

SYNTHESIS



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extraordinary **Knee**

An ankle becomes
a knee for child
with sarcoma

PAGE 12

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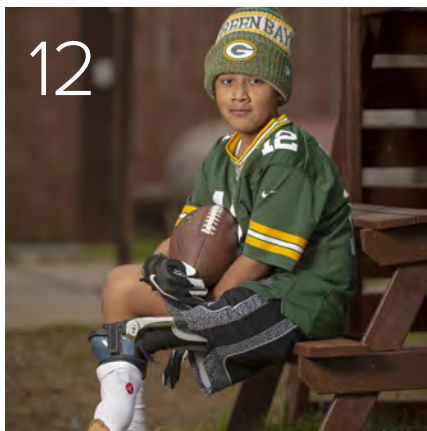


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THE MAGAZINE OF UC DAVIS COMPREHENSIVE CANCER CENTER

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BREAKING BARRIERS TO BEAT CANCERSM

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Dear Reader,

How people heal after a cancer diagnosis can be as different as the individuals who experience it. For some, it's regaining the ability to run for a football. For others, it's finding creative ways to face cancer's emotional toll. And some find refuge in the hope that a revolutionary new kind of treatment will make the life-saving difference.



In this special issue of *Synthesis*, you will read about all of those approaches to healing. In our cover story, for example, you will meet Jorge Portugal-Herrera, a 9-year-old boy with Ewing's sarcoma who endured a complex and disfiguring surgery to save his life — and have a chance to fulfill his dream of playing sports.

In "Writing for Their Lives" we introduce you to several people who have found their voices in a special writing class at the Cancer Center that allows participants to tap into their grief, fear and other emotions through writing and encouraging group discussion.

And you'll meet Bobby and Jerri Hughes, who opted for a novel cellular therapy treatment for Bobby's stubborn lymphoma. The couple has derived great comfort in knowing that CAR T therapy may finally be the treatment that keeps him alive.

This issue also introduces you to the exciting and unusual world of Justin Siegal and his work using online crowdsourcing to help find a needle in a haystack: the answer to a global carcinogen — aflatoxin, a fungus that infects commonly consumed crops and can cause liver cancer in many parts of the world.

We hope you enjoy these and other stories in this issue of *Synthesis*. If you have suggestions for future editions, please contact our editor, Dorsey Griffith, at dgriffith@ucdavis.edu.

Primo "Lucky" Lara

DIRECTOR, UC DAVIS COMPREHENSIVE CANCER CENTER

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Experimental compound may help prevent cancer progression

A study in mice of an anti-inflammatory compound developed in the lab of Cancer Center member Bruce Hammock has found that it suppresses inflammation that can occur from cell debris after cancer treatment and stimulate further cancer growth and recurrence.

“We are excited about this research and its potential,” said Hammock, a distinguished professor in the UC Davis Department of Entomology and Nematology. “Chemotherapy and surgery, the mainstays of conventional cancer treatment, can act as double-edged swords.”

The research by a 13-member team, including from Harvard Medical School, was published in the *Proceedings of the National Academy of Sciences (PNAS)*.

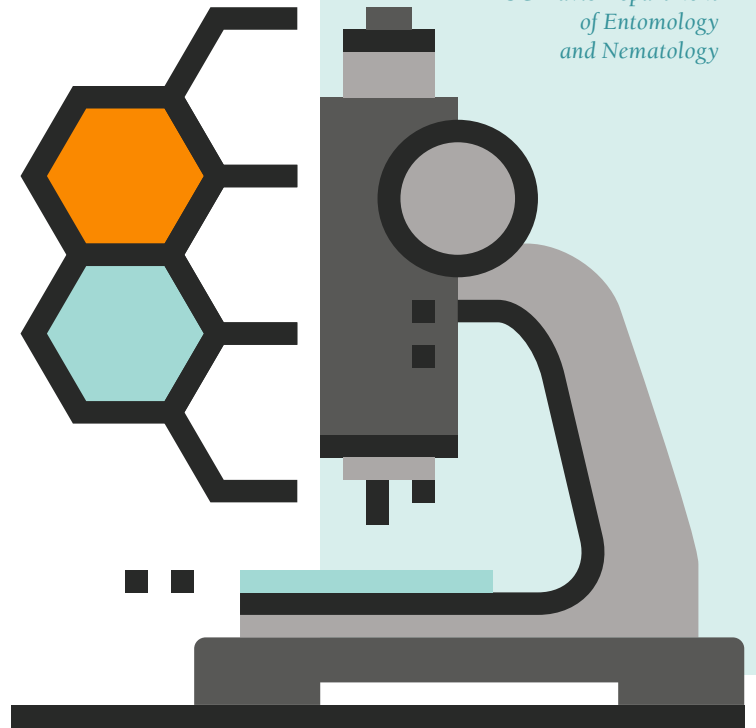
The team treated mouse models of ovarian cancer with a dual lipid pathway inhibitor discovered several years ago in the Hammock lab. It integrates two anti-inflammatory drugs (COX-2 inhibitor and soluble epoxide hydrolase (sEH) inhibitor) into a single molecule with the aim of reducing tumor angiogenesis and metastasis.

