



## RESEARCH PROGRESS REPORT SUMMARY

**Grant 03032-MOU:** Early Detection of Canine Osteosarcoma

**Principal Investigator:** Jaime Modiano, VMD, PhD

**Research Institution:** University of Minnesota Office of Sponsored Projects Administration

**Grant Amount:** \$497,469.60

**Start Date:** 4/1/2022      **End Date:** 3/31/2025

**Progress Report:** End-Year 1

**Report Due:** 3/31/2023      **Report Received:** 4/3/2023

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### **Original Project Description:**

Funding for the research is provided through the collaborative efforts and generosity of the Golden Retriever Foundation®, Great Dane Club of America Charitable Trust, Irish Setter Club of America Foundation, Irish Wolfhound Foundation and Irish Wolfhound Club of America, Leonberger Health Foundation International, Rottweiler Health Foundation, and the AKC Canine Health Foundation, which will oversee grant administration and scientific progress.

Primary bone cancers (called osteosarcomas) affect more than 8,000 dogs, and possibly as many as 50,000 dogs per year in the United States. Although the risk for bone cancer is greatest in large and giant breeds, it is a health concern for many breeds. The impact of the problem is highlighted by the fact that osteosarcoma accounts for up to 10-20% mortality in some breeds. While osteosarcoma is treatable, only 30-40% of dogs that receive the standard of care survive one year or longer, and fewer than 20% are alive at two years. In addition, some dogs suffer significant treatment-related morbidity. Thus, better strategies to manage this cancer are needed. Given the current understanding that size and longevity are two major factors associated with osteosarcoma risk, and the challenges of treating this disease once it is established, investigators have focused efforts on developing tests that allow detection of osteosarcoma at or near its origin. Early detection, in turn, will enable the deployment of strategic prevention in dogs at high risk. This project will place special emphasis on Irish Wolfhounds, Rottweilers, Great Danes, Golden Retrievers, Irish Setters, and Leonbergers, without neglecting other breeds (or mixed breed dogs) at risk. The central goal is to develop a blood test for early detection of osteosarcoma as the initial step in the implementation of the long-term strategy of early detection and targeted prevention. Success in this effort will be foundational to implement the test in clinical practice and to provide access to prevention. Investigators propose that this approach—combining early



detection and targeted prevention—is a novel and potentially transformative strategy to address the unmet health need for dogs at risk of bone cancer. This project may also add to the proof-of-concept that will enable using this type of approach to reduce the impact of cancer in humans.

**Publications:**

None to date

**Presentations:**

1. Makielski, K. Development of a Canine Osteosarcoma Early Detection Test: The COED Study. Presented at the inaugural ACVIM Research Colloquium & Networking Event, June 24, 2022, Austin, TX.
2. Makielski KM. Molecular Signatures of Disease Behavior. Masonic Cancer Center Seminar Series, December 20, 2022, Minneapolis, MN.
3. Makielski KM, Modiano JF. Assessment of biological aging and cancer risk using liquid biopsies. ACVIM 2023, 6/15/23-6/17/23. (Accepted).
4. Makielski KM, Khammanivong A, Labe CH, Schulte AJ, Kreager LE, Rendahl AK, Cutter GR, Spector LG, Weigel BJ, Modiano JF. Identification of serum exosomal gene signatures associated with prognosis in pediatric osteosarcoma. FACTOR Osteosarcoma Conference 2023, Atlanta GA, 6/22/23 – 6/24/23 (Accepted for oral presentation).

**Report to Grant Sponsor from Investigator:**

In this study, we aim to identify blood biomarkers that can be used to assign a probability of developing osteosarcoma to otherwise healthy dogs at risk for this disease. We have a large set of samples and are also collecting new samples for this project. The control (old and new) samples will include healthy dogs and dogs with cancer. These samples are used to identify the patterns that are exclusively present in dogs with cancer, and specifically in dogs with bone cancer. The experimental group will include healthy dogs at risk for development of bone cancer. This risk is based on age (older than 4.5 years) and on size. Dogs from six breeds will have preference in recruitment, although large dogs of other breeds and mixed breeding will be eligible to enroll. A gift from the Irish Wolfhound Foundation in advance of this project was instrumental in helping us to finalize the infrastructure. It also allowed us to pilot enrollment of 25 dogs to make sure the protocols were efficient and reasonable. Recruitment for the experimental group was launched at the end of August of 2022 and we began enrolling dogs and receiving samples, in random order, in October 2022. As of March 15th, 2023, we have collected 196 new samples for both parts of this project. We estimate enrollment will be complete on or about the end of year 2 of the project. A test for predicting the occurrence of bone cancer in dogs would be extremely valuable to veterinary medical community and dog owners worldwide. This proposal applies artificial intelligence technologies to describe patterns associated with the formation of these cancers.



We have also used this project as a vehicle for training to engage young scientists and encourage them to pursue careers in canine health research. Ms. Courtney Labe is a second-year veterinary student who has demonstrated exceptional excitement about this project and has accepted a Summer Scholar position in the lab, and Ms. Lauren Kreager is a technician (Researcher-2) hired into our group last year who will also be contributing to the project. Both have expressed an interest in continuing on a path that includes research, and specifically research that aims to improve the health and wellbeing of companion dogs as a major component of their future careers.