

CCAH UPDATE

SPRING 2022



From the Director

The year of 2022 remains a challenging time with the pandemic, the brutal invasion of Ukraine, climate change and wildfires, deep political schisms, and issues of racial and gender inequity and inequality. Despite the conditions of the world around us, we still must advance on matters of health and wellness. We remain committed to these ideals. For more than 25 years now, with your help we've been responding to the health and wellness needs of companion animals and their families.

In this issue we update you on some of that work. From our expanded clinical trials to basic science research that will fuel the next medical breakthroughs, the **Center for Companion Animal Health** addresses the most pressing health problems that dogs, cats and other small companion animals face. Thanks to your support, we have been able to increase our resident grant program to include those seeking advanced training in

fellowships. In fact, we have just reviewed and approved four new resident grants and one for fellows. We now review these four times a year, allowing us to quickly implement new studies that help prevent, treat and diagnose disease while training the next generation of clinician scientists. I received my first grant from the CCAH when I was a resident in training 22 years ago, and I know how

important it was in launching my research career.

We are also leading the way in addressing animal welfare issues. By joining forces with other groups and the state, our Koret

Shelter Medicine Program is tackling the problems facing shelters and the homeless animals we serve. It is very exciting that the

Million Cat Challenge is expanding its focus to include dogs. In addition, with the California for All Animals program, which is funded by the state, we will help shelters create safer environments and move us to a time where no animals will be unnecessarily euthanized

because they cannot find a home. This is huge!

With your continued help, we will continue to make the world a better place for all of our companions. May you and yours remain safe and well.

My best,

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

Michael had



ENGINEERED TISSUEMay Heal Injured Joints

Undergraduate biotechnology major Enmian Chang (left) and Dr. Natalia Vapniarsky discuss cell growth during the tissue engineering study.

Dogs with joint injuries may be helped in the future thanks to a CCAH-funded study to engineer new tissue. A team of researchers and orthopedic surgeons, led by Dr. Natalia Vapniarsky, has developed a strategy to create new cartilage from cells derived from the patient's injured tissue.

Osteochondritis dissecans (OCD) is a joint disease that causes pain and inflammation due to cartilage detachment. Surgical removal of the damaged cartilage is necessary and provides temporary pain relief, but dogs may never regain normal joint function due to the persistence of a cartilage defect and associated osteoarthritis.

The team found that OCD chondrocytes (cells taken from the injured, discarded cartilage) can be cultured and engineered into viable tissue comparable to native cartilage. While not at this stage yet, the manufactured tissue may one day be transplanted back into the patient to restore normal function of the affected joint.

Using OCD chondrocytes surgically removed from three injured dogs, the team successfully engineered new canine

cartilage tissue in approximately two months. The cell growth was so efficient that a 3mm in diameter surgical fragment yielded enough cartilage constructs to completely cover the articular surface of six shoulder joints.

The research team tested the strength of constructs created from OCD chondrocytes to those of healthy articular cartilage (HAC). They went a step further to recreate constructs from HAC chondrocytes taken from the legs of dogs who had an amputation for other diseases or injuries to see if growing cartilage from diseased OCD cells made them inferior to those derived from normal cartilage cells. The research found them to be comparable, and in some cases the OCD-derived cartilage even outperformed the HAC chondrocytes in tests.

"I think in the future, we will be able to offer some solutions for older dogs with degenerative joint disease such as replacement of parts or entire joint components using engineered tissue," Vapniarsky said.

COVER STORY

Clinical Trials from page 1

Dr. Boaz Arzi, a veterinary dentist and oral surgeon, and his team at the **Veterinary Center for Clinical Trials** (VCCT), were conducting a clinical trial to evaluate the use of a PET/CT scanner—the only one of its kind in use in veterinary medicine and partially funded by CCAH donors—as a diagnostic tool for oral pain of unknown origin in pets. PET, or positron emission tomography, is an advanced imaging modality gaining traction in veterinary medicine, as it is known to detect tissue lesions that do not show up on other imaging techniques. The scan of Texas proved successful, finding a very focal area of inflammation within the underside of his tongue that was consistent with a foreign body reaction, likely from a plant awn. Texas then underwent surgery to remove the abnormal tissue.

"Texas' case was a major conundrum as no one could figure out what his issues were," said owner Mindy Katz. "It was that PET/CT scan that determined the issue and probably saved his life."

Texas is one of hundreds of pets helped by UC Davis clinical trials that are evaluating novel diagnostics, techniques, and medications that hold promise for advancing the accepted protocol of care. Thanks to CCAH donors, more than \$525,000 is currently funding 23 new trials through the VCCT.

