



03003: Suppression of Extracellular Glutamate Efflux & mGluR1 Signaling to Impede Canine Hemangiosarcoma Cell Growth

University of Illinois: Principal Investigator: Timothy Fan, DVM, PhD Total grant amount: \$170,000
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Abstract: Canine splenic hemangiosarcoma (cHSA) is a highly malignant solid tumor that results in near universal fatality. The occult nature of splenic cHSA poses a clinical dilemma, as all too often, pet dogs harboring this deadly disease behave normally until the manifestation of overt, and often catastrophic, clinical symptoms. While emergent medical interventions including splenectomy and whole blood transfusions can often be life-saving, therapeutic benefit is usually transient given the remarkable proliferative capacity of cHSA cells. Unfortunately, most pet dogs will eventually decompensate from the rapid reseeding or metastases progression of cHSA within the peritoneal cavity or lungs.

Attempting to improve outcomes in dogs diagnosed with cHSA, most veterinary investigations have focused on evaluating systemic treatment options that might exert cytoreductive activities, yet survival times in dogs treated with cytotoxic combinations remain disappointing. An alternative strategy that has received limited attention is the exploitation of metabolic vulnerabilities that might exert cytostatic effects; and in the setting of non-terminal tumor burden, cytostasis of cancer cells might afford the opportunity for maintaining high quality-of-life and prolongation in survival times.

This investigation explores extracellular glutamate efflux and metabotropic glutamate signaling in sustaining cHSA cell proliferation. If the investigators' hypothesis is true, current FDA drugs can be repurposed to inhibit glutamate efflux and serve as novel adjuvant strategies for curbing the explosive outgrowth of cHSA cells. Targeting the metabolic dependency of glutamate efflux and consequent paracrine metabotropic signaling could improve the clinical management and survival of pet dogs afflicted with this deadly vascular malignancy.

Contribution: \$2500

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