

### **Genetics Unravel Clues to Gliomas**

**S**ometimes a trip to the water cooler delivers more than a refreshing drink—it can also lead to productive research collaborations that shed light on topics of critical concern to animals and humans. Dr. Danika Bannasch, the Maxine Adler Endowed Chair in Genetics, recalls numerous impromptu discussions in the hallways of the Center for Companion Animal Health (CCAH) with Dr. Peter Dickinson, a veterinary neurologist. For decades, he'd been puzzled by why he saw a higher incidence of gliomas among specific dog breeds, particularly in brachycephalic canines such as boxers, bulldogs and Boston terriers.

"What is it about brachycephaly and gliomas?" Bannasch recalls him asking her. "You're the geneticist—why don't you find out!"

Bannasch and Dickinson joined a team with two Swedish scientists that used genome mapping across 25 dog breeds to identify three candidate genes associated with glioma development in canines. The study, published in *PLoS* 

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"The big pathways altered in humans are likely to be altered in dogs as well..."

– Dr. Peter Dickinson



Dedicated to improving the health of companion animals

## A Message from the Director

One of the primary missions of the CCAH is providing funds to inspire innovation that advances the health of companion animals. We accomplish this through many avenues, one of which is by funding resident projects that teach bright clinicians to design and launch a study with a common disease or injury under direct mentorship of a faculty member. These projects allow residents to improve their knowledge in a chosen field of specialization, and expose them to the principles of clinical research, critical thinking, hypothesis design and data mining that encompass this type of investigation, while advancing animal health – a win win.

We also support innovation by providing initial seed funds to faculty in an area of research they wish to explore. This can lead to important discoveries and develop the data needed to apply for external grants for a larger base of support. For example, our colleagues Drs. Danika Bannasch and Peter Dickinson used initial CCAH grant funds (\$15,000) to conduct a genetic analysis of canine gliomas, which we report on in this issue. The sequencing data they gleaned from this initial study led to an NIH funded grant of \$500,000, on which they are co-investigators with other faculty from the veterinary school and the UC Davis National Cancer Institute-Designated Comprehensive Cancer Center. This NIH grant will hopefully produce outcomes that benefit both dogs and people.

Inspiring innovative learning and research collaborations are made possible through the generous support of our donors—our partners in discovering new knowledge and treatments for our animal companions.

Thank you,

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Michael S. Kent, MAS, DVM, DACVIM, DACVR Director, Center for Companion Animal Health

#### "Your devotion inspires our commitment."

– Dr. Michael S. Kent



### Gifts from the Heart Matter Most

Did you know that you can send a heartfelt gesture in celebration or sympathy of a loved one or beloved pet? With a gift to the Companion Animal Remembrance and Endearment (CARE) Fund, your honorees are sent a special letter from the director of the CCAH notifying them of your meaningful tribute. Gifts to the CARE Fund benefit companion animal health studies.

For more information visit: www.give.ucdavis.edu/Go/care or call 530-752-7024.

# A short story of Sheller Medicine

t wasn't long ago that an animal that so much as let out a sneeze in a shelter was euthanized. A sick animal was seen as risk to the entire population; there simply were no resources, training or protocols in place to guide shelter professionals in managing the health of large populations of companion animals.

Fifteen years ago, the first shelter medicine residency training program was launched at UC Davis by Drs. Niels Pedersen and Janet Foley, in response to a sheltering community seeking more humane outcomes for their patients. Dr. Kate Hurley '99, the world's first shelter medicine resident, was tasked with finding the commonalities between herd health and companion animal care.

Today, animal shelters worldwide lean on the discoveries made by this initial team and the handful of shelter medicine programs that have emerged since. Millions of animal lives have been spared as a direct result of the advances made in this expanding field.

In November 2015, the first shelter medicine certification exam made it possible for veterinarians to

earn board certification from the American Board of Veterinary Practitioners. This past November, eight new graduates brought the total number of Shelter Medicine board-certified veterinarians to 12.

A growing number of students are choosing shelter medicine

as a career motivated by the lure of saving thousands of lives a year.

