PURINA PRO PLAN

GERMAN SHEPHERD DOG Update

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HEMANGIOSARCOMA RESEARCH

Molecular Study Seeks to Inhibit Cancer Growth

HEMANGIOSARCOMA STUDY AIMS TO DETER CANCER GROWTH

TO HELP GERMAN SHEPHERD DOGS

"Vinnie" (CH Lindenhill's Vinnie The Viper) died quickly at age 7 from hemangiosarcoma when a tumor in his spleen ruptured. His breeder-owners Sheila and Michael Metz of Roseville, Minnesota, adored their handsome male.

Longtime German Shepherd Dog breeders Sheila Metz and her husband, Michael, of Roseville, Minnesota, had never had cancer in their dogs. When their handsome 7-year-old black-and-tan male, CH Lindenhill's Vinnie The Viper, lost his appetite and his energy, they didn't consider cancer to be a possibility.

"Vinnie" was special. He made the Top Ten competition at the 2005 and 2006 German Shepherd Dog Club of America National Specialties. The sire of several healthy litters, Vinnie had just traveled with the Metzes to the 2010 National Specialty in Farmington, Utah. Although he went for fun rather than to compete, Vinnie was "awesome, he greeted everyone like an ambassador for the breed," Metz recalls.

A trip to the veterinarian the next day plays through Metz's mind like a slow-motion movie. Its ending radicalized her view of canine cancer, particularly of hemangiosarcoma, one of the most deadly ones.

"Our veterinarian took a blood sample from Vinnie and was concerned," she says. "Next, he took radiographs, which were unremarkable, and then an ultrasound of Vinnie's abdomen showed the problem."

Looking over the veterinarian's shoulder, Metz saw tiny star-like images on the screen. "The veterinarian suspected hemangiosarcoma," she says.

As though he was reacting on cue, Vinnie collapsed. The hemangiosarcoma tumor in his spleen had ruptured.

"I saw Vinnie take a last breath, and then he passed away," says Metz, her voice catching as she remembers the moment. "There were no signs — until it was too late."

One year later, it was déjà vu for the Metz family when another dog was diagnosed with hemangiosarcoma. Their 13-year-old black-and-tan housedog, Lindenhill's Pom Pom, clearly did not feel well. "I thought 'Fanny' may have pyometra," Metz says. "I didn't think of hemangiosarcoma."

The veterinarian performed an ultrasound and extracted fluid from Fanny's abdomen. The diagnosis was hemangiosarcoma.

"I let her go," says Metz. "Fanny was 13, and there was no point in her suffering."

Hemangiosarcoma is an aggressive tumor that arises from blood vessels. It most commonly occurs in the spleen, liver, heart, and muscle, though it can be found in other locations as well. The tumor cells spread to other parts of the body early in the course of disease, so it is common for multiple organs to be involved at diagnosis.

The stats on current treatment options for canine hemangiosarcoma are dim. Given the propensity for this tumor to bleed, dogs can die before treatment begins. If diagnosed early, the standard of care involves surgical removal of the tumor, if possible, followed by chemotherapy. Even with treatment, a dog typically survives at most from six to eight months.

German Shepherd Dogs are among the large breeds — along with Golden Retrievers, Boxers and Portuguese Water Dogs — considered at high-risk for hemangiosarcoma. This suggests there could be a genetic link, though heredity is likely not exclusively responsible for the development of this cancer as several breeds and mixed-breeds of dog can be affected.

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 bleeding from the tumor. Most dogs have an advanced form of the cancer when it is discovered, explaining why severe internal bleeding and sudden death are not unusual.

Hemangiosarcoma most commonly occurs in the spleen, though it can originate in other organs such as the heart, liver, kidneys, skin, muscle, and bone. The cancer occurs most commonly in dogs older than 6 years of age. It is believed to arise from primitive endothelial cells that normally form blood vessels. Consequently, tumors often are comprised of disorganized, abnormal blood vessel-like structures that are prone to spontaneous bleeding events, which can be self-limiting, causing intermittent lethargy, or can be severe and life-threatening, associated with collapse. The tumor cells are very aggressive and have typically spread to other organs by the time a diagnosis is made.

