UC DAVIS
VETERINARY MEDICINE

CCAH UPDATE

FALL 2024

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Preventing Deadly FIP in Cats

Feline infectious peritonitis (FIP) is a devastating disease caused by feline coronavirus. Assistant Professor Terza Brostoff and a team of UC Davis infectious disease and biomedical engineering professionals have spent the past three years creating a vaccine to prevent the often fatal condition in young cats.

In early 2021, during the height of the COVID-19 pandemic when multiple mRNA coronavirus vaccines were being developed in human medicine, laboratory technician Hongwei Liu had the idea that the same techniques could be applied to developing an FIP vaccine. Liu has spent 20 years in molecular biology, virology, and immunology and was a laboratory technician in Dr. Niels Pedersen's groundbreaking FIP research. She approached Professor Patricia Pesavento about developing an mRNA vaccine for FIP who quickly helped pull together a multidisciplinary team.

With a background in infectious disease and vaccine development, Brostoff was chosen by Pesavento to lead the project. Joining them were Simon Anthony, Lark Coffey, Kenneth Jackson and Hannah Savage from the School of Veterinary Medicine; Joseph Dutra, Justin Fontaine, and Dennis Hartigan-O'Connor from the School of Medicine; and Randy Carney from the Department of Biomedical Engineering.

See FIP in Cats on page 4

From the Director

Research drives innovation. In reading this issue, you will see how your donations to the CCAH impact critical research discoveries. The cover story details our continued work to develop an FIP vaccine for cats. This is an amazing on-going collaborative effort to take what was learned from the human coronavirus pandemic and apply it to our feline companions.

This dovetails with one of our new grants that supports Dr. Krystal Reagan and her team in starting a new drug trial to treat FIP. Stay tuned in future issues for more on that! None of this would be possible without the ground breaking work of our Center's founder, Dr. Niels Pedersen, and our partnership with SOCK-FIP, including the recent Wolfe Estate gift (described in our last issue.)

There are two more stories that I want to highlight: a new TMJ replacement developed by a team lead by Dr. Boaz Arzi, and the work of Dr. Carrie Palm and her team in using a minimally invasive procedure to remove kidney stones in dogs.

Finally, we get to honor one of our own in this issue. Dr. Kate Hurley, who runs our Shelter Medicine program, was recognized with the school's highest honor for its graduates—the Alumni Achievement Award. She has built our life-saving program from the ground up and influenced shelter medicine across the world. I am in awe of all that she has and continues to accomplish—locally, statewide, nationally and globally. She has literally helped save millions of the most vulnerable dogs and cats.

Without you we can't continue to innovate, so thank you again for all you do for animals and helping us achieve our mission of improving animal health!

My best,

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

Dr. Palm and team performing a minimally invasive percutaneous kidney stone removal.

Stone Removal Now
SAFER, MORE EFFICIENT

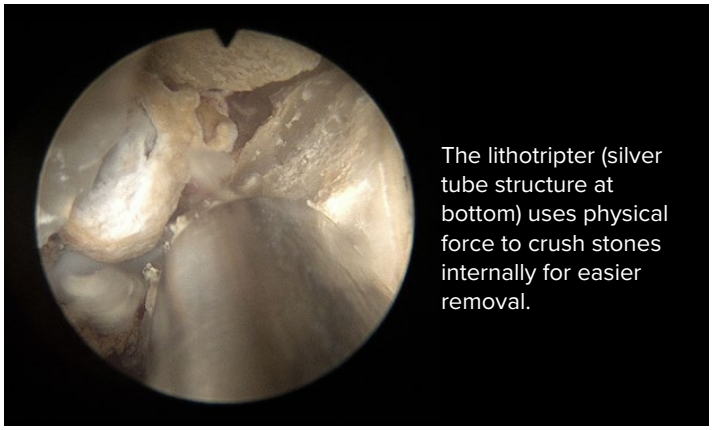
Historically, veterinary surgeons rarely removed kidney stones in dogs, largely due to procedure risks. In humans, these stones are commonly removed through advanced minimally invasive techniques. Those procedures are now available to veterinary patients at UC Davis, thanks to an anonymous gift to the Center for Companion Animal Health.

