

Finding a **CURE**

After devoting a half century of his life to studying feline infectious peritonitis (FIP), a deadly feline coronavirus, Dr. Niels Pedersen now finds himself in the unusual position of responding to media inquiries about SARS-CoV-2, the human coronavirus that causes COVID-19.

The drug he discovered to be highly effective in curing FIP, known as GS-441524, turns out to be a close antiviral cousin of remdesivir—the first drug found to speed people's recovery from COVID-19 in clinical trials.

"While coronaviruses are found in most animal species, they don't attract a lot of attention unless they are particularly virulent or deadly," said Professor Emeritus Pedersen. "This COVID-19 pandemic has drawn attention to the parallels between human and veterinary medicine that hopefully will help the public understand the critical connections between human and animal health."

Pedersen has a soft spot for cats after growing up with them on his family's poultry farm. When he came to UC Davis in the 1960s, FIP was still a mysterious disease with an unknown cause that killed the majority of infected cats. Over the decades, he and other scientists discovered the feline coronavirus behind FIP but finding a vaccine or an effective treatment proved difficult. That's where Pedersen poured his research endeavors—finding a cure for FIP.

Dr. Brian Murphy joined the UC Davis faculty in 2007 and after Pedersen semi-retired in 2010, took over the feline coronavirus program. Murphy was first author on the groundbreaking 2018 article in *Veterinary Microbiology* showing GS-441524 had been successful in curing all 10 FIP-infected cats in a small study. A follow-up field trial of 31 cats had a high success rate as well.

These study results seemed to herald the breakthrough that Pedersen had been seeking for decades. But for desperate pet owners seeking a cure, obtaining this new drug would prove elusive. Gilead, the biopharmaceutical company that developed GS-441524, withheld the rights for its use in animals because it might interfere with FDA approval for a prodrug form called remdesivir. The hope is that remdesivir will be approved by the FDA for general use in human viral diseases like COVID-19, thus paving the way for approval and legal use of GS-441524 for animals by veterinarians.

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A Message from THE DIRECTOR

The world has definitely changed since I last wrote. When our spring newsletter went out, the country was just beginning to feel the impact of so many things—the ongoing pandemic along with a greater realization of our nation's social and racial inequities. While it is not easy, we have all had to adjust how we live and work. Perhaps now more than ever we recognize the importance of family, including our companion animals.

Health and wellbeing of our companion animals is at the core and heart of what we do. It is what drives us. It is a point of unity that we can all agree on and fight for.

We have learned to adjust at the <u>CCAH</u>. For our administrative staff, it means working remotely as much as possible. For our researchers, it means changing how labs operate to increase safety, and in some cases shifting project priorities.

While <u>clinical trials</u> were impacted during the early days of the pandemic with decreased hospital functioning, many are open again and new ones are starting. We have also funded, with your generous support, several studies that directly address the impact the virus has on dogs and cats by looking at exposures. Thankfully, so far it appears that there is little risk to them, even while the virus has been so devastating for people. We are also working harder than ever to find treatments for the coronavirus of cats, FIP, that kills so many of our feline friends.

We also have to keep in mind that COVID-19 hasn't stopped other diseases from impacting the lives of our companion animals and research on them remains vitally important. This is why we at the CCAH are moving forward with our research to bring better treatments to the clinic and hope you will work with us, so that together we will continue to make this world a healthier and happier place.

Stay well, stay safe and my best,

Michael put

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

A Legacy of LOVING ANIMALS

aidee Stade had a passion for animals—especially dogs. She helped many homeless animals by volunteering at her local Society for the Prevention of Cruelty to Animals. While she passed away in 2014, her commitment to animals lives on through a legacy gift to the Center for Companion Animal Health (CCAH).

Stade enjoyed the companionship of several dogs during her life. A friend remembers her sitting in the sunny alcove of her San Francisco Bay Area home surrounded by adoring canines. Most recently, Stade shared a special bond with Coco, a Maltese mix rescue, and considered her like a child. They did everything together. One of their favorite activities was going for walks several times a day and making new friends along the way. They were well loved in their neighborhood.

Carrying out Stade's wishes, estate trustee Katie Rodden was determined to find an organization that shared Stade's dedication to improving animal lives. Rodden learned about the CCAH from a friend. After visiting the school and being impressed with the compassionate care that all patients receive, Rodden was convinced that supporting the CCAH was a fitting tribute to Stade's legacy of improving the lives of companion animals.

"This gift would have meant so much to Haidee," Rodden said. "She was an avid animal lover all her life and was drawn to helping them. She didn't like to see animals suffer."