“The dual inhibitor here follows earlier work we did with it, blocking breast and lung tumors in mice,” Hammock said. “It is already being clinically evaluated for its therapeutic properties in other diseases.”

Lead researcher Dipak Panigrahy, a former Harvard physician turned full-time researcher, described chemotherapy and surgery “as our best tools for front-line cancer therapy, but chemotherapy and surgery create cell debris that can stimulate inflammation, angiogenesis and metastasis. Thus, the very treatment used by oncologists to try to cure cancer is also helping it survive and grow. Overcoming the dilemma of debris-induced tumor progression is critical if we are to prevent tumor recurrence of treatment-resistance tumors which lead to cancer therapy failure.”

“We are excited about this research and its potential... Chemotherapy and surgery, the mainstays of conventional cancer treatment, can act as double-edged swords.”

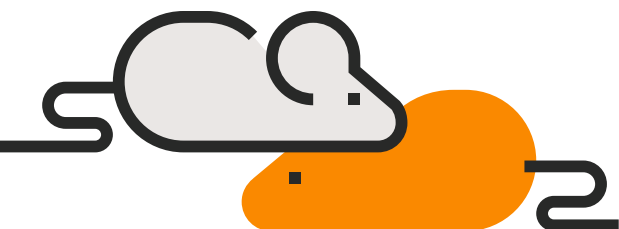
Bruce Hammock
UC Davis Department
of Entomology
and Nematology



The tumor cell debris generates a “cytokine surge” that can result in a perfect storm for cancer progression, and the dual inhibitor acts as a surge protector,” Panigrahy said. “Our studies potentially pave the path for a new strategy for the prevention and treatment of chemotherapy-induced resistance with potential to translate to the clinic. If successful, this approach may also allow us to reduce the toxic activity of current treatment regimens.”

American Cancer Society statistics show that among women, ovarian cancer ranks fifth in cancer deaths. A woman’s risk of ovarian cancer is about 1 in 78; every year more than 14,000 die from the disease.

“We are exploring all options to translate this compound to cancer patients especially in combination with current cancer therapies such as chemotherapy, radiation, immunotherapy, or surgery which either directly or indirectly may generate tumor cell debris,” Panigrahy added. “Our next step is to investigate whether our findings are consistent with clinical studies involving human cancer.”



FOR HARD-TO-REACH TUMORS AT THE BACK OF THE THROAT, ROBOTS CAN ASSIST SURGEONS TO REMOVE CANCERS IN A LESS INVASIVE WAY.

But this high-tech approach has a drawback: the surgeon's inability to assess through touch whether they've been able to get all of the cancer.

An innovative new device developed by UC Davis biomedical engineer Laura Marcu is helping to change that. Based on fluorescence lifetime imaging microscopy (FLIm), the device can be used in tandem with robotic surgery to distinguish between cancerous and benign tissue, guiding the physician in real time to achieve a more precise surgical outcome for the patient.

In a first-in-human, proof-of-principle study published in *Scientific Reports*, a *Nature* publication, UC Davis researchers reported on their ability to successfully integrate the FLIm tool with a surgical robot to allow real-time evaluation of the different tissue types in patients undergoing oral cancer surgery without using contrast agents. First studied in animal models, the technology

has now been used in about 30 human patients with cancers of the tonsil and base of the tongue.

"We are the first to demonstrate implementation of augmented reality in patients and in conjunction with robotic surgery," said Marcu, a professor and Cancer Center member.