The generous gift, earmarked specifically for large breed canine equipment, allowed the CCAH to purchase a Boston Scientific Swiss LithoClast® Trilogy Lithotripter. In addition to kidney stones, this equipment can remove bladder stones in large dogs.

Urolithiasis, or stones in the urinary tract, occur commonly in dogs and can lead to life-threatening consequences if not treated or removed. Smaller stones in the lower urinary tract can be removed using laser lithotripsy, which breaks up the stones so that fragments can be removed minimally invasively. However, this technique does not work effectively on larger stones in the upper urinary tract (kidneys) or for a large number of bladder stones.

In the past, invasive surgical removal of larger stones by opening a dog's kidney was the accepted treatment protocol but was associated with high morbidity rates. Given this, even when stones caused significant problems, such as urine flow obstruction or chronic infections, it was very rare to remove the stones. This new device can be inserted minimally invasively through the skin (percutaneous) and into the kidney where stones can be broken up into small pieces using a combination of ultrasonic (mechanical vibrations) and ballistic (jackhammering inflexible stones) energy. The lithotripter can then suction up the stone fragments to remove them from the patient.

Following the procedure, a small stent is placed into the urinary tract to prevent stone fragments from blocking the ureter (tube that carries urine from the kidney to the ureter). When the procedure goes smoothly, this minimally invasive technique often allows the patient to return home the following day.



The lithotripter (silver tube structure at bottom) uses physical force to crush stones internally for easier removal.

Ella had kidney stones broken down and removed during a minimally invasive procedure using the new lithotripter. The technology used a combination of jackhammer-like force and ultrasound energy to break down the stones before suctioning and removing the remaining small fragments.

Dr. Carrie Palm and a team of surgical and internal medicine specialists recently performed the first known minimally invasive percutaneous kidney stone removal in Ella, a 7-year-old female spayed Briard using the new equipment. After a successful procedure in a large canine patient, the team has also removed kidney stones in two smaller dogs with a modified percutaneous technique. Palm has now presented her finding at a scientific meeting to introduce the technique beyond UC Davis.

"We are so thankful to have the generous support of compassionate donors that allow us to provide relief for our patients in a safe, efficient manner," Palm said.

With support of the UC Davis School of Medicine Urology Service, the school is uniquely positioned to lead research efforts with this equipment to further advance veterinary medicine. In addition to the huge benefit to patient care, this device has tremendous research potential, including projects focusing on minimally invasive treatment of different stone types in multiple anatomical locations and in numerous species.

FIP in Cats

from page 1

Funding was acquired from the Center for Companion Animal Health, SOCK-FIP, and the Morris Animal Foundation.

Developing a vaccine depends greatly on overall knowledge of a pathogen to determine what type of vaccine will be most effective. The team studied the development of COVID-19 mRNA vaccines and the strategies used to ensure they were successful at mounting an immune response. With that knowledge base, the research team began to adapt the process for kittens.

> **"This is a new platform that's never been tried in cats. There have been very few studies on mRNA vaccines in animals intended for animals."**
>
> – Dr. Terza Brostoff, Assistant Professor

While a USDA-approved vaccine for FIP was developed nearly 40 years ago, it is not recommended due to the potential for antibody-dependent enhancement (ADE) later seen in immunized cats, worsening the effects of the disease. Brostoff set out to create a vaccine based on a completely different platform and strategy.

"This is a new platform that's never been tried in cats," Brostoff said. "There have been very few studies on mRNA vaccines in animals intended for animals."

All coronaviruses have four structural proteins—three on the surface of the virus and one present on the inside of the virus. ADE occurs when the vaccine directs the immune system to target viral surface proteins which paradoxically enhance disease.

"A new vaccine cannot get around the antibody dependent enhancement question if we continue to use an mRNA vaccine where it is directed at one of the surface proteins," said Brostoff.

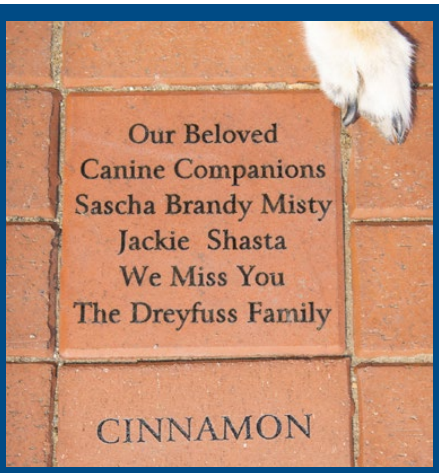
After three years of research and development, Brostoff and her team have successfully created an mRNA vaccine that targets structural proteins inside the virus and does not cause ADE.