MAKING STRIDES with Evidence-Based Medicine

Dogs and cats treated for gait abnormalities caused by injury or disease just "got a leg up" with a new piece of equipment aimed at better analyzing their stride pattern. Thanks to CCAH funding, the school recently acquired a Tekscan Strideway pressure walkway that allows clinicians and researchers to better gauge a patient's step pattern, and make decisions about their optimal care and recovery.

To fully understand a patient's gait abnormalities associated with leg, neck, or back injuries, musculoskeletal and neurologic diseases, or gait abnormalities, veterinarians and researchers rely on objective, quantitative ways to assess locomotor function. The Strideway system complements the force plates in the school's J.D. Wheat Veterinary Orthopedic Research Laboratory (VORL), which captures extensive information, but only for one gait step. The new pressure walkway expands the capabilities to quantify pressure, vertical force, and stride parameters (timing and spacing) on all limbs for several strides during walking, trotting or landing. The system also expands a clinician's ability to assess neurologic and muscular gait deficits and can be used on a wider range of animal sizes.

"This equipment is incredibly helpful for our multi-user laboratory



Veterinarians use the pressure walkway to analyze the gait of Rufus, a patient in Dr. Beverly Sturges' spina bifida clinical trial.

to support scientifically rigorous research for our faculty, residents, and students, as well as engaging collaborators across campus to facilitate our academic environment," said Dr. Sue Stover, director of VORL.

The system quantifies functional gait abnormalities in muscle, nerve, bone, and joint diseases, and captures data to inform evidence-based medical recommendations for treatments. The system is already in use for several clinical trials and research projects. The Strideway system provides key outcome measures for Dr. Beverly Sturges' clinical trial on bulldogs with spina bifida in conjunction with physicians and researchers at the School of Medicine. In addition, gait abnormalities are being quantified in a muscle disorder, myasthenia gravis, in dogs. The system will also be used for cat and small dog orthopedic studies, evaluation of tumor treatments, and assessment of other clinical trial outcomes.

Beyond assisting clinicians, the multi-purpose walkway will benefit residents, graduate students, and DVM students who incorporate evidenced-based research into their training.

The CCAH supports research to improve the health of companion animals in a range of areas, including cancer, genetics, anesthesia, behavior, surgery and nutrition. Completed studies have led to innovative treatments and therapy options, better understanding of disease and genetic defects, and new knowledge for improved animal health.

"Ms. Stade's gift is a wonderful tribute to her generosity and kindness to all creatures and will make a difference for countless companion animals for many decades to come," said CCAH Director Michael Kent. "We are sincerely grateful to her. By funding critical health research, she will help beloved animal companions like Coco enjoy healthier and longer lives."



Coco, Haidee Stade's companion and friend, was one of several dogs to touch her life and inspire her love of animals.

Dogs and Cats Examined for Exposure to SARS-COV-2

While it is rare, we now know that our pets can contract COVID-19. The USDA has documented nearly three dozen animals (dogs, cats, lions, tigers) who tested positive in the U.S. All have had contact with COVID-positive human owners in their households, or caretakers. However, it is unclear if more animals are infected but are asymptomatic.

To better understand how widespread exposure is, researchers need to know what percentage of animals have been in contact with the virus. A team of UC Davis School of

Medicine researchers—including Drs. Stefan Keller, Tracey Goldstein, Jane Sykes and Danielle Carrade Holt—are examining exposure prevalence of dogs and cats to SARS-CoV-2, the virus that causes COVID-19, as well as to other coronaviruses that infect animals and humans. In February, they started saving blood samples from dogs and cats brought to the UC Davis veterinary hospital for treatment. To date, they have saved more than 4,000 samples and will continue saving them through 2020.

"We know that cats can show clinical signs, but most dogs don't show signs of illness," said Goldstein. "So far we know it's reverse zoonosis, meaning animals are not



Researchers hope to discover the prevalence of animals exposed to the SARS-CoV-2 virus.

the source infection—exposure is from their infected humans."

Since it is difficult to detect a virus by traditional PCR testing in animals, as we don't know when exposure may have occurred, researchers will be looking for antibodies in the animals' blood—an immune response to the virus.

"We know from experimental studies that dogs and cats can be infected, and cats can transmit the virus to other cats, but we don't know how relevant that is in a natural setting," Keller said. "Our goal is to get an idea of how common exposure is in dogs and cats under real-life conditions."

In addition to assessing exposure to SARS-CoV-2, the researchers will also look for antibodies to other human and animal coronaviruses to get a more complete picture of the coronavirus types and frequency of circulation within and between species.

