



Gene Mutation for Heart Disease in Newfoundland Dogs Identified page 2

Dear Friends:

Patience and persistence. These are two words that researchers in all fields learn early in their careers—and that we at the CCAH both support and understand. While some research breakthroughs happen quickly, many are the result of work that unfolds over months, years, and even decades. Most of the time, it is only through careful, meticulous trial and error that we can unlock the causes of diseases and develop new treatments to address them.

In this issue, we tell the story of two CCAH-supported research groups that have applied both of these principles in their work with great impact. In one case, researchers recently found the genetic cause of a serious heart condition in dogs they've been studying for years. In the other, a research team figured out how to safely treat a painful disease in cats that has perplexed veterinarians for decades—leading to one of the biggest breakthroughs in veterinary medicine in recent years.

At the CCAH, we are dedicated to ensuring that researchers get the support they need to make discoveries like these that contribute new knowledge to the field—and make a vital difference in the health and well-being of companion animals. This means providing seed money to fund researchers who have the vision to tackle the most difficult problems that these animals face. Funds from our donors are used to support this groundbreaking research.

It's probably important to note that we don't fund every project we see. Rather, researchers submit proposals that are then reviewed by our Scientific Advisory Board, which is made up of experts in many fields of veterinary medicine. Together, we review each proposal to find those that hold the most promise to positively impact the lives of dogs, cats, and other companion animals. Sometimes this means taking a chance on a project that may not work—or may, as in one of the stories featured in this newsletter, lead to “an amazingly exciting moment in research.”

It's moments like this that drive the CCAH to make sure that our teams have the resources they need to move the whole field of veterinary medicine forward—one disease at a time.

My best,

Michael Kent, MAS, DVM
Director, Center for Companion Animal Health

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Gene Mutation for Heart Disease in Newfoundland Dogs Identified

Newfoundlands—those massive, furry, black dogs—have captured many a heart with their hallmark size, sweet nature, and loyalty. Unfortunately, these gentle giants' own hearts are all too often afflicted with a potentially lethal congenital disease called subvalvular aortic stenosis (SAS).

SAS is the most common inherited heart disease in dogs—but it is far more prevalent among Newfoundlands than many other breeds.

But now, thanks to a groundbreaking new study, that may be changing. Recently, a team of veterinary researchers—led by Dr. Josh Stern, DVM, chief of the UC Davis Veterinary Medical Teaching Hospital's cardiology service—discovered a genetic mutation responsible for SAS in Newfoundland dogs. This discovery has the potential to help breeders and owners eradicate this deadly disease from Newfoundland breeding lines.

What Is SAS?

Subvalvular aortic stenosis is a genetic disease that causes an abnormal ring or ridge of tissue to form below the heart's aortic valve, making it difficult for blood to be pumped out of the heart and around the body. Diagnosing and treating SAS, however, is particularly challenging because the disease can vary greatly in its severity. Dogs with the severe form are likely to die before they are 4 1/2 years old, even with therapeutic drugs. But dogs with the mild form can live a completely normal lifespan—which means they often go undiagnosed. "Unfortunately, these dogs may get bred and propagate this lesion within the population," says Dr. Stern.

Veterinarians may discover the disease when they detect a heart murmur and conduct further diagnostic tests such as chest X-rays, an echocardiogram, or an electrocardiogram. However, often the first sign that a dog has SAS may be a collapse, fainting spell, or even sudden death.



Dr. Josh Stern (left) examining a Newfoundland dog.

Finding the Mutation

The discovery of the SAS mutation in Newfoundlands did not happen overnight. Dr. Stern started collecting DNA samples from Newfoundlands a decade ago, while he was still a veterinary student at The Ohio State University. "I started looking at Newfoundland pedigrees and trying to piece together how this disease was inherited," he explains. Eventually he began to try to identify a mutation responsible for the disease.

Dr. Stern and his fellow researchers began by conducting a "whole genome" analysis, scanning thousands of genes for abnormalities.

This analysis revealed that the mutation associated with SAS resides in a gene called PICALM. This same mutation has been linked to the formation of plaque-like lesions in the brains of people with Alzheimer's disease.