Many kittens in high population situations, like shelters, become infected with the coronavirus that causes FIP. Most will only sustain minor gastrointestinal (GI) illness and recover. A few, however, will not clear the virus before it becomes FIP.

"Our hope is that if we can vaccinate kittens before, or soon after, they've already been infected with the GI tract form of coronavirus, that they're going to be able to make an immune response that allows them to get rid of the virus before the switch to FIP happens," said Brostoff. "The ADE concern has been eliminated by not targeting the surface proteins on the virus."

Most kittens begin receiving vaccinations by 6-8 weeks of age. The switch to FIP generally does not occur until 6 months to 2 years of age. If kittens receive this new FIP vaccine during the beginning immunization stage, they should be properly protected against the disease.

The team recently published the research and development results in the medical journal, *Vaccines*. They have filed a patent for the vaccine, and are seeking funding for initial clinical studies in kittens.



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Dedication to Advancing CANINE HEALTH

Dr. Harriet Benson and her beloved canine companion Buster.

Dr. Harriet Benson, a lifelong enthusiast of the Dachshund breed, has had nine of these lovable dogs over the years, including 14-year-old Bandit and 11-year-old Buster.

Benson described her Dachshunds as having terrific personalities, each with endearing qualities. Bandit is a selective, slow eater and less social than Buster, who is affectionate and independent. One of their favorite activities is riding in the car.

“I have enjoyed the companionship of both smooth and long-haired doxies, like Bandit and Buster,” Benson said. “They have all brought me lots of joy. I can’t imagine life without having one.”

Benson first learned about the CCAH when her veterinarian, Dr. Williams L. Klein, from the Village Square Veterinary Hospital made a meaningful gift to the center’s Companion Animal Memorial Fund in memory of her beloved Dachshund Monte, who passed away from a mast cell tumor. Donations to this fund make significant impact supporting clinical health research to improve treatment for diseases affecting companion animals.

After learning about the CCAH and its mission, Benson herself became inspired to support its work since 2004, including a planned gift to advance canine health research.

“We are tremendously grateful to Dr. Benson for her dedicated partnership and honored by her support of our work to make the lives of animals better, healthier and longer.”

– Dr. Michael Kent, CCAH Director

“I am especially interested in research that will benefit cherished dogs like my Bandit and Buster,” Benson said. “I recognize that science and research are key to advancing companion animal health and make breakthroughs possible.”

“We are tremendously grateful to Dr. Benson for her dedicated partnership and honored by her support of our work to make the lives of animals better, healthier and longer,” said CCAH Director Michael Kent.

The CCAH supports research to improve the health of companion dogs in a range of areas, including anesthesia, behavior, nutrition, oncology and surgery. Completed studies have led to new treatments and therapy options, better understanding of disease and genetic defects, and knowledge leading to advancements in canine health.

Drs. Brian Leonard and Sangwan Park examine a dog's cornea.

IMPROVING Dry Eye Disease

When Dr. Sangwan Park first came to UC Davis in 2019 as a post doctorate in Ophthalmology, she was immediately impressed with the combination approach of research with clinical practice to identify new diseases and monitor disease progressions.

"There aren't many institutions that allow trainees to do both research and clinical training—I could do that here, so I knew I wanted to stay and pursue my residency training," said Park, who received her DVM ('12) and Ph.D. ('18) degrees at Seoul National University.

Park joined the Vision Science Lab led by Drs. Brian Leonard and Sara Thomasy and has been working to improve outcomes in canine patients with dry eye disease. In a study, "Investigation of meibomian gland dysfunction in dogs using ocular surface and tear film imaging," she developed a new method to quantitatively assess meibomian gland function.

