of many dedicated breeders, we have received samples from ITP affected dogs and controls for DNA banking and genetic analyses. We have already found some significant differences in the immune cell profiles of Cocker Spaniels compared to other breeds of dogs. We are now exploring these differences to determine whether they make Cockers at particular risk for autoimmune diseases. We are also looking for similar patterns in each new case of ITP as they are enrolled in our study.

2. In-depth immunoprofiling of newly diagnosed ITP cases

We have set up a multi-institution collaboration among three veterinary academic and referral centers (Cornell University, Iowa State University, and Cornell University Veterinary



Specialists) to enroll active ITP cases. We have developed a novel in depth immune profile system and a new bleeding severity scoring system. The new bleeding score system is important to standardize grading of each dog's clinical status and relate physical exam findings to laboratory test results. Ultimately, the markers of disease severity that we identify will help veterinarians reserve aggressive treatment for only those ITP affected dogs at risk for significant blood loss.

Together these endeavors will provide a better understanding of the cause of ITP and new approaches to treatment, including individualized therapy of ITP patients based on disease severity.