

# FINAL REPORT



## Curbing Tumor Growth and Chemotherapy Resistance in Canine Hemangiosarcoma

Erin Dickerson, PhD, University of Minnesota, D17CA-059

### **RESULTS: Propranolol shows promise as a treatment for hemangiosarcoma in dogs.**

Morris Animal Foundation-funded researchers at the University of Minnesota are looking at new ways to block hemangiosarcoma tumor growth and cancer spread. They are specifically studying propranolol, a drug commonly used to treat certain forms of heart disease as a promising, new treatment for hemangiosarcoma.

Propranolol was previously found to inhibit the growth of a similar tumor in humans known as angiosarcoma. The team and others showed the addition of propranolol to treatment protocols for angiosarcoma patients can improve overall patient survival by slowing tumor growth. The team wanted to see if this would hold true for dogs and better understand the mechanisms by which propranolol worked to maximize its potential as a promising treatment for canine hemangiosarcoma.

In studies using hemangiosarcoma cell lines, the team found propranolol blocks key metabolic or nutrient pathways, preventing tumor cells from dividing and slowing tumor growth. Identifying metabolic changes induced by propranolol provides opportunities to combine propranolol with other FDA-approved drugs and refine combination drug approaches. The team currently is testing some of these drug combinations in the laboratory, including doxorubicin, a common chemotherapy drug used to treat hemangiosarcoma. The team showed propranolol works with doxorubicin to kill tumor cells, and propranolol can partially restore the sensitivity of doxorubicin-resistant hemangiosarcoma cells to the chemotherapy; chemotherapy resistance is a major stumbling block to successful treatment for this cancer.

Further studies in mouse models show propranolol alone inhibits tumor growth, suggesting it may work as a single agent therapy. Propranolol also worked better than doxorubicin alone in reducing tumor growth in mice. Further study is underway to better understand if these drugs can work together to improve treatment success in dogs.

Findings from these studies may help change standard-of-care treatment for canine hemangiosarcoma. Data already is being used to help inform a multi-center clinical trial to determine if propranolol in combination with doxorubicin will improve the overall survival of dogs with hemangiosarcoma compared to doxorubicin alone. While the team cannot yet report the results from the clinical trial, their data from follow-up studies suggest responses to propranolol may depend upon the genetic mutations found within the tumors, meaning that some dogs may derive greater benefit from the addition of propranolol to standard of care treatment than others. The team is conducting ongoing studies to confirm these findings.

### **PUBLICATION:**

Propranolol Sensitizes Vascular Sarcoma Cells to Doxorubicin by Altering Lysosomal Drug Sequestration and Drug Efflux (*Frontiers in Oncology*, February 2021)

**Thanks to the generous sponsors of this study!**