



PURINA
PRO PLAN

GOLDEN RETRIEVER Update

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B-CELL LYMPHOMA RESEARCH

Biomarkers May Help Detect
Cancer Risk & Outcome

GOLDEN RETRIEVER LYMPHOMA STUDY

LOOKS AT EFFECT OF EPIGENETICS IN GENE EXPRESSION



Golden Retrievers take a hard hit when it comes to canine cancer, thus cancer is a leading health concern for breeders and owners of Golden Retrievers. Lymphoma, a cancer that originates in the lymphocyte cells of the immune system, is estimated to affect one in eight Golden Retrievers. One-third of cases are diffuse large B-cell lymphoma.

Due to the relatively high prevalence of lymphoma in the breed, a dog's genetic background may have an important role in whether a Golden Retriever develops the cancer. Lifetime experiences — such as a dog's age, environment and lifestyle — also contribute to lymphoma development in an individual dog. These factors, called epigenetics, affect gene expression and have the ability to silence genes that would otherwise stop cancer growth in affected dogs.

Importantly, unlike gene mutations, one form of epigenetic change occurs via DNA methylation, a process in which methyl groups are added to a DNA molecule without changing the sequence of DNA. While gene mutations permanently change the DNA sequence, methylation changes can be reversed, thus allowing a gene to regain normal function.

Cancer researcher Jeffrey Bryan, DVM, PhD, DACVIM (Oncology), associate professor of veterinary oncology and director of the



Comparative Oncology Radiobiology and Epigenetics Laboratory at the University of Missouri, says, “The unique DNA methylation signature of B-cell lymphoma potentially will allow us to develop biomarkers to help detect Golden Retrievers at risk for lymphoma, as these changes occur early in the cancer formation process. The possibility of developing effective medicine or dietary therapeutics could become a reality with improved diagnostic and prognostic capabilities.”

Dr. Bryan [completed a four-and-a-half-year study in December 2017 on the epigenetics that alter gene expression](#) and occur over the lifetime of a Golden Retriever. The \$404,813 study was jointly funded by the AKC (American Kennel Club) Canine Health Foundation and the Golden Retriever Foundation.

A longtime supporter of canine cancer studies, the Golden Retriever Foundation provided funding in 2013 for one-half of \$1.5 million for two lymphoma studies sponsored

through the AKC Canine Health Foundation. Besides Dr. Bryan’s research, funding of \$1.06 million supported a study to develop markers to diagnose and guide therapy of lymphoma and hemangiosarcoma based on heritable and acquired genetic mutations. This research involved collaborators at the University of Minnesota, North Carolina State University and the Broad Institute of MIT and Harvard.

Rhonda Hovan, research facilitator for the Golden Retriever Club of America, explains that the parent club and the Golden Retriever Foundation have worked together since 1998 to change a culture of secrecy about cancer. “In the beginning, no one wanted their bloodline associated with cancer,” she says. “Today, participating in research is considered to be a responsibility and a badge of honor.”

The shift toward an openness about cancer and other diseases also resulted in Golden Retrievers

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LEARN MORE ABOUT LYMPHOMA AT GRCA NATIONAL SPECIALTY

Jeffrey Bryan, DVM, PhD, DACVIM (Oncology), associate professor of veterinary oncology at the University of Missouri, will present his lymphoma research Oct. 3 at the Golden Retriever Club of America National Specialty at Purina Farms in Gray Summit, Missouri. [Click here](#) for information.

To view a webinar presented by Dr. Bryan on lymphoma and sponsored by the AKC Canine Health Foundation, [click here](#).

WHEN CANINE LYMPHOMA HITS HOME

One in eight Golden Retrievers develops lymphoma, and one-third of cases are B-cell lymphoma. Whether a dog has an aggressive or low-grade type of lymphoma impacts the prognosis. Some dogs live for years after chemotherapy treatment and careful monitoring for the cancer's return. Here is the journey these Golden Retrievers and their owners took in dealing with lymphoma.

