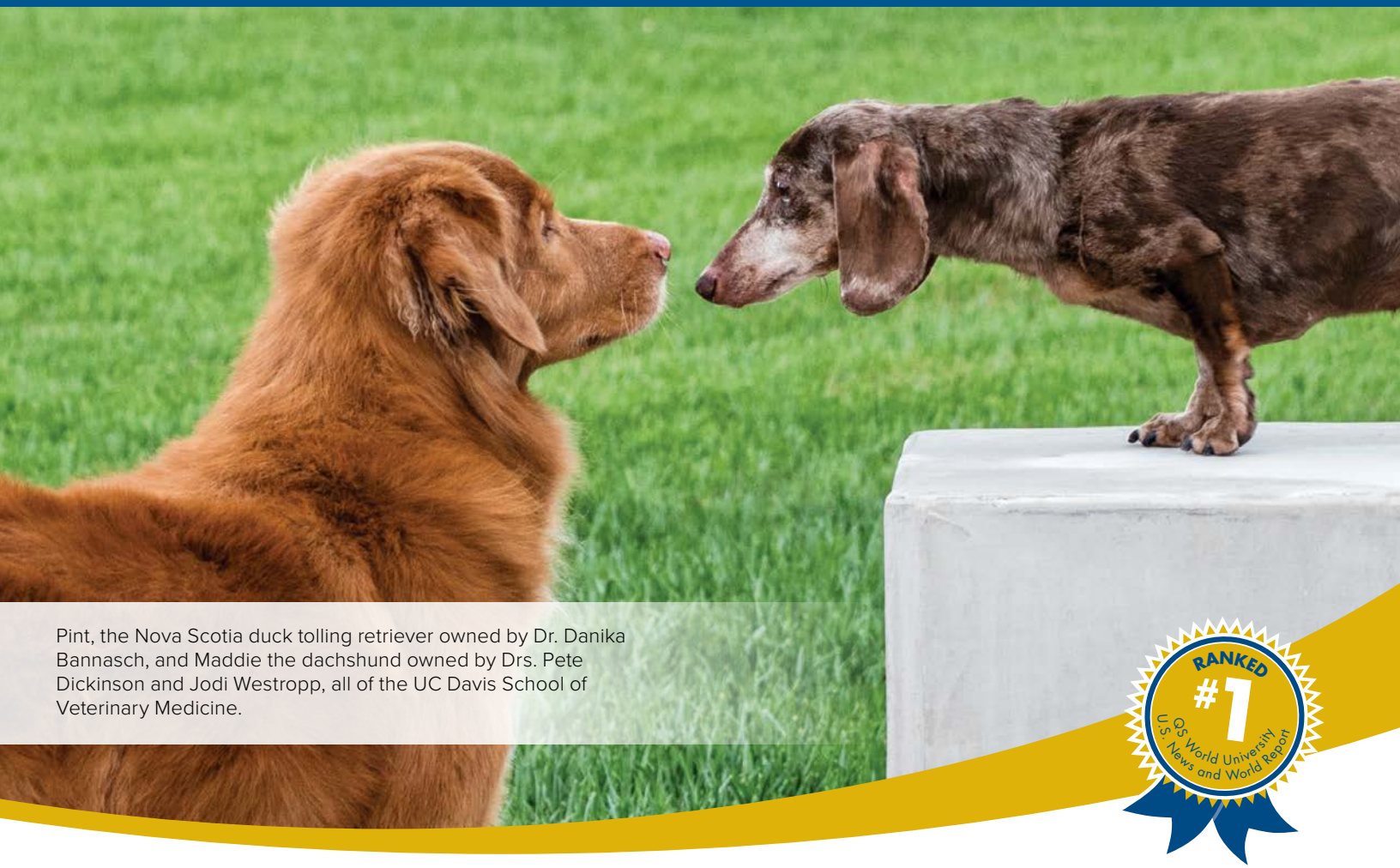
CCAH Update
UC DAVIS SCHOOL OF VETERINARY MEDICINE
SPRING 2018



Pint, the Nova Scotia duck tolling retriever owned by Dr. Danika Bannasch, and Maddie the dachshund owned by Drs. Pete Dickinson and Jodi Westropp, all of the UC Davis School of Veterinary Medicine.

