RESEARCH PROGRESS REPORT SUMMARY

Grant 02502: Precision Medicine for Canine Lymphoma

Principal Investigator:	Nicola Mason, BVetMed, PhD
Research Institution:	University of Pennsylvania
Grant Amount:	$86,400.00
Start Date: 3/1/2018	**End Date:** 2/29/2020
Progress Report:	End-Year 1

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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:

Wang G." Bringing precision medicine into veterinary oncology." American Association of Cancer Research (AACR), Atlanta, Georgia. Apr 2nd 2019.

Report to Grant Sponsor from Investigator:

The clinical response of dogs with lymphoma to chemotherapy is highly variable. Although up to 85% of dogs respond initially, most patients relapse and eventually succumb to their disease. Remission times of dogs with lymphoma are highly variable, some patients relapse within weeks, while others enjoy remission times of several 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 that occur 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. This data can then be used to select therapies that specifically target the driver mutations/ pathways present in each patient’s tumor. The ultimate goal is to direct the most effective therapy for that tumor type to the patient early in the course of disease to improve outcome. 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. We have designed a next generation sequencing panel that aims to rapidly identify which genes are mutated in a patient’s lymphoma. We are now in the process of validating this panel and optimizing the experimental workflow and bioinformatics associated with it. Once our panel is validated, we will use it to determine the specific mutational profiles within canine lymphoma samples and whether these may predict patient response to CHOP-based chemotherapy. In the future and outside the scope of this award, we aim to build on this work and forge collaborations with pharmaceutical companies to gain access to therapies that specifically target mutated pathways within each patient’s tumor and determine whether a personalized approach to canine lymphoma can improve patient outcome.