One of those trials is helping male cats with potentially fatal urethral obstructions. Dr. Jamie Burkitt and the emergency team see at least three male cats per week in the ER with dangerous urethral obstructions. These blockages often recur in male cats, require hospitalization, and are expensive to treat. Since they are the result of a chronic disease process, many owners are forced to euthanize their cats when the costs become prohibitive.

Burkitt is conducting a clinical trial to determine whether the size of the urinary catheter used to allow bladder drainage during hospitalization affects recurrence of urethral obstructions.

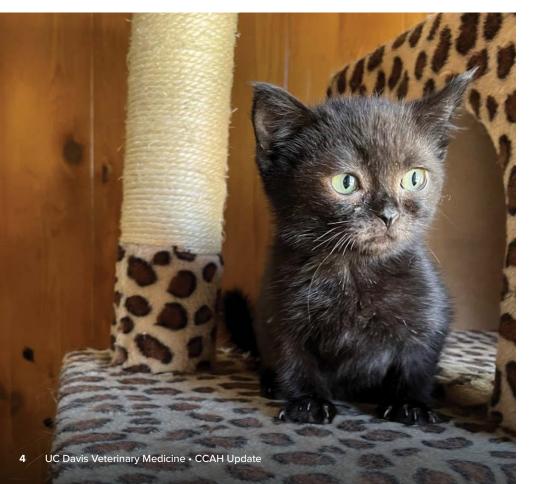
"This CCAH funding is absolutely vital," said Burkitt. "It's the only reason that we're able to do this study. Since this funding decreases client financial burden, the main client roadblock is gone, and it ultimately supports the ideal care of the cat. Without that funding, we would not be able to do this study."

Other trials include investigating alternative treatments of nasal and prostate cancer in dogs, studying genetic components of eye diseases, understanding more about chemotherapy drugs in dogs, and analyzing 3D surgical techniques for laparoscopic adrenalectomies.

Dr. Karen Vernau, faculty advisor for the Orphan Kitten Project, is conducting multiple collaborative clinical trials for a spectrum of cat health issues. Atlas, a newborn kitten, was treated for an ocular infection brought on by an upper respiratory tract infection. Vernau and ophthalmologist David Maggs are testing the safety and efficacy of an oral drug to treat eye infections known to work in older cats but with little history of use in kittens. Atlas' eye infection cleared brilliantly during the trial.

Additional trials conducted by Vernau are looking at the effects of early life experience on growth, health, and behavior of orphaned kittens; testing the efficacy of a probiotic to reduce diarrhea in kittens, as well as an oral medication to treat ringworm in kittens; and improving the care of kittens with hypothyroidism.

Donations to CCAH are changing the lives of current patients and potentially changing the course of veterinary medicine for future generations of pets.





HIGHLIGHTS

OF DONOR-FUNDED CCAH RESEARCH STUDIES

Through the generous philanthropic assistance of our donors, the CCAH funds over 70 research proposals annually. Here are some of the studies we recently supported:

- New anti-viral therapies against Feline Infectious Peritonitis (FIP)
- A blood test to help diagnose intestinal obstructions
 - GI disease in working dogs: improving overall performance and health
- A novel suturing device in laparoscopic gastropexy
- Iron levels in blood donor dogs



Genetic underpinnings of fibrocartilaginous embolism in dogs



Improved respiratory monitoring in dogs



Using flow cytometry in dogs with mast cell tumors to determine grade and possible spread



Antimicrobial resistance in dogs and cats



Treating ocular herpes in cats

Thank you for making a difference!

The Million Cat Challenge LETS THE DOGS IN!

The Million Cat Challenge (MCC), a six-year feline lifesaving drive that has saved nearly 4 million cats, has broadened its focus to include dogs, and introduced new initiatives to meet the challenges faced by today's animal shelters.

The Challenge—powered by a UC Davis and University of Florida partnership—addressed the "before, during, and after" for any cat at risk of shelter entry. The program sought to institutionalize the Five Key Initiatives, a spectrum of interventions designed to match the needs of shelters, pets and their people.

Although the Challenge blew past the goal of saving 1 million cats, neither program co-founders nor the shelters involved were ready to call it a day when the program was slated to end.

This pandemic era has left many families at risk of surrendering their pets. Evictions, and housing and job insecurity are putting unprecedented stress on families. Veterinary care is often unavailable due to severe veterinary staffing shortages. MCC co-founder Dr. Julie Levy knew that many of the same barrier-busting interventions that helped cats could be adapted to help keep other pet species with their people.