FLIm measures the autofluorescence properties of certain molecules in tissue in the form of wavelength (or color) and lifetime (or the time a molecule emits light). Since tumor tissue is made up of molecules different from those in normal tissue, tumors also have different fluorescence properties. This allows the autofluorescence to encode diagnostic information to help the surgeon as he removes tissue.

"The FLIm features are augmented instantaneously in the surgeon's field of view so the surgeon can see tissue properties that cannot be seen otherwise," Marcu said.

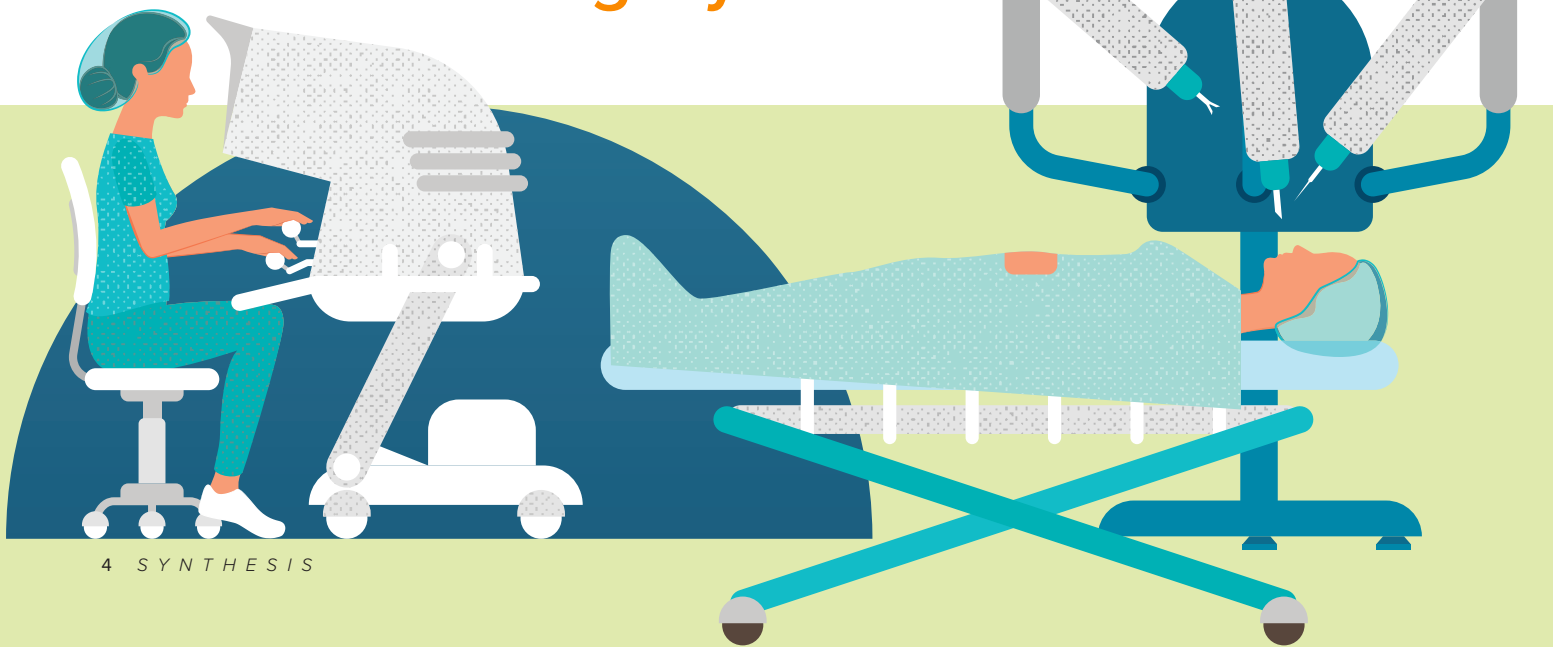
Marcu teamed up with Cancer Center member D. Gregory Farwell, professor and chair of the UC Davis Department of Otolaryngology — Head and Neck

Surgery, to use the device to help guide him during complex oral cancer surgeries. When Farwell began using the robot to do complex head and neck surgeries, the two figured out a way to incorporate the device with the robot's technology.

"These tumors are very difficult to access, and they traditionally required extensive surgery that involved cutting the jaw and reconstructing the jaw to allow us to get back there," Farwell said. "In selected patients we can use the robot to gain access to tumors that historically we could not get to less invasively."

