



## 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:** \$14,580  
**Start Date:** 6/1/2019      **End Date:** 5/31/2021  
**Progress Report:** Mid-Year 2  
**Report Due:** 11/30/2020      **Report Received:** 10/12/2020

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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:

Joshua G. Henry DVM, Gregory Shoemaker#, Many Beth Hannon, Joseph J Wakshlag DVM, PhD. The effect of cannabidiol on canine neoplastic cell proliferation and MAP Kinase activation during autophagy and apoptosis. In preparation.



**Presentations:**

I have 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 from Investigator:**

We have completed a lot of the proposed work related to the effects of CBD on cell death and autophagy and the upregulation of the MAP kinase pathway which appears to be involved, however the main mechanism of apoptosis has not been elucidated which may just be directly related to the autophagy induction. This is a global response in all of the cell lines and has real implication for us to look at other G protein signaling which is not within the scope of this project. The other area that we were in the middle of investigating is the induction of mitochondrial toxicity before the COVID epidemic hit. Once we are back up and running in the laboratory, we will be looking into mitochondrial insult using some standard assays including DHR free radical damage and mitochondrial permeability testing. This will complete the project and we are hoping it will lead to a further publication. That said, we have completed the other aspect of the project related to doxorubicin co-treatment and have also done vincristine co- treatment showing some synergy between vincristine and CBD in the cell culture system which is part of the publication below. Unfortunately, the COVID pandemic has lasted longer than expected and we have not been able to initiate any laboratory work until recently. This laboratory has just been approved as of September 15th and we are doing experiments to fulfill reviewer comments regarding the paper submitted and are about to initiate the mitochondrial toxicity assays.