"The Million Cat Challenge was wildly successful, ultimately more than tripling its goal of saving the lives of one million shelter cats and supporting the adoption of proven catfriendly methods across more than 1,500 North American shelters," said Dr. Julie Levy of the Maddie's® Shelter Medicine Program at the University of Florida. "Now in that same spirit, we're inviting shelters and veterinary practices to join us in reimagining community-centered sheltering and care, and reserving shelter care for animals with no other options."

The newly-renamed Maddie's® Million Pet Challenge (MMPC) has been awarded a five-year \$7.4 million grant from

Maddie's Fund®, a national family foundation established by Dave and Cheryl Duffield to revolutionize the

Dave and Cheryl

Ouffield to

evolutionize the

status and well-being of companion animals.

The MCC evolution includes a collaboration of the UC Davis Koret Shelter Medicine Program (KSMP), the Maddie's® Shelter Medicine Program at University of Florida, Open Door Veterinary Collective, and Team Shelter USA.

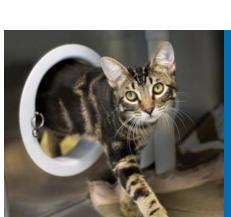
TEAMING UP FOR PETS & PEOPL

Under the new program, experts will deploy to communities across the country to offer free consultations to shelters and veterinary clinics on how to keep pets with their families and out of shelters. They will also teach veterinary clinics a financially sustainable model that removes cost as a barrier to providing care.

"Our goal is for every animal in every community to be assured what we call the Four Rights," said KSMP Program Director Kate Hurley. "That means providing every animal with the Right Care in the Right Place, at the Right Time, and with the Right Outcome. This is the new normal that communities and pets deserve, and we want to help them get and stay there."

This program is available at no cost to participants, thanks to Maddie's Fund®.

"The combination of the Million Cat Challenge coupled with Open Door Veterinary Collective is an evolution to meet the moment," said Mary Ippoliti-Smith of Maddie's Fund® Executive Leadership Team. "We have every faith the Maddie's® Million Pet Challenge will create an extraordinary opportunity for animal welfare and our nation's communities in keeping pets and people together."



#ShareTheLove

On February 14th, the Koret Shelter Medicine Program spread the love to California animal shelters when they launched the long-awaited <u>California For All Animals</u>, an initiative created to end euthanasia of healthy and treatable animals in California animal shelters, with \$5,000 welcome grants and portal grants for every eligible shelter!

HANDS-ON CLINICAL RESEARCH INSPIRES EXCELLENCE

Dr. Jennifer Chan '19 distinctly remembers when she knew she wanted to be a veterinarian. As a high school sophomore, she attended a day-long open house at the **UC Davis School of Veterinary Medicine** where she got hands-on experience at various animal health labs.

"I remember I got into the car and I said to my dad, 'I'm going to become a vet and I'm coming to UC Davis," she said. "I was so impressed that the veterinary students could tell me everything on a horse and then look at a cat and tell me a bunch of information about that animal too."

Soon after Chan enrolled in veterinary school at UC Davis, she caught the attention of her current residency advisor, Dr. Lynelle Johnson.

"Jennifer came to me as a first-year student and said, 'Hey, I think I'd like to do some research," Johnson said. "As soon as she told me about her project, I said this gal is something else."

Chan wrote and secured a grant funding a study on fluoroscopy and its efficacy on measuring chest wall expansion. Working with Johnson and Dr. Rachel Pollard, a radiologist, Chan conducted a study that encompassed 50 patients. Chan then partnered with a classmate to expand the project's scope to include assessing effects of fluoroscopy on the cardiac cycle. She produced two publications from the project and presented her findings at the American College of Veterinary Internal Medicine national meeting in Washington DC.

When she graduated in 2019, Chan was awarded the school medal—the highest honor for a graduating DVM student in recognition of outstanding academic and clinical performance. She completed an internship at North Carolina State University, one of the top programs of its kind in the country, before coming back to UC Davis for residency.

"I decided to pursue a residency because I liked the variety that internal medicine offers," Chan said. "When I was a student, I felt like all the complex and interesting cases were referred to internists, and I wanted to be the person seeing those diverse cases."

Under Johnson's mentorship, Chan has received resident support from the CCAH to execute a clinical trial dedicated to finding better care options for dogs who experience chronic cough. The purpose of this study is to determine whether or not inhaled steroids can reduce cough severity and frequency to an acceptable level.



Dr. Jennifer Chan (left) and her residency advisor, Dr. Lynelle Johnson.

"The benefit of this research project is that we can find treatments that have minimal side effects and work in treating this chronic ailment that is very common in dogs." Johnson said.