FLIm uses light to excite molecules in tissue and measure how long they emit light of their own after they are excited. Different types of molecules emit light at different rates. FLIm can measure the rates, and that information is used to distinguish between different types of tissue. The device employs fiber optics to deliver and collect the light. Marcu and Farwell are recruiting up to 80 more patients to further develop and refine the technique. Marcu also plans to team with urological surgeons to use the device for prostate cancer patients.

Optical device aids robot-assisted cancer surgery





“Working in tandem with other leading clinicians and scientists around the country and beyond, I believe we can make the difference so desperately needed.”

UC Davis team takes on pancreatic cancer with SU2C grant

UC Davis scientist Julie Sutcliffe and surgical oncologist Richard Bold have been awarded a \$1 million “New Therapies Challenge” grant from the Pancreatic Cancer Collective in an effort to improve survival for people with the disease.

The Collective is a strategic partnership of the Lustgarten Foundation and Stand Up To Cancer (SU2C). The UC Davis team was one of seven to receive the grant, which could be augmented by an additional \$4 million in the second round of funding.

The UC Davis team will use the grant to build on nearly 15 years of work undertaken in Sutcliffe’s laboratory, which developed advanced imaging techniques to pinpoint pancreatic cancer using positron emission tomography with a specially synthesized peptide that binds to tumor cell receptors. The team will now develop the radiotherapy that can be delivered through a radioactive isotope using the same peptide. The radiotherapy will attack a protein called integrin $\alpha v \beta 6$, which is significantly upregulated in pancreatic cancer and is a marker for cancer aggression.

“We have an opportunity through this funding to take our diagnostic agent and turn it into a therapy,” said Sutcliffe, professor in the Departments of Internal Medicine and Biomedical Engineering. “Over the next few months we will design and synthesize the targeted therapy, test its efficacy in animal models and prepare for translation to the clinic by the end of the 14-month proposal.”

Sutcliffe noted that similar radiotherapies have been developed and are in clinical trials for treatment of prostate cancer, neuroendocrine pancreatic cancer and other neuroendocrine tumors.

“There is a clear need right now for more effective pancreatic cancer treatment,” said Bold. “There is very little out there and the 5-year survival rate is not improving.”

At year’s end the UC Davis team will report their results to the Collective, and teams deemed to have the most promising treatment approaches will advance to the second round and receive \$4 million to support clinical trials.

Sutcliffe said she is proud and thrilled to be part of the international SU2C effort.

“It is a great honor to receive this prestigious grant and the opportunity to improve outcomes for people diagnosed with pancreatic cancer,” she said. “Working in tandem with other leading clinicians and scientists around the country and beyond, I believe we can make the difference so desperately needed.”

KIT LAM BECOMES THE SUE JANE LEUNG PRESIDENTIAL CHAIR IN CANCER RESEARCH

Kit Lam, chair of the UC Davis Department of Biochemistry and Molecular Medicine, is the inaugural holder of the Sue Jane Leung Presidential Chair in Cancer Research.

The presidential chair is the result of a \$1.5 million gift to UC Davis from the family of Sue Jane Leung and a \$500,000 contribution from the UC Office of the President. Lam also serves as co-director of the UC Davis Comprehensive Cancer Center’s Cancer Therapeutics Program.

