



**UC DAVIS**

**VETERINARY MEDICINE**

*Center for Companion Animal Health*

# CCAH UPDATE

SPRING 2024

## Longevity is in the Genes

**Golden retrievers** are one of the most popular breeds of dogs. But research shows they have up to a 65% chance of dying from cancer. UC Davis researchers set out to find if certain genetic factors could help their survival rate. Instead of searching for genes associated with a cancer diagnosis in the breed, they chose to look for genes associated with longer life.

Their study, published in the journal *GeroScience*, found that variants of a gene, **HER4**, long known to be important in human cancers were also associated with an increased lifespan of nearly two years.

“We assume that the majority of golden retrievers have a genetic predisposition to cancer, but if some of them are living to be 14, 15 or 16, we thought there could be another genetic factor that is helping to mitigate the bad genes, and the gene that popped out for us is **HER4**,” said co-corresponding author Robert Rebhun, Maxine Adler Endowed Chair in oncology at the UC Davis School of Veterinary Medicine.

**HER4**, also known as **ERBB4**, is a member of the family of human epidermal growth factor receptors. It is the same family of genes in humans as **HER2**, a gene well-known for making cancer cells grow quickly. Rebhun said dogs get many of the same kinds of cancers as humans, which could make this discovery important for humans, as well.

See Golden Retrievers on page 4





# From the Director

**The center exists to improve the life and welfare** of companion animals and their families. This issue highlights some of the ways that we—and by extension you—accomplish this in both the short and long term. You can read about our response to the wildfires in Maui that separated many cats from their families and our efforts to help house them while they found their families or new homes. You can also learn about how we invest in the future, whether through award-winning resident research that teaches us how to use existing drugs better, mentoring undergraduate research that prepares the future leaders of veterinary medicine, helping new faculty jump start their research careers at UC Davis, or carrying out the basic science research that may help us unlock clues to longevity. These efforts have impact now and in the future.

UC Davis has long been known as a pioneer in research to improve the lives of animals; the CCAH is a big part of that endeavor. The teams we build and the people we attract are our strongest resources. If you take the best people and give them the support they need, amazing things can happen. You can read about one of our newest team members, Dr. Jessica Lawrence, who recently joined me as part of our radiation oncology group. She really sums it up when she talks about the family she's found at the veterinary school and the environment that allows us to take what we see in the clinic and let it guide our research so that we can improve patient care.

Through some targeted gifts, we have been able to fund exciting new research into improved control for surgery-related pain in cats, better treatment for brain tumors in dogs, and building a cell-based model to test drugs for canine cardiac disease. I look forward to reporting the finding of these and other studies in future CCAH Updates. We are also currently

reviewing our equipment funding requests to provide our researchers the tools they need in order to carry out groundbreaking research.

Artificial Intelligence (AI) is working its way into many different fields including veterinary medicine and we have supported research and will continue to support this type of research to improve animal health. On a lighter note, we have also used AI to create the cover image for this issue. Using Adobe Firefly we asked it to create a picture of multiple golden retrievers of different ages in a field. To see the result, take a look at the cover.

The CCAH is entirely funded through the generosity and care of supporters like you. We leverage the funds you invest with us to have the biggest impact. Thank you for joining us in our efforts—we could do nothing without you.

My best,



Michael Kent, DVM, DACIMV (Oncology),  
DACVR (Radiation Oncology) Director, CCAH



Quilt in photo donated to the CCAH by Nancie Wiseman Attwater. Photo: CCAH

# Alternative Chemotherapy Administration SHOWS PROMISE

When medical oncology resident Dr. Evangelia Makrygiannis started her training, she sought to conduct research that would change the way oncologists practice. One of her faculty mentors, Dr. Katherine Skorupski, offered a variety of ways to achieve that goal. They decided on exploring alternative methods of administering a chemotherapy drug in dogs that was having success in human medicine.

Gemcitabine is FDA approved in human medicine for treatment of aggressive cancers, but less used in veterinary medicine due to limited research and variability in published dosing schemes. Recent research in human medicine suggests that longer fixed dose rate (FDR) infusions are more effective than the quicker 20 to 30-minute injections previously used in veterinary medicine, where FDR dosing had not been studied.

More than a decade ago, UC Davis oncologists wondered whether the drug would be more efficacious when dosed similar to how it is used in human medicine—delivered over two hours. So, they began to administer gemcitabine in FDR for advanced cancers when other avenues of treatment were exhausted. Makrygiannis decided to research the results.

