RESEARCH PROGRESS REPORT SUMMARY

Grant 02643-A: Examination of the Effects of Cannabidiol on Canine Neoplastic Cell Apoptosis/Autophagy and Potential for Chemotherapy Resistance or Sensitivity

Principal Investigator: Joseph Wakshlag, DVM, PhD

Research Institution: Cornell University

Grant Amount: $13,528

Start Date: 6/1/2019 **End Date:** 5/31/2021

Progress Report: FINAL

Report Due: 5/31/2021 **Report Received:** 8/13/2021

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Original Project Description:

Currently the use of cannabidiol (CBD) rich extracts for canine oncology patients is common, yet there is no data in canine oncology regarding the effects of CBD on canine cancer cells. Oncologists are wary of CBD use in their patients due to a lack of knowledge regarding the effects of CBD during chemotherapy. Initial studies on cytotoxicity by the research team show that CBD has cytotoxic activity on a variety of canine cancer cell lines at modest concentrations in the laboratory. These effects cause apoptosis, or programmed cell death, within a very short time frame, suggesting a discrete mechanism. The objective of this study is two-fold; 1) to determine if co-treatment of cancer cells with a common chemotherapeutic (doxorubicin) and CBD at varying concentrations affects chemotherapeutic cytotoxicity, and 2) to examine the molecular framework of the cell death response looking at the most commonly implicated pathways targeted in canine cancer treatment, including mechanisms of cell signaling and autophagy (removal of damaged cells).

Publications:

Henry, J. G., Shoemaker, G., Prieto, J. M., Hannon, M. B., & Wakshlag, J. J. (2020). The effect of cannabidiol on canine neoplastic cell proliferation and mitogen-activated protein kinase activation during autophagy and apoptosis. *Veterinary and Comparative Oncology,* e12669, e12669. https://doi.org/10.1111/vco.12669

Presentations:

I have already presented the data at NAVC this past January and Dr. Henry has presented the doxorubicin and apoptosis data this past fall at the NY State Veterinary Conference

Report to Grant Sponsor:

The objective of the project was to examine the effects of CBD on canine cancer cell growth proliferation with aims towards understanding the signaling pathways involved and the apoptotic response related to CBD. A second aim was to understand the influence of CBD co-treatment with chemotherapeutics such as doxorubicin and vincristine. Both of these aims are outlined and presented in the publication listed above and is a comprehensive review of our results from this project. Investigators found that CBD is effective at hindering cell proliferation and induction of autophagy and apoptosis rapidly across neoplastic cell lines. Further clinical trials are needed to understand its efficacy and interactions with traditional chemotherapy.

Over the last 6 months we have completed some of the mitochondrial data that was no part of the initial publication and was the third aim of our study to further examine mitochondrial influence on the overall apoptotic response. Flow cytometry assays are not showing that mitochondrial perturbations do not supersede the apoptotic response in these cell lines and that CBD treatment does not act as a potent free radical scavenger or generator that may be influencing mitochondrial function during CBD treatment.