GRANT PROGRESS REPORT REVIEW

Grant: 00615B: *Heritable and Sporadic Genetic Lesions in Canine Lymphoma*

Principal Investigator: Dr. Matthew Breen, PhD

Research Institution: North Carolina State University

Grant Amount: $149,369.00

Start Date: 8/1/2008 **End Date:** 7/31/2010

Progress Report: 18 month

Report Due: 1/31/2010 **Report Received:** 2/10/2010

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.)

Original Project Description:

Background: Certain dog breeds are prone to develop certain types of cancer. Between the late 1960's and the early 1980's researchers related the risk of lymphoma for different dog breeds. Yet, there has been little progress since then to define factors that account for this risk. As part of ongoing programs supported by the AKC CHF, the researchers recently showed that the breed-specific risk of lymphoma extends beyond the simple disease condition to a tendency for specific forms of lymphoma. More importantly, the researchers showed there are frequent chromosomal abnormalities that separate with specific forms of lymphoma and that are more common in Golden Retrievers than in other breeds. This suggests breed-specific profiles of genetic abnormalities will be found in canine lymphoma.

Objective: To continue this work, the researchers are using contemporary "array-based" technologies to identify genes that map to these regions and how they contribute to the disease. The researchers anticipate that the results from this work will allow them to predict how genetic factors influence the occurrence of abnormalities in these genes, and will set the groundwork to identify specific genes associated with breed-dependent cancer risk.

Original Grant Objectives:

Objective 1: Test the hypothesis that deletions of chromosome 14 are associated with high grade (diffuse large) B cell lymphoma, gain of chromosomes 15 and 36 are associated with high grade (lymphoblastic) T cell lymphoma, and these abnormalities occur significantl more frequently in Golden Retrievers than in other dogs.

Objective 2: Define the minimal region of loss for each of these regions using high-resolution arrays.

Publications:

- Manuscript in preparation to report on the findings of this first pass 1Mb data set.

Report to Grant Sponsor from Investigator:

Mid way through the second year of this two-year project we have used genome wide assessment of DNA copy number variation to profile tumor DNA from over 200 dogs diagnosed with lymphoma. Preliminary analyses of these genome wide data have identified several high frequency aberrations and a large number (>100) of small (<1-2Mb) regions. Already we have identified a series of genetic abnormalities that are associated recurrently with B cell and with T cell canine lymphoma and have early indication of further subtype associations. In the final six months an additional 40 cases of T cell lymphoma will be profiled by 1Mb aCGH analysis to strengthen that component of the project. When considering the breed specific nature of copy number changes of dog chromosomes 14, 15 and 36, the data indicate that these copy number aberration are no longer associated specifically with golden retrievers. However, there are a number of changes along the length of these chromosomes that may be breed specific, as well as numerous other regions of the genome. These regions will be evaluated over the coming weeks to determine those that are most significantly associated with breed. Over the past six months we also have developed a high-resolution form of cytogenetic analysis that allows us to increase the resolution of our search for key regions 75 fold and simultaneously reduce the cost to analyze each case. We have selected a subset of our patient population that presented with recurrent changes and will process these using this new higher resolution analysis. This will further refine the boundaries of the changes we have defined, lead to the identification of regions of the genome and thus hone in on key genes of interest.