Enter another mentor Dr. Luke Wittenburg, who helped Makrygiannis understand the pharmacology behind the FDR dosing scheme. He explained that longer infusions allow more cells to become susceptible to the drug. Makrygiannis retrospectively investigated 36 dogs treated at UC Davis from 2013-22 with the FDR gemcitabine infusions. She found that treatment was well tolerated with eight dogs (25%) achieving partial remission and 10 dogs (31%) maintaining stable disease—a better response than most published results of the quicker treatments in similar circumstances.

“This data shows promise that FDR administration may be more effective, particularly with squamous cell carcinoma, the cancer that reacted best,” said Makrygiannis. “To give those animals weeks to months more with good quality of life despite their cancer diagnosis is so rewarding.”

Makrygiannis presented the research at the 2023 Veterinary Cancer Society conference, where it won the Amiya K. Patnaik



Medical oncology resident Dr. Evangelia Makrygiannis (center) conducts research under the mentorship of Drs. Luke Wittenburg and Katherine Skorupski. Photo: Michael Bannasch

Memorial Award for best research poster presentation. Many attendees took interest in revisiting the use of this old drug in a new way.

The trio hope that with further indications of efficacy, gemcitabine will be more commonly used, and that this study opens new avenues of research that can be achieved with future funding.

“I feel fortunate to work alongside these mentors,” said Makrygiannis. “Together, we were able to better understand a drug that can help our patients, especially with this new protocol.”



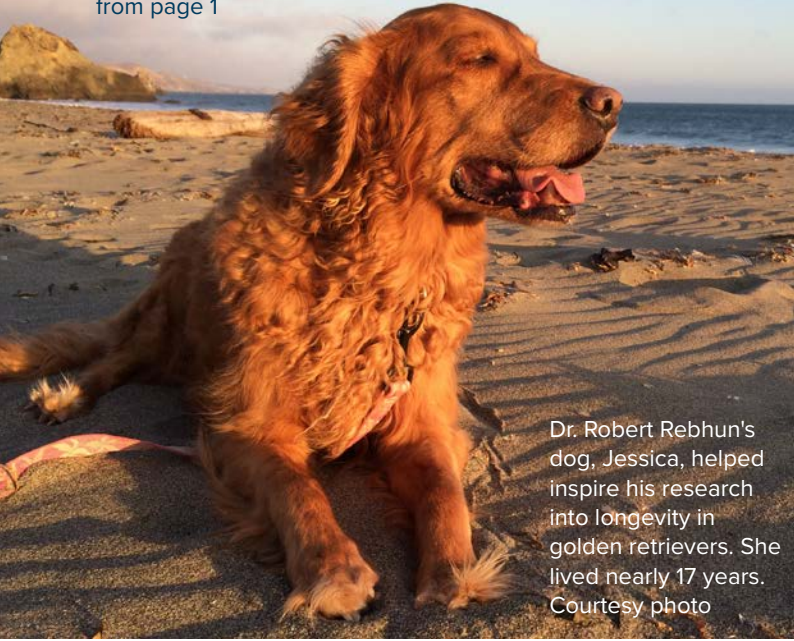
While much of CCAH research is focused on dogs and cats, the center also supports research into the health of exotic companion animals. A recent study in orange-winged Amazon parrots discovered that the drug atorvastatin can be used to fight high cholesterol and other heart issues that affect companion parrots. The drug, commonly known as Lipitor, is the most prescribed human medication in the U.S., successfully used for nearly 30 years. By determining the drug’s pharmacokinetic parameters in parrots—the body’s absorption, distribution, metabolism, and excretion of the drug—the research team concluded its relevance in companion avian medicine.



## COVER STORY

### Golden Retrievers

from page 1



Dr. Robert Rebhun's dog, Jessica, helped inspire his research into longevity in golden retrievers. She lived nearly 17 years. Courtesy photo

"If we find that this variant in HER4 is important either in the formation or progression of cancer in golden retrievers, or if it can actually modify a cancer risk in this population, that may be something that can be used in future human cancer studies," he said.

#### Hope for golden retrievers

More than 300 golden retrievers were part of the study. Researchers compared the DNA from blood samples of golden retrievers that were alive at 14 years of age to those that died before age 12. They found that dogs with certain

variants of the gene survived longer, on average 13.5 years compared to 11.6 years.