Chan said the project has stimulated further interest in research because it proves "research can be clinically applicable for our pets."

"I don't think the study would have been possible without the support of generous CCAH donors," Chan said. "We wouldn't be able to investigate this trial and we'd still be doing anecdotal medicine. Being able to tell an owner, this has worked and this is how much it's going to cost—those are important things."

Johnson agreed and added that the funding helps boost morale and is vital for giving veterinarians of tomorrow hands-on experience doing clinical trials.

"Gifts to support our work really pushes us to do more," she said. "Every person who gives stimulates us to do better."



ADVANCED DIAGNOSTICS for Feline Intestinal Lymphoma

From left: Drs. Bill Vernau, Stefan Keller and Peter Moore have developed a new diagnostic tool for feline intestinal lymphoma.

Intestinal lymphoma is the most common cancer in cats, but its diagnosis can be tricky. Symptoms of decreased appetite, weight loss, diarrhea, and vomiting mimic inflammatory bowel disease. Proper disease identification can be crucial to providing patients the most appropriate treatment.

UC Davis researchers recently developed next generation clonality assays as critical new molecular tests to distinguish inflammatory bowel disease from intestinal lymphoma in cats. Clonality tests look at the DNA in lymphocytes in a patient's sample and see if they all originate from the same cell, as they would in cancer, or if they have different targets, as they would in inflammatory diseases.

"We still have a poor understanding of how this disease develops in cats," said veterinary pathologist Stefan Keller. "But now we have a better toolkit to investigate the condition in greater detail, which should help clinicians to provide the best possible treatment and management."

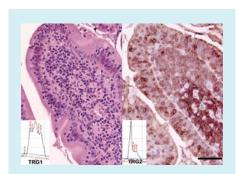
When Keller came to UC Davis to pursue a residency and then his PhD in 2009, Drs. Peter Moore and Bill Vernau (originally Moore's graduate student) had been tackling the issue of how to better diagnose feline intestinal lymphoma for years. They were frustrated that routine microscopic analysis of tissue samples often wasn't

sufficient for getting the job done, which affected patient management. They needed more tools in the toolbox and that is where clonality assays came in.

"These clonality tests are DNA specific and have to be developed for each species independently," explained Vernau, a self-proclaimed "crazy cat guy" who has helped his family

foster more than 700 kittens through the Orphan Kitten Project over the past 7 years.

While clonality assays had been used for several decades in human medicine, Moore and Vernau pioneered their use in veterinary medicine by developing them first for dogs in the late 1990s. It was soon apparent they needed the same assays for cats. However, they had to first go through the laborious process of generating the feline genetic sequence.



Cat small intestinal biopsy sample (routine HE and CD3 immunohistochemistry stains) that does not demonstrate clonality with the previous molecular clonality PCR assay (TRG1, left), versus clear indication/evidence of clonality, confirming small T-cell lymphoma, with the newly developed next generation molecular clonality PCR assay (TRG2, right).

CREATING A BRIGHTER FUTURE

For Shelter Animals

Christine Lynch and UC Davis alumnus William C. Tanner have a special place in their hearts for shelter animals, especially their feline companions Abby, Baxter, Biscuit and Tobias—who once faced uncertain futures. Lynch has made a difference in the lives of countless cats, dogs and other companion animals at their local shelter in Puyallup, Washington, where she has volunteered more than 7,000 hours over the past 14 years.



Biscuit

"Bill and I are committed to creating a brighter future for animals and were inspired to support the Koret Shelter Medicine Program (KSMP)," Lynch said. "The program has transformed how shelters are built and operate."

To advance the life-saving mission of the KSMP, Lynch and Tanner contributed a current-use gift and included the program in their estate plans, creating the Christine Lynch and William C. Tanner Shelter Medicine Program Endowment—to improve the quality of life for animals for many future decades. They also established a scholarship fund to support the next generation of veterinary leaders.

"We are so grateful to Chris and Bill for their support and for making sure we can put their good deed to work now," said Dr. Michael Kent, CCAH director. "Their passion for our work is heartening."



From left: CCAH Director Michael Kent, Christine Lynch, William C. Tanner and Koret Shelter Medicine Program Director Kate Hurley.

Lynch and Tanner first learned about the KSMP during a tour of the school in 2018. They were thrilled to find out that the program offers facility design consultations to shelters.

"Chris and I were impressed with the science behind installing portals in cages and how they create a healthier environment for cats living in shelters," Tanner said.