The current standard of care is surgical removal of the primary tumor, depending on the tumor location, followed by chemotherapy. If the tumor cannot be removed due to its location, chemotherapy with or without local radiation therapy may benefit a dog. Treatment is meant to prevent fatal blood loss and to extend life but is seldom curative. Chemotherapy may delay the recurrence of metastasis, which occurs in virtually every dog diagnosed with the cancer.

Due to the propensity for spontaneous bleeding events, it is not uncommon for dogs to die before treatment can begin. If a dog survives an initial bleeding event but does not have surgery, survival is typically less than one to two weeks. With surgery and chemotherapy, the expected survival is six to eight months.

"Fanny" (Lindenhill's Pom Pom), shown with owner Michael Metz, was diagnosed with hemangiosarcoma at age 13.

Recognizing the challenges and slow progress in developing new approaches for the diagnosis and treatment of hemangiosarcoma, the AKC (American Kennel Club) Canine Health Foundation has launched the Hemangiosarcoma Research Initiative. The fundraiser for hemangiosarcoma research is supported by the American Kennel Club and the Golden Retriever Foundation, which are matching gifts up to $300,000 received in 2018. Currently, the AKC Canine Health Foundation is actively supporting four hemangiosarcoma studies totaling over $906,089.

One of the studies focuses on learning whether it is possible to inhibit a molecular pathway linked to the origin, development and spread of many cancers — including hemangiosarcoma — and thus deter cancer growth before it begins. The AKC Canine Health Foundation is providing funding of $168,857 for the three-year study underway at Tufts University, with support from the German Shepherd Dog Charitable Foundation. Collaborating on the research are cancer scientists at the Broad Institute of MIT and Harvard.

A NEW LOOK AT CANCER

The lack of treatment advances for hemangiosarcoma over the past 30 years is disheartening. "There have been no advances in treating this cancer since I began my residency in 1992," says Cheryl London, DVM, PhD, DACVIM (Oncology),

research professor at the Cummings School of Veterinary Medicine of Tufts University and Tufts School of Medicine. "The current treatment protocol is largely based on whether the tumor can be removed, and if there is obvious evidence of tumor spread at the time of diagnosis."

The lead investigator of the molecular PI3K/AKT/mTOR pathway study, Dr. London is optimistic that it is possible to stop the growth and spread of the cancer. Her research, all conducted via cell culture work based on *in vitro* cancer cell growth from hemangio-

DOUBLE YOUR DONATION VIA THE HEMANGIOSARCOMA RESEARCH INITIATIVE

German Shepherd Dog breeders and owners can help advance research by contributing to the Hemangiosarcoma Research Initiative, a matching-gift challenge in which the American Kennel Club and the Golden Retriever Foundation are matching donations up to $300,000 received in 2018 to the AKC Canine Health Foundation.

Currently, the AKC Canine Health Foundation is supporting over $906,089 for four hemangiosarcoma studies, with additional studies under review. "The AKC Canine Health Foundtion is committed to funding canine cancer research to benefit all dogs. Through our current Hemangiosarcoma Research Initiative, we are finding and funding more innovative research to tackle this devastating disease," says Diane Brown, DVM, PhD, DACVP, CEO of the AKC Canine Health Foundation.

"The partnerships we have with Purina, the American German Shepherd Dog Charitable Foundation, the Golden Retriever Foundation, and many other concerned donors and dog lovers allow us to identify and invest in critical research to answer questions about why dogs get cancer and how to improve early diagnosis and provide promising treatments for dogs," she says.

To view abstracts of the current studies funded by the AKC Canine Health Foundation's Hemangiosarcoma Research Initiative click here and scroll down.

sarcoma tumor samples from dogs and people, involves examining the intricacies of how the pathway works. Humans develop a similar type of cancer called angiosarcoma, though it is rare with only 300 to 500 new cases annually.

"Inhibitors of the PI3K pathway have shown promise in blocking the growth of hermangiosarcoma cells in laboratory research," explains Dr. London. "Exactly how this happens is not known, but we do know that hemangioscaroma tumors sometimes contain genetic mutations that activate the PI3K pathway and thus enable the cancer to grow and spread."