"Two years in a dog's life is equivalent to 12-14 years in humans, which is pretty significant," said co-corresponding author Dr. Danika Bannasch, Maxine Adler Endowed Chair in Genetics.

She emphasized the finding is still one small piece to the complex puzzle of what could cause a golden retriever to get cancer.

"There are going to be many genes involved in a dog's predisposition to getting cancer, but the fact that the gene associated with longevity is also a gene involved in cancer was really interesting," Bannasch said.

The study also found the gene variant seemed to be most important to the longevity of female dogs compared to male dogs. HER4 has been shown to interact with hormones such as estrogen and may also play a role in processing environmental toxins.

Rebhun said the next step is to enroll a larger population of golden retrievers in a study to see if they can reproduce these results and discover how this genetic variant may impact expression or function of the gene.

In addition to co-first author of the study Dr. Daniel York, other co-authors include Drs. Michael Kent, Flora De Graaf, Stephanie Ryan, Paula Yoon, and Jamie Peyton of UC Davis; Kevin Batchner and Madison Luker of UC Davis; and Dr. Joshua Stern of North Carolina State University.

The study was funded in part by the CCAH, Maxine Adler Endowed Chair Funds, and private donor funds specifically designated for longevity studies in golden retrievers.

## Lasting Impact on FELINE HEALTH

A gift to SOCK FIP at the CCAH from the estate of the late Dale Wolfe will make a tremendous impact on advancing feline health, especially in the field of feline infectious peritonitis (FIP)—a nearly always fatal disease in young cats.

Wolfe's gift will create the Feline Infectious Disease Research Endowment and establish the Save Our Cats and Kittens from Feline Infectious Peritonitis (SOCK FIP) Endowed Chair in Feline Infectious Disease Research.

"Dale, through his generous estate gift, has chosen to honor the SOCK organization and its almost five-decade commitment to support feline health research at UC Davis," said Professor Emeritus Niels Pedersen, world-renowned expert in feline infectious diseases. "The SOCK organization has played a critical role



in funding research at the school—with the control of feline leukemia virus (FeLV) infection and its varied associated diseases; the discovery and characterization of feline immunodeficiency virus (FIV); and finally the discovery of the cause of FIP, its pathogenesis and a cure. It is my hope, and the hope of the SOCK organization, that the Feline Infectious Disease Research Endowment created by the Wolfe estate gift will support future discoveries critical to the health of our feline companions."

In addition to infectious disease research, the CCAH supports studies to improve the health of cats in a range of areas, including cardiology, genetics, nutrition and oncology. Completed studies have led to innovative treatments and therapy options, a better understanding of disease and genetic defects, and new knowledge for advancing feline health.

"We are very grateful to Dale and the SOCK organization for their dedication to feline health, bringing hope to beloved cats and their caring families," said CCAH Director Michael Kent.



# Fostering FUTURE LEADERS

DVM/Ph.D. student Matt Kramer with Dr. Michael Kent (left) and Dr. Jennifer Larsen (right).  
Photo: CCAH

**While still an undergraduate student**, Matt Kramer approached Dr. Michael Kent about conducting a research project. Kent had an idea for a study and wanted to encourage a bright aspiring scientist, so he teamed up with Dr. Jennifer Larsen, chief of the Nutrition Service to mentor Kramer.

“Matt was a promising student that we wanted to see go to veterinary school,” said CCAH Director Kent. “This project was a way to help foster his research interest and help create a future leader in veterinary medicine.”

While conducting the study as an undergraduate, Kramer was hired as a patient care assistant with the Radiation Oncology Service. After graduation, while applying to veterinary school, he was exposed to different types of research when he was hired by Dr. Xinbin Chen, who runs one of the school's basic science oncology laboratories.

Now a student in the DVM/Ph.D. program, Kramer attributes that first taste of research as a driving force that led to where he is today—on a path Kent envisioned with a future as a clinician-scientist and possibly an academic leader.

**“We are very proud of Matt, who showed a lot of initiative and a real acumen for research, even before starting veterinary school.”**

– Dr. Jennifer Larsen, DVM, Ph.D.

