



RESEARCH PROGRESS REPORT SUMMARY

Grant 02091-MOU: Differentiating between Localized and Disseminated Histiocytic Sarcoma in Bernese Mountain Dogs

Principal Investigator: Dr. Elaine A Ostrander, PhD

Research Institution: National Human Genome Research Institute

Grant Amount: \$10,300.00

Start Date: 8/1/2014 **End Date:** 7/31/2015

Progress Report: Mid-Year 2 (FINAL)

Report Due: 7/31/2015 **Report Received:** 1/29/2016

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:

Canine histiocytic sarcoma (HS) is a disease arising chiefly from cells called histiocytes, which play an important role in the immune system. While HS is relatively uncommon among most dog breeds, it is present at high frequency in Bernese mountain dogs (BMD) and Flat-coated retrievers (FCR), with more moderate incidence reported in Labrador retrievers and Rottweilers. For BMDs, HS accounts for over 25% of deaths and the average survival time is just 49 days from diagnosis. Commonly, this cancer is divided into two subtypes: localized, a tumor rising in a single organ or limb and often metastasizing to other organs, and disseminated, multiple tumors arising at the same time (often referred to as malignant histiocytosis). Survival time is nearly 5x greater for dogs diagnosed with localized HS compared to disseminated HS. However, no clinical guidelines exist to differentiate between these two subtypes and diagnosing subtypes remains largely clinically subjective. We seek to develop clinical indicators of the differences between localized and disseminated HS. We will do this by comparing gene expression in tumors and complement this approach by investigating a marker that is crucial for tumor cell immortalization and cancer progression. Together, these experiments will provide us with the first insight into the differences that exist between these two types of HS tumors. Such information will be crucial to aid in the diagnosis and treatment options available to clinicians, providing a powerful step forward in treating this devastating cancer.



Publications:

Schoenebeck, JS, and Ostrander EA (2014). Insights into morphology and disease from the dog genome project *Ann Rev of Develop Biol* 30:535-60.

Report to Grant Sponsor from Investigator:

Histiocytic sarcomas are highly aggressive cancers, often appearing as multiple tumors distributed throughout the body, making them very difficult to anticipate or treat. Though the disease is rare in the general dog population, histiocytic sarcoma is very common in Bernese mountain dogs and Flat-coated retrievers, and has been identified in Rottweilers and Golden retrievers at rates higher than the general population. In order to find the mutations within these breeds that are responsible for the development of HS we have sequenced the entire genome of six dogs with histiocytic sarcoma from three breeds. By comparing these sequences to 78 genomes from unaffected breeds, including the BMDs close cousin the Greater Swiss mountain dog, we have identified rare variants that appear only in affected dogs. The initial analysis of these genomes has identified a new region on chromosome 34 that is unique to affected BMD and Rottweilers that has not been identified through GWAS studies. Additional analyses are underway and are expected to provide new insights into the genetic basis of HS susceptibility. The identification of the specific mutations that lead to histiocytic sarcoma will enable the development of genetic tests for early detection and improved breeding strategies as well as increase the treatment options for dogs that have been affected.