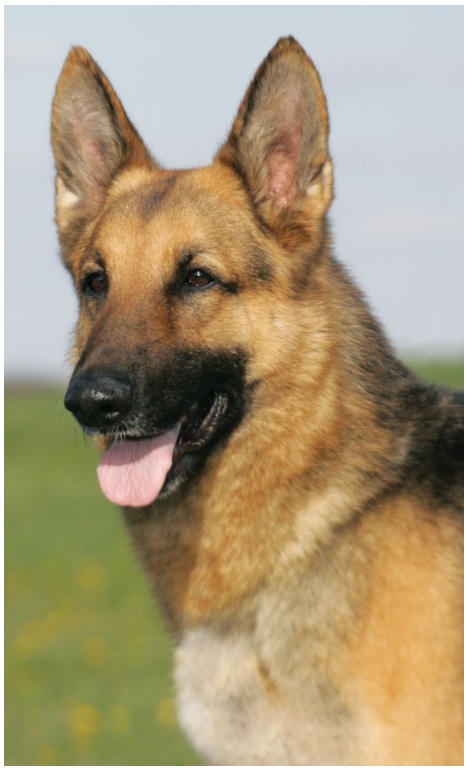
The investigation centers on finding combinations of small-molecule inhibitors with the power to kill cancer cells and turn off the PI3K pathway. "Ultimately, our goal is to develop new, more effective combination therapies to treat this disease both following surgery and at the time of relapse after chemotherapy has been completed," she says.

The ability to improve treatment options will come none too soon. Owners of affected dogs wrestle with the high cost of treatment and a survival rate of six to eight months — even with treatment.

Dogs treated for hemangiosarcoma with surgical removal of the tumor followed by chemotherapy seem to recover and do well for a while. In reality, the tumor may have already spread cancer cells throughout the body. The threat of metastasis is a genuine concern realized all too often.

"Our research will help develop novel methods to inhibit tumor growth and also new techniques to identify tumors earlier in the course of the disease before a bleeding event occurs," Dr. London says.

Metz hopes the research will lead to answers soon. "I am excited to



now be working with a nice 6-year-old male," she says. "Every day, I hope he stays healthy."

Reflecting on whether she would continue breeding and owning German Shepherd Dogs given the breed's susceptibility to this cancer, she says, "Absolutely, I would. As heartbreaking as this diagnosis is, I can't imagine life without a German Shepherd Dog. Finding new ways of diagnosing and treating hemangiosarocma would be welcome news for all dog owners." ■

Purina appreciates the support of the American German Shepherd Dog Charitable Foundation (AGSDCF), particularly Ginny Altman, current vice president and health liaison of the Foundation, and a past president and former chair of the Health and Genetics Committee of the GSDCA, in helping to identify this topic for the *Purina Pro Plan German Shepherd Dog Update.* The AGSDCF board of directors also helps to identify topics.

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Cheryl London, DVM, PhD, DACVIM (Oncology), Cummings School of Veterinary Medicine of Tufts University and Tufts School of Medicine

PURINA PUPPY CHOW ENHANCES NUTRITION FOR PUPPIES

During the first year of life, puppies need more protein than adult dogs and essential nutrients to support their growth and development. *Purina Puppy Chow* is launching three newly formulated formulas in October that provide 30 percent more protein than *Purina Dog Chow* Complete Adult dog food. The new formulas have added vitamin C, an antioxidant, and contain DHA, an essential omega-3 fatty acid, for brain and vision development. They also contain antioxidants to support a healthy immune system. Look for new packaging featuring children and puppies on these *Puppy Chow* formulas: Complete, Tender & Crunchy, and Natural. *Purina Puppy Chow* is sold at grocery stores, major pet food retailers and online.

LEARN MORE

PURINA DOG CHOW SALUTES VETERANS WITH SERVICE DOG SALUTE CAMPAIGN

Purina Dog Chow is donating up to $500,000 to support Tony La Russa's Animal Rescue Foundation's (ARF) veteran's program. The campaign, called *Dog Chow* Service Dog Salute, will benefit ARF's expanding veterans program that matches veterans with rescue dogs whom they train to become their own service dogs. Here's how it works: Through Veteran's Day, Nov. 11, *Dog Chow* will donate $1 for each unique share on Facebook of the BuzzFeed video featuring the powerful stories of veterans and rescue dogs brought together by ARF (up to $250,000). In addition, the brand will donate 5 cents from the sale of each specially marked bag of *Purina Dog Chow* Complete Adult With Chicken dog food (up to $250,000) through Nov. 11. Located in Walnut Creek, California, ARF has rescued more than 38,000 dogs and cats since it began in 1991.

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PURINA PROCLUB

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