RESEARCH PROGRESS REPORT SUMMARY

Grant 02751-A: Luteinizing Hormone Receptor Activation Induces Migration and Adhesion in Neoplastic Canine Lymphocytes

Principal Investigator: Michelle Kutzler, DVM, PhD

Research Institution: Oregon State University

Grant Amount: $14,580

Start Date: 2/1/2020 **End Date:** 7/31/2021

Progress Report: FINAL

Report Due: 7/31/2021 **Report Received:** 7/26/2021

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

Original Project Description:

Luteinizing hormone (LH) is secreted from the brain (pituitary) in sexually intact dogs to stimulate synthesis of estrogen and testosterone in females and males, respectively. However, LH is secreted at concentrations up to 20 times higher following gonad removal with spaying or castration because hormonal negative feedback is lost. Although LH is considered to be a reproductive hormone, there are dozens of non-reproductive tissues in dogs that contain receptors for LH including immune system cells, specifically lymphocytes. Lymphoma is a common malignant cancer of dogs involving lymphocytes, and spayed/castrated dogs are reportedly 3-4 times more likely to develop lymphoma. Conventional chemotherapy results in remission in approximately 60-90% of cases with a median survival time of 6-12 months. Preliminary work has identified LH receptors in canine lymphoma tissue and demonstrated LH-receptor-induced proliferation of neoplastic lymphocytes in vitro. This study aims to determine if LH receptor activation induces adhesion and migration of neoplastic lymphocytes in vitro. Characterizing the role of LH receptor in neoplastic lymphocyte proliferation may help guide future lymphoma treatment options.

Publications:

Abstract published in the Society for the Study of Reproduction Abstract book: "Wanli Li, Michelle Anne Kutzler: Luteinizing Hormone Receptor Gene Expression in Canine Neoplastic Lymphoma Cells is Upregulated by Treatment with Human Chorionic Gonadotropin. 2020;4 (abstract #1850)."

Abstract published in the journal Clinical Theriogenology: "Dietz A, Kutzler M: Luteinizing hormone receptor activation stimulates endothelial adhesion of neoplastic canine T-lymphocytes. Clin Theriogenology 2021;13:302."

Kutzler, M. A. (2020). Possible Relationship between Long-Term Adverse Health Effects of Gonad-Removing Surgical Sterilization and Luteinizing Hormone in Dogs. *Animals: An Open Access Journal from MDPI*, *10*(4). https://doi.org/10.3390/ani10040599

Presentations:

2020 Society for the Study of Reproduction Poster: "Wanli Li, Michelle Anne Kutzler: Luteinizing Hormone Receptor Gene Expression in Canine Neoplastic Lymphoma Cells is Upregulated by Treatment with Human Chorionic Gonadotropin

2021 Society for Theriogenology Conference presentation: "Dietz A, Kutzler M: Luteinizing hormone receptor activation stimulates endothelial adhesion of neoplastic canine T-lymphocytes."

Report to Grant Sponsor from Investigator:

In the United States, spaying and neutering of dogs and cats is commonly performed to prevent the birth of unwanted pets. However, surgically removing the ovaries or testes may have unexpected consequences. Dogs that have been spayed or neutered have an increased risk for developing obesity, urinary incontinence, hypothyroidism, hyperadrenocorticism, diabetes, cruciate ligament tears, hip dysplasia, and cancer. Lymphoma is three to four times more common in spayed and neutered dogs compared to dogs left intact. In addition, dogs that are neutered before one year of age are three times more likely to develop lymphoma than dogs neutered after one year of age. This funded study is investigating the hormonal and cellular relationships between spaying/neutering and the development of lymphoma so that new treatments will be available in the future to extend life expectancies of dogs with cancer.