"Cami"

*Starduck's Change of Venue to Cambria NAJ
NAP CGC*

Cami was 5 years old in 2013 when owner Diana Maberry of Rancho Cucamongo, California, discovered enlarged lymph nodes in the dog's groin area when brushing her. Diagnosed with B-cell lymphoma, Cami was treated with multi-drug (CHOP) chemotherapy for 26 weeks, going



Cami

into remission in the second week. Cami continued to train and compete in agility until the chemotherapy affected her ability to jump. The remission lasted 15 months before Maberry again found enlarged lymph nodes. A second round of CHOP chemotherapy combined with an antibody therapy led to a 25-month remission. In early 2016, Cami developed an incurable nasal disease, possibly due to her weakened immune system, and was euthanized at age 7.



Kicker

"Kicker"

Tanglewood's Special Team Player CGC

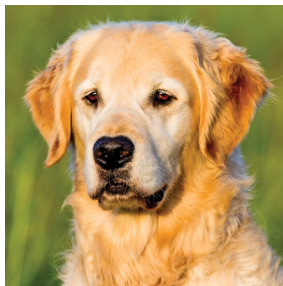
A therapy dog with an easygoing, gentle temperament, Kicker was diagnosed with lymphoma at age 10 when owner Jo Anne Fusco of Memphis, Tennessee, found a large lump on his neck. The veterinarian found four other lumps behind the dog's stifles (knees). Kicker began CHOP chemotherapy right away and went into remission, so he was never tested to learn the type of lymphoma he had. By contributing his DNA to a study sponsored by Morris Animal Foundation, he helped to advance lymphoma research. Kicker and Fusco were charter members of the pet therapy program at St. Jude Children's Research Hospital in Memphis. Kicker, who lived the longest of the original four therapy dogs, was the only dog to be nominated for St. Jude's Volunteer of the Year award. He also was recognized at the 2008 Westminster Kennel Club Dog Show for his therapy work. Kicker and Fusco continued their therapy work up to two weeks before he died. Beating the odds, Kicker survived four years after his cancer diagnosis before passing away in 2015 at age 14 from pancreatitis.

"Cooper"

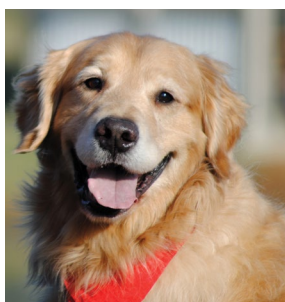
Harvestimes Need For Speed

Cooper was 11 years old when he was diagnosed with B-cell lymphoma in September 2015. He began CHOP chemotherapy and went into remission right away. A few months later, the cancer returned, and Cooper did a second round of chemotherapy. During the second chemotherapy, Cooper took part in a study at the University of Pennsylvania working to develop

a vaccine to fight the cancer. Owner Paige Jones of Middleburg, Virginia, says it was only a matter of weeks after the second chemotherapy ended before the lymphoma returned. After several rescue chemotherapy drugs failed, Cooper passed away naturally in December 2016. Throughout his treatment for cancer, Cooper continued to travel with his family to field trials, serving as the equipment manager. "He was happiest doing things with us," Jones says.



Cooper



Samson

"Samson"

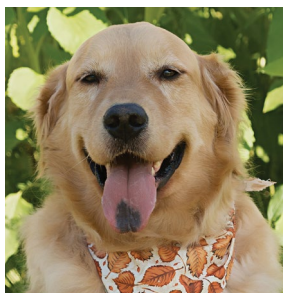
Shilo's What Legends Are Mayd Of CGCA TDI

A cuddly therapy dog who was naturally intuitive and mellow, Samson loved visiting patients at hospitals, cancer centers and hospices with owners Rachel and Mark Conwell of Columbus, Ohio. He also was a handsome dog who once took Best of Opposite Sex in Sweepstakes at a Golden Retriever specialty show. Samson was diagnosed with T-zone lymphoma, a subtype of T-cell lymphoma, in October 2017. He died in April 2018 from aspirate pneumonia, possibly due to his compromised immune system.

