



## 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:** 1/31/2016

**Progress Report:** End-Year 2 (FINAL)

**Report Due:** 1/31/2016                      **Report Received:** 3/4/2016

**Recommended for Approval:** Approved

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*(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:**

In preparation.

### **Report to Grant Sponsor from Investigator:**

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.

In this study period we completed data collection for a two-pronged attack on canine ITP:

1. In-depth immunoprofiling of newly diagnosed ITP cases

We developed new assays that provide more detailed information on the immune response and the platelets that are targeted for destruction in ITP dogs. We have found abnormalities in several of these assays that appear to differentiate dogs with immune platelet destruction from dogs with thrombocytopenia caused by other diseases. We are now completing additional laboratory analyses and beginning the statistical analyses to determine which factors are



significant in predicting disease severity. These predictors will have direct clinical applications in both disease diagnosis and helping to guide treatment intensity to minimize the side effects of immunosuppressive agents.

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

Through the efforts of many dedicated breeders, we have collected samples from more than 50 dogs, including ITP affected dogs and healthy OES and CS as controls for genetic analyses. We have also evaluated peripheral blood counts and lymphocyte subsets in 20 healthy Cocker Spaniels and 20 healthy Old English Sheepdogs. We have found some interesting differences in the immune cell numbers and subsets in Cocker Spaniels and OES compared to other breeds of dogs. Subsequently, we looked at the mediators these cells produce (cytokines) and again found interesting differences between these breeds and dogs of other breeds. These banked samples and immune profile data will be used for case control studies to identify any genetic risk factors for developing ITP. Ultimately, identifying genetic risk factors could help prevent this disease.