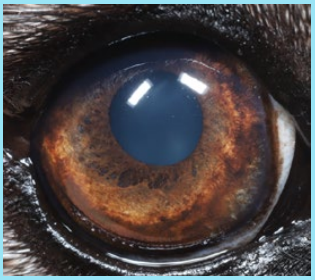
Meibomian glands are located along the edge of the eyelids and secrete oil to coat the eye's surface and help keep tears from evaporating. That protects eyes from infection and keeps them healthy. Meibomian gland dysfunction is the most common cause of dry eye disease for humans and although it is common in older dogs, very few studies have previously evaluated this condition in canines.

"Being able to quantitatively assess the lipids of the tear film and the glands that make those lipids will help us diagnose and quantify changes so we can track patients and disease progression," Leonard said. "With newly developed therapies, we can also track their improvements."

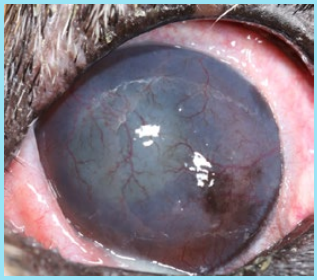
> **"There aren't many institutions that allow trainees to do both research and clinical training—I could do that here, so I knew I wanted to stay and pursue my residency training."**
>
> – Dr. Sangwan Park

Upcoming Clinical Trial

1. Age: Greater than 7 years of age
2. Breed: any breed
3. Clinical Signs: unilateral or bilateral clinical signs of EDED (mucoid to mucopurulent discharge, conjunctival hyperemia/chemosis, evidence of keratitis)
4. Diagnostics:
   a. Tear film breakup time (TFBUT) of < 6.3 s (two standard deviations lower than control animals in prior study)
   b. Schirmer tear test I (STT-I) value of > 10 mm/min
5. Only dogs identified as EDED will be included in this treatment study.



Normal ocular surface in dogs



Typical ocular surface appearance for tear deficiency in dogs

"If we're successful in canine patients with spontaneous disease, that improves the positive predictive value of moving forward into human clinical trials."

– Dr. Brian Leonard

The UC Davis group is the only comparative ophthalmology research team in the U.S. actively investigating tear film disorders. They are starting a clinical trial with a novel lipid therapy to replace the lipids that are missing in a dog's tear film. Other team members include postdoctoral fellow Nayone Araujo, 2nd year Ophthalmology resident Erinn Mills, DVM/Ph.D. student Erin Hisey, and DVM student Brian Puentes.

"If we're successful in canine patients with spontaneous disease, that improves the positive predictive value of moving forward into human clinical trials," Leonard said. "If it works in the dog, there's a really good chance it will work in humans, and we expect to see improvements in tear film stability in both canine and human patients."

The project has been funded by a CCAH grant with additional support from the American Kennel Club and Canine Health Foundation. The team also received a CCAH equipment grant for a Tear Scope (Ocular Surface Analyzer) they can use to quantitatively assess the lipids of tear film and the glands that make them.

"We really value the team approach at Davis—without it, you can't accomplish these audacious goals," Leonard said.

Park said she's grateful to contribute a better understanding of this poorly known condition and improve treatment for their patients.

HIGHLIGHTS

OF DONOR-FUNDED CCAH RESEARCH STUDIES

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

- Stem cell research to study canine dilated cardiomyopathy
- Developing a novel diagnostic test for feline infectious peritonitis (FIP)
- Using Artificial Intelligence (AI) for more accurate diagnosis of intestinal disease in cats
- Evaluating how two commonly used drugs effect the heart rhythm of dogs being treated for ventricular arrhythmias
- Developing an immunotherapy to overcome immunotherapy resistance in canine high-grade gliomas

Reassessing Vitamin B6 Needs IN AGING CATS

Researchers Drs. Cecilia Giulivi (left) and Jennifer Larsen with Mango.

In all animals—cats included—B vitamins play an important role in optimal health, especially as they age. These minerals aid in the proper utilization of protein and synthesis of neurotransmitters. With insufficient B vitamins, your feline companion may suffer fatigue, weakness, nausea, digestive issues, nerve issues, skin infections, and anemia. But how much should they be getting in their daily diet?

