RESEARCH PROGRESS REPORT SUMMARY

Grant 02655-E: 2019 Clinician-Scientist Fellowship - University of Minnesota

Principal Investigator: Jaime Modiano, VMD, PhD

Research Institution: University of Minnesota

Grant Amount: $12,000

Start Date: 1/1/2019 **End Date:** 7/31/2021

Progress Report: End-Year 2

Report Due: 1/31/2021 **Report Received:** 1/31/2021

(The content of this report is not confidential and may be used in communications with your organization.)

Original Project Description:

Dr. Wood completed a dual DVM/PhD training program at the University of Wisconsin, School of Veterinary Medicine followed by a small animal medical and surgical internship at the University of Missouri Veterinary Health Center. She is currently a medical oncology resident at the University of Minnesota Veterinary Medical Center.

Dr. Wood's research focuses on the molecular mechanisms and signaling pathways active at the boundary of tumor tissue and normal tissue in translational cancer models (those that may translate from one species to another). Specifically, her project will examine the methylation patterns of specific dog lymphocyte subsets. The data will then be used to define the lymphocyte subsets that infiltrate canine osteosarcoma and improve our understanding of the immune system's role in this serious type of bone cancer.

Publications: None at this time.

Presentations:

Wood, C. "Characterizing canine lymphocyte subsets to identify tumor infiltrating cells." University of Minnesota, Veterinary Clinical Sciences Grand Rounds. March 21, 2019

Wood, C. "Wnt and the Immune System in Canine Osteosarcoma." Invited Research Seminar, Cornell University. April 3, 2019

Wood, C. “Wnt and the Immune System in Canine Osteosarcoma.” Invited Research Seminar, University of Wisconsin – Madison. November 26, 2019

Report to Grant Sponsor from Investigator:

T-cells, or T-lymphocytes, are disease-fighting white blood cells that are “programmed” to recognize foreign antigens – small bits of protein that are unique to viruses, bacteria, and other pathogens. T-cells can also recognize abnormal proteins that are made by cancer cells, providing a level of protection against cancer, and making them useful in the treatment of cancer.

The cells we call “naïve T-cells” have never encountered the antigen that they are programmed to recognize. Thus, when they “see” the antigen for the first time, they (1) take longer to become activated and (2) follow a certain path of activation to secrete proteins that help initiate an immune response. As part of the response, the single activated T-cell divides repeatedly, creating a “clone army” against the invading pathogen (or tumor). The immune response is terminated once the danger is eliminated, but some T cells in the “clone army” remain behind to protect against future invasion. These are called “memory T cells.”

We know that the process of turning a naïve T-cell into a memory T-cell includes changes in the 3-dimensional structure of DNA. These changes are partially due to the addition of methyl groups (“methylation”). When there are many methyl groups, the DNA clumps like a ball of string. This prevents cellular machinery from accessing the genes encoded by that portion of DNA. When there are fewer methyl groups, the DNA remains un-clumped and accessible. These 3D changes can regulate which genes are turned on to make new proteins, and which are silenced.

While we have learned quite a bit about DNA methylation in humans, the precise changes that occur in canine T cells, in either their naïve or memory state, has not been examined in detail. Our goal is to determine how methylation differs between these two states. We use blood samples from healthy dogs and culture techniques to collect both naïve and memory T cells, and then will use special genetic sequencing to evaluate the methylation changes. This information will help us to learn more about the function of the canine immune system and how we can use it to fight bone cancers.

We have established the methods needed for analysis. But the COVID-19 pandemic negatively impacted our ability to make progress during much of 2020. As we enter a new year, we are hopeful in progress being made against the pandemic, and confident that we will soon be able to resume our work at 100% capacity. We anticipate data collection will be completed by the end of Spring/Summer 2021.