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: 12 month

Report Due: 7/31/2009 **Report Received:** 8/31/2009

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:

CHF615B now has been active for one year. During this time we have used genome wide assessment of DNA copy number variation to profile tumor DNA from 100 dogs diagnosed with lymphoma. This sample set comprises 70 Golden retrievers and 30 non-Golden retrievers. Preliminary analyses of these genome wide data have identified several high frequency aberrations and a large number (>100) of small (<1-2Mb) regions. The next stage of this project is to further refine these changes and identify the minimum regions of shared aberration. Now that we have completed the first pass of the data we have unveiled the pathology and clinical information for each case and have begun to evaluate the data in the context of these parameters. 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. Over the next 6-12 months we will select a subset of our patient population that present with recurrent changes and move forward with even higher resolution analysis to further refine the boundaries of the changes. This will lead to the identification of regions of the genome and thus hone in on key gene of interest.