Unlocking the Genetic Code to Disease

What determines your dog’s reddish coat or their long, fluffy tail? Genetics — or the study of how particular physical traits are passed from parents to offspring. This scientific field also applies to understanding disease inheritance.

Drs. Danika Bannasch and Josh Stern at the Center for Companion Animal Health approach genetic studies from several angles. Bannasch identifies mutations in an animal’s genetic code or DNA that correlate to a particular disease to develop tests that can decrease that disease incidence. Stern's approach is more clinically based as he unravels the genetic mechanism of a disease to develop novel therapies.

A recent example involved hypertrophic cardiomyopathy (HCM), a heart disease that affects 1 in 7 cats. Stern and other researchers led a clinical trial to look at how a cat’s DNA alters how it responds to clopidogrel, a commonly prescribed life-saving medication to prevent blood clots in cats with HCM. Data showed that nearly 20% of cats had resistance to the therapy.

“This study was about figuring out why some cats weren’t responding as expected to clopidogrel therapy and leading us towards a more effective prescription,” said Stern, who also serves as the chief medical officer for the UC Davis veterinary hospital. “Understanding how genetic mutations in cats reduce the effectiveness of this treatment can help us personalize medicine for them, just as physicians do for particular human diseases.”

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From the Director

As you know, our Center’s focus is to improve animal health. To do this, we take a multi-pronged approach of combining basic science, translational and clinical research. Throughout this issue we highlight some of the work you have helped fund in these areas, as well as some exciting news for shelters and a new comparative oncology training program.

The underlying genetic causes of health and disease are discussed in our cover feature on genetics with Dr. Danika Bannasch. The translation of these techniques to answer clinical questions is highlighted with Dr. Josh Stern’s work, looking to see how genetics affect whether or not a patient will respond to a particular treatment. We also help fund equipment to develop novel procedures such as the new 3D laparoscope, and the research undertaken at the J.D. Wheat Veterinary Orthopedic Research Laboratory to treat orthopedic disease with innovative techniques and tools. Our goal is to ensure that we assemble the best teams with the funding and equipment needed to achieve results.

We also recognize the necessity to engage more talented people in research. This means helping in their training. Whether it is a clinical resident who is learning to conduct a clinical research project, such as Dr. Paula Rodriguez, or the training of DVM/PhD students and postdoctoral fellows with the help of our new T32 grant, we are committed to the future of animal health research.

Again, thank you for supporting the Center and making this all possible.

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

New Pain Relief FOR BIRDS

Through research funding, CCAH provides residents many opportunities not found at other veterinary schools. Following completion of her veterinary degree at the University of Georgia, Dr. Paula Rodriguez is now a resident in the Companion Exotic Animal Medicine and Surgery Service. A CCAH grant is allowing her to conduct a research project entitled “Pharmacokinetics and safety of oral grapiprant with wildlife medicine and wanted to focus her research on ways to improve inflammatory drug for the first time in birds. Rodriguez has always been involved involved in falconry.

The pressure-sensing walkway measures weight distribution and analyzes gait patterns.

TEAMWORK Makes the Dream Work

Make no bones about it, the researchers at the UC Davis J.D. Wheat Veterinary Orthopedic Research Laboratory (VORL) are a team. They’re the first to point out that the collaborative environment, along with help from supporters like CCAH donors, are key to translating science to improved patient care.

VORL provides technical support, equipment, and training for anyone interested in musculoskeletal research. From examining new ways to repair fractures in the notoriously brittle bones of rabbits to 3-D printing canine jawbones, researchers identify situations where success rates have been less than ideal in the clinic, and work to develop solutions.

“We have a very energetic, collaborative environment where everyone works in teams,” said VORL founder Susan Stover. “That’s the part I really love.”

Named after a former UC Davis professor of equine surgery, the laboratory’s focus was initially on orthopedic research in horses. The work quickly transcended species and now covers companion animals and exotics. The technology has advanced too. The facility houses a range of systems used for clinical trials, understanding orthopedic diseases, and developing new treatments. Capabilities range from quantifying locomotion, specialized imaging, biomechanical testing, 3-dimensional modeling and manufacturing for surgical planning and artificial parts, to cell and molecular biology.

