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: 18 month

Report Due: 6/30/2011 **Report Received:** 6/14/2011

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 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.

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 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:

- Scott M, Duckett M, Modiano J, Yang C, Martinez H, Iverson B, Nunez R. (2010). Ambient temperature stabilization of feline and canine tumor cell RNA for use in gene expression assays. GenVault Technical Application Note for GenTegra™. http://www.genvault.com/downloads/case-studies-and-applicationnotes/ambienttemperature-stabilization-app-note.pdf

Report to Grant Sponsor from Investigator:

The initial batch of samples for gene expression profiling has undergone QC and data for QA should be available before the end of June. Samples arrayed will allow us to assess effects of tumor location, breed, and unique tumor biology. We also will complete next-generation RNA sequencing on select samples and have collected additional material that can be added to the analysis as needed. We have continued a systematic search for molecules that inhibit hemangiosarcoma growth and survival. The HTS system is working and has allowed us to identify prospective targets that may improve therapy. The project studying the EGF_uPA ligand targeted toxin is progressing to clinical studies. Nonetheless, data from a non-overlapping, complementary project indicate it will be important to consider tumor-stroma interactions to develop effective treatments.