

CCAHUPDATE

SPRING 2021



Tackling Canine

Conquering a complex disease like canine glioma takes scientific expertise, a passion for generating data, and, of course, financial support. But the secret sauce to a successful scientific endeavor for Drs. Christine and Ryan Toedebusch has been the team approach they found when

The couple met at the College of Veterinary Medicine at the University of Missouri, where Ryan was working on a PhD in biomedical sciences, and Christine was concurrently pursuing a PhD while doing a residency in

"To be honest, we weren't sure this was going to work—being in the same lab and living together,"

But they've proven to complement each other with different skill sets that allow them to generate new research questions and find ways to answer them. Their big picture questions revolve around microglia, the brain's resident immune cells, in the context of brain tumors such

"There's so much we don't know about microglia in general or what they do in canine glioma," said Christine, who serves as an assistant professor of surgical and radiological sciences. "It's important to figure out the pathophysiology."

See Canine Glioma page 4



From the Director

As we are now more than a year into the pandemic with its staggering toll on life, our way of life and the economy – evident both at an individual level and in our strained systems – I am humbled by the dedication people still have to making the world a better place. This has always been our mission at the Center; we do this by positively impacting the lives of animals and their families. More than ever, our families, which for most of us include our pets, have been so important in helping us get through this past year. We at the school, the hospital and the CCAH work every day to make the lives of our companion animals healthier and better.

In this issue we will show how our donors are making this possible—all the work we do is funded through your dedication to the cause and your trust in us. From our shelter medicine team's innovative initiatives that have saved over 3 million cats and created a new model for how animals are sheltered, to our ophthalmology group's efforts to save the vision of dogs and cats with corneal ulcers, to our neurologists' groundbreaking work in brain tumors, we are tackling problems that need to be solved. These are just a few of the areas where your donations have helped us bring a bit more light to the world. We are optimistic, and we are making great strides on so many fronts.

All of us at the Center hope this finds you and your family well and safe in these difficult times.

My Best,

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

ROBOTICS

Aid Cancer Treatments

Thanks to an anonymous donation to the CCAH, radiation therapy for cancer treatment is now quicker, safer, and more accurate. With the purchase of a PerfectPitch 6 degrees of freedom (6-DoF) couch for the Radiation Oncology Service's linear accelerator (shown in photo at left), radiation outcomes will improve for thousands of animals and open doors to novel treatments and research.

The 6-DoF couch, which the patient lies on during a radiation treatment, has more movement capabilities than the previous couch that moved in and out, left and right, up and down, but it could not pivot or dip in these directions to compensate for small rotations. These additional movements allow for countless additional positions which are more accurate and sustainable.

To pinpoint the radiation dose to a tumor, a radiation oncologist will utilize cone-beam computed tomography (CBCT) scans to help properly position the animal on the couch. The 6-DoF couch can automatically decide on just how much the table needs to move (even the slightest of degrees) once the clinician sets the coordinates in accordance to the CBCT scan.

Dr. Katherine Hansen noted the new couch has been the most beneficial in treating nasal tumors, front limb bone tumors, and spinal cord tumors—by reducing the number of CBCT scans needed to perfectly position the animal and cutting anesthesia time by as much as 15 minutes.

The 6-DoF couch is also helping to reduce planning target volumes—an error margin needed for treating extra area beyond the tumor because of potential movement, such as an animal breathing and imperfections in patient position.

"The smaller you can make your error volumes, the better you can deliver stereotactic radiation," said Hansen. "This will open the door for stereotactic radiation to be delivered to more areas than we thought we could treat."

The new couch has also been a launching pad for two novel research projects — supported by the CCAH donor-funded resident research grant program — comparing tabletop devices to accompany linear accelerators, and the use of thermoplastic immobilization devices to improve the consistency of day-to-day setups for animals receiving multiple treatments on a daily or weekly basis.