Portals are one of the most effective ways to reduce stress and disease in shelters and to increase adoption rates for homeless animals. They provide a cost-effective way to change housing from cramped cages to double-sided cat condos with separate eating/sleeping and bathroom areas.

"Our research has shown that low-stress housing saves lives," said Dr. Kate Hurley, KSMP's director. "We are energized by Chris and Bill, who share our vision for a better future for shelter animals. Together, we can dream even bigger!"

Thankfully, the recent explosion in high throughput sequencing has facilitated the development of a new generation of assays with better performance. Even with the technology more widely available, researchers must be able to analyze the data and that's where Keller's strength in bioinformatics helps the team.

"As important as generating results is interpreting results," Vernau said. "Together, we have a really strong team with different skills and the drive of a talented, persistent grad student."

The team represents a multigenerational effort in tackling this disease. Keller came to UC Davis because he wanted to pursue a PhD with Moore, like Vernau had done in the late 90s. As part of his PhD, Keller worked on developing clonality assays. After his PhD was finished in 2015, Keller

went on to a faculty job at the University of Guelph, Canada before he returned to UC Davis in 2019 as an assistant professor. His research now as a faculty member has further refined the diagnostic clonality tests he helped work on as a PhD student. The CCAH helped provide the funding for Keller's PhD training research and did the same for Araya Radtanakatikanon, a graduate student of Vernau's and first author of the latest study published in the Journal of Veterinary Internal Medicine.

"We had to be like groupies stalking our idols to get to UC Davis," Keller joked. "But it has paid off. Because of this research supported by the CCAH, we have better tests for diagnosing intestinal lymphoma in cats, and also a greater knowledge of the basic science of the feline immune system. And that's the key to appropriate treatment for affected cats."



Melanoma is often a deadly disease in dogs and people. Immunotherapy has shown promise in treating humans with cancer, but when it comes to dogs, veterinary medicine has been more limited in using that therapeutic to date. This is due to a lack of specific dog immunotherapies and the necessary diagnostic panels to determine what types of immune cells are affected by their cancer.

Veterinary oncologist Michael Kent and veterinary immunologist Liz Sparger, along with colleagues at the veterinary school and <u>UC Davis Health</u>, recently published a study in the journal <u>Frontiers</u> that identifies some of the T cell phenotypes involved in dogs with malignant melanoma that differ from those in healthy dogs. This study was funded by CCAH donors.

"In our immune system, we have T cells that promote immunity and T cells that suppress the immune response. In normal life, this is important so we don't get severe allergic reactions," explained Kent, who serves as CCAH director. "Unfortunately, this is also a way that cancer can evade the immune system. T regulatory cells, in particular, are involved when tumors learn how to suppress an immune response."

The purpose of the five-year study was to look at blood and tumor tissue from cases of canine melanoma before the patient started receiving treatment. Researchers were able to use the shared resource of the flow cytometry core at the **Comprehensive Cancer Center**, and create flow cytometry panels to determine what types of T cells were present and if immunosuppression was happening.

Dogs presenting to the UC Davis veterinary hospital with a diagnosis of a malignant melanoma and no prior treatment $\,$

were recruited to the study. Healthy client-owned dogs served as controls and were recruited through clients and staff. The researchers found not only a higher number of regulatory T cells in dogs with melanoma, but were also able to determine their ability to respond to immune stimulation.

Kent said this collaborative study with human health physicians is an example of building tools to aid clinicians in the future—in human and veterinary medicine.

"If you don't have the tools, you have to build them," Kent said. "We didn't have the tools, so we're building them."

These tools are a step toward better treatment for not just melanoma, but different types of cancer as well. They also serve as a model for developing similar flow cytometry panels for cats, and this work is currently underway.

"These panels will inform us of changes in different immune cell populations that may contribute to cancer-related immune suppression, as well as changes associated with effective cancer control," said Sparger. "Accordingly, this information may be used to identify immune biomarkers for cancer prognoses, either positive or negative, for individual feline or canine cancer patients. Lastly, this type of information may identify immune cell populations that can be targeted for cancer immunotherapeutics useful for specific cancer types in both pet dogs and cats."

Next steps are to come up with strategies to reverse the immunosuppression, and to get a better response to the tumor.

"These panels will be used to help us evaluate how our patients are doing in future clinical trials and if they're responding to treatment," Kent said.

THANK YOU!

Companion Animal Memorial Fund Honor Roll



Thank you to our Companion Animal Memorial Fund veterinary partners for honoring the memory of beloved pets and making an impact on animal health. We are pleased to recognize the more than 220 veterinarians and clinics who donated to this fund in 2021. Thanks to you, we are 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.

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