Other researchers collaborating on the study were Drs. Stephen N. White of Washington State University; Linda B. Lehmkuhl of MedVet Medical and Cancer Centers for Pets; and Nanette M. Nascone-Yoder and Kathryn M. Meurs, both of North Carolina State University.

As a result of this study, there is now a DNA-based test that can be used to screen Newfoundland dogs for the mutation. "Our hope now is that breeders will be able to make informed breeding decisions and avoid breeding dogs that harbor the mutation, thus gradually eliminating the disease from the Newfoundland breed," says Dr. Stern. The test is now available through the Veterinary Genetics Laboratory at the UC Davis School of Veterinary Medicine.

The finding also has implications for the study and treatment of SAS in children, who can also be affected by the disease. Because the genetic basis of the disease in people is not yet fully understood, "knowledge of this gene may be really

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Ensuring the Future of Feline Health

Cats hold a special place in the hearts of the more 36 million households across the country that have them as pets. Understanding the unique health issues and care needs of feline companions is important to the devoted families who love them.

For more than 40 years, the UC Davis School of Veterinary Medicine has been a leader in identifying and addressing health problems in cats. Researchers and clinicians have made significant advancements in a number of areas, including infectious disease, genetics, nutrition, and cancer.

Notably, Dr. Niels Pedersen has made great strides in understanding infectious diseases through his veterinary career and is recognized as a world authority in feline health. He is particularly proud of the role of UC Davis in conquering feline leukemia virus infection, discovering and characterizing feline immunodeficiency virus, and



Dr. Niels Pedersen

better understanding feline infectious peritonitis.

While much has been accomplished, new knowledge impacting feline health is still on the horizon—such as improving diets, understanding behavioral issues and obesity, and preventing and treating diabetes and inflammatory disease. Also, genetics holds the promise of developing tests to identify, manage, or prevent certain disorders and diseases.

To ensure that innovations in feline health continue, the Feline Health Research Endowment Fund was established. This fund will provide necessary research support for future generations of veterinarians.

For more information about the Feline Health Research Endowment Fund, please contact the Office of Development at (530) 752-7024.

Gene Mutation for Heart Disease (continued from page 2)

important for researchers in human medicine,” explains Dr. Stern. “I would foresee further research looking at PICALM’s role in heart development in the future.”

The Work Continues

Dr. Stern and his fellow researchers are continuing to unravel the mysteries of PICALM in order to learn more about how the mutation works. “Finding the mutation is great,” Dr. Stern says, “but understanding how it does what it does is really the important part for us, because eventually we’d like to develop novel treatment options for those dogs that are severely affected.”

They are also studying why SAS is mild in some dogs while causing severe symptoms in others, as well as “looking feverishly” to find the mutations that cause the disease in six other breeds, says Dr. Stern. The CCAH is providing seed funding for that work—as well as other UC Davis research designed to better understand the causes and treatments for various forms of inherited heart disease.

Given how devastating these diseases can be for animals and their families, says Dr. Stern, “I think inherited heart disease is one of the most important disease types to study.”

Learn more about the SAS study and other upcoming cutting-edge cardiology research projects at UC Davis in our Q+A with Dr. Stern, posted on the CCAH website at: http://www.vetmed.ucdavis.edu/ccah/local-assets/pdfs/q_a_stern_final.pdf

Subvalvular aortic stenosis (SAS) test available

SAS test ordering, pricing, and information are available through the Veterinary Genetics Laboratory website: www.vgl.ucdavis.edu or by calling (530) 752-2211.

If your dog has been previously DNA tested you can simply add the SAS test by logging in to your MyVGL account and choosing “Add Test to Existing Sample.”

Researchers Discover Revolutionary Treatment for No. 1 Eye Problem in Cats

In early 2013, life was looking bleak for a cat named Sadiqi. “Her right eye was swollen and entirely closed, and her left eye was crusty and bloody,” explains owner LeAnne Crowell, of Washoe Valley, Nevada. Worse, they’d been like that for months. “She was so depressed, staying in her tree all day,” says Crowell. “Her quality of life was terrible.”

Like 97 percent of cats, Sadiqi has feline herpesvirus type-1, a disease that stays latent in a cat’s body for life and can cause recurrent and painful eye problems—including conjunctivitis, a condition in which the tissues of one or both eyes become inflamed or infected. According to Crowell, Sadiqi’s case was the most persistent that her veterinarian had ever seen.

