



RESEARCH PROGRESS REPORT SUMMARY

Grant 01822: Beyond the Genome: The Intersection of Genes and the Environment in Canine Cancer

Principal Investigator: Dr. Robert K Wayne, PhD

Research Institution: University of California, Los Angeles

Grant Amount: \$29,923.00

Start Date: 1/1/2013 **End Date:** 12/31/2014

Progress Report: End-Year 2 FINAL

Report Due: 12/31/2014 **Report Received:** 2/2/2015

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:

DNA methylation plays a central role in regulating gene expression in both normal and pathological states, with abnormal patterns of methylation having been observed in cancer. However, methylation remains an unexplored dimension of canine disease. Here, we propose to establish the pattern of normal variation in methylomes (the genome-wide collection of methylated sites) from an array-based analysis of a variety of domestic dog breeds. Differences in methylation found between breed lineages will be complemented by the study of gene expression to understand how methylation regulates levels of expression. This information can potentially be used to predict pathways of canine disease. Further, we will focus our attention on aberrant methylation in dogs with melanoma, a likely candidate for epigenetic control. We will establish a public web-based resource to serve as a repository for the dog methylomes. The collection of methylomes we generate will contribute to the growing resources that are available for investigation of disease etiology as well as advancing therapeutic approaches. These data will provide a new resource for understanding how gene regulation through methylation affects phenotype, disease and overall canine health.



Grant Objectives:

- To collect and assemble the multiple canine methylomes
- To establish a publically available repository and resource

Publications:

Manuscript in submission.

Report to Grant Sponsor from Investigator:

DNA methylation plays a central role in regulating gene expression in both normal and pathological states, with abnormal patterns of methylation having been observed in cancer. However, methylation remains an unexplored dimension of canine disease. Here, we propose to establish the pattern of normal variation in methylomes (the genome-wide collection of methylated sites) from an array-based analysis across a variety of domestic dog breeds. Differences in methylation found between breed lineages will be complemented by the study of gene expression to understand how methylation regulates levels of expression. Our preliminary analyses have focused on a proof-of-principle approach, surveying the differences in methylation of the X chromosome between male and female dogs. Our expectation is that females will display increased levels of methylation due to the inactivation through methylation of an X chromosome for dosage compensation. We do indeed observe this result, and thus are confident that we have the statistical resolution to detect differential methylation across autosomes as well. We focus on methylation as an aspect of gene regulation that could complement gene mapping studies traditionally completed for exploring the genotype-phenotype link. We propose that methylation data can potentially be useful in predicting pathways involved in canine disease risk and progression. We will establish a publically available web-based resource to serve as a repository for the dog methylomes. The collection of methylomes we generate will contribute to the growing resources that are available for investigation of morphology, disease etiology, advancing therapeutic approaches, and overall canine health.