Kramer’s research surveyed 128 UC Davis canine oncology clients over a 16-month period to see if and how they modified their dogs’ diets following a cancer diagnoses. He found that 48% changed their dog’s food, and 55% altered food and/or supplements. Many owners made these decisions without consulting veterinary expertise, prompting veterinarians to consider consulting with clients about the importance of following dietary guidelines.

“Our findings really underscore the importance of collecting a dietary history during veterinary visits,” said Larsen. “This information enables us to address any concerns proactively and to assess for any nutritional risk factors such as an unbalanced diet. We are very proud of Matt, who showed a lot of initiative and a real acumen for research, even before starting veterinary school.”

Kramer’s dual DVM/Ph.D. degrees will take eight years to complete. With up to four additional years for an internship and residency, which he hopes to pursue, Kramer will have more than a decade invested in reaching his ultimate career goals.

“That’s a really big commitment,” said Kent. “And we, as a leading veterinary institution, need to make just as big of a commitment to these students. It’s important that we train future primary care veterinarians and specialists alike, but if we don’t train people like Matt, then there’s no future for veterinary medicine. By training the next generation of researchers, medicine advances. It’s through these dual degree programs that we foster the next generation of faculty and researchers.”



# Compassionate Giving to the **COMPANION ANIMAL MEMORIAL FUND**

**Dr. Alison Pillsbury '88** has provided exceptional care for animals for more than 30 years in Sutter Creek, California, and the surrounding Amador County. She helps fulfill the emergency veterinary needs of the community and offers general health care practice for the pets and wildlife of Amador County through a practice established in 2015—Acorn Hills Animal Center/Amador Veterinary Emergency Clinic.

Voted best Veterinarian and Veterinary Clinic by her community for numerous years, Pillsbury and her team of 12 are committed to providing compassionate, state-of-the-art care for their patients. They recognize the special bond between families and their pets. When a client loses a beloved companion, the clinic makes a thoughtful tribute to the animal by donating to the CCAH's Companion Animal Memorial Fund (CAMF).

"A heartfelt acknowledgment letter from the UC Davis School of Veterinary Medicine honoring a pet is so very meaningful to a client," Pillsbury said. "It's an incredible expression conveying the importance of that animal companion. Families treasure these letters and often hold on to them for life. A letter to a child or young adult can open a pathway to a future career in veterinary medicine or science exploration."

Acorn Hills Animal Center recognizes that a donation to the CAMF program brings hope. Thanks to these donations, the CCAH is making great strides advancing shelter medicine and carrying out research that leads to new diagnostics and treatments improving the health of cats, dogs and other cherished pets.

**"A heartfelt acknowledgment  
letter from the UC Davis  
School of Veterinary Medicine  
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— Dr. Alison Pillsbury



Acorn Hills Animal Center/Amador Veterinary Emergency Clinic team members (front) Kyndle Mehlhaff; (middle row from left) McKenzie Allen, Camille Rexford, Dr. Alison Pillsbury with Labrador retriever Bindy; (back row from left) Shahrie Glisson-King, Lisa Vanderpool, Megan Blackmer, Cheyenne Kinny and Mary Thorton. Courtesy Image.

"As a graduate of the school, not only do I believe in supporting the institution that made me who I am, but like all my clients, I too am in awe of the pets that have shared my life and made me a better human being and veterinarian," Pillsbury said. "They are my life."

In addition, Pillsbury generously gives back through her service on the school's Dean's Leadership Council since 2008—comprised of distinguished leaders in their fields who volunteer their time, provide insight and advice to the dean, and demonstrate the power of philanthropy.

# Welcome DR. JESSICA LAWRENCE

**Dr. Jessica Lawrence** joined the Department of Surgical and Radiological Sciences as a professor of radiation oncology on February 5th, 2024. Previously, she was Assistant Professor of Medical Oncology (2009-2012) at the University of Georgia and with the University of Edinburgh, Royal (Dick) School of Veterinary Studies in Scotland as a Senior Lecturer and the Head of Oncology (2012-2016).

After realizing that her long-term passion lay in radiation oncology rather than medical oncology, she shifted her focus and most recently was an associate professor of Veterinary Radiation Oncology with tenure at the University of Minnesota (2016-2024). She believes that the ever-accelerating improvements to radiation oncology, especially technological advances, constantly feeds her intellectually curious nature. Lawrence's research focuses on how radiation therapy stimulates and suppresses the immune system and how these immune changes affect tumor control.

