RESEARCH PROGRESS REPORT SUMMARY

Grant 02383: Identifying Cellular Mechanisms of Inflammation During Canine Tick-Borne Diseases

Principal Investigator: Christine Petersen, DVM, PhD

Research Institution: University of Iowa

Grant Amount: $207,526.00

Start Date: 9/1/2017 **End Date:** 12/31/2019

Progress Report: End-Year 2

Report Due: 8/31/2019 **Report Received:** 8/29/2019

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Original Project Description:

Tick-borne diseases are found in all 50 states of the United States and are the most common vector-borne disease diagnosed in people in the US. The predominant disease is Lyme disease, caused by *Borrelia burgdorferi* and related species (sensu lato). Other important canine tick-borne diseases include those caused by *Anaplasma platys*, *Anaplasma phagocytophilum* (Anaplasmosis), *Babesia canis*, *Babesia conradea* and *Babesia gibsonii* (Babesiosis), and *Ehrlichia canis*, *Ehrlichia chaffiensis* and *Ehrlichia ewingii* (Ehrlichiosis). Many of these diseases also affect people. Dogs can serve as sentinel species for human disease and there are many areas where the immune responses and disease outcomes are very similar in people and dogs, meaning that important lessons can be learned by sharing information between human and animal health (One Health). The researchers will further investigate the dog's immune system to determine which immune cells are responsible for the cure or creation of canine tick-borne disease. Through understanding which cells are responsible for causing disease, the goal is to then specifically target the molecules they produce using immunotherapy or immune modulation to improve treatment of tick-borne diseases in all dogs.

Publications: None at this time.

Presentations:

Natural Killer cell subsets during Lyme Disease: Pathogen control and pathogenesis. Breanna M Scorza.

- Oral presentation: Immunology Grand Rounds, University of Iowa Hospitals & Clinics, Iowa City, IA. November 2018.

Impact of Tick-Borne Co-Infections on Canine Leishmaniosis: Circulating Natural Killer Cell Populations. Breanna M Scorza, Kurayi Mahachi, Erin C Cox, Angela Toepp, Jennifer Foltz, Dean Lee, and Christine A Petersen.

- Oral presentation: Parasitology Group Meeting, University of Iowa, Iowa City, IA. January 2019.
- Oral presentation: Immunology Student Seminar, University of Iowa, Iowa City, IA. December 2018.
- Poster presentation: American Society for Tropical Medicine and Hygiene Conference. New Orleans, LA. October 2018.
- Poster presentation: Center for Immunology and Immune-based Diseases. Iowa City, IA. August 2018.
- Poster presentation: American Association of Immunology. Austin, TX. May 2018.

Characterization of circulating Natural Killer cells in canines exposed to tick-borne infections. Breanna M Scorza, Kurayi Mahachi, Angela Toepp, and Christine A Petersen.

- Poster presentation: Great Plains Emerging Infectious Disease Conference. Iowa City, IA. March 2018.

Altered circulating NK cell response during *Ehrlichia* and *Leishmania* infection and potential role in progressive disease. Breanna M Scorza, Kurayi Mahachi, Erin C Cox, Jennifer Foltz, Dean Lee, Jill Saucier, Phyllis Tyrrell, Christine A Petersen.

- Poster presentation: Great Plains Emerging Infectious Disease Conference. Iowa City, IA. March 2019.
- Oral presentation: World Association for the Advancement of Veterinary Parasitology conference. Madison, WI. July 2019.
- Oral presentation: Center for Immunology and Immune-Based Diseases Retreat. Iowa City, IA. August 2019.
- Oral presentation: Woods Hole Immunoparasitology conference. Woods Hole, ME. April 2019.

Report to Grant Sponsor from Investigator:

We have successfully identified sporting and hunting dogs at different clinical stages of Lyme Disease and sampled blood from them in the field. We have confirmed our field diagnoses with a specialized assays performed by IDEXX Laboratories. Currently, we analyzed ~70% of our projected sample size of dogs with Lyme exposure. In the lab, we have analyzed the percentage of Natural Killer immune cells and some markers of the activation state of these NK cells in the blood. We have found one subset of these cells increases during canine Lyme disease. The NK cells from dogs with symptomatic Lyme Disease showed a statistically enhanced inflammatory response, indicating that these cells may contribute to clinical disease. We also found a serum cytokine that was elevated in dogs that were asymptomatic after Lyme disease exposure, thus this cytokine could be skewing the NK cell subset

toward a less inflammatory phenotype. Our final experiment, which we have troubleshot and obtained working protocols for, will determine if NK cells from dogs in each Lyme subgroup have different cell killing properties. Our overall goal is to determine differences between dogs with asymptomatic versus symptomatic Lyme, in order to better understand which cell types, or inflammatory factors produced by them, are helpful for controlling the disease. Based on these results, therapies targeted towards decreasing NK cell-mediated inflammation, or to increase serum cytokines associated with NK differentiation, may help dogs maintain an asymptomatic state following Lyme Disease exposure. Throughout this study, we have established a good working relationship with the caretakers of the hunting and sporting dogs and have collected enough samples to meet our statistical needs for these experiments. We plan to submit the results of these assays for publication this fall.