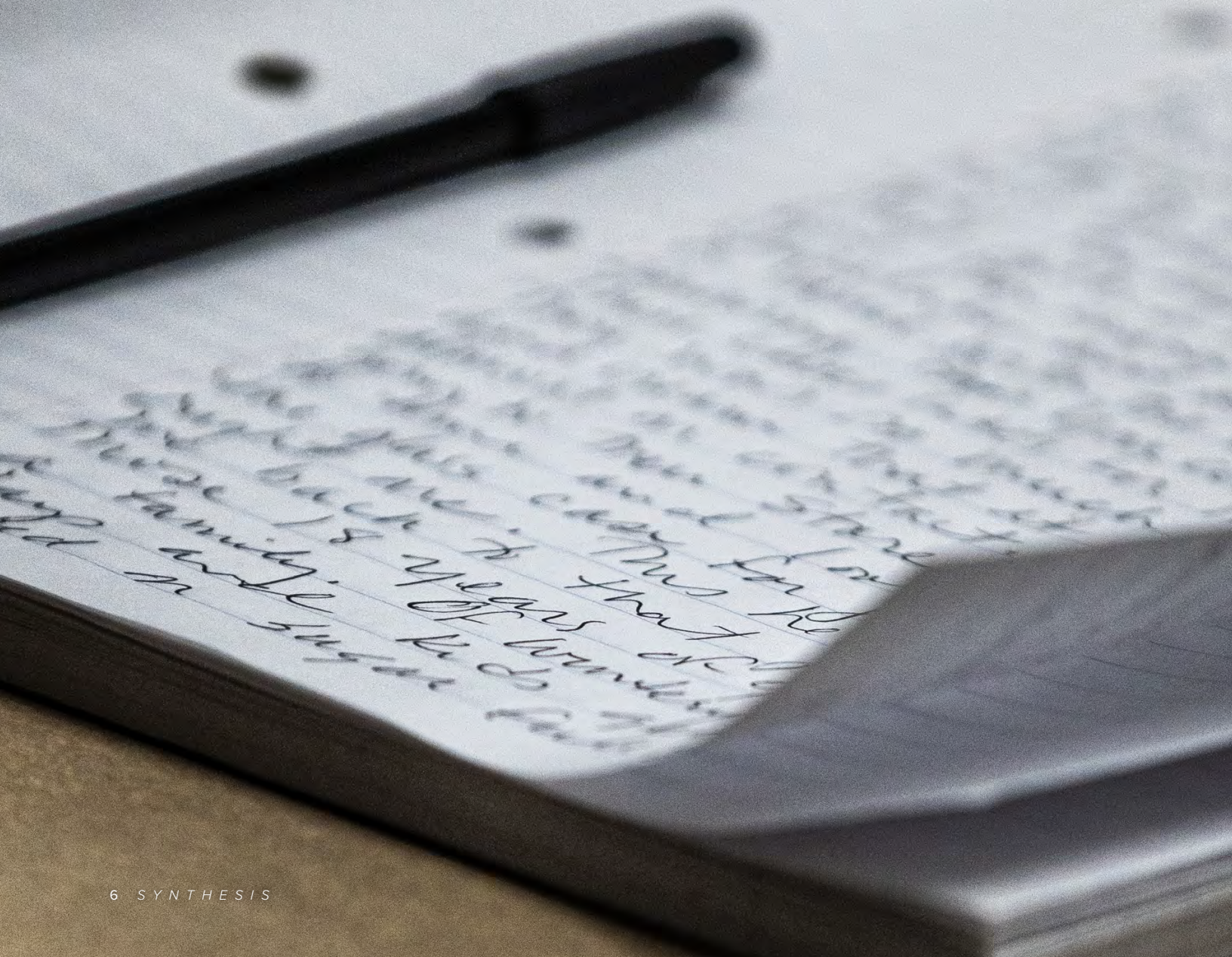
Sue Jane Leung, who never smoked, was diagnosed with lung cancer in 2006 and fought the disease with tenacity until her death five years later. Her daughter, Lucinda Hsu, and her husband, James Leung, a UC Davis engineering graduate, decided to make the gift to UC Davis to honor Sue Jane’s strength and determination.

Lam, who has pioneered novel approaches to cancer drug delivery, said the generous gift from the Leung family will allow the Cancer Center and Department of Biochemistry and Molecular Medicine to build a world-class cancer drug development and drug delivery program.

“The Department of Biochemistry and Molecular Medicine and I are very grateful for the Leung family’s generosity, and their foresight in supporting research in the development of novel cancer therapy,” Lam said.



Writing



for their lives

Workshop promotes recovery through pen and paper

CHERYL PALETZ, A RETIRED NURSE, HAS A TENDENCY TO

“stuff it,” to take the feelings that surge up inside and push them back down until she’s riddled with anxiety.

So when her husband of 25 years, Gary Paletz, was diagnosed with acute lymphoblastic leukemia in May 2018, and when the chemotherapy he received in rural Oregon nearly killed him, something had to give.

“It’s like, I have to get this out because if it doesn’t come out, I don’t do well,” she says. “My stress and emotions are all over the place, and I feel lost and alone.”

After some focused research, the couple found the UC Davis Comprehensive Cancer Center and oncologist Brian Jonas. Soon, they had packed up their lives, bought a fifth-wheel vehicle and moved onto a friend’s property in Elk Grove. Gary is now undergoing intensive treatment



at UC Davis Health, which includes both inpatient and outpatient chemotherapy.

And here they found help for Cheryl, too, in Writing as Healing, a free workshop of the Cancer Center’s Supportive Oncology Program for anyone looking for a safe place to write whatever needs to be written.