"What's so fascinating about radiation therapy is that it can both arm the immune system and make it recognize and attack cancer cells," Lawrence said. "It can also disarm the immune system and suppress the immune system's ability to see cancer cells, infiltrate tumors, and kill cancer, so it's this ability of radiation to do both that we need to study. We need to figure out how to harness the power of radiation oncology to stimulate the immune system, and combine it with systemic therapies to improve outcome and therefore quality of life. Harnessing the power of the immune system, we can hopefully marry better treatments with less toxicity."

**"I've realized what a family UC Davis is and it's kind of this dream of being part of a work group that feels like the right fit."**

– Dr. Jessica Lawrence

Lawrence is currently working with Dr. Lindsey Sloan, a radiation oncologist and clinician-scientist, at the University of Minnesota to study a type of immune cell called the myeloid-derived suppressor cell (MDSC) to see if canine MDSC share features with human MDSC. Lawrence anticipates this research overlaps with work being done by Drs. Michael Kent and Rob Rebhun at the CCAH and Dr. Bob Canter at UC Davis Health.

Beyond the newfound research opportunities, Lawrence emphasizes her excitement to be part of the UC Davis veterinary medicine community.

"I've realized what a family UC Davis is and it's kind of this dream of being part of a work group that feels like the right fit," Lawrence said. "Everyone is there to make sure the pet gets the best care, and we can work as a team to figure out the research questions to ask in order to improve that care. Seeing the collegiality, kindness, and support that people give each other has really impacted me."

The CCAH, through our generous donors, have helped fund her research startup costs which will accelerate her work on combining radiation therapy and immunotherapy in our fight against cancer.



Dr. Jessica Lawrence with Dr. Michael Kent's dog, Danson.  
Photo: Trina Wood



# The CCAH Joins Community to **HELP MAUI'S CATS**

**Last August**, a hopscotching wildfire set the island of Maui ablaze. Residents were forced to flee their homes without warning, some jumping into the ocean to save their lives. More than 100 people lost their lives and more than 8,000 residents were displaced. Animals that live outside tried to escape as their habitats burned; indoor pets were separated from their owners as they fled. More than 500 feline survivors lost their home/habitat, their people, and everything familiar to them.

Maui Humane Society (MHS) quickly stepped up to help reunite and house victims of the fire, but the number of animals in distress surpassed their capacity. To manage the crisis, the MHS tapped the UC Davis Koret Shelter Medicine Program (KSMP) and the small but mighty team from FieldHaven Feline Center—who gained experience in the Paradise fires and featured in the documentary *Fire Cats*. All parties were committed to reuniting pets with their families where possible and providing a second chance at life when reunification wasn't. But a community cat rescue effort of this scale had never been attempted.

Housing the cats proved to be the most immediate challenge. Typically, feral and unsocialized cats should be confined as little as possible. The stress of housing and handling often makes



Outdoor enclosures offer environmental choice to free-roaming cats not used to being inside. Photos: Denae Wagner

free-roaming cats sick and causes their health to rapidly deteriorate. In a situation where both people and animals are experiencing a crisis, cats are housed longer than is advised and the risk of a stress-induced disease outbreak is high.

KSMP housing expert Dr. Denae Wagner and KSMP Director Dr. Kate Hurley traveled to Maui for nearly three weeks and went to work designing structures to suit the needs of cats with longer stays, including housing suited for both indoor and outdoor living. They focused on space to exhibit natural behaviors that offered some form of environmental choice—a key component in reducing the stress in animals in captivity. The next challenge was, what could they use to build? The store aisles were empty and ordering more supplies and materials was proving neither reliable nor timely. Undeterred, the team began to compile whatever was available. Prototypes were constructed from donated pop-up cages, chicken wire, card tables, Rubbermaid bins all fashioned together with zip-ties.



**“In the face of adversity, the Maui Humane Society’s initiative to build outdoor cat housing stands as a testament to the resilience and unity of the community,”**

– Dr. Denae Wagner



A community of volunteers came together, some physically on the island and some participating through Google sheets and text threads, to build the emergency shelter. Together the team created Cat Hales (a hale is a traditional Hawaiian house) that offered elevated spaces, sun decks, soft places, playhouses and cool retreats.