RANKED #1 QS World University U.S. News and World Report

Unraveling the Genetics of Disc Disease in Dogs

For the past century, veterinarians have observed intervertebral disc disease more commonly in dogs with short legs (dachshund, French bulldog, and Pekingese to name a few), but they couldn't pinpoint why—until now.

School researchers recently announced the discovery of a genetic mutation across breeds that is responsible for chondrodystrophy (the skeletal disorder leading to shorter legs and abnormal intervertebral discs) in a study published in the *Proceedings of the National Academy of Sciences*.

"Dogs with intervertebral disc disease (IVDD) are 50 times more likely to have this mutation," said veterinary geneticist and one of the paper's authors Danika Bannasch. "That's an incredibly strong correlation with disc disease."

Identifying the cause of this painful condition is the first step to alleviating pain and suffering, Bannasch said. Because of this work, there is now a genetic

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UCDAVIS VETERINARY MEDICINE
Center for Companion Animal Health

Dedicated to improving the health of companion animals

A Message from the Director

Once again, I have the pleasure of updating you on some of the exciting impactful work coming out of the center—determining the underlying cause of disease which is critical to prevention and treatment. We highlight three research discoveries in this issue and the collaborative environment at the School of Veterinary Medicine that makes these stories possible.

Here at the school we bring together unique teams that work across disciplines. By teaming up clinicians who can identify and treat a disease with other clinicians and basic scientists, who have the tools and knowledge to help answer research questions, we can tackle the toughest problems facing animal health. Our teams also benefit from state-of-the-art laboratories with access to electronic medical records going back decades in a teaching hospital that sees 50,000 patients a year.

All of the work that we do—each grant we fund; every piece of equipment we provide; each resident we help train; each discovery we make; every dog, cat, bird, rabbit or other companion animal we treat—is thanks to friends like you who care about improving animal health and support our center.

Thank you and my best,

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

P.S. (spoiler alert) – And how about saving a million cats?
Go Shelter Medicine—that's impact!

The Behavior of Drugs

Dr. Luke Wittenburg joined the faculty in 2016, thanks to an anonymous gift to the Center for Companion Animal Health (CCAH), with a focus on the clinical pharmacology of chemotherapeutic agents. By better understanding how chemotherapy drugs function in animals, Wittenburg hopes to make an impact on translational medicine and foster further collaboration between the CCAH and the School of Medicine.

Dr. Luke Wittenburg studies the pharmacology of cancer drugs.

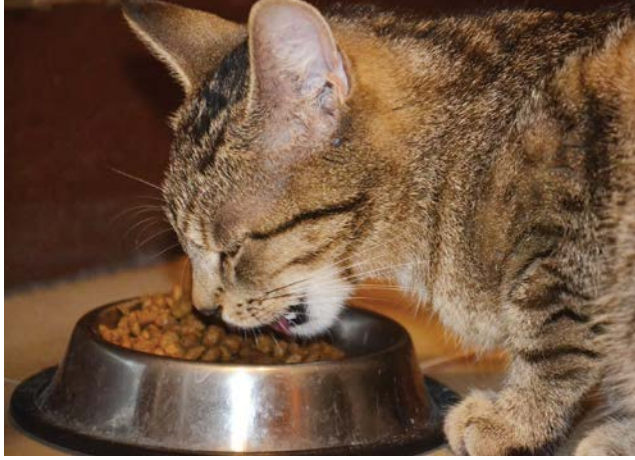
Working closely with clinical oncologists and researchers in both veterinary and human medicine, Wittenburg is currently addressing two main areas. First, he hopes to identify novel targets and therapeutics with translational possibilities for osteosarcoma. Since the disease is similar in dogs and humans, researchers are testing effects of potential drugs in dogs that may also help humans. His benchtop research is currently testing a compound initially developed for leukemia in humans that is showing positive effects on bone cancer in dogs.

Second, Wittenburg is studying the clinical pharmacology of chemotherapeutics in veterinary species. Collaborating with veterinary oncologists conducting clinical trials, he analyzes how animals process these medications and their toxicity and efficacy. Two clinical trials currently in progress at the veterinary hospital involve the drugs Vinblastine and Cyclophosphamide.