"Bruin"

Birdwing Sunday Playoff

Bruin was diagnosed with B-cell lymphoma one month after turning 3 years old. He breezed through three rounds of CHOP chemotherapy, with minimal side effects, each time going into remission after the first dose. Owner Alexa Grella of Middleton, Massachusetts, says Bruin's cancer never slowed down the fun-loving retriever who enjoyed walks, playing fetch, weekend trips to the lake, and being with his family. Grella lost Bruin to an unrelated disease, dilated cardiomyopathy, five days before his 6th birthday.



Bruin



Roxy

"Roxy"

UOCH URO3 Sunfire's Solid As A Rock UDX2 OM2 BN RAE TKA

Six-year-old Roxy is the second Golden Retriever of owner Pat Franckowiak of Grand Rapids, Michigan, to be diagnosed with lymphoma. The first one, "Libby" (U-CDX Hilltops Just Having A Blast AM/CAN/ASCA CDX), died in 2005 at age 13. Franckowiak was bathing Roxy before an obedience competition when she felt a lump in the groin area. An immune-suppressant drug may have contributed to Roxy developing the cancer, Franckowiak says. Roxy underwent CHOP chemotherapy, and thus far, after 13 months, she is in remission and back to showing in competitive obedience.

GOLDEN RETRIEVER OWNERS CAN HELP

The University of Missouri canine oncology research team is seeking DNA from the lymph nodes of normal dogs and fresh or frozen tissue samples from dogs diagnosed with lymphoma. To participate, please contact Debbie Tate or the Oncology Clinical Trials Service at 573-882-7821.

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being among the first breeds to participate in the Canine Health Information Center (CHIC) DNA Repository sponsored by the Orthopedic Foundation for Animals and the AKC Canine Health Foundation. The Repository collects and stores DNA extracted from blood or cheek swabs from healthy dogs and dogs affected with diseases so that these samples are readily available to researchers as they begin new studies. Pedigrees and health histories also are collected because this information is critical to the usefulness of the samples for future research.

“Golden Retrievers have the largest number of samples banked of all breeds,” Hovan says. “In addition to DNA stored with CHIC, GRCA members have donated about 1,000 tissue samples from dogs with cancer and other diseases directly to research studies.”

A NEW LOOK AT CANCER

Epigenetics are an emerging area of importance in understanding cancer, though few studies have been done in dogs. In humans, epigenetic DNA methylation changes have been found to underlie the development of lymphoma.

Along with colleagues Anne Avery, VMD, PhD, of Colorado State University, and Heather Wilson-Robles, DVM, DACVIM (Oncology), of Texas A&M University, Dr. Bryan studied the DNA methylation changes associated with B-cell lymphoma in 29 Golden Retrievers. Each dog’s methylation profile had a distinctive fingerprint reflecting those changes.

“The aggressive forms of lymphoma are painfully prevalent in Golden Retrievers,” Dr. Bryan says. “Our goal in studying this disease was to identify a means of detecting risk, reducing risk, improving early detection, and making treatment more effective.



“We showed that B-cell lymphoma has distinct methylation profiles that distinguish it from all other lymphocytes that are not cancerous. Some of the markers of that profile appear in dogs that do not yet have lymphoma, so now we want to know if those markers in apparently healthy dogs indicate the risk for disease. This will enable us to develop biomarkers of each class of lymphoma and identify new therapy targets for affected dogs.”

A challenging and complex cancer to understand, lymphoma includes more than 30 subtypes of canine cancer. Some lymphomas are classified aggressive, high-grade disease because they progress rapidly and become fatal within one or two months. Others are indolent, low-grade cancer that progresses slowly over months or years.