"It is amazing how far we've come in just 15 years—it shows how hungry the field was for this information," said Dr. Kate Hurley, director of the Koret Shelter Medicine Program. "While I don't think any of us thought we'd be studying for another exam at this point in our careers, we're terrifically excited to be part of the first wave of certified shelter medicine experts."

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*Genetics*, may provide insights into how these often untreatable brain tumors form in dogs and possibly in humans.

A second breakthrough concerning gliomas in dogs came a few months later and provided further definition of the candidate genes while suggesting a common pathway in dogs and humans. The research team, led by Dickinson, also included Drs. Dan York, Robert Higgins, Richard LeCouteur, Bannasch and researcher Nikhil Joshi. Results appeared in the *Journal of Neuropathology & Experimental Neurology*. The study was supported by donors to the CCAH, UC Davis, The Paul and Borghild T. Petersen Foundation and the Maxine Adler Endowment.

"Cancer is cancer," says Dickinson, who has spent the past 17 years researching gliomas in dogs and pursuing a canine model to develop translational therapies in humans. "The big pathways altered in humans are likely to be altered in dogs as well. The details may vary but it's likely to be the same big picture overall, so it's smart to use dogs as a model to identify potential genes for gliomas in humans." Because spontaneous gliomas are the most common form of malignant primary brain tumors in humans and occur at a similar frequency in canines, human neurooncologists have been interested in the association of gliomas in dogs and humans for a long time. Until recently, they didn't have the tools to answer the questions of whether there were particular genes associated with the tumors in both species.

"Now we have the tools for meaningful clinical translation," Dickinson says. "With advanced imaging and treatment equipment in a veterinary hospital setting, we can almost recapitulate what doctors do for humans in dogs."

He is particularly interested in one of the three candidate genes identified, P2RX7, which is involved in immunity in the brain and may be a target for future therapeutic action.

"We've shown association, now we need to prove causation," Dickinson said. "Can we show that the genes we've identified are really responsible for the increased incidence of tumor formation in specific dog breeds?"

# Investigating Safer Sedation for Cats

Advancing patient care is one of the primary goals of the CCAH. Sometimes one of the best ways to achieve that is to fund research projects that lay a foundation for larger clinical trials that eventually make their way into practice. Thanks to CCAH donors who support these endeavors, veterinary anesthesiologist Bruno Pypendop



veterinary anesthesiologist Bruno Pypendop recently published a study in *Veterinary Anaesthesia and* 

Analgesia that may lead to safer sedation techniques for cats.

His research examined the cardiovascular effects of dexmedetomidine, with or without MK-467, when given intravenously to cats. Dexmedetomidine is widely used to sedate animals or provide pain relief. However, the drug does come with adverse cardiovascular effects such as vasoconstriction and decreased heart rate.

"Our study showed that by adding MK-467 when administering dexmedetomidine, we can blunt some of its cardiovascular side effects without affecting its anesthetic/ analgesic properties," Pypendop said.

He pointed out that young, healthy cats are better able to tolerate the effects of dexmedetomidine, while older, sicker cats are more likely to suffer adverse effects, so its use is often avoided.

Several studies from Finland show MK-467 to be effective at mediating some of the negative cardiovascular effects in dogs and Pypendop was asked by colleagues there to pursue this initial study on cats. With the help of two primary CCAH grants, Pypendop

and his team was able to launch an investigation into the efficacy of using MK-467 in cats. He approached the Winn Feline Foundation for further funding with the support of a matching commitment from the CCAH.

"Getting the initial evidence is really important as proofof-concept and/or for garnering additional funding for larger clinical trials in the future," Pypendop said. "Having the two faculty grants from the CCAH helped us attract the additional funding we needed to accomplish that."

While MK-467 is still being explored through research and not commercially available, Pypendop said the drug shows promise as a means of improving sedation and anesthesia for cats, especially for older felines or those with systemic disease.

# Devoted to Improving Canine Health

Dogs hold a special place in Bille Sarzin's heart, largely because of the life-changing work they do—some as service dogs assisting those with disabilities, others as search and rescue dogs saving lives when disaster strikes. Since dogs help people in so many ways, she wanted to do something to help them, inspiring her to support the Center for Companion Animal Health (CCAH).