Cheryl Paletz, center, during Writing as Healing workshop session.

Life is an Ocean

BY CHERYL PALETZ

Life is an Ocean

Depths unknown

Waves obliterating...

In-Out, Close-Far, Happiness –
Sorrow, Pain-Peace, Joy-Loss...

Churning, white frothy storm
Threatening.

Danger explodes, crashing ashore.

Devastation.

Changed in an instant,

Forever.

Life is an Ocean,

Depths unknown–

Uncharted territory.

Overwhelming panic,

Breathing impossible.

The sneaker wave “LEUKEMIA”

Fiercely attacking –

Pulling, Dragging,

Taking, Suffocating

One fierce, terrifying jolt –

Drowning in despair,

Sinking in quicksand.

Life is an Ocean

Depths Unknown

Uncharted Territory.

Moving forward impossible.

Going back not an option.

Stuck, Stranded in the NOW.

Facing a landscape unknown...

Life is an Ocean,

Depths unknown...

Charting new territory.

Hope whispering across
the gentle breeze,

The thick misty, morning fog lifting,

Hyper vigilantly living a day at a time

Charting new territory.

Life is an Ocean, depths unknown.

For Cheryl, it was just what the doctor ordered.

“I’ve always loved to write,” she says. “I’ve had several ideas for books in my head, but I never got to it. I felt the need to start writing about our journey. I need to write. It comes from my gut.”

Held twice a month, the Writing as Healing sessions draw people with all kinds of experiences, from addiction recovery, to coping with a loved one’s illness or loss, to personal medical challenges.

“I’ve seen people talk about finding their voice and having insights as they are writing,” says Terri Wolf, a registered nurse and trained writing facilitator who began the program years ago and continues to co-facilitate it. “They see something new for themselves and see a way out.”

The writing prompts that Wolf offers vary from free, timed writing to poems by well-known authors and even games.

During a session recently, Wolf passed around dice with a single word on each side. Each participant shook the dice, then used the words they landed on — like “waste,” “fertile” and “obey”

to stimulate their writing. This was repeated for several rounds. Some writers wrote single stories; others wrote shorter, unrelated poems or prose.

Wolf gives participants the opportunity to share their writing with the group and reminds everyone not to critique one another.

“Think of this as a brand new baby,” she says. “You wouldn’t go into someone’s house and comment about the way the new baby looks.”

Brad Buchanan, a retired English professor and two-time cancer survivor, says the approach is very freeing, “a totally different paradigm.”

“It’s all about encouraging the writer to put words on the page and not be judged and to get immediate positive feedback in whatever form,” says Buchanan, who also serves as a co-facilitator. “This is totally different from anything that happens in a creative writing class where, ultimately, everyone knows they will be evaluated.”

Buchanan derives many benefits from the workshop. Besides giving back to “the cancer center that has saved my life multiple times,” he has found the



Cheryl Paletz visiting her husband, Gary, at UC Davis Medical Center.

approach unique in terms of helping him cope with recovery from a number of health crises.

The 48-year-old has had two types of lymphoma, a stem cell transplant in 2016 and a chronic condition related to the transplant called graft vs. host disease, which caused temporary blindness that required corneal transplants and that still affects his vision.

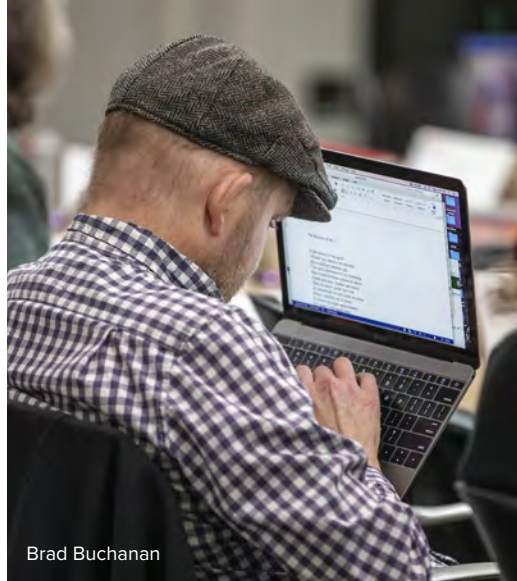
Buchanan likens Writing as Healing to a yoga practice.

