



GRANT PROGRESS REPORT REVIEW

Grant: 01131: *Genetic Background and the Angiogenic Phenotype in Cancer*

Principal Investigator: Dr. Jaime F Modiano, VMD PhD

Research Institution: University of Minnesota

Grant Amount: \$254,871.00

Start Date: 1/1/2010 **End Date:** 12/31/2012

Progress Report: 6 month

Report Due: 6/30/2010 **Report Received:** 7/1/2010

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.)

Original Project Description:

Background: Certain dog breeds are prone to develop certain types of cancer; yet, there has been little progress to define genes or other factors that account for this risk. The researchers' recent work on hemangiosarcoma is the first to clearly demonstrate that a dog's genetic background, defined by "breed," can influence the type of genes that show up as tumors. This means that certain breeds are diagnosed with specific cancers more frequently than others because of the behavior of tumors after they show up, and not simply because they show up more frequently. Specifically, this may apply to the observed tendency for hemangiosarcoma seen in Golden Retrievers, German Shepherd Dogs, and Portuguese Water Dogs. In addition, one-size-fits-all therapies may be not enough to effectively treat this disease.

Objective: This project will continue the researchers' observations on gene appearance profiles in hemangiosarcoma from Golden Retrievers to German Shepherd Dogs and Portuguese Water Dogs, and it also will define how new targeted therapies may effectively control the disease in these and other dog breeds.

Original Grant Objectives:

Objective 1: Use microarray technology and contemporary bioinformatics to establish unique gene expression signatures in HSA samples from each breed.

Objective 2: Test the how small molecule inhibitors that act directly and indirectly on angiogenic pathways affect HSA cells derived from dogs of each of these breeds.

Objective 3: Examine how attenuating vascular endothelial growth factor receptors affects pro-inflammatory environments generated by HSA cells.

Publications:

Report to Grant Sponsor from Investigator:

Certain dog breeds are prone to develop certain types of cancer; yet, there has been little progress to define genes or other factors that account for this risk. Our recent work on hemangiosarcoma is the first to clearly demonstrate that a dog's genetic background, defined by "breed," can influence the profile of genes that are expressed by tumors. Among other important implications, this implies that certain breeds are diagnosed with specific cancers more frequently than others because of the behavior of tumors after they arise, and not simply because they arise more frequently. Specifically, this may apply to the observed predisposition for hemangiosarcoma seen in Golden Retrievers, German Shepherd Dogs, and Portuguese Water Dogs. Here, we have begun to test this premise by evaluating genome-wide gene expression profiles in these three breeds. We also have started complementary experiments to determine if potential treatment targets behave equally in dogs from different breeds. Our preliminary results suggest that differences at the molecular (submicroscopic) level in these tumors will indeed influence their behavior and their response to treatment approaches.