



## GRANT PROGRESS REPORT

**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:** 7/31/2010

**Progress Report:** 6 month

**Report Due:** 1/31/2009

**Report Received:** 3/2/2009

**Recommended for Approval:** Approved

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### Original Project Description:

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. For this project, we will use contemporary technologies 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 our colleagues at the University of Michigan and the Broad Institute, we 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.

### Original 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:**

- Rachael Thomas, Huixia J. Wang, Pei-Chien Tsai, Cordelia F. Langford, Susan P. Fosmire, Cristan M. Jubala, David M. Getzy, Gary R. Cutter, Jaime F. Modiano and Matthew Breen. Influence of genetic background on tumor karyotypes: evidence for breed-associated cytogenetic aberrations in canine appendicular osteosarcoma. Chromosome Research (in press).

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

From PI:

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 have discovered that these tumors contain a high degree of genetic abnormalities. 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. CHF947A has been active for just six months and during this tumor we have profiled tumor DNA from 75 dog OSA patients and have identified genetic abnormalities recurrently associated with dog OSA. In addition, using larger sample number of three breeds, Greyhounds, Rottweilers, and Golden Retrievers, we have identified genomic abnormalities that appear to be associated more frequently with one breed. Over the coming six months we will complete our genomic analysis of 100 canine OSA cases, reevaluate our data and then perform higher resolution analysis to further refine the data and define key genes of significance.