"I am greatly impressed with the work at the CCAH, especially in their energetic efforts to help dogs enjoy longer and healthier lives," Bille said. "I appreciate their collaborative approach, encouraging work across veterinary and human medicine disciplines to find the best solutions to diseases, some afflicting both dogs and people."

Bille has been a loyal annual supporter of the CCAH since 2000 and is recognized as a distinguished member of the Dean's Circle. Planning for the future, she also directed a portion of her estate to the school and is honored through the Heritage Society for Animals. "I first met Bille about a decade ago and have been honored to get to know her," said Dr. Michael Kent, CCAH director. "We are deeply grateful to Bille for her generous support and her devotion to improving canine health. She is an important partner in our commitment to advancing our knowledge and treatment options for diseases that affect all of our animal companions."

For information about making a gift to the CCAH and to learn more about the Dean's Circle and Heritage Society for Animals, please contact the Office of Development at 530-752-7024.

Bille Sarzin is enjoying a visit with Spring, a four-year-old, careerchanged golden retriever from Guide Dogs for the Blind. Spring now spreads her happiness and love of life throughout the community as a member of the Furry Friends organization.



### **Companion Animal Memorial Fund – Honor Roll**

We gratefully acknowledge veterinary clinics and practitioners who made heartfelt tributes to beloved pets through a gift to the Companion Animal Memorial Fund. This fund helps to support clinical research to better identify, diagnose, treat and prevent animal diseases and conditions including cancer, genetics, nutrition, infectious diseases, endocrinology, immunology, anesthesiology and internal medicine. The following supporters contributed \$500 or more to the memorial fund from March to December, 2016.

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# Training a New Generation of Faculty

Success is what happens when chance meets preparation—but sometimes you need a little nudge to grab the opportunity. Dr. Derek Cissell, a new assistant professor of diagnostic imaging, was completing a Ph.D. in the lab of Dr. Kyriacos Athanasiou, a renowned bioengineer on campus, when a faculty position opened in radiology. Cissell had completed a four-year residency in radiology at UC Davis before pursuing his doctorate and knew it was the perfect opportunity to combine research and teaching.

While Cissell was reluctant to apply before finalizing his Ph.D., his mentors pushed him to do so. Thankfully, he did.

"The position here was a once-in-a-life-time opportunity," Cissell says. "It was definitely a case of being in the right place at the right time."

The seed to pursue specialty training had been planted in veterinary school at the University of Pennsylvania—a suggestion also made by Drs. David Wilson and John Madigan who mentored him at UC Davis while he completed a two-week externship in the large animal clinic in 2004. That experience proved critical in bringing him back to California in 2007 to begin the radiology residency. During his residency, Cissell co-authored some research projects that were funded by generous donors to the CCAH.

"I realized during the residency that I really enjoyed teaching as well," he says. "To combine academia and

teaching, I knew I'd have to take the next step and pursue a Ph.D."

So Cissell returned to his first college interest of engineering and joined the Athanasiou lab where Dr. Boaz Arzi was completing his post-doc training. Cissell collaborated with him on the pioneering procedure of



Derek Cissell

regenerating mandibular bone in dogs.

Cissell's current research interests focus on using imaging to evaluate tissue function and disease noninvasively in the musculoskeletal system, particularly cartilage. While on clinics, Cissell works in large animal radiology and in CT, MRI and nuclear medicine. He's always been interested in musculoskeletal biomechanics, particularly in horses, since his undergrad years when Cissell played polo.

When he's not in clinics or the lab, Cissell enjoys driving a tractor and fixing fences on his 10-acre property west of Davis. He also recently acquired his first horse, an off-thetrack Thoroughbred named Mambo who needed to heal from a stress fracture in his pelvis. With luck, Cissell says he will be able to pull his old polo gear out soon and start smacking a ball around the backyard.

