RESEARCH PROGRESS REPORT SUMMARY

Grant 02489: Tumor-permissive Collagen Signatures in Canine Mammary Gland Tumors: Development of Prognostic Markers and Targeted Therapies for Improved Outcomes

Principal Investigator: Susan Volk, VMD, PhD

Research Institution: University of Pennsylvania

Grant Amount: $162,700

Start Date: 3/1/2018 **End Date:** 2/29/2020

Progress Report: Mid-Year 2

Report Due: 8/31/2019 **Report Received:** 8/29/2019

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Original Project Description:

Mammary gland tumors (MGT) are the most common malignancies in intact female dogs, and the resulting premature death and morbidity in this sub-population of dogs represents a significant health problem. While genetic alterations within tumor cells can promote their uncontrolled growth and ability to spread to distant sites, recent work indicates that normal, non-malignant cells and extracellular matrix (ECM) within the surrounding tumor stroma also regulate the growth and spread of cancer. The investigators have identified cancer-associated stromal (collagen) signatures in canine MGT biopsy samples that predict clinical outcome better than commonly used markers. These predictive markers may improve the veterinary oncologist's ability to accurately predict which dogs truly need aggressive treatment from those that do not. Notably, their laboratories have shown that inhibition of a collagen-degrading enzyme (Fibroblast Activation Protein (FAP)) and increasing a tumor-suppressive collagen (type III collagen (Col3)) prevent the formation of these tumor-inciting signatures in other species (mouse and human)[*not funded by CHF]*. This work suggests that if these novel targets can suppress tumor-permissive collagen signatures in the dog, we can treat canine MGT more effectively. The goals of this project are 1) to identify additional collagen signatures which predict clinical outcome in dogs, 2) determine how they direct tumor cell behavior and 3) develop therapies that prevent formation of tumor-inciting collagen signatures in canine MGT. Based on the investigators' published and preliminary data, they predict that identifying and targeting tumor-inciting collagen signatures will lead to improvements in both diagnosis and treatment of dogs with malignant MGT.

Publications: None at this time

Presentations: None at this time.

Report to Grant Sponsor from Investigator:

Mammary gland tumors (MGT) are the most common malignancies in intact female dogs and recent work indicates that normal, non-malignant cells and extracellular matrix (ECM) within the surrounding tumor stroma regulates the growth and spread of cancer. Our recent study has identified cancer-associated collagen signatures in canine MGT biopsy samples that predict clinical outcome better than commonly used markers. In studies not funded by CHF, our lab has shown that increasing a tumor-suppressive collagen (type III collagen (Col3)) prevents the formation of these tumor-inciting signatures in other species (mouse and human). Building on these results, we have recently used a novel imaging technique to look at collagen types in MGT samples. Our data suggests that type of collagen as well as the amount and type of collagen cross-linking in tumor samples may be useful in predicting clinical outcome of patients. Our studies also reveal factors that drive formation of these tumor-permissive collagen signatures as well as the ways in which they direct cell activities to direct tumor aggression. Finally, laboratory work suggests these findings can be used to develop clinical therapies. Based on our published and new data, we predict that identifying and targeting tumor-inciting collagen signatures will improve both diagnosis and treatment of dogs with malignant MGT.