Although Vinblastine is commonly used to treat feline lymphoma, there is currently no information on how the drug is distributed and eliminated in cats. Even when the same standard dose is administered to all cats, there can be large differences in how effective it is and in side effects. Wittenburg aims to describe the pharmacokinetic profile of the drug to find answers that begin to explain these differences.

Cyclophosphamide is another chemotherapy drug used to treat lymphoma. Wittenburg is measuring whether altering the dosing regimen might enhance the drug's activity or make it less effective. He hopes to gain a better understanding of the drug's variability with results from clinical situations of animals with naturally occurring forms of disease.

Is the Answer in the Blood?



Can a blood test determine if a cat will tolerate certain diets?

Determining the best diet for cats with food allergies can be tricky. Researchers at the Center for Companion Animal Health (CCAH) may be one step closer to using a simple blood test to help figure that out.

Former nutrition resident Dr. Aarti Kathrani led a CCAH-funded pilot study to measure a cat's production of cytokines – inflammatory proteins secreted by the immune system that influence response to things like bacteria, viruses, and even food. Hydrolyzed diets, where the protein has been broken down into such small pieces that it is no longer recognized by the immune system, are often used for cats with food allergies.

If blood samples can measure cytokines in response to a hydrolyzed diet, clinicians may be able to determine the best hydrolyzed diet for a particular cat.

Results from the study suggest that the immune systems of healthy cats were able to recognize hydrolyzed forms of tolerated proteins, and also that certain cytokines may be useful markers for dietary tolerance in cats. The next steps will involve exploring this test in food allergic cats. Further investigations may lead to a test to more precisely guide diet choices to treat food allergies.

Gaining a Better Look at Health of Golden Retrievers

A new study provides further evidence that golden retrievers are more prone to developing cancer than other dog breeds, and also sheds light on the controversy over whether their spay/neuter status affects longevity and risk for getting cancer.

Veterinary oncologist Michael Kent sought to determine the association of golden retriever deaths related to cancer, age and spay/neuter status in a large epidemiological study published in the journal *PLOS ONE*. His research team relied on electronic medical records of golden retrievers that were necropsied at the veterinary hospital from 1989-2016. Of a total of 652 golden retrievers included in the study, 65 percent of them died from cancer.

"It's profound that so many goldens are getting cancer," said Kent, who also serves as director of the Center for Companion Animal Health (CCAH). "We also found that if a golden retriever is spayed or neutered, they live a lot longer than intact dogs of the same breed—by many years."

The study, funded by CCAH donors, was made possible by the extensive medical records at the hospital. The center recently made a large financial contribution to modernize this recordkeeping system to ensure not only the best care for our patients, but also to support these types of studies.

"Having this database is a huge resource which allows us to delve into these larger questions on health and disease and longevity," Kent explained.

Among the 652 dogs included in the study, the average age of death was 9.15 years. In 424 of those, cancer had led to their death. Among dogs dying from a cause other than cancer, the median age of death was 6.93 years while those dying from cancer lived a median of 9.83 years.

While there was no significant difference in the proportion of intact and castrated males dying from cancer, a greater proportion of spayed females died of cancer compared to intact females, although spayed dogs lived on average more than 3.5 years longer than intact female golden retrievers.

"This gives a little more evidence that spay/neuter isn't going to negatively impact how long a golden retriever will live," Kent said. "We also found that similar to humans, as dogs get older, they're more likely to have cancer."

The researchers didn't find a difference between spay/neuter in the types of cancer the dogs got, but overall, they identified hemangiosarcoma as the most common cancer that causes death in golden retrievers, followed by lymphoid cancers. The next step is to look at the genetic basis for longevity in the breed to try to unravel why goldens experience such a high incidence of cancer.

Other study co-authors include Drs. Danika Bannasch, Jenna Burton and Robert Rebhun from UC Davis, and Gillian Dank from the Koret School of Veterinary Medicine in Israel.

Aengus is a beloved companion of dedicated CCAH donor Mary Ann Peters.