Funding for this study was made possible by the efforts of Dr. Michael Kent, director of CCAH, to fast track the grant approval.

"The pace of COVID-19 research is incredibly fast," Keller said. "The fact that the CCAH reviewed our proposal immediately and granted us funding promptly allowed us to jump-start this project. It is special to have an intramural funding organization that can respond to situations such as this one, and we are grateful to be backed by the CCAH."

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"It's very frustrating because we were faced with having this huge discovery, a great discovery," Pedersen told ABC News in June. "We had a drug that could safely and effectively cure most cats with FIP. This was a dream of 50 years."

The UC Davis team has switched focus to testing a viral protease inhibitor, GC376, which they also found to be effective in curing cats of FIP. That drug is licensed by Anivive, which is pursuing FDA approval to use the drug in cats. A clinical trial is slated to begin at UC Davis later this year.

In the meantime, desperate cat owners are obtaining knock-offs of GS-441524 on the black market and sharing information about how to get and use the drug on the FIP Warriors Facebook page. While it is illegal for veterinarians to administer the drug, many owners report success in saving their cats' lives with the unapproved product. "It's a tough position for cat lovers trying to save their pet," Murphy said. "We've shown that we can cure FIP although some forms of the disease are more difficult to treat than others. We are now working on a combined therapy approach for these more difficult to treat patients. The challenge is to get approved, affordable and effective drugs in the hands of veterinarians to save more lives."

Generous donors to the CCAH helped fund safety and efficacy studies of GS-441524 and GC376 at UC Davis. CCAH funding also supported Murphy's graduate student, Sarah Cook, as well as student research assistant, Diego Castillo, for two years. CCAH covered a portion of equipment needs and through a faculty grant, will fund the upcoming clinical trials. Additional funding came from Kansas State University, the State of Kansas, Winn Feline Health, Save Our Cats and Kittens from FIP, Morris Animal Foundation, and many individual cat lovers. The team is also grateful for the initial help provided by Gilead Sciences, Inc., that allowed for laboratory and field studies involving their antiviral compounds, including GS-441524.

Leading THROUGH CRISIS

When the state of California ordered people to shelter in place on March 20, 2020, animal shelters across the state, and soon the nation, were left in a crunch. Despite being deemed essential, staffing infrastructure is not in place to weather such a storm at most welfare organizations.

In truth, many municipal shelters struggle to meet the personnel headcount required to perform essential duties in the best of times; one positive COVID-19 test, resulting in a mandatory quarantine for remaining staff, could shut down the building and render the shelter unable to serve their community in crisis. Standard safeguarding tactics, such as working in teams and splitting shifts, is simply out of reach for many of these already lean-staffed organizations.

Luckily, two years ago, the UC Davis Koret Shelter Medicine Program (KSMP) began investing in a more scalable, online approach to shelter consultations and information sharing, a decision that enabled the small program to hit the ground running in the face of crisis. Coupled with the popular resource library housed on the website, KSMP's online infrastructure and teaching modules were immediately repurposed to guide the sheltering community through the pandemic. In collaboration with a handful of other national organizations, KSMP developed protocols online to help shelters pivot their most essential programs-such as foster care and adoption-reducing the touchpoints for frontline staff and enabling them to reserve contact, and limited PPE, for emergencies and animal drop off and pick up.

To meet the demands of increased website traffic and rapidly changing content, KSMP expanded their online suite to include a portal that houses the most recent and thoroughly-vetted COVID-specific recommendations in quick, digestible modules that allow directors to stay fresh on the newest information without getting bogged down in the overwhelming amount of content being served up daily. Additionally, the expanded portal includes an online community platform that allows shelters to share and connect in groups and forums that are specific to region, topic or type. A calendar helps track the daily webinars and trainings being offered by dozens of organizations. Within weeks of launching, the portal was already serving nearly 1,000 shelter leaders who are enrolled in learning modules and sharing resources with other shelters across the nation.

A few weeks after the shelter-inplace order was issued, KSMP was already shifting gears from developing and disseminating protocols to launching the California Animal Shelter COVID Action Response— a group whose purpose is spelled out in its tagline: "Driving change together." Shelters from across the state joined weekly Zoom calls to learn about the latest guidance, tools for



implementation, and to get a weekly dose of community support.

Topics included everything from resilience in the face of budget cuts, telemedicine, virtual adoption tactics, leveraging online software, diversity, equity and inclusion and, most recently, expanding surrender prevention programs (e.g., food pantries, emergency foster placements and kitten kits) in preparation for the largest wave of the housing and economic crisis to hit.

