

PROGRESS REPORT



Finding Ways to Block Hemangiosarcoma Tumor Growth

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Morris Animal Foundation-funded researchers at the University of Minnesota are investigating how hemangiosarcoma cells use cholesterol and lipids to fuel cancer growth. Since healthy, non-cancerous cells are less dependent on cholesterol and fat for growth, the team is looking at novel ways to block tumor cells from using these metabolic fuels while sparing normal cells.

Using cell lines to test their hypothesis, researchers are evaluating whether two beta blockers, propranolol and carvedilol, can disrupt lipid metabolic pathways. Beta blockers are used in human medicine to reduce disease progression and increase survival time in people with angiosarcoma, a cancer similar to canine hemangiosarcoma. An added benefit is propranolol and carvedilol already are used in veterinary medicine to treat heart disease and high blood pressure in dogs. If these drugs eventually prove useful for hemangiosarcoma, it will be easier to translate their use to the clinic.

So far, tests in cell lines confirm that hemangiosarcoma cells appear to scavenge cholesterol and lipids from the environment around the tumor. Early data show propranolol and carvedilol block hemangiosarcoma cells from taking up and processing these essential nutrients. The tumor cells then activate survival mechanisms to compensate for nutrient loss, and prolonged activation of these pathways appears to lead to cell stress and eventually tumor cell death.

The team also continues to evaluate the therapeutic effects of propranolol and carvedilol alone and in combination with chemotherapies. They found that propranolol and carvedilol synergize with different chemotherapy drugs, and that some combinations are vastly superior to others. One specific finding is propranolol increases hemangiosarcoma cell lines' sensitivity to the anti-cancer effects of doxorubicin. The group recently has launched a concurrent clinical trial to determine whether this combination improves the outcome of dogs with hemangiosarcoma.

Hemangiosarcoma is an aggressive disease that most commonly affects large breed dogs. It accounts for 2% to 3% of all canine tumors with a mean age at diagnosis of 9 to 12 years. The cancer is nearly 100% fatal and new treatments are desperately needed. Findings of the study may allow for an improvement in the treatment of canine hemangiosarcoma, a disease that has seen few advancements over the past 30 years.

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