GRANT PROGRESS REPORT REVIEW

Grant: 00947A: *Heritable and Sporadic Genetic Lesions in Canine Osteosarcoma*

Principal Investigator: Dr. Matthew Breen, PhD

Research Institution: North Carolina State University

Grant Amount: $147,912.00

Start Date: 8/1/2008 **End Date:** 7/31/2011

Progress Report: 24 month

Report Due: 7/31/2010 **Report Received:** 9/9/2010

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. The below Report to Grant Sponsors from Investigator can be used in communications with your club members.)

Original Project Description:
Background: Certain dog breeds are prone to develop certain types of cancer. Yet, there has been little progress to define the genes that account for this risk.

Objective: For this project, the researchers' goal is to identify genetic abnormalities that are shared by bone tumors and segregate with risk in two dog breeds (Rottweilers and Golden Retrievers) where the disease is prevalent. In collaboration with their colleagues at the University of Michigan and the Broad Institute, they have identified preliminary regions of the genome that may influence risk in Rottweilers. The work described here represents a next step to pinpoint specific genes that are associated with breed-dependent risk, and to predict how heritable factors influence bone cancer in Rottweilers, Golden Retrievers, and other dogs.

Grant Objectives:
Objective 1: Test the hypothesis that genome-wide high-resolution, genome-integrated aCGH will identify breed specific and/or histologically specific cytogenetic aberrations within the canine genome, which may reveal key cancer-associated genes.

Objective 2: Define i) minimum regions of small copy number aberrations and ii) boundaries of larger regions of recurrent copy number imbalances, each to within single BAC clones (identified in aim 1), using high-resolution custom tiling-path BAC arrays.

Objective 3: Test the hypothesis that deletion of WT1 and PTEN occur significantly more frequently in Rottweilers than in Golden Retrievers and will investigate these key aberrations and their clinical significance in other breeds comprising our sample population.

Publications:

- Thomas, R., Wang, H., Tsai, P.-C., Langford, C., Fosmire, S., Jubala, C., Getzy, D., Cutter, G., Modiano, J., Breen, M., 2009, Influence of genetic background on tumor karyotypes: Evidence for breed-associated cytogenetic aberrations in canine appendicular osteosarcoma. Chromosome Research 17, 365-377.

Report to Grant Sponsor from Investigator:

Osteosarcoma (OSA), bone cancer, is the most common primary malignant bone tumor, occurring spontaneously in both humans and dogs. In humans, around 900-1000 cases of OSA are diagnosed per year while in dogs more than 8000 cases are reported per year making the disease incidence in dogs nine times the incidence in humans. Previous research focusing on human and dog OSA has discovered that these tumors contain a high degree of genetic abnormality. Several studies on human OSA have indicated that some genetic abnormalities in humans are correlated with a poor prognosis. Currently, only a little is known about how genes influence the risk and progression of bone cancer in dogs. In order to assess the degree of genetic abnormalities in dogs, we are looking genome wide for genomic changes associated with canine OSA. In this study we evaluated the genomic status of 123 cases of canine osteosarcoma at 1Mb resolution and identified recurrent genetic abnormalities. In addition, using larger sample numbers of four breeds (Greyhounds, Rottweilers, Great Pyrenees and Golden Retrievers) we have identified several genomic abnormalities that appear to be associated more frequently with one breed. Using a higher resolution form of analysis (27kb), and combining our data for canine osteosarcoma with new data we generated from human samples, we have narrowed the search for key genes of comparative value and have begun to evaluate the role of these genes in both dogs and people.