Disc Disease in Dogs Continued from page 1

test offered through the school's Veterinary Genetics Laboratory (VGL) that breeders, owners and veterinarians can use to make informed breeding decisions and to identify those dogs at greatest risk so they can be monitored and treated proactively.

Veterinary neurologist Pete Dickinson, a co-investigator, has witnessed all too often the correlation of unique shapes and debilitating disease in the neurology clinic.

"IVDD is the most common neurological condition we deal with in the clinic," Dickinson said. "It's the herniation of those abnormal discs that can lead to paralysis in the worst cases."

Treatment can be quite costly and prohibitive for some.

"The disease cost our clients approximately $1.7 million last year on cases that were severe enough to lead to surgery," Dickinson said.

Thanks to an extensive biorepository amassed at the UC Davis veterinary hospital over the past 15 years, Bannasch and her team were able to look at the DNA from cases with IVDD from a variety of dog breeds. The hunt for the actual mutation took hours of hard work from DVM/Ph.D. student Emily Brown, who completed her doctoral thesis using this project.

"There's a lot of literature that points to chondrodystrophy in dogs as an exciting animal model for degenerative disc disease in people," said Bannasch, who also holds the Maxine Adler Endowed Chair in Genetics. "Now that we know more about IVDD, it could make for a better animal model."

This study, funded by our generous donors, is part of the Center for Companion Animal Health's long-term commitment to genetic research to improve the wellbeing of companion animals.

For more information about the genetic test, contact the VGL at 530-752-2211.

Honoring Beloved Pets

Jonathan Ferrini has provided a loving home to several homeless dogs and cats through the years. He describes them as "adopting" him and changing his life forever. Because of the difference his beloved pets made in his life, Ferrini wanted to honor their memory in an impactful way by giving to the Center for Companion Animal Health (CCAH). With his heartfelt generosity, Ferrini joins the CCAH in their commitment to improve the lives of animal companions through genetic research, unlocking the causes of inherited diseases.

Jonathan Ferrini

One of Ferrini's cherished pets was Duke—a young, emaciated golden retriever that he found in the fall of 1991. For the next 15 years, this once homeless dog became an important part of his life. They were best friends until Duke succumbed to a degenerative orthopedic disease.

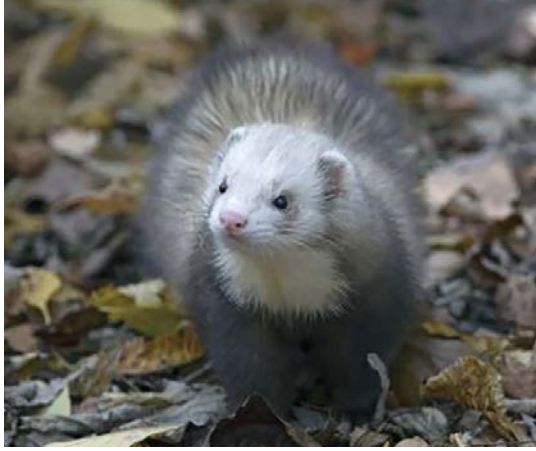
In tribute to Duke and his other pets, Ferrini established an endowment to create the Belzer, Duke, Midas, Thomas and Willy Ferrini Award for Genetic Research, recognizing exceptional, promising scientists.

"I wanted to remember my pets in a special way by funding cutting-edge advances in companion animal medicine," Ferrini said. "Genetics is the foundation of understanding and treating diseases that will help pets like those I have cherished."

The current award recipient is Emily Brown, who works in Dr. Danika Bannasch's genetics lab. Brown completed an undergraduate degree in Animal Science with a focus in genetics at UC Davis. She then launched immediately into the veterinary school, adding the Veterinary Scientist Training Program for a Ph.D. in her second year.

Brown participated in a major research project in the Bannasch lab and helped discover a genetic mutation across dog breeds responsible for chondrodystrophy (the skeletal disorder leading to shorter legs and abnormal intervertebral discs) and was first author on the paper published in the *Proceedings of the National Academy of Sciences* and highlighted in this newsletter.

Pet Ferrets at Risk



Domestic ferrets are known for their playful, mischievous antics. They are also known to be at risk for genetic disorders and disease due to a lack of genetic diversity. A collaborative team of UC Davis and University of Wyoming researchers published these findings in the journal *Evolutionary Applications*.