Named Floyd

Floyd was a ball fanatic with the heart of a retriever. The muscular black and white Boston terrier would play fetch for hours with Ananda and Chuck Nettnins before collapsing in his water trough to cool off.

A few months after his death in April 2016 from hemangiosarcoma, a cancer of the vascular endothelium or the blood vessel walls, the Nettnins discovered a secret stash of more than 20 balls hidden under their couch.

To honor Floyd and all the fun memories he gave them, the Nettnins wanted to do something special. They had recently opened a brewery called Three Stacks and a Rock, so they created a new American strong ale, A Beer Named Floyd. For each pint sold, the Nettnins generously donate \$1 to the Companion Animal Memorial Fund (CAMF) in his memory.

"We love dogs so much and wish they had more opportunity to survive horrible diseases like cancer, especially hemangiosarcoma," Chuck said. "We will continue to fundraise and donate as much as possible even in these tough times."

The Nettnins first learned about CAMF several years ago when their veterinarian Dr. A.J. Hardy, DVM '80, of the Lifetime Animal Care Center, donated to this fund in memory of their first Boston terrier, Ladelle, who also succumbed to hemangiosarcoma.

When the Nettnins learned that nearly one in four dogs develop cancer, they too decided to donate to CAMF and raised funds by selling their handcrafted dog treats. Floyd's passing and the recent loss of their third Boston terrier, Darby, from cancer made their commitment to supporting this fund even stronger. In memory of Darby, her veterinarian Dr. Richard Knighton, DVM '86, of the Los Osos Pet Hospital also made a donation to CAMF.

CCAH Director Michael Kent described memorial tributes as a

special way to ensure that beloved animal companions will never be forgotten. The CAMF program supports discoveries in diverse animal-health areas, such as cancer therapy, infectious diseases, nutrition, kidney failure, heart disease, diabetes, and genetic disease.

"We are grateful to Ananda and Chuck for their deep commitment to animal health. Floyd, Ladelle and Darby will always be remembered," Kent said. "The memorial tributes from Dr. Hardy and Dr. Knighton are a meaningful way to honor these loyal canine companions.

For information about the Companion Animal Memorial Fund, visit ccah.vetmed.ucdavis.edu/giving.

Chuck Nettnins with Ladelle (left) and Floyd (right).



"We love dogs so much and wish they had more opportunity to survive horrible diseases like cancer, especially hemangiosarcoma. We will continue to fundraise and donate as much as possible even in these tough times."



Canine Glioma from page 1

Microglia are very small cells and make up about 10-15% of total cell volume in the mammalian brain. One of their main roles is to maintain homeostasis by fighting infection and invaders, but they can also create havoc. In certain diseases, microglia can go rogue and cause more problems than they fix. That seems to be the case with glioma in particular, Christine explained, where they are heavily recruited into the tumor microenvironment. Once there, the tumor reprograms them to make molecules for the tumor's continued growth.

With the help of the CCAH, the Toedebusch lab just completed a study examining the microglia signature in canine gliomas. This study revealed that canine gliomas are very similar to human gliomas, with microglia heavily infiltrating the tumors and producing many molecules that promote glioma growth. A molecule of particular interest to the Toedebusch lab is Olfactomedinlike 3. It is upregulated in both human and dog brain tumors, although not much is known about it. Their research has focused on what this molecule is doing inside the microglial cells, and what effect this protein has on other cell types in the tumor environment.

"There's a lot we don't understand about how the dog gets a glioma in the first place and what contributes to its progression," Christine said. "Until we better understand those, it will be challenging to identify treatment. It's clear that the standard of care, which is surgical removal and radiation, just doesn't work so we need to get more savvy and find precise targets that we can go after. We need to keep digging, and basic science allows us to uncover pathways and break down the nuances of how this tumor grows and develops."