The temporary shelter allowed the Maui Humane Society the time needed to find a permanent solution, like developing a partnership with a local sanctuary, building a working cat program, and finding new families and habitats for the cats that were unable to be returned. It also allowed the MHS to continue focusing on trapping the cats that remained hidden in the fire zone.

Wagner reflects on completing a project that had never been done before.

“In the face of adversity, the Maui Humane Society’s initiative to build outdoor cat housing stands as a testament to the resilience and unity of the community,” she said. “Through collaborative efforts, we were not only able to provide practical solutions for the displaced cats, but seeds were sown of a more compassionate and interconnected community where the well-being of all things is a shared responsibility. I’m proud that we were able to represent UC Davis in that effort.”



Different types and sizes of enclosures, the ability to hide and climb allow cats to exhibit natural behaviors which reduces fear, anxiety and stress.



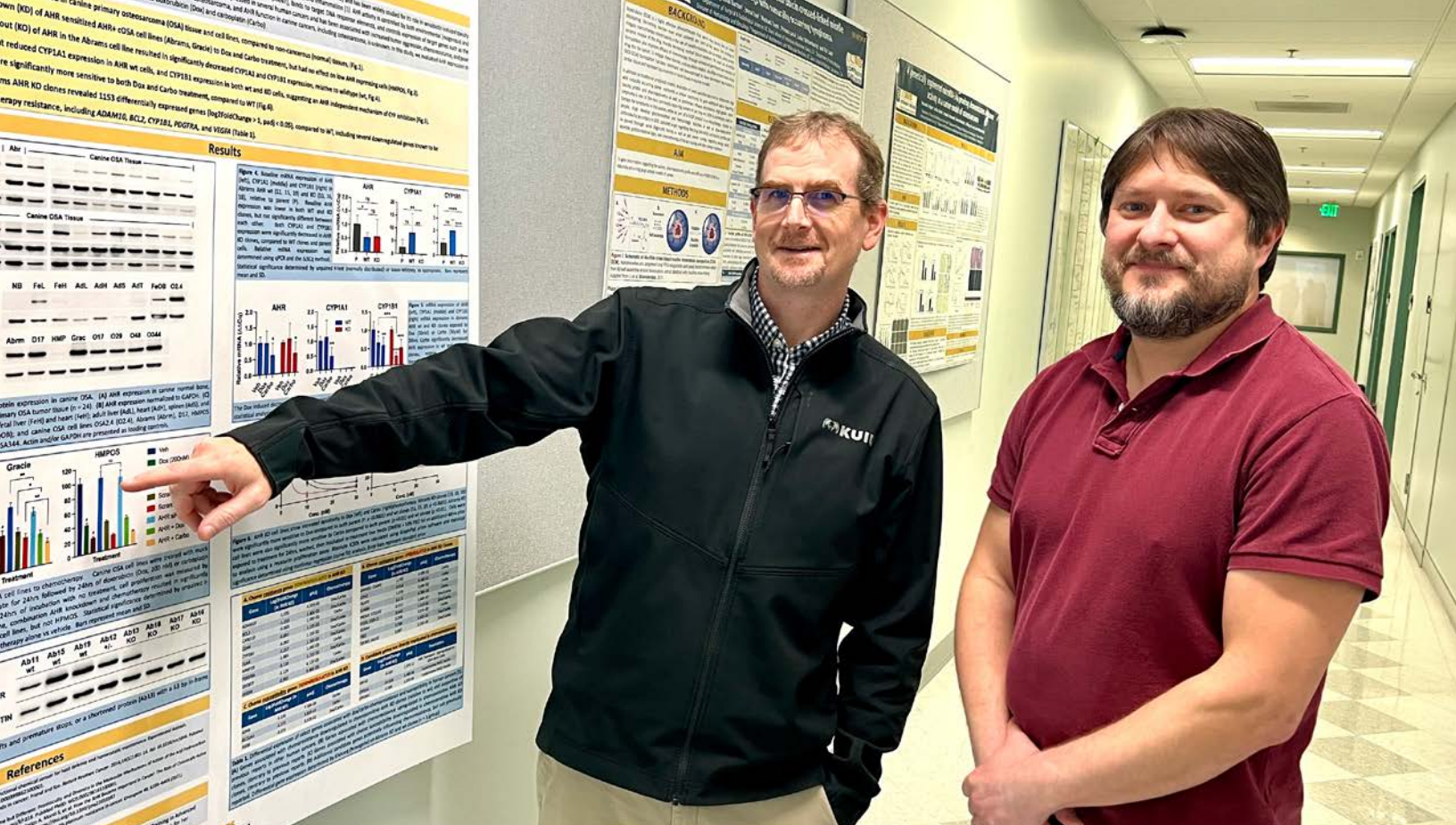
## GIFTS from the Heart

Are you looking for a heartfelt way to show that you care? Honor someone special—a beloved pet, friend or family member—with a donation made in their name to the Companion Animal Remembrance and Endearment (CARE) fund. Your gift will help support studies that improve the health of our animal companions. We will brighten your honoree’s day with a letter sharing your meaningful tribute.