UC Davis researchers Cecilia Giulivi, Andrea Fascetti and Jennifer Larsen set out to answer that by assessing Vit B6 at the molecular level in cats. They collected blood samples and conducted biochemistry tests on two feline populations: a cohort of 60 healthy cats maintained under strictly controlled conditions and fed a balanced diet at the Feline Nutrition and Pet Care Center, and a cohort of 57 cats randomly selected between December 2022 to January 2023 that visited the Veterinary Medicine Teaching Hospital to seek care under different circumstances.

In a study published in *Scientific Reports*, they identified 17% of the cats as vitamin B6 deficient, which was slightly surprising to them since the cats didn't show clinical signs of deficiency. Key associated factors were the diagnosis of an infectious, chronic or acute condition, followed by age and body condition score.

"Because these deficiencies are not associated with obvious symptoms, cats who may need more vitamin B6 are not being treated or diagnosed," said Larsen, chief of the veterinary hospital's Nutrition Service. "This study suggests we need to adjust the nutritional requirement for B6 based on age."

The study also supports that vitamin B6 supplementation may be indicated in junior to adult animals diagnosed with an infectious, chronic, or acute conditions or healthy cats with body weight ranging from optimal to overweight.

Giulivi, a molecular biochemist and molecular biologist, was interested in assessing concentrations of vitamin B6 through a functional biomarker. She said the approach used in this study for cats sets the groundwork for similar studies in different species, including humans.

"If the same is happening—and it is happening—in humans as they age, then we can't say the requirement for this vitamin is the same for us in our 60s or 70s as it was in our teens," Giulivi said. "So maybe we need to go back and recalculate

"As we seek to prolong the health span of our feline companions, we want to keep them as healthy as possible, and this study suggests that appropriate levels of B6 play a role in that."

– Dr. Jennifer Larsen

the reference values normalized by age and sex as the identified deficiencies were subclinical with an uncertain impact on their health with time."

Larsen pointed out that nutritional deficiencies can be impacted by many different things—how long has the diet been deficient in this vitamin, how low is the amount, is there a genetic component, is there a physiological change that increases or decreases the requirement such as pregnancy or disease?

"We haven't previously defined whether a cat's need for vitamin B6 increases with age," Larsen said. "But as we seek to prolong the health span of our feline companions, we want to keep them as healthy as possible, and this study suggests that appropriate levels of B6 play a role in that."

Other researchers involved in the CCAH donor-funded study include: DVM student Vy Chu (through the Students Training in Advanced Research program), and Maria Montano.

Dr. Kate Hurley Honored with ALUMNI ACHIEVEMENT AWARD

When Dr. Kate Hurley first donned the uniform of a California State Humane Officer for the Santa Cruz SPCA in 1989, only about 1 of 4 cats left the shelter alive. A single sneeze or cough was a death sentence. Six years later, Hurley enrolled in veterinary school with a desire to change those odds.

Graduating in 1999 was just the beginning. That year, more than 25,000 animals were euthanized in shelters within thirty minutes of UC Davis, surpassing the entire small animal caseload of the veterinary teaching hospital.

Hurley knew professionals responsible for shelter-housed animals needed a home for credible, evidence-based information to keep more of those animals alive. She returned to UC Davis to earn her Master of Preventive Veterinary Medicine in 2003, becoming the world's first Shelter Medicine resident, and beginning the journey of bridging that gap. She then took over the Center's Shelter Medicine Program, which she heads to this day.

Hurley prioritized getting lifesaving information to those doing the work. She co-published www.sheltermedicine.com, the first animal shelter guidelines and still the most widely used authoritative repository of free shelter expertise, leveling up the standard of care for all.

To secure a foothold for future generations of veterinarians dedicated to improving the lives of animals in shelters, Kate trained the first four residents in Shelter Medicine and served as chair of the organizing committee for a new specialty in Shelter Medicine Practice through the American Board of Veterinary Practitioners. Today we celebrate more than 35 boarded specialists!

By 2012, Hurley was ready to go from moment to movement. Together with Dr. Julie Levy (University of Florida), they launched the Million Cat Challenge—the world's largest feline lifesaving initiative. The challenge is responsible for more than 5.3M (and counting!) lives saved. Most recently, Hurley's program at the Center was awarded $50 million in funding for California animal shelters, an unprecedented move by Governor Gavin Newsom to support the paradigm shift in sheltering.