While this pandemic has created new challenges for shelter operations, it has opened further opportunities for online collaborations to save more lives of animals in shelters.

A Bright Spot

We have reported on the life-saving benefits of installing cage portals in issues past. After nearly half of animals in shelters were able to be evacuated thanks to foster care assistance during this pandemic, KSMP and the Million Cat Challenge spotted an opportunity to install these cage-joining doors in shelters across North America. Portalmania2020 was launched and, within weeks, pet-loving organizations were stepping up to help. Over \$100,000 was raised and 3,400 portals were

awarded to 120 shelters nationwide. The campaign provided a muchneeded bright spot in a time of darkness. Interested in helping? Please visit: <u>www.millioncatchallenge.org/get-involved/portalmania-2020</u>

COMPASSIONATE CARE Inspires Research

Dr. Tommaso Rosati came to UC Davis for his residency in small animal emergency and critical care because of its outstanding reputation for research as well as clinical expertise. But he could not have anticipated the level of compassionate care he found here and became involved with during the aftermath of the Camp Fire in 2018.

"People treat animals like family here," said Rosati, who grew up in Florence, Italy. "I was extremely impressed with the quick turnaround to treat all animals coming in from the fires who needed a high level of care."

Rosati developed a special bond in particular with Mr. Banana, one of more than 70 cats brought to the veterinary hospital in the fire's aftermath. The months of caring for him taught Rosati a lot about giving patients the best opportunities and pushing the boundaries of veterinary medicine.

The desire to provide optimal outcomes for patients also drove Rosati to undertake a research project with the help of a CCAH resident grant to evaluate the best way to determine a cat's response to Clopidogrel, a drug used to stop blood clots from forming.

In cats with hypertrophic cardiomyopathy (HCM), Rosati explained, they can develop large clots in their femoral arteries and lose function of their back legs. The only way to prevent this is to stop clots forming in the heart, so this drug is often prescribed. The problem with Clopidogrel is that is has an intrinsic resistance; approximately 15 percent of cats don't respond to this treatment.

"The current standard of care is to administer Clopidogrel to cats with HCM and cross fingers they are in the 85 percent category of those who respond to the drug," Rosati said. "We wanted to evaluate various methods of determining if a cat was responding appropriately to the medication, so we can better treat those cats with HCM."

Rosati and other clinicians working with the CCAH evaluated three different devices to monitor responses to Clopidogrel in 31 cats enrolled in the study: a novel viscoelastic test (Viscoelastic Coagulation Monitor, VCM), thromboelastography (TEG) and light transmission aggregometry (LTA). Currently, the LTA is the standard way of measuring effectiveness, but it's a sophisticated machine and most clinics don't have access to it. TEG has been around more than a decade, but the technology is not yet available to small clinics and requires special handling. The newest technology, VCM, is a portable machine developed for human battlefield applications.

"We were hoping this new VCM technology would provide a more widely available and affordable test for cats with HCM," Rosati said. "Unfortunately, the results did not support that. LTA still provides the most reliable results."

The research still provides valuable information for clinicians, Rosati said, because it indicates they should continue to look for more accessible technology and helps raise awareness of Clopidogrel resistance. That's helpful for veterinarians to know if a feline patient still exhibits symptoms that indicate a need to change medications or the dosage.

Rosati completed his residency this past summer and has just taken his board examinations. He is now returning to Europe to look for an academic position where he can teach as well as treat.

> "I look forward to having my own resident someday to transmit what I've learned," Rosati said. "I received a lot of one-on-one mentorship at UC Davis to ensure excellent understanding of physiology and organism function. I want to pass that passion on to others."

> > Dr. Karl Jandrey (left) served as one of Dr. Tommaso Rosati's mentors during his residency at UC Davis.



Friends of Companion Animals HONOR ROLL

Thank you for making a difference for our animal companions! 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 companion animal we treat—is thanks to friends like you. With your partnership, we advance the knowledge and treatment options for improved companion animal health. We are pleased to recognize donors who contributed \$1,000 or more to the Center for Companion Animal Health from period July 1, 2019 to June 30, 2020.

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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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HIGHLIGHTS of Donor-Funded CCAH Research Studies

Here are a few of the 30 research projects we recently funded through your generous support:

- New treatments for epilepsy in dogs, lymphoma in dogs and decreased blood pressure in cats undergoing anesthesia.
- Studies to better understand disease including blood clotting in cats, fatty acids in food, leptospirosis in cats, FIP in cats, wildfire burns in cats and brain tumors in dogs.

With your help we will continue to find ways to improve animal health and welfare.

Center for Companion Animal Health

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