Honor a loved one by visiting [give.ucdavis.edu/Go/care](https://give.ucdavis.edu/Go/care) or calling 530-752-7024.







# Better Understanding CHEMORESISTANCE

Drs. Daniel York and Robert Rebhun with the poster study presented at the most recent Veterinary Cancer Society meeting.

**When Drs. Daniel York and Robert Rebhun** began looking into longevity in golden retrievers despite the breed’s genetic predisposition for cancer (see cover story), they became interested in the aryl hydrocarbon receptor (AHR)—a ligand activated transcription factor best known for regulating the CYP1 family of cytochrome P450 genes.

“This receptor is overexpressed in several human cancers and has been associated with increased tumor aggression, chemoresistance, and poor patient prognosis,” York said. “But there wasn’t any real data to show how AHR affected canine cells. So, we developed knockout cell lines to analyze that.”

Initially, it appeared to the researchers that AHR may have a role in regulating the HER4 gene, which was associated with an increased lifespan in goldens. It is the same family of genes in humans as HER2, a gene well-known for making cancer cells grow quickly.

**“There wasn’t any real data to show how AHR affected canine cells. So, we developed knockout cell lines to analyze that.”**

– Dr. Daniel York

Although the researchers did not observe direct regulation of HER4 by AHR, they did find that AHR regulates a protein that activates HER4 known as Nueregulin-1, indicating an indirect effect on HER4. In addition, their research showed that, within osteosarcoma cells, AHR regulated several genes associated with chemotherapy resistance. Those results took them on a different path of scientific inquiry.

The result of that inquiry led to a poster presentation at the 2023 Veterinary Cancer Society meeting. Their results suggest AHR expression may be a useful biomarker to predict response to chemotherapy in canine osteosarcoma and further identifies AHR as a potential therapeutic target.

Another interesting observation that came out of the study that isn’t in the poster itself, York explained, is that several identified AHR regulated genes, including the cytochrome P450 genes, are involved in chemo-induced cardio toxicity. It may be that manipulating AHR activity could affect the cardio toxicity associated with chemotherapy. However, because a large number of genes influence this toxicity, more studies are needed to evaluate that.

“By inhibiting AHR, we may be able to kill tumors faster, but with unknown consequences to the heart,” York said. “There’s a lot to look into.”





# THANK YOU!

## Friends of Companion Animal Honor Roll

**Thank you to our Companion Animal Memorial Fund veterinary partners** for honoring the memory of more than 16,000 beloved pets. Through your meaningful tributes, you brought comfort to their caring families and made a big impact on animal health. We are pleased to recognize the 173 veterinarians and clinics who donated to this fund in 2023, raising \$179,000.

A Gentle Rest	Chico Animal Hospital	Laguna Veterinary Hospital	Reedley Veterinary Hospital
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**VETERINARY MEDICINE**

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The CCAH is dedicated to advancing studies in veterinary medicine—encompassing new ways to prevent, diagnose and treat diseases including cancers, genetic and immune disorders, infectious diseases, kidney and heart diseases, and nutritional disorders in companion animals. We welcome visitors to come and learn more about our mission and programs. To schedule a visit, please call 530-752-7295. *The University of California does not discriminate in any of its policies, procedures or practices. The university is an affirmative action/equal opportunity employer.*



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# 2023 CCAH Annual Report

Want to learn more about the CCAH?  
The CCAH Annual Report highlights  
the activities and impacts of the  
CCAH on companion animal health.

To view report, visit:  
<https://ccah.vetmed.ucdavis.edu/news/ccah-annual-report>

Photo: Nico Pryt

## Center for Companion Animal Health

Business office: 530-752-7295 • Small animal clinic appointments: 530-752-1393



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