Many are familiar with the phrase "Be the change you wish to see in the world," but Hurley truly lives by that advice. Her dedication for advocating for shelter animals her entire career earned Hurley the school's esteemed Alumni Achievement Award.

In nominating Hurley for the award, Dr. Patricia Pesavento wrote: "Kate is a soft-spoken, humble, powerful, and generous colleague, who has advocated, initiated, and heralded permanent new expectations, globally, to raise every possible facet of care for sheltered animals."

"I feel so humbled by the kind words of my colleagues and this recognition of all the work that's moved shelter medicine from a twinkle in a few peoples' eyes, to a boarded specialty in veterinary medicine with a robust body of research, teaching, and practice," Hurley said. "In truth I don't think I deserve any kudos as it has been simply an honor and joy of a lifetime to be able to do this work with such amazing colleagues and friends on all sides, and of course for all the short-legged dogs, one-eyed cats, and other temporarily displaced creatures that look to us for care in the most vulnerable moments of their lives."

New Hope for TMJ DISORDERS

(l. to r.) Biomedical engineer Tanya Garcia, orthopedic surgeon Dr. Denis Marcellin-Little, and oral surgeon Dr. Boaz Arzi showcase their new TMJ replacement prothesis affixed to 3d-printed small dog (left) and cat (right) skulls.

UC Davis veterinary medicine researchers are revolutionizing treatment for pets with non-functioning temporomandibular joints (TMJ)—the joint that connects the lower jaw to the skull. Thanks to generous donations for faculty research to the Center, the team has developed a TMJ replacement prosthesis (TMJR) for cats and dogs to restore functionality that has been lost due to injury or disease.

"The only recourse we have had in the past for these animals is to remove all the affected structures in the jaw to enable opening the mouth," said Dr. Boaz Arzi, chief of the Dentistry and Oral Surgery Service. "While this allows the patient to eat and drink, there is no longer functionality to the joint, and their mouth can never close properly again."

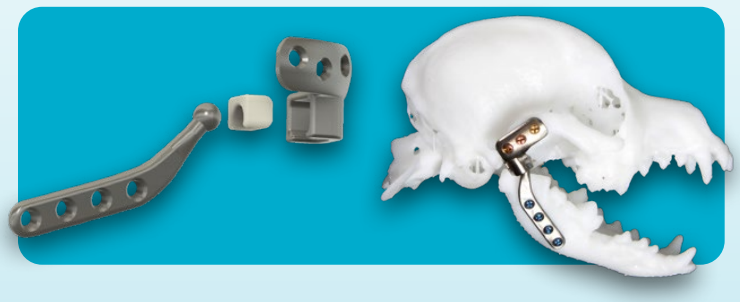
Due to an increased number of patients with fused jaws, Arzi figured there must be a better way to not only salvage the joint, but improve functionality and quality of life. He joined forces with Dr. Denis Marcellin-Little, a UC Davis veterinary orthopedic surgeon well versed in implant design and production, and Tanya Garcia, a biomedical engineer in orthopedic research.

The trio created a TMJR implant loosely based on the FDA-approved TMJR used in humans but designed with the needs of animals in mind. Their initial research was recently published in the *American Journal of Veterinary Research*, and patent pending status has been achieved on the device.

To evaluate the mechanical properties of the joint, the team tested the TMJR on dog and cat cadavers. Varying bite forces and other functions were applied to the implant to evaluate its behavior and capabilities. The implant resulted in joint motion not demonstrably different from the native TMJ, with the ability to fully open and close the mouth with stability. This led the group to conclude that a novel TMJR may be implanted into patients and allow normal jaw motion.

As the team establishes a path to clinical use, their work continues to assess the implant's strength and durability. They are currently testing "load to failure," to determine the maximum force that the joint can withstand. Following that, "fatigue testing" will take place—a process that will open and close the joint 250,000 to 500,000 times to test its longevity.

The hospital will soon begin evaluating suitable patients to be the first cases in a pre-clinical trial of the TMJR implant for compassionate use.



THANK YOU!

Friends of Companion Animal Honor Roll

Thank you for the impact you make in our companion animal's lives! We are grateful for the gifts from our many friends who are helping us continue our mission to improve animal health. We are pleased to recognize donors who contributed $1,000 or more to the Center for Companion Animal Health from July 1, 2023 to June 30, 2024.

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