

**BIOMEDICAL & VETERINARY SCIENCES  
GRADUATE PROGRAM**



**ANNOUNCES**

The Master of Science Seminar and Examination of

**Stacy Lauren Clothier**

**“Immune Checkpoint Molecule Expression in Canine  
Lymphoma and Canine Reactive Lymphoid  
Hyperplasia”**

**Monday, September 9th, 2019  
2:00 PM  
VMIA Classroom 220**





Stacy is from Media, PA and graduated from Villanova University with a BS in Biology. She completed a masters in laboratory animal science from Drexel University followed by her DVM from Western University of Health Sciences in southern CA in 2010. After veterinary school, she completed a one-year rotating small animal internship at a private specialty hospital in southern CA and then worked in small animal general and emergency practice. In 2015, she began a combined veterinary clinical pathology residency and Biomedical and Veterinary Sciences MS program at the Virginia-Maryland College of Veterinary Medicine. She achieved board certification in veterinary clinical pathology from the American College of Veterinary Pathologists in 2018.

**Funded by**

- AstraZeneca
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- VMCVM Office of Research and Graduate Studies

### **Awards and Academic Achievements**

- Diplomate, American College of Veterinary Pathologists (Clinical Pathology) 2018

### **Lay Language Abstract**

Lymphoma, a cancer of the white blood cells in the body, is one of the most common malignancies in dogs. Although treatment with a multi-agent chemotherapy protocol results in high remission rates, the remission duration is usually less than one year, with the majority of patients relapsing. In an effort to improve remission rates and survival times, scientists have been working to develop therapeutic interventions that target specific points in the development and replication cycle of a cancer cell. One such strategy, targeting checkpoint molecules programmed death (PD)-1 and PD-L1, has shown promise for several different types of human cancers, including lymphoma.

PD-1 is a receptor on T cells, which together with its ligands, PD-L1 and PD-L2, decreases lymphocyte function when activated. This is a protective mechanism, acting to inhibit sustained harmful inflammation in a normal healthy dog. Some cancers have taken advantage of this pathway, increasing expression of PD-L1 or PD-L2 in order to evade detection by the immune system. To date, little is known regarding the role and expression of these immune checkpoint molecules in dogs with lymphoma. We sought to evaluate if PD-1, PD-L1 and PD-L2 expression is significantly increased in canine lymphoma compared to reactive lymphoid hyperplasia controls.

Tissue samples were collected from two sources. Cytology samples of lymphoma and reactive lymphoid hyperplasia were collected by fine needle aspiration from clinical patients. Formalin fixed paraffin embedded tissue

samples of lymphoma and reactive lymphoid hyperplasia were collected from the archived tissue bank. Using a molecular analysis technique called quantitative reverse transcription PCR (qRT-PCR) we measured the amount of messenger RNA (mRNA) encoding PD-1 and its ligands PD-L1 and PD-L2 in lymphoma and in reactive lymphoid hyperplasia controls.

In our results we did not observe an upregulation in the expression of checkpoint molecules in canine lymphoma relative to canine reactive lymphoid hyperplasia. This suggests there may be a limited therapeutic application for PD-1 and PD-L1/PD-L2 blockade in canine lymphoma. Although these results do not suggest that checkpoint inhibitors would be useful for treatment, they give insight into the mechanisms of unchecked lymphocyte proliferation in canine lymphoma.

### **Publications**

**Clothier SL**, Zimmerman K, Hanks C, Sponenberg P, Weiss T. What Is Your Diagnosis? Coelomic effusion in a skittering frog. *Veterinary Clinical Pathology*. (In press)

**Clothier SL**, Johnson-Delaney C. Invited book chapter: Hematology of Mustelids (Otters, Minks, and Ferrets). In: *Schalm's Hematology 7th edition*. Submitted for editorial review, Spring 2019.

**Clothier S**, Barrett S, LeRoith T, Klahn S, Huckle W. Immune Checkpoint Molecule Expression in Canine Lymphoma and Canine Reactive Lymphoid Hyperplasia. (manuscript in preparation).

### **Presentations**

**Clothier S**, Barrett S, LeRoith T, Klahn S, Huckle W. Immune Checkpoint Molecule Expression in Canine Lymphoma and Canine Reactive Lymphoid Hyperplasia. 2019 ASVCP/ACVP Annual Conference. San Antonio, TX. (accepted poster presentation).

**Clothier S**, Ernst M. Case Presentation: Mastocytomia with Secondary Paraneoplastic Eosinophilia in a Cat. Southeastern Veterinary Pathology Annual Conference. Tifton, GA. May, 2019.

**Clothier S**, Boes K, Cecere T, Wilkinson A, Grant D. Case Discussion: Central Diabetes Insipidus and Erythrocytosis Secondary to Metastatic Lymphoma in a Dog. American College of Veterinary Pathology Annual Conference. Washington, DC. November, 2018.

**Clothier S**, Barrett S, LeRoith T, Klahn S, Huckle W. Expression of Programmed Death/Programmed Death Ligand (PD-1, PD-L1/PD-L2) in canine neoplastic versus non-neoplastic lymphocytes. Virginia Maryland College of veterinary medicine Annual Biomedical and Veterinary Science Graduate Research Symposium. Blacksburg, VA. March 2018 (Poster presentation).

**Clothier S**, Boes K. Case Presentation: Histoplasmosis with Secondary Immune-Mediated Hemolytic Anemia in a Cat. Southeastern Veterinary Pathology Annual Conference. Tifton, GA. May 2018.

**Clothier S**, Boes K. Mystery Slide Session: Gastric Squamous Cell Carcinoma in Peritoneal Fluid of a Horse. American College of Veterinary Pathology Annual Conference. Vancouver, British Columbia. November, 2017.

**Clothier S**, Boes K, Barrett S. Case Presentation: Barium Peritonitis in a Dog. Southeastern Veterinary Pathology Annual Conference. Tifton, GA. May, 2017.

**Clothier S**, Boes K. Mystery Slide Session: Snake Envenomation, Dog Blood Smear. American College of Veterinary Pathology Annual Conference. New Orleans, LA. December, 2016.

## Examination Graduate Committee

### **Major Advisor/Chair:**

William R. Huckle, MS, PhD  
Associate Professor, Cell Biology and Pharmacology  
Department of Biomedical Sciences and Pathobiology

### **Graduate Advising Committee Members:**

Tanya LeRoith, DVM, PhD, DACVP  
Clinical Professor, Anatomic Pathology  
Department of Biomedical Sciences and Pathobiology

Sarah Barret, DVM, PhD, DACVP  
Clinical Assistant Professor, Clinical Pathology  
Department of Biomedical Sciences and Pathobiology

Shawna Klahn, DVM, DACVIM (Oncology)  
Clinical Associate Professor, Oncology  
Department of Small Animal Clinical Sciences



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