Lymphoma stems from lymphocytes, a type of white blood cell that helps the immune system fight off infection. Lymphocytes are highly concentrated in organs having an immune function role, such as lymph nodes, the spleen and bone marrow.

Multicentric lymphoma, the most common type, affects lymph nodes throughout the body, with enlarged lymph nodes being the obvious clinical sign. The second most common type is alimentary lym-

phoma, which arises in the lymphocytes of the intestines. Mediastinal lymphoma affects the thymus and mediastinal lymph nodes in the chest. Extranodal lymphoma affects a specific organ, such as the skin, eyes, kidneys, lungs, or central nervous system.

Among the signs of lymphoma noted by owners are:

- Enlarged, non-painful lymph nodes in the neck, over the body or behind the stifles (knees)
- Sudden onset of extreme thirst and urination
- Sudden difficulty breathing
- Sudden onset of redness of the eyes, which can quickly lead to blindness
- Hemorrhage or bleeding

“It’s important to know which type of lymphoma a dog has because this impacts the treatment and prognosis,” explains Dr. Bryan. “For example, the prognosis for a dog with high-grade B-cell lymphoma is poor without treatment — less than two months. With appropriate chemotherapy, usually involving multidrug chemotherapy, a dog will likely live more than a year. Low-grade lymphoma cases could survive years with proper monitoring.”

The most accurate way to improve diagnostics, classify cancer type and determine prognosis is using flow cytometry, a sophisticated laser technology that measures the amount of DNA in cancer cells, combined with a biopsy, which characterizes the lymphoma type, he says. The cost of diagnosing and treating the cancer can be several thousand dollars.

The recently completed study provided ground-breaking insights showing the ability to identify tumor-initiating cells from lymphoma biopsies and to characterize stem-like cells by surface markers and DNA methylation changes. “Identifying these cells will aid thera-

peutic strategy development,” Dr. Bryan says. “By performing these in parallel, the markers from each can be combined, correlated and translated into biomarkers of risk, diagnosis and prognosis to advance the prevention and management of lymphoma in Golden Retrievers.”

A clinical trial already has begun to evaluate drug therapies that may alter methylation and improve the efficacy of chemotherapy. The ability to counteract problematic DNA methylation could have far-reaching results, not only for treating affected dogs but also for blocking cancer in at-risk dogs. “Disruption of normal DNA methylation is common to all cancers, and it appears to be a change before overt cancer even develops,” he says.

Hovan is optimistic. “Dr. Bryan’s work has moved us further down the pathway toward identifying ways to reduce a dog’s risk for developing lymphoma and possibly other cancers,” she says. “This research is particularly exciting because it may provide us with tools to help dogs avoid cancer by managing food, lifestyle and other choices we make for them. The promise of this study is that it may empower owners to make decisions or changes that actually make a difference with the science to back it up.”

Reflecting on the progress, Dr. Bryan says, “Our aim is to strike at the root of the cancer before it manifests. There are new frontiers in understanding the mechanisms of cancer that may make us more effective at predicting, diagnosing and fighting cancer in dogs.” ■

Purina appreciates the support of the Golden Retriever Club of America, particularly Rhonda Hovan, GRCA research facilitator, in helping to identify this topic for the *Purina Pro Plan Golden Retriever Update*.

ONGOING LYMPHOMA RESEARCH FUNDED BY THE AKC CANINE HEALTH FOUNDATION

The AKC Canine Health Foundation currently is providing funding totaling more than \$670,000 for eight canine lymphoma studies. “We are committed to funding canine cancer research to benefit all dogs, and this includes lymphoma as well as several other important types of cancer,” says Diane E. Brown, DVM, PhD, DACVP, CEO of the AKC Canine Health Foundation.

“The partnerships we have with Purina, the Golden Retriever Foundation and many concerned donors allow us to identify and invest in critical research to answer questions about why dogs get cancer and how to improve early diagnosis, ultimately with a goal of providing better treatments for dogs.”

To view abstracts of these studies, see page 30 when you [click here](#).

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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