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# ROTTWEILER Update

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## HEMANGIOSARCOMA RESEARCH

Artificial Intelligence Aids Early Detection of Cancer

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# ROTTWEILERS MAY BENEFIT FROM HEMANGIOSARCOMA RESEARCH ADVANCES

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## DOUBLE YOUR DONATION VIA THE CANINE CANCER RESEARCH INITIATIVE

Recognizing the challenges and slow progression in the development of new approaches for diagnosing and treating canine cancer, such as hemangiosarcoma, the AKC (American Kennel Club) Canine Health Foundation (CHF) has launched the [Canine Cancer Research Initiative](#). This fundraiser for cancer research is supported by the American Kennel Club, which will match donations and CHF Donor Advised Fund transfers to the Canine Cancer Research Initiative up to \$250,000 in 2019. The match is provided to support research of canine-specific cancers. Currently, the AKC Canine Health Foundation is supporting four hemangiosarcoma studies totaling over \$906,089.



The heart-crushing agony of losing a beloved dog to cancer is bad enough. When the cancer is a silent killer that snares its victims without a sign of illness, it can be traumatic. This is how it often goes with hemangiosarcoma, a cancer believed to be responsible for the deaths of tens of thousands of dogs in the U.S. each year.

Susan Cohen of East Longmeadow, New Hampshire, still sheds tears when remembering how quickly “Tedy” (V-1 CH Exodus Heart Of A Patriot UD BH HIC TT CGC TDI), a 9 ½-year-old male Rottweiler she bred, faded from life. His passing impacted many

Rottweiler lovers, partly because it happened at the 2015 Colonial Rottweiler Club Specialty in Lancaster, Pennsylvania.

“That morning at the hotel, Tedy kept trying to steal my clothes as I was getting dressed,” Cohen says. “He was happy, having fun. I had taken his picture throughout the week, posting photos of ‘Tedy, the Roving Reporter’ on my Facebook page.”

The energetic, spirited Rottweiler showed beautifully in the Veterans class. When the audience cheered, he got excited and acted silly. Tedy also was a therapy dog who could be gentle when visiting Alzheimer’s patients. Cohen describes him as a



**“Tedy,” left, and his dam, “Lola,” are pictured after a therapy dog visit. Both died of hemangiosarcoma. Tedy passed away at age 9, and Lola died at age 11.**



breed ambassador, a resilient dog who adjusted to whatever was going on around him.

After showing in the Veterans class, Tedy's co-owner, Carol Costa of Taunton, Massachusetts, took him out for a walk. "Something was not right," Cohen says. "He was going down fast. He suddenly was weak, and his gums were pale."

She and Cohen rushed Tedy to an emergency clinic, where radiographic tests showed he was rapidly bleeding out from tumor masses wrapped around his heart, liver and spleen. The veterinarian said it looked like hemangiosarcoma, an aggressive cancer that can cause severe internal bleeding and sudden death. He told them Tedy was going into shock. He was dying.

They made the decision to euthanize him, so he wouldn't suffer.

"Carol had to call her husband, John, and tell him that Tedy had died and wouldn't be coming home," Cohen says. "It was so hard for all of us."

Cohen thought of her heart dog, "Miss Lola" (CH Keerocka's Ingenua CD RA CGC TDI), who died of

hemangiosarcoma in 2013 at age 11. Lola, who was Tedy's dam, was weak and breathing heavily. A tumor was wrapped around her heart. She, too, was euthanized, only hours after appearing normal.

Back at the specialty show, word spread about what happened to Tedy. The Colonial Rottweiler Club nominated Tedy for the Rottweiler Health Foundation Circle 2000 Registry, which memorializes special Rottweilers by raising funds to support health research. Nominees are inducted when fundraising reaches \$2,000. The next year at the specialty, Tedy was inducted into the Circle 2000 Registry.

"As a breeder, you try to make the best choices you can," says Cohen. "It's tough though when a direct cause is unknown. Hemangiosarcoma is like a silent epidemic with our dogs."

