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:** 2/29/2020

Progress Report: Mid-Year 2

Report Due: 8/31/2019 **Report Received:** 9/27/2019

(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:

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 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. 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, determine whether profiling may predict patient outcome and ultimately whether specific therapies that target the individual patient’s aberrant oncogenic pathway(s) provide superior treatment outcomes when compared with conventional, untargeted chemotherapy.