Through VORL’s more than 25 years of operation, the CCAH – and its donors – have played integral roles in its growth and sustainability. One of the original motivations for establishing VORL was to centralize specialized equipment, an area for which funding is traditionally challenging to obtain. Over the years, support from the CCAH has enabled the purchase of new equipment and software, as well as upgrades and maintenance for existing equipment.

“Without CCAH equipment funding, many of the advances that we have made would have been significantly delayed,” said orthopedic surgeon Denis Marcellin-Little.

Support from CCAH has also helped with more focused projects for junior researchers and residents, as well as proof-of-concept projects. This has a trickle-down effect, providing opportunities for undergraduates and veterinary students to participate in research.

“Most universities don’t have funding mechanisms for residents, so they depend on a faculty member to have funding for their projects,” said orthopedic surgeon Amy Kapatkin. “We have this advantage of resident training grants that enable UC Davis to jump start residents’ research careers.”

Clinical applications made possible by VORL research include novel ways to treat spinal fractures, enhanced standard of care for repairing mandible fractures, and the use of CT scans to predict the possibility of fractures and optimize treatments in dogs with osteosarcoma.

“What CCAH is doing is a tremendous boost to state-of-the-art technology,” said Marcellin-Little. “When we combine clinical knowledge with basic science, we can really push the envelope in novel ways.”
Training Future Comparative Oncologists

UC Davis is taking a major leap forward in training the next generation of scientists engaged in basic and translational cancer research for animals and humans, thanks to a prestigious National Institutes of Health (NIH) T32 grant. The grant supports institutions to develop or enhance research training opportunities for pre- and postdoctoral fellows to be trained in comparative oncology. The university has been awarded approximately $1.9M over five years for the UC Davis Comparative Oncology T32 program, which is comprised of members from the School of Veterinary Medicine, School of Medicine, and the Comprehensive Cancer Center.

“This is the first time that the UC Davis Schools of Veterinary Medicine and Medicine have been awarded this level of support for an innovative Comparative Oncology Training Program,” said CCAH Director Michael Kent, a veterinary oncologist who serves as a co-principal investigator (PI) of the program. “It signals that the NIH recognizes the importance of One Health and that we can learn a lot about cancer by studying and treating animals with cancer.”

Kent will be serving as co-PI along with Dr. Robert Canter, a surgical oncologist from UC Davis Health, and Dr. Xinbin Chin, a professor and basic science cancer researcher in the veterinary school.

“Tackling complex cancer research problems should include investigators with broad experience across animal and human species, presenting a unique opportunity for DVMs and MDs to have a crucial role in basic and translational research,” Canter said. “Veterinarians can strengthen comparative approaches essential to multidisciplinary research accelerating innovative treatments for animals and humans, while medical doctors bring a patient-centered approach linking biology with clinical therapy.”

Five individuals at a time will be supported by the funding over a five-year period. Twenty-seven faculty members from five academic departments will provide training and mentoring.

The UC Davis Comprehensive Cancer Center is one of 51 centers around the country that receive National Cancer Institute designation and funding. The UC Davis center received its comprehensive status five years ago and is the only one in the U.S. to have a formal program dedicated to comparative oncology.

“This is team science at its best,” Kent said. “With this NIH grant, we will be at the forefront of training the next generation of clinicians to do research in comparative oncology.”

Genetic Code from page 1

Bannasch and Stern also pointed out the translational value of genetic studies for people. Last fall, several faculty members at the school published a study in the journal, Genes, that identified the mutation for succinic semialdehyde dehydrogenase (SSADH) deficiency in Saluki dogs. It’s a rare neurological disease that closely resembles a similar condition in humans.

“We were able to help establish the only translational large animal model for the development of novel therapeutic strategies for people who suffer from this condition,” said Bannasch, who holds the Maxine Adler Endowed Chair in Genetics. Genetic studies have changed dramatically in the past several decades with the evolution of advanced molecular tools, she explained. We’ve come a long way from the 1950s when scientists spent many years using cross breeding and large pedigrees to identify chromosomes associated with disease.

Whole genome sequencing now makes it possible to test a single dog for an inherited disease and enable rapid, effective treatment.

