



GRANT PROGRESS REPORT

Grant: 00613: *The Prognostic Significance of Chromosome Aneuploidy in Canine Lymphoma*

Principal Investigator: Dr. Matthew Breen, PhD

Research Institution: North Carolina State University

Grant Amount: \$113,929.00

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

Progress Report: 6 month

Report Due: 1/31/2009 **Report Received:** 3/2/2009

Recommended for Approval: Approved

Original Project Description:

Lymphoma is the most common life-threatening cancer in dogs, accounting for up to 24 percent of all canine malignancies. A large proportion of canine lymphomas are generally responsive to standard of care using multi-agent chemotherapy, increasing both the length and quality of an affected dog's life. However, there is considerable variation in the extent of response to therapy and overall survival time. This indicates that there is a need to develop more refined modes of classification, which are of prognostic significance. In human lymphoma, the application of cytogenetics has been used to demonstrate the presence of recurrent chromosome aberrations that have both diagnostic and prognostic significance. In previous studies we have identified recurrent chromosome aberrations in canine lymphoma, including copy number changes (aneuploidy) of dog chromosomes 6, 15, 16, and 18. In this project we will use molecular cytogenetics to analyze a collection of over 300 archival lymphoma specimens, derived from dogs that were all treated with the same chemotherapy protocol as part of a clinical trial. This approach will allow us to determine if these frequent copy number aberrations are of prognostic significance. This project offers the potential to increase the sophistication of diagnosis and prognosis for canine lymphoma.

Canine lymphoma accounts for almost a quarter of all cancers in the dog. Despite improvements in veterinary medicine, the response to treatment for canine lymphoma continues to be highly variable with no reliable means to predict response. In human lymphoma the presence of characteristic chromosome aberrations has been shown to have both diagnostic and prognostic significance. With previous funding from the AKC CHF we have identified a series of recurrent chromosome aberrations in canine lymphoma, some of which also correlate with different subtypes of lymphoma. In this project we will test for the presence of these chromosome

aberrations in over 300 cases of canine lymphoma derived from dogs that were all treated with the same chemotherapy protocol as part of a clinical trial. This approach will allow us to determine if these frequent chromosome aberrations correlate with the duration of disease free interval in the study population and thus are of prognostic significance. This project therefore offers real potential to increase the sophistication of diagnosis and prognosis for canine lymphoma and thus provide a means to improve the health and welfare of dogs diagnosed with lymphoma.

Original Grant Objectives:

Objective 1: Test the hypothesis that recurrent chromosome copy number aberrations (aneuploidy) in canine lymphoma have prognostic significance.

Publications:

Report to Grant Sponsor from Investigator: (Lay Update allowed to be reproduced)

From PI:

During the first six months of this two year projects, we have shown that pooling DNA from overlapping BAC clones results in a more robust fluorescent signal than using a single BAC clone and provides a higher signal to noise ratio. We have generated the DNA used for the probes being used for this project en masse. Cells have been isolated from 120 of our 315 archival patient samples and prepared for multicolour FISH analysis. Thus far we have performed FISH analysis of the first 100 archival cases and have acquired images for each these cases. Data for the copy number of each of the four loci are being assessed and statistical evaluation indicates that at least one of the four loci may be associated with disease free interval. Over the next six months we will continue processing cases, aiming to reach 200 cases by July 2009.

At the midpoint of year 1 we are ahead of our anticipated schedule.