# Exercise Improves Parrot Health

**S** ince most captive parrots lead a sedentary lifestyle, a group of UC Davis researchers was interested in learning what effect this had on the birds' overall health. Was their inactivity a contributing factor in susceptibility to high cholesterol (hypercholesterolemia) and hardening of arteries (atherosclerosis)? Exercise has been shown to be an important component to manage breakdown of fat (lipid metabolism) in human and poultry studies, and the researchers were curious if increased exercise could improve parrot health as well.

Wild parrots spend more than 50 percent of their waking time being active, foraging for food and flying several miles a day. Captive parrots, however, spend more than 90 percent of their waking time inactive. This extremely high level of inactivity seemed an obvious point to improve the health and welfare of captive parrots.

Dr. Joanne Paul-Murphy, a faculty veterinarian specializing in zoological medicine as well as animal welfare, with her post-doctoral graduate student, Dr. Kate Gustavsen, collaborated with other scientists to conduct a study with Amazon parrots. Eight birds were placed in an exercise group, while four made up a sedentary control group.

The exercise group performed 30 minutes of flight and 30 minutes of walking for five days every week. The sedentary group continued to live as typical companion birds. Body weight, chest girth and lipid panels were measured at three time points over several months. Lipid panels included total cholesterol, high-density lipoprotein cholesterol (HDL-C) (the "good" cholesterol), low-density lipoprotein cholesterol, and triglycerides.

## Can Probiotics Help Obese Cats?

UC Davis nutritionists are researching new options to combat cat obesity



With obesity in cats being a major health problem, veterinary nutritionists at the school are tackling the issue with new approaches. One method they are exploring is the use of probiotics to assess its effect on food intake, body composition and metabolic parameters in healthy, overweight and obese cats. Probiotics are live microorganisms introduced into the body to confer a health effect, usually benefits to the digestive system. They have been used

for various purposes, most notably to treat diarrhea or chronic gastrointestinal disease. However, research into their use as potential weight loss tools in companion animals is lacking.

Recently, a resident research project conducted by Dr. Aarti Kathrani (mentored by faculty members Drs. Jennifer Larsen, Philip Kass and Andrea Fascetti) studied the use of probiotic *Enterococcus faecium* strain SF68 on 20 cats (eight in the control group). Studies in mice and humans showed the probiotic to reduce food intake, promote weight loss and improve metabolic profiles. The veterinarians were hopeful to find similar outcomes in cats.

"Unfortunately, we did not see that outcome with cats in our limited study," Larsen said. "We did see some trends, though, before the 8-week study ended. There was potential for a different outcome if the study lasted longer or if we included more cats."

Researchers hope to launch additional projects with a longer or broader study to see if those trends, such as movement toward greater lean body mass in the cats, could point to probiotics having a positive effect on weight loss and overall health. A potential future clinical trial of probiotics could help determine if this could be a new tool to fight obesity in pets.

Donors supporting the Center for Companion Animal Health funded this research project. Findings were presented in poster format at the 2016 American Academy of Veterinary Nutrition annual meeting, and discussed by Kathrani at House Officer Seminar Day last spring where dozens of research projects are presented by UC Davis residents. As the veterinary school with the largest advanced training program in the world, UC Davis is able to offer its house officers (residents, interns, fellows) valuable research opportunities not available at other institutions.

The exercised birds lost significant weight and showed decreased body measurements compared to the unexercised birds. HDL-C measurements were significantly higher about midway through the study, but returned to near baseline by the end. The investigators think the reason that the birds' HDL-C did not stay elevated for the second half of the study was because the birds learned ways of avoiding the flight exercise, even though they continued to enjoy the walking exercise.

This study supports the theory that exercise has a positive effect on parrots' health, and further research is needed to determine the amount of exercise necessary to validate long-term positive changes in the parrots' health and welfare.

An Amazon parrot on an exercise "treadmill." 🕨



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- Improving minimally invasive surgery techniques for cats (Dr. Philipp Mayhew)
- Developing new pain medications for pet birds (Dr. David Guzman)
- Reducing heart toxicity in dogs undergoing chemotherapy (Drs. Joshua Stern and Catherine Belanger)
- Using PET scans to look for tumor spread in dogs with melanoma (Drs. Jennifer Willcox and Mathieu Spriet)

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