RESEARCH PROGRESS REPORT SUMMARY

Grant 02519: Prevalence of *Bartonella* spp. Infection in Dogs with Cardiac and Splenic Hemangiosarcomas Within and Between Geographic Locations

Principal Investigator: Edward Breitschwerdt, DVM

Research Institution: North Carolina State University

Grant Amount: $219,026

Start Date: 2/1/2018 **End Date:** 1/31/2021

Progress Report: End-Year 2

Report Due: 1/31/2020 **Report Received:** 2/1/2020

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Original Project Description:

Splenic masses comprise ~50% of all canine splenic disease. Despite advances in imaging and pathologic definition, the etiology and medical relevance of splenic lesions in dogs are often ambiguous. While some splenic tumors are benign, approximately two-thirds are highly malignant and carry a poor prognosis. Hemangiosarcoma (HSA) accounts for the majority of canine malignant splenic tumors and occurs in many large dog breeds, including mixed breeds. A less common site of HSA localization is the heart (cardiac HSA). Risk factors for both cardiac and splenic HSA remain unclear, confounding development of preventative strategies. The investigators recently reported a high prevalence of species of the bacterial genus *Bartonella* in dogs with HSA from North Carolina, suggesting a potential role in the initiation and/or progression of this cancer. *Bartonella* species exist worldwide and are transmitted by blood-sucking arthropods (e.g. ticks, fleas) and their presence in splenic tissue could potentially be explained by the fact that the spleen is primarily responsible for removal of blood-borne parasites from the systemic circulation. The investigators will perform a comprehensive examination of the potential association between *Bartonella* infection and HSA by comparing the prevalence of *Bartonella* DNA in tumor and blood samples from both splenic and cardiac HSA cases, and also within and between distant geographical locations in the US. Ultimately, demonstration of a robust association between *Bartonella* infection and the development of HSA may lead to new opportunities for improved diagnosis, treatment and prevention of this devastating cancer.

Publications:

Lashnits, E., Neupane, P., Bradley, J. M., Richardson, T., Thomas, R., Linder, K. E., Breen, M., Maggi, R. G., & Breitschwerdt, E. B. (2020). Molecular prevalence of *Bartonella*, *Babesia*, and hemotropic *Mycoplasma* species in dogs with hemangiosarcoma from across the United States. *PLOS ONE*, *15*(1), e0227234. https://doi.org/10.1371/journal.pone.0227234

Presentations:

Lashnits E, Abstract oral presentation: Molecular prevalence of *Bartonella, Babesia*, and hemotropic *Mycoplasma* species in dogs with hemangiosarcoma. American College of Veterinary Medicine Annual Forum, Phoenix, AZ, June 12-15, 2018.

Breitschwerdt EB. The genus *Bartonella* and vasoproliferative cancers in dogs and humans. presented at the AKC Canine Health Foundation National Parent Club Canine Health Conference in St. Louis, MO August 9-11, 2019.

Report to Grant Sponsor from Investigator:

We are on track to accomplish all of our aims for this study. We were able to obtain the initial set of samples on April 26, 2018 so we had a short delay in starting this study. We have now completed all Year I study aims, with the exception of immunohistochemistry and FISH localization of *Bartonella* organisms within various cell types. We have published a manuscript to the Journal of Clinical Microbiology, representing additional research from our AKC-CHF study #02287, which allowed us to define the Western Blotting (WB) criteria for serodiagnosis of bartonellosis in dogs. That work required additional time and research effort to validate WB testing. We are very excited with the qPCR and ddPCR results obtained from the fresh frozen hemangiosarcoma tissues provided by the NIH-CCOGC. The results strongly support a role for Bartonella spp. in the etiopathogenesis of hemangiosarcoma in dogs. The regional study should provide additional insight as to the issue of potential causation. All three of the regions have identified, collected and shipped all necessary samples from their region. These samples will be tested by ddPCR, which has required months of validation, over the next six months.