Figuring out how to collect data to answer those basic science questions is where Ryan's expertise shines. In graduate school, his technical skills garnered Ryan the nickname "golden hands," for his ability to complete delicate and nuanced experiments, often on his first attempt. His attention to detail and creativity makes him the perfect project scientist to run the Toedebusch lab.

"His technical abilities and the intellect he brings to be able to figure out how to do these studies and make it happen for us is huge," Christine said. "With me having 50% clinical responsibilities and being on committees, we wouldn't be where we are if I didn't have him in the lab."

Ryan's diverse scientific background in exercise physiology, cardiovascular disease and neuroscience allows him to troubleshoot experiments and figure out how to do new things like using CRISPR gene editing, making recombinant proteins and generating antibodies needed for studies.

"I kind of have scientific ADD in that I have too many interests," Ryan said. "But that's the most enjoyable thing for me—having different things on the burner, being able to switch gears and continue to advance our scientific goals."

In addition to their teamwork in the lab and among her colleagues in the Neurology Service, Christine emphasized that the access to funding – from CCAH grants to the Comprehensive Cancer Center – made it possible to hit the ground running when they arrived at UC Davis. CCAH has been instrumental in building the success of the Toedebusch lab by providing seed funding for pilot studies that will lead to larger national grants.

"You've got to make that investment early on to make really productive teams for them to be successful in the future," said Michael Kent, director of the CCAH. "To get the publications, it takes a while to get the big grants and when we believe in a team, we have to back it. Everyone who donates to CCAH is backing them as well so together we can do great things."



Dr. Ryan Toedebusch took advantage of the move to UC Davis in July of 2018 and rode to California from Missouri in 34 days. "I'd always wanted to do a bicycle tour across the country," he said. "I loved every second of it, but when I hit the Pacific in San Francisco, I realized I had to turn around."



Envisioning a Clearer Future

Corneal ulcers are among the most common ocular diseases treated by the hospital's Ophthalmology
Service. Injury, dry eye, or even minor trauma can cause an ulcer. If not dealt with appropriately, these painful lesions can become infected, rupture, and ultimately lead to blindness and eye loss.

Currently, the service treats ulcers with topical medications, and in some cases, surgery.

"We take multiple approaches – surgical and medical – that can work in concert with each other," said Dr. Brian Leonard.

Thanks to donor-funded CCAH grants, veterinary ophthalmologists are conducting research to better understand corneal ulcers and to investigate alternative therapies that may improve patient outcomes. For example, Leonard is looking to augment medical therapies while his colleague, Dr. Bianca Martins, studies surgical interventions.

Leonard's research addresses antibiotics needed in treating infected corneal ulcers and the resistance that bacteria have acquired to these drugs. Cells that line the surface of the eye make small molecules called antimicrobial peptides (AMP) that naturally fight bacteria. Leonard has identified three molecules that can cause a 300-fold increase of AMP production. This boost to the animal's own immune system dramatically improves its ability to kill bacteria with only a droplet. He is also working on developing cell lines that mimic the cornea, which will allow development and testing of new medications in the laboratory.

Martins and Dr. Sara Thomasy have launched a clinical trial to expand on research initiated at the University of Zurich, which suggested that collagen crosslinking (CXL) with a drug called riboflavin may be a safe and effective means of treating corneal ulcers. This latest large-scale trial will compare the efficacy and safety of CXL with standard treatments in dogs at UC Davis and several other institutions. In some cases, the cornea starts to melt, resulting in the need to strengthen the cornea with surgical grafting. That process, however, can lead to scarring and loss of corneal transparency, hampering vision. The trial will determine if CXL can help stiffen the cornea without the need for surgery.

"UC Davis has the largest comparative ophthalmology department in the world," Leonard said. "CCAH grants support our laboratory and research teams, allow us to purchase needed equipment for clinical use, and advance our imaging program to evaluate and diagnose challenging cases. I don't know of another program in the country that has such interconnectivity among those three realms. The support from CCAH donors allows us to achieve this."