"Understanding the genetics of pet ferrets is important in terms of learning how to better treat them and hopefully prevent disease," said Dr. Michelle Hawkins, a UC Davis specialist in avian and exotic animal medicine.

Hawkins said the study was launched almost a decade ago after a hallway conversation at a professional meeting with anatomist and Missouri-based photographer, Bob Church, who wanted to study the dental patterns of diverse domestic ferret populations. Hawkins and her colleague Dr. Susan Brown, an exotic animal veterinarian in Illinois, were interested in determining the genetics of some cancers in ferrets.

Hawkins got in touch with Dr. Holly Ernest, a conservation geneticist who was then at UC Davis, as she had studied microsatellite DNA in wildlife species to determine population differences. Together, they designed a genetic study, funded by donors to the CCAH, to piggyback onto Church's already-funded dentistry study as he traveled around the globe, collecting dental specimens, oral swabs and tail hairs for genetic analysis from 765 ferrets in 11 countries for a comprehensive look at their genetic diversity—or lack thereof.

During this period, Ernest moved from UC Davis to the University of Wyoming and her post-doctoral student, Kyle Gustafson, was recruited to help complete the lab work and write the manuscript as first author.

The team reported that domestic ferrets in North America and Australia had extremely low genetic diversity, while ferrets in Europe had higher genetic diversity. Low genetic diversity created as a result of too few individuals contributing to the gene pool is known as a genetic bottleneck and is exacerbated when animals are bred for human-desired traits such as coat color.

"Because we understand that low genetic diversity is a significant contributor to certain diseases, including cancers, it makes sense to consider how breeding programs can use this information to enhance their genetic diversity," Hawkins said.

While keeping ferrets as pets in California and Hawaii is not yet legal, an estimated 500,000 to 1 million are kept as pets in California. They are allowed in 48 other states. The researchers recommend that North American breeding programs would benefit by incorporating genetically diverse ferrets from other countries such as Europe, where genetic diversity is much higher. However, international importation and exportation laws limit the potential for introducing new genetic material in some locations, such as Australia and New Zealand. In those places, breeders should actively minimize inbreeding among ferrets. Further breeding programs should also be cautious to ensure diseases are not introduced through international transportation.

"This global collaboration amongst veterinarians, breeders, and pet owners is an amazing example of how working together to address these very common and deadly medical issues may help save lives in the future," Hawkins said.

In addition to investing in future veterinary scientists, Ferrini is ensuring that the impact of genetic research will continue for generations to come through a planned gift to the CCAH.

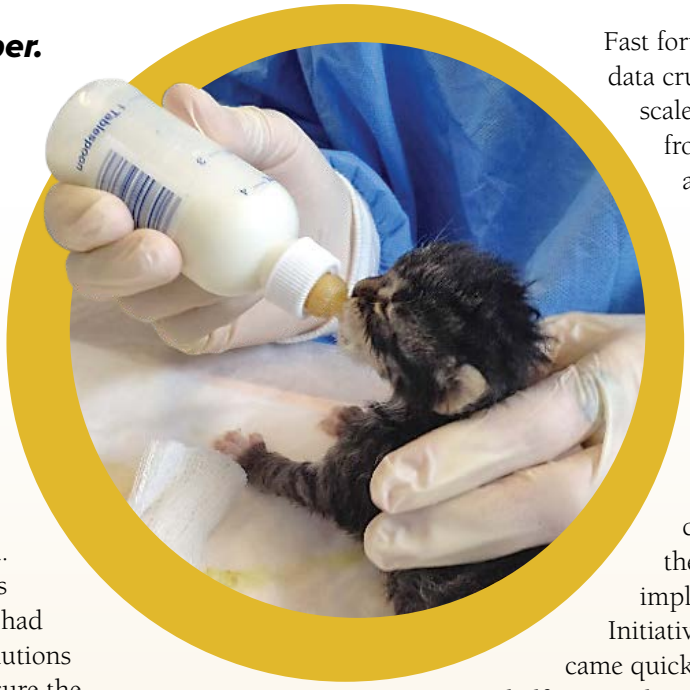
To recognize his enduring commitment to animals, the school honors Ferrini as a member of the school's prestigious Heritage Society for Animals.