### CLASSIFYING TUMORS

Hemangiosarcoma is an unpredictable cancer that develops painlessly. As with Tedy and Lola, it is often advanced by the time it is discovered. Severe internal bleeding and

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sudden death are not unusual with the disease. A dog's breed, age, gender, diet, and environment are not likely to impact the progression of this cancer, experts say.

"It is virtually impossible to pigeon-hole this tumor into categories that work for other cancers," says Jaime F. Modiano, VMD, PhD, the Perlman Endowed Chair in Animal Oncology at the University of Minnesota. "The most challenging aspect of studying this disease has been accepting that many, and perhaps most, of our preconceived notions about what we thought we knew about the disease were incorrect. In order to make progress, we needed to start with a blank slate."

Filling that blank slate eventually led to employing artificial intelligence to analyze large and complex data sets that look for defined algorithms and statistics to identify the cancer.

This type of analysis could lead to more accuracy in classifying hemangiosarcoma tumors based on their patterns, explains Dr. Modiano.

At the 2018 Connective Tissue Oncology Society meeting in Rome, Dr. Modiano's research group introduced artificial intelligence as a way to interpret the results of a test designed to detect cells associated with the presence of hemangiosarcoma in the circulation of dogs. It is yet to be determined whether these cells in the blood are precursors to the tumor, actual circulating tumor cells, or cells that are a component of the niche that allows the tumors to grow and eventually metastasize.

"The goal is to deploy a blood test that can detect hemangiosarcoma in its earliest stages before tumors actually form and to pair that detection with rational, targeted

## WHEN A DOG HAS HEMANGIOSARCOMA

A silent disease, hemangiosarcoma develops painlessly. The only hints that a dog may have the cancer are recurring lethargy and pale mucous membranes due to anemia. Most dogs have an advanced form of the cancer when it is discovered, which explains why severe internal bleeding and sudden death occur frequently and unexpectedly.

Although this cancer can affect any dog of any age and gender, it is most common in older dogs; more than half of the dogs that develop hemangiosarcoma are over 10 years old. It usually originates from a cell in the bone marrow that settles in the thin layer of cells that line the interior of blood vessels. Although the most common sites for tumor formation are the spleen, skin, heart, and liver, the tumor cells have access to the blood supply, allowing them to potentially seed and grow in virtually any organ in the body.

The disorganized growth of tumor cells in the walls lining the blood vessels disrupts normal blood flow, leading to blood clots and hemorrhage. Mini-hemorrhages can heal quickly with dogs showing only mild signs, but severe hemorrhage from within a tumor can be fatal.

Sadly, most dogs die before treatment can begin. Without treatment, dogs may die in a few hours or possibly within one to two weeks. With treatment, the expected survival is four to six months, though this is dependent on the tumor's location. Tumors that occur in or under the skin typically are less aggressive, and dogs whose visible tumors are accessible tend to do better with the standard of care.

The standard of care is surgical removal of accessible tumors, depending on the location, followed by chemotherapy. Treatment is meant to prevent fatal blood loss and to extend life, but is seldom curative. Chemotherapy delays the recurrence of metastasis, which occurs in virtually every dog diagnosed with the cancer.

About 5 to 15 percent of dogs with hemangiosarcoma will survive a year or longer, even with conservative treatment. Because there currently are no reliable tools to determine which dogs are likely to be long-term survivors, anecdotal evidence of long-term survival with alternative therapies is an unreliable indicator of efficacy and could create false hope and unrealistic expectations for owners and veterinarians. Thus, it is recommended that treatment should be based on objective data.

drugs that can prevent or significantly delay tumor formation and tumor progression," Dr. Modiano says.

The researchers at the University of Minnesota have been studying hemangiosarcoma for many years. In 2019, [they will complete a three-year study, the Shine On Project](#), which was supported with \$432,000 contributed by the Golden Retriever Foundation, the American Boxer Club Charitable Foundation and

the Portuguese Water Dog Foundation, breeds that show a high prevalence of this cancer.