“CCAH donors make all the science we bring to the public possible—and the improvements we’re able to make in animal’s lives,” Stern said. “Their support has provided seed money that leads to critical larger funding, including four National Institutes of Health grants in recent years. Even if it’s a small amount, it gives us a huge advantage.”

Pioneering 3D Minimally Invasive Surgery

Louie, an 8-year-old male Boston terrier with Cushing’s disease, was cured after undergoing the world’s first laparoscopic adrenalectomy on an animal utilizing 3D technology at the UC Davis veterinary hospital. The pioneering surgery was made possible by generous CCAH donors who enabled the purchase of a three-dimensional scope used for minimally invasive surgical procedures.

Soft Tissue Surgery Service faculty member Ingrid Balsa led the surgery to remove a tumor in Louie’s right adrenal gland that was causing the condition. Cushing’s disease causes a dog’s adrenal glands to produce too much cortisol, a chemical that controls many aspects of a dog’s body, including its weight, ability to fight infections, blood sugar levels, and many other vital functions.

As a pioneer in minimally invasive procedure, UC Davis has been performing laparoscopic surgeries for many years, including adrenalectomies. Normally, these surgeries are guided by an on-screen two-dimensional (2D) image from a camera in the scope. Surgeons are able to navigate the animal’s body proficiently after a learning curve, however they lose depth perception with a 2D image which may lead to surgical errors or prolong surgical time.

The new 3D scope greatly improves on the 2D technology. With two cameras in the scope instead of one, two images are presented on-screen. When viewed with 3D glasses, the two images are fused together due to the polarization of the glasses, creating a 3D image on the monitor, helping veterinarians to better navigate their surgical field.

While 3D technology has been used in human surgeries for several years, it is a new advancement for veterinary medicine. Studies on human procedures have shown 3D surgeries decrease surgical time and decrease surgical errors, and the school’s faculty hope to see those advantages realized for their veterinary patients.

“I hope this allows us to push the envelope for different types of surgeries that we could consider performing in a minimally invasively fashion,” said Balsa, who will continue to investigate 3D capabilities with fellow faculty surgeon Philipp Mayhew. “I think this will also provide a stepping stone for resident training in regard to laparoscopic procedures, which have different instrumentation and techniques compared to traditional open surgeries. The 3D scope will remove loss of depth perception in laparoscopy.”
Animal Shelter Program leadership in the field and its long history of working with the policy's goals. He cited the program's reputation for materials, and perform in-person consultations to help achieve to set up a grant process, create and distribute educational should be euthanized.”

state’s long-held policy that “no adoptable or treatable animal for animal shelters and reflects the governor’s commitment represents the first time a state has earmarked grant funds statewide Animal Shelter Assistance Program. The program in July that includes $45 million in one-time support for a change the landscape for vulnerable animals and their families. “This truly is a generational investment that has the potential to “Thank you for making a difference in the lives of our beloved animal companions! With your partnership, we are able to advance the knowledge and treatment options for dogs, cats, birds, rabbits and other pets. Science and research are the keys to advancing companion animal health, and we will continue to work for all species to live healthy, long lives with their families. As the work that we do is thanks to friends like you. We are pleased to recognize donors who contributed $3,000 or more to the Center for Companion Animal Health from July 1, 2020 to June 30, 2021.

State Funds KSMP-Led Animal Shelter Program

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THE CCAH at Work

139 Faculty Projects

Dogs...................90
Cats....................35
Pig .....................1

Rabbits...............4
Fish ....................2
Multispecies ......7

19 Research Pieces of Equipment Purchased, Totaling: $259,902

37 Newly Submitted Projects Totaling: $516,732

29 Resident Projects

Dogs....................17
Cats.....................2
Birds ....................2

Rabbits...............2
Fish .....................1
Multispecies ......5

Gifts from the Heart

Are you looking for a heartfelt way to show that you care? Honor or memorialize someone special—a beloved pet, friend or family member—with a donation made in their name to the Companion Animal Remembrance and Endearment (CARE) fund. Your gift will help support studies that improve the health of our animal companions. We will brighten your honoree’s day or show a grieving loved one that you care with a letter sharing your meaningful tribute.

Honor a loved one by visiting give.ucdavis.edu/Go/care or calling 530-752-7024.