“Sometimes you go somewhere you had no idea you would go and you say things you never suspected you wanted or needed to say,” he says. “It’s like yoga, which gives you stretches you didn’t know you needed, and doing them makes you more limber.”

Like others, Seanain Snow came to the workshop with a variety of personal and family challenges. Her father has been through prostate cancer and is now battling multiple myeloma. Her 15-year-old son has Marfan syndrome, a genetic connective tissue disease for which he later had a heart transplant.

“I’ve seen people talk about finding their voice and having insights as they are writing,” says Terri Wolf, a registered nurse and trained writing facilitator who began the program years ago and continues to co-facilitate the program. “They see something new for themselves and see a way out.”

“There is an immense amount of grief parents experience when our children have health problems,” she says. “We grieve the wonderful, healthy childhood we wanted them to have and all the activities they aren’t able to do. The writing process helps me see and



accept those things, and really grieve where I need to grieve, and then move on from it.”

For caregivers like Snow and Paletz, Writing as Healing allows them to be more available to their loved ones.

“There is still a family that needs me to not be stuck in grief in the hospital or wherever we happen to get stuck,” says Snow.

Paletz gets in touch with her own emotions — and needed perspective.

“I am mourning my house, the doggy door, the rhododendrons,” she says, sitting at her husband’s hospital

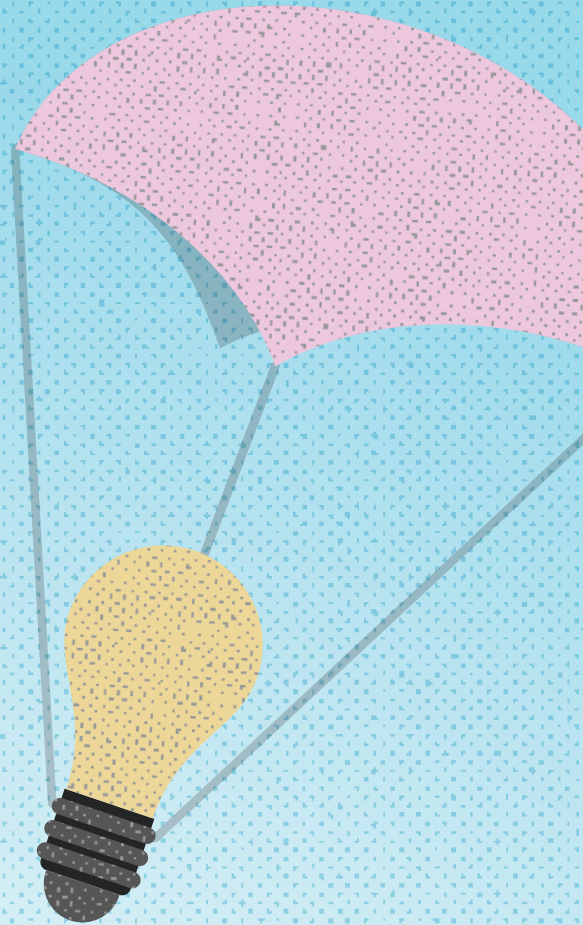
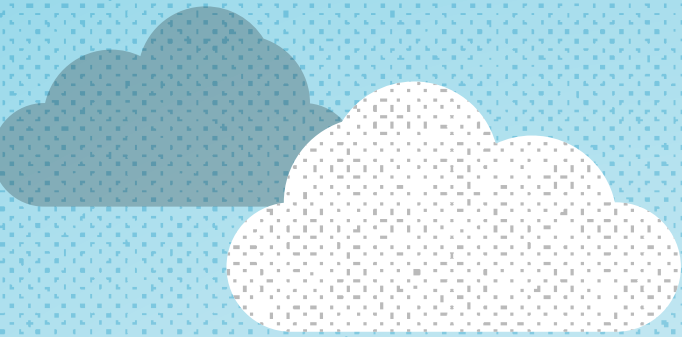
bedside during a recent chemotherapy infusion. “But he is my home, and we are going to get through this.”

For more information about Writing as Healing, visit the Cancer Center website community calendar at health.ucdavis.edu/cancer/events.

