RESEARCH PROGRESS REPORT SUMMARY

Grant 02502: Precision Medicine for Canine Lymphoma

Principal Investigator:	Nicola Mason, BVetMed, PhD
Research Institution:	University of Pennsylvania
Grant Amount:	$86,400
Start Date: 3/1/2018	**End Date:** 2/28/2021
Progress Report:	Mid-Year 3
Report Due: 8/31/2020	**Report Received:** 11/9/2020

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

Original Project Description:

The clinical response of dogs with lymphoma to multi-agent chemotherapy is highly variable. Although up to 85% of dogs respond initially, some relapse within weeks, while others enjoy remission times of two years. This heterogeneity in clinical response is in part explained by the recognition that "lymphoma" is not a single disease entity, but consists of different subtypes that can be characterized on a molecular level by mutations in specific genes. As in human medicine, it follows that different lymphoma subtypes, driven by different molecular mechanisms, may respond better to therapies that are specifically selected to inhibit the driver mechanisms within that patient's tumor. Recent work using sophisticated genetic sequencing tools (next-generation sequencing (NGS)) has begun to shed light on the different molecular subtypes of canine B cell lymphoma, and specific therapies aimed at targeting patient-specific driver genes and pathways are being developed. To enable targeted therapies to move into the clinic, a personalized diagnostic tool must be developed that can rapidly and cost-effectively determine the mutational profile of a patient's cancer allowing selection of the most effective drug for that patient. The investigators aim to develop a NGS diagnostic test that can be employed on standard biopsy samples to identify molecular drivers of a patient's lymphoma (personalized diagnostics), enabling the most appropriate targeted therapy to be selected for that patient. In addition, they aim to determine whether specific mutational profiles within canine lymphoma identified by their NGS panel are predictive of clinical outcome.

Publications: None at this time.

Presentations:

This work was included as part of a presentation entitled: Bringing precision medicine into veterinary oncology; given by Dr. Guannan Wang at the following locations.

Mari Lowe Comparative Oncology Seminar, The Penn Vet Cancer Center, Jan 2019, Philadelphia, PA
American Association for Cancer Research (AACR) Annual Meeting 2019, Mar 2019, Atlanta, GA
Corporate workshop at Association of Molecular Pathology (AMP2019) Annual Meeting Nov 2019, Baltimore, MD

Dr. Wang also described some of this research in her YouTube presentation which can be found at: https://www.youtube.com/watch?v=TQNzmozP12Y

Report to Grant Sponsor from Investigator:

The clinical response of dogs with lymphoma to multi-agent chemotherapy is highly variable. Although up to 85% of dogs respond initially, some relapse within weeks, while others enjoy remission times of two years. This heterogeneity in clinical response is in part explained by the recognition that "lymphoma" is not a single disease entity but consists of different subtypes that can be characterized on a molecular level by mutations in specific genes. As in human medicine, it follows that different lymphoma subtypes, driven by different molecular mechanisms, may respond better to therapies that are specifically selected to inhibit the driver mechanisms within that patient's tumor. Recent work using sophisticated genetic sequencing tools (next-generation sequencing (NGS)) has begun to shed light on the different molecular subtypes of canine B cell lymphoma and specific therapies aimed at targeting patient specific driver genes and pathways are being developed. To enable targeted therapies to move into the clinic, a personalized diagnostic tool must be developed that can rapidly and cost-effectively determine the mutational profile of a patient's cancer allowing selection of the most effective drug for that patient. Supported by the AKC-CHF, we have developed a NGS diagnostic test that can be employed on standard biopsy samples to identify molecular drivers of a patient's lymphoma (personalized diagnostics). This will enable targeted therapies to be selected based on their ability to inhibit the molecular pathway that is driving that specific patient's tumor. We are in the process of using our NGS panel to evaluate 100 canine lymphoma samples and determine their tumor mutational burden and molecular drivers. In addition, we aim to determine whether specific mutational profiles within canine lymphoma identified by our NGS panel, are predictive of outcome. This is an important first step toward bringing personalized diagnostics that aim to improve the outcome of patients with B cell lymphoma, into the veterinary clinic.