"The unprecedented collaboration among these three breed club foundations and their dedication to canine health have driven this project forward, helping to make a significant difference for all dogs," says Dr. Diane Brown, CEO of the AKC (American Kennel Club) Canine Health Foundation, which adminis-

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Jaime F. Modiano, VMD, PhD, the Perlman Endowed Chair in Animal Oncology, University of Minnesota

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ters and manages the grant. “This approach to a particularly aggressive form of cancer in dogs has the potential to eventually change the landscape and improve outcomes for all dogs diagnosed with this horrible disease.”

Prior to the start of the Shine On Project, Dr. Modiano and his team developed a blood test to detect the “suspect cells” in dogs diagnosed with hemangiosarcoma. They also independently developed a promising chemopreventive drug called eBAT, which is a targeted bacterial toxin that is exceptionally safe and

has demonstrated efficacy in the treatment of hemangiosarcoma.

With Shine On, their focus turned to refining the test to identify dogs at risk for developing hemangiosarcoma and those that have the suspect cells present in their blood but have no evidence of a tumor, and then using eBAT to attack the hemangiosarcoma stem cells and kill them before they have a chance to form a tumor.

“Few cancers are more deadly than hemangiosarcoma,” Dr. Modiano says. “The frequency of this cancer underscores the need for developing specific treatments in dogs and opens the door to help improve our understanding of sarcoma tumors that occur infrequently in humans.”

The three phases of the Shine On Project are ongoing. They are:

- **Phase 1:** Defining the parameters for using the blood test to confirm the presence of hemangiosarcoma cells to help distinguish between dogs that have the cancer from those that do not. About 80 dogs have been studied, and the preliminary analysis suggests that a family of algorithms separates the four categories of samples being collected: 1) no evidence of disease, 2) benign splenic abnormalities, 3) hemangiosarcoma, and 4) cancers other than hemangiosarcoma.
- **Phase 2:** Determining whether blood testing for hemangiosarcoma cells will help predict when tumors become resistant to treatment and thus when a dog in remission might relapse. More than 20 dogs have been studied, indicating that the number of suspect cells in blood is relatively stable until animals are treated. This number decreases with treatment, and so it is expected to help track the duration of remission. In future research, the team hopes to gain insights into how therapy management might



extend remission times and prevent unexpected life-threatening bleeding episodes.

- **Phase 3:** Establishing how well the blood test works for early detection and how well eBAT works to eliminate hemangiosarcoma cells before tumors have a chance to form. About 140 dogs are enrolled in this part of the study. Although the analysis is in its early stages, Dr. Modiano says that patterns found in the blood suggest that the test may be helpful in identifying risk for pathological conditions, including splenic abnormalities and cancers. “We are using artificial intelligence to analyze data from Phase 3,” says Dr. Modiano. “As we hone on the patterns, the accuracy of how we classify samples will improve based on those patterns. Ultimately, we will assign classifications by predicting, or inferring, the probability that unknown samples belong to particular groups that were defined in the training phase.”

As Shine On continues, the research team plans to keep enrolling dogs in all phases of the study. Dr. Modiano and his team also are exploring how they can expand the Shine On approach to include other cancers and chronic conditions that are responsible for significant morbidity and mortality of canine companions.

Reflecting, Dr. Modiano says, “Our goal is to reduce the health burden of this cancer in dogs and humans, who develop the rare cancer angiosarcoma, which is similar to hemangiosarcoma. A method to detect hemanigosarcoma in its earliest stages and an effective mechanism for preventing it would be a giant leap forward in the management of this disease.”

Cohen, like many other Rottweiler breeders and owners whose lives have been impacted by hemangio-



sarcoma, welcomes the possibility of recognizing the cancer sooner. “The ability to diagnose this cancer early and to identify risk factors would be a tremendous help,” she says. “It is absolutely heartbreaking to lose a dog to this cancer. If we could one day understand how to minimize the risk, it would be wonderful.” ■

Purina thanks Roberta Kelley-Martin, president of the Rottweiler Health Foundation, for helping us to identify this topic for the *Rottweiler Update*.

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