To learn more about supporting genetic research at the CCAH and becoming a member of the Heritage Society for Animals, please contact the Office of Development at 530-752-7024.

Emily Brown with her Nova Scotia duck trolling retriever, Gilly.

Saving a Million Cats—One at a Time

"Some is not a number. Soon is not a time."



This quote by Donald Berwick, CEO of the Institute for Healthcare Improvements and leader of the 100k Lives Campaign, galvanized Drs. Julie Levy and Kate Hurley to launch a lifesaving campaign of their own. Instead of human lives, their goal was to save cats from unnecessary euthanasia in shelters across North America.

For years, the veterinarians (and UC Davis DVM alumni) had shared ideas, schemes and solutions to improve the health and ensure the adoption of shelter animals. They understood animal homelessness was a multifaceted problem—one that seemed perpetual and insurmountable.

"But we knew that was not the truth," said Levy, who leads a shelter medicine program in Florida. "We had witnessed individual shelters rally to extraordinary achievements in spite of modest budgets, dilapidated buildings and other challenges. The closer we looked, the clearer it was to us that there was an equation and the results were, in fact, predictable despite shelter hardships. There are a handful of steps every shelter can take that almost guarantee real, quantifiable results."

Both agreed on what was missing: a package that included a clear goal, an action plan, and a good dose of hope.

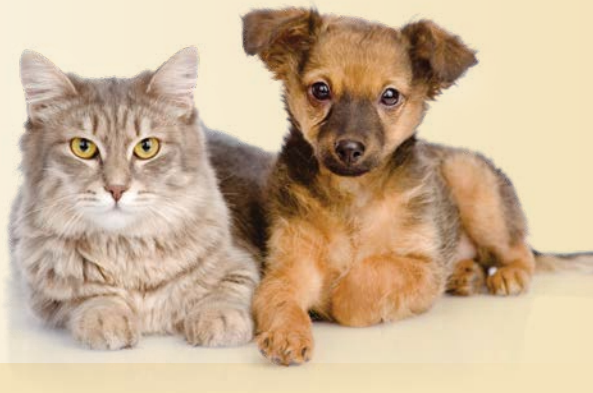
Fast forward through a period of intense data crunching, the study of large-scale change and a generous gift from Maddie's Fund, and Levy and Hurley's hopes and dreams coalesced into one huge project: The Million Cat Challenge. The goal was to use five straightforward strategies to save one million cats from euthanasia in North American animal shelters over a five-year period (2014-2018).

Shelters were eager for a community platform where they could share their journey implementing each of the Five Key Initiatives. The results of their efforts came quickly as the campaign hit the halfway mark one year earlier than planned, all while new shelters continued to commit to saving "at least one more cat life" daily. In the fall of 2017, more than one thousand shelters celebrated the million mark together with more than a year left in the campaign. At the time of this article, the final tally is being calculated and will be revealed later in the spring. As for Hurley and Levy, their eyes are still fixed on the future.

"The goal of the challenge was to save lives, of course, but it was really about creating irreversible change," said Hurley, director of the Koret Shelter Medicine Program at UC Davis. "What we all want is for every shelter to be able to offer the right outcome for every animal. We hope that will be the ultimate legacy of the Million Cat Challenge."

Neonatal kittens are the tiniest winners of the Million Cat Challenge. Without their mother, underage kittens require 24/7 care, something most shelters are not equipped to provide. Foster networks (like the Orphan Kitten Project run by UC Davis DVM students) have expanded and communities are stepping in to help, but there is still much to learn about their care. Donors to the CCAH provided funding for a $150k grant to the Koret Shelter Medicine Program for Drs. Karen Vernau and Dr. Tony Buffington to determine best practices to ensure the highest quality care possible for these youngsters.

Thank You



We gratefully acknowledge veterinary clinics and practitioners who have made heartfelt tributes to beloved pets through a gift to the Companion Animal Memorial Fund. This fund supports 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 $400 or more to the memorial fund from January to December 2017.

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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.

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- Studying the effect of a platelet drug on cats that throw clots

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