Meet the **Resident Researcher**

Dr. Andréa Minella (on right) is in her third year of an ophthalmology residency after completing a PhD in Comparative Medicine and Integrative Biology where she focused on feline inherited eye diseases. The opportunity to continue research drew her to UC Davis.

"I would miss research if my residency didn't include it," said Minella. "Clinical medicine is wonderful—you can make an immediate impact on each patient. But with research, you have the ability to make a broader impact (on countless animals) if you discover a new treatment."

Currently, Minella and faculty mentor Dr. Sara Thomasy are utilizing a CCAH resident research grant to investigate the efficacy of a drug in preventing corneal scar tissue following an injury. To target the specific molecular process that causes the scar formation, researchers have found the enzyme tissue transglutaminase 2 (TGM2) to be involved in the scar tissue formation process across multiple body tissue systems, including the eye. In theory, if TGM2 can be inhibited, scar tissue formation can be slowed or eliminated.

While investigating TGM2 inhibitor compounds, Minella found one as an ingredient in an already FDA-approved eye drop for a different disease. The drug has not been tested for its scar inhibitor property, so Minella is investigating whether the eye drop has a high enough concentration of the compound to also act as a TGM2 inhibitor. If successful, it may be possible to have the drug re-branded as a TGM2 inhibitor and market ready in a short timeframe, preventing dogs from going blind.

Managed Admissions Lead to Permanent Change

What Can Animal Shelters Learn From the Pandemic?



The pandemic has brought many challenges to our lives, but conversely, it may have benefitted animals who would have landed in a shelter or were already living in one. It's also highlighted the life-saving success of following the Koret Shelter Medicine Program's (KSMP) animal sheltering management model, Capacity for Care (C4C).

"The goal of C4C is to provide the right care for every animal that needs it, in the place that's best positioned to provide that care," said program director Dr. Kate Hurley. "Not every animal is best served by entering a shelter."

When the pandemic hit, stay-at-home orders forced us to slow down and examine the necessity of our every action. For shelters, that meant non-emergency animals were first served outside shelter walls whenever possible—a core tenet of C4C.

In general, Hurley explained, we are working to undo a historically common idea that an animal shelter should provide uncontrolled admission for healthy animals, even though we know the value of appointment-based services in so many other areas of our lives.

"We expect to make appointments everywhere from going to the doctor to the DMV, yet we often haven't afforded shelters that same opportunity to manage the flow of animals coming in their doors every day," Hurley said. "It's been a tough nut to crack, and ironically the pandemic helped us crack it."

The Million Cat Challenge, a campaign that celebrated its 3 millionth life saved in January, was launched in 2014 to spread solutions to this chronic crisis state. Primary solutions included: appointment-based services; a community-based approach to animal sheltering; and changing public perceptions about how and where we should help animals that are found outside, lost, or homeless.

"Year-end data for 2020 collected at animal shelters have shown us, again, that a community-based model is where we need to land," said Dr. Cynthia Karsten, one of the KSMP veterinarians. "Nearly 1 million animals were spared a needless night in a cage by being cared for outside the shelter walls. Euthanasia of healthy animals is down fifty percent. Animals are being cared for in foster homes. Shelters are able to provide expanded support and resources to assist. In many ways, it's the model we've been working toward for many years."

With a year of community-based sheltering under our proverbial belt and the data to prove its efficacy, we have built the foundation to continue using C4C guidelines in shelters even after the pandemic is over.



Thank you to our Companion Animal Memorial Fund veterinary partners for making a difference! Through your meaningful tributes, you honored the memory of beloved pets and brought comfort to their caring families. Your gifts have also made an impact on improving animal health—enabling us to make great strides in advancing cancer treatment, identifying genetic causes of certain diseases, saving shelter animals, and discovering other life-saving knowledge and treatments. We are pleased to recognize the veterinarians and clinics who donated to this fund in 2020.

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