Historically, no good treatment options have existed for cats with severe herpes-related eye disease. That is, until Dr. Sara Thomasy, a vision researcher in UC Davis’ Murphy-Russell Laboratory, and Dr. David Maggs, a UC Davis professor of veterinary ophthalmology, along with a team of other veterinarians, launched the first of many investigations into famciclovir, a drug used in people to treat cold sores and other diseases caused by the human versions of herpesvirus.

Their research led to one of the biggest breakthroughs in modern veterinary medicine.

Though safe for humans, famciclovir belongs to a family of drugs that have proved toxic—and even fatal—in cats.

So when Drs. Thomasy and Maggs learned that veterinary ophthalmologists around the country were starting to use the drug to treat herpes-related eye problems—yet just estimating the dose—they felt it was critical to study the drug. “These veterinarians were reporting that it was working really well,” says Dr. Thomasy. “But they were experimenting with a potentially toxic drug.”

“We had to move really slowly so that we didn’t endanger any cats’ lives,” adds Dr. Maggs.

After an initial safety study, they launched a second study looking at the drug’s efficacy. In that study, 10 cats with feline herpesvirus received famciclovir three times daily and 6 cats with the virus received a placebo.

The results were both quick and astounding. “We had six cats that were sneezing, just feeling awful, not eating, and looking terrible,” explains Dr. Thomasy. “Then we had 10 cats that were playing and looked amazing. And we saw that difference in just a few days.”

“It was an amazingly exciting moment in research,” says Dr. Maggs. “These cats were virtually normal compared to the cats on the placebo.”

As a result of their work, famciclovir has become standard treatment for a disease that has stymied veterinarians for

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On the left is a picture of what Sadiqi’s eye looked like when she presented for evaluation. On the right is Sadiqi’s eye after treatment with famciclovir, developed in part with four grants from the CCAH. Also pictured is Sadiqi happy at home.

UC Davis Veterinary Students Learn High-Quality Spay and Neuter Surgery

Thanks to donations and grants to the Koret Shelter Medicine Program

Earlier this year, veterinarian Kristi Ellis joined the UC Davis Koret Shelter Medicine Program as its first-ever shelter medicine spay and neuter instructor—a position funded by PetSmart Charities® as well as other donations and grants to the CCAH. As part of her post, Dr. Ellis coordinates student clinical rotations at the Yolo County Animal Services Shelter, where she teaches them how to perform high-quality, high-volume spay and neuter surgery.

A 2002 UC Davis Veterinary School graduate who spent the last seven years as lead veterinarian at the Oregon Humane Society in Portland, Oregon, Dr. Ellis brings deep experience with spay and neuter surgery to the program. “I love teaching and I love shelter medicine, so it’s the perfect fit for me,” says Dr. Ellis. “I also love spay and neuter—not just the procedure but getting personal satisfaction from knowing that I’m helping to solve the overpopulation problem.”

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Dr. Ellis examining a foster kitten.

New Treatment for Feline Eye Disease (continued from page 4)

decades. “It has completely revolutionized our ability to treat the most common form of conjunctivitis in cats,” says Dr. Maggs. “It has changed the way we practice veterinary medicine.”

After several courses of the drug, Sadiqi’s eyes are now clear, and she has transformed from depressed to playful. “We were lucky to live just a few hours from the leading experts on this condition,” says Crowell. “And we are grateful to have our little kitty back.”

For Drs. Maggs and Thomasy, the research continues. Because famciclovir is a very complex drug, they are continuing their work to unlock its mysteries—including finding a dosage that will be effective in 99 percent of cats. “Figuring out what dose to give is normally a simple step, but with this drug it’s been an incredibly complex step, taking us eight or nine years so far to date—and we’re still not there,” says Dr. Maggs.

Recently, the team started working with zoos—and also with a cheetah conservancy in Namibia—to look at the usefulness

of famciclovir in nondomestic cats. They are also studying herpesvirus in the shelter setting, where it remains the most common reason for the euthanasia of shelter cats. And they are looking at whether famciclovir might be used not just to treat outbreaks but to prevent them in the first place—which, if so, could revolutionize the field of veterinary ophthalmology all over again.

