Saluki Health Research, Inc. supported AKC/CHF grants

Summary of progress reports received May 2010

Grant 00613: The prognostic Significance of Chromosome Aneuploidy in Canine Lymphoma. Principal investigator: Matthew Breed, PhD. Research institution: North Carolina State University. Grant amount: $113,929. Start date: 8/1/2008. End date: 7/31/2010.

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 responsive to chemotherapy, increasing both the length and quality of an affected dog's life. However, there is considerable difference in the response to therapy working and overall survival time. This shows that there is a need to develop more improved forms of classification. In human lymphoma, the use of cytogenetics has been used to show the presence of frequent chromosome abnormalities that have both diagnostic and predictive importance. In previous studies the researcher have identified frequent chromosome abnormalities in canine lymphoma, including copy number changes (aneuploidy) of dog chromosomes 6, 15, 16 and 18.

Objective: In this project the researchers will use molecular cytogenetics to study a collection of lymphoma specimens, taken from dogs that were all treated with the same chemotherapy procedure as part of a clinical trial. This approach will allow us to determine if these frequent copy number abnormalities are able to predict response. This project hopes to increase the sophistication of diagnosis and life expectancy for canine lymphoma.

Report to grant sponsor from investigator: During the first year of this two-year project, we showed that pooling DNA from overlapping BAC clones results in a more robust fluorescent signal in interphase analysis than using a single BAC clone and provides a higher signal to noise ratio. We generated the DNA used for the probes being used for this project en masse. Cells were isolated from 200 of our 315 archival patient samples and prepared for multicolor FISH analysis. Cytogenetic analysis of the first 150 archival cases was completed. Data for the copy number status of each of the four loci being tested in this project was assessed and statistical evaluation has indicated that one of the four loci may be associated with disease free interval. During the previous six months we continued to evaluate the data from these 150 cases and have developed a robust regression analysis that allows us to now predict duration of disease free interval. This model is based on performing a cytogenetic evaluation of just two regions of the genome (one of which was investigated as part of this project) in lymphoma cells. We now will begin to evaluate the status of the key regions of interest in cells from new lymphoma patients to test the predictive power of our test.

Grant 00947A: Heritable and Sporadic Genetic Lesions in Canine Osteosarcoma. Principal investigator: Mathew Breen, PhD. Research institution: North Carolina State University. Grant amount: $147,912. Start date: 8/1/2008. End date: 7/31/2010.

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.

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.

Report to the 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 have evaluated the genomic status of 123 cases of canine osteosarcoma and have identified recurrent genetic abnormalities. In addition, using a larger sample number 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, we have narrowed the search for key genes and have begun to evaluate the role of these genes in canine osteosarcoma.