All of these projects stem from the CCAH’s foresight in investing in the team’s very first famciclovir study, says Dr. Maggs. “This was really ‘out there’ research when the CCAH began funding our work,” he says. “I really commend them for taking the risk.” It’s a risk that has helped thousands of cats already, and millions more to come.

Learn more about the famciclovir breakthrough and how it came about in our Q+A with Drs. Thomasy and Maggs, posted on the CCAH website at: http://www.vetmed.ucdavis.edu/ccah/local-assets/pdfs/q_a_maggs_thomasy_final.pdf

Thank You!

Friends of Companion Animals Honor Roll

We gratefully acknowledge Friends of Companion Animals members for supporting the CCAH and advancing animal health and well-being. The following benefactors contributed \$1,000 or more from July 1, 2012 through July 31, 2014, with gifts totaling over \$5.9 million.

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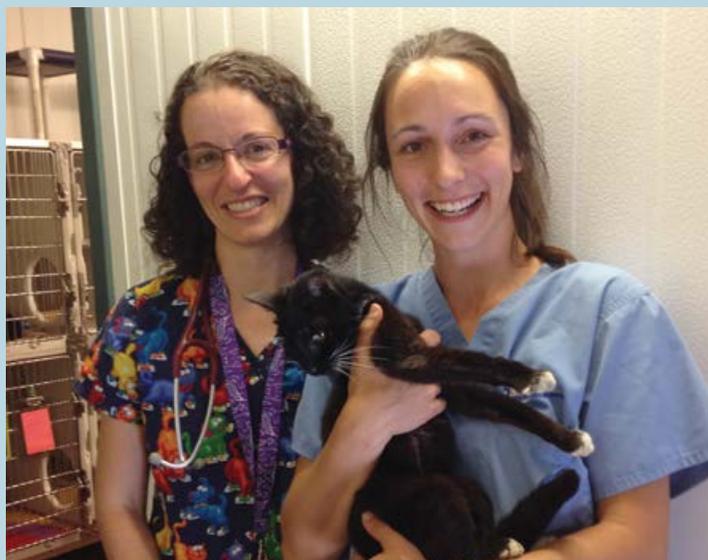
Quality Spay and Neuter Surgery

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Dr. Ellis works with up to two students at a time in the shelter's mobile surgery unit, supervising and teaching them as they assist with and perform spay and neuter surgeries. Each student does an average of 30 such surgeries, half of which are pediatric, over the one to three weeks of their rotation.

Previously, shelter medicine students studied other components of shelter medicine but were not getting surgical experience—and the hands-on experience they get now is invaluable. “The students are so excited to be here and to learn spay and neuter,” says Dr. Ellis, adding that students are also gaining a better understanding of how shelters operate and their importance. “The feedback I've gotten from students is very positive, and the shelter is enjoying having them here. So it's a win-win for everybody.”

The UC Davis Koret Shelter Medicine Program is expanding in other ways as well—adding more teaching components and increasing the number of critical research projects that its students and faculty pursue. “In this way, we are helping to improve how individual shelters work,” says CCAH director Dr. Michael Kent. “And we're ensuring that the next generation of veterinarians is trained to understand the problems shelters face—and to continue our work in this important area.”



Dr. Ellis and senior veterinary student (class of 2015) Jess Sands with a shelter cat.



Senior veterinary students performing surgery at Yolo County Animal Services.

Friends of Companion Animals Honor Roll (continued from page 6)

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CANCER CORE LABORATORY AT THE CCAH



At the CCAH we are committed to ending suffering and death caused by cancer. We are in this fight for the long haul. Through cancer specific endowments and ongoing gifts from donors we have and will continue to fund the research needed to beat this devastating and deadly disease. We understand that this is not an easy task and are committed to putting the resources and time necessary to make cancer cures a reality for companion animals and their families. This means funding research looking at the causes, mechanisms and treatment of cancer. Only by taking this three pronged, long term approach can we hope to make cancer one of those diseases that we helped to cure.



Our cancer core laboratory at the CCAH is an exciting place where translational research takes place—meaning we are taking what we learn in the lab and move it to the clinic, developing new treatments. Some of the types of cancer we are funding research projects on include lymphoma, melanoma, bladder cancer, nasal tumors and brain tumors.

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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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