Side FX

BY BRAD BUCHANAN

a sleazy B-movie into which you’ve been cast for a cameo role by a famous director before the auditions have taken place because you are special or have specialized in getting certain dramatic effects a character actor with a tragic demeanor who works cheap and is right in line with the studio’s low production values you play the role of the unlucky patient the one to whom all the bad stuff happens: nausea, headaches, sleeplessness, fever, sweats, constipation, irregular heartbeat all the things they warn you about before you sign the legal disclaimer that exculpates the respected script doctor you make it, somehow to the cheesy last scene—unsteady recovery played as redemption—that you welcome nevertheless because it ends like everything else and maybe it’s better than the chance you missed to star in your own chemical bromance



**A new
target for
triple-negative
breast cancer**



Chen Lab tackles hard-to-treat disease

Early-stage breast cancer can be curable, but one type presents major treatment challenges: triple-negative breast cancer (TNBC). “Triple negative” means these tumors lack the receptors for estrogen, progesterone and HER2, so TNBC patients don’t have access to important targeted therapies, such as Herceptin or Tamoxifen.

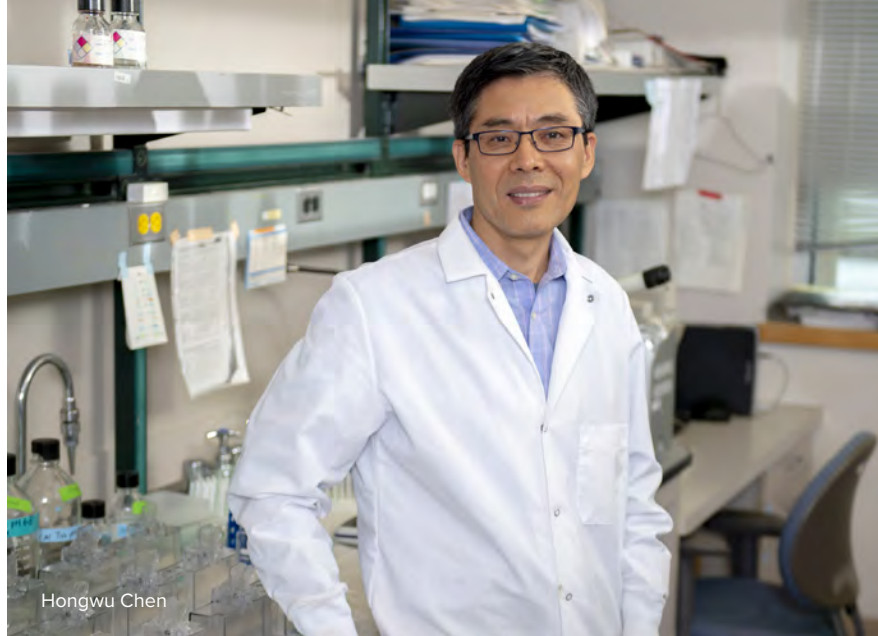
As a result, treating TNBC is like climbing a mountain without hand or footholds. There’s nothing to latch onto, keeping TNBC survival rates well below those of other types of breast cancer. To complicate matters, TNBC often learns to resist existing treatments. And though TNBC may sound like a single cancer, it’s really many.

“TNBC is actually many different kinds of cancer,” says Hongwu Chen, professor in the Department of Biochemistry and Molecular Medicine and a Cancer Center researcher. “Some of them are very aggressive and are more likely to relapse after treatment.”

But Chen may have a lead on a potential new target against TNBC: ROR- γ (ROR-gamma). This molecule, a member of the same protein family that includes estrogen and progesterone receptors, may play a significant role in TNBC growth.

“Our study in 2016 established ROR- γ as an important player in prostate cancer,” says Chen. “Continued study showed it plays a role in other cancers, including breast cancer and particularly triple-negative breast cancer.”

Chen’s early research has been promising, and was recently recognized by the National Cancer Institute (NCI) with



a five-year, \$2.16 million grant. The NCI wants to close the survival gap between TNBC and other breast cancers, and hitting ROR- γ may be a path forward.

The ROR- γ story

Chen’s lab has been following a number of clues that ROR- γ could be a good therapeutic target. Previous studies have shown the protein is overexpressed in some cancers, including prostate and TNBC. This added activity could be enabling rampant tumor growth.

ROR- γ is a nuclear hormone receptor protein. In other words, it’s activated by the human body’s hormonal signals and turns on specific genes.

“Cancers such as TNBC have hyper-activated cholesterol biosynthesis that allows tumor cells to make a lot of it, which is in turn used as a component in their cell membranes to allow rapid tumor growth,” says Chen. The NCI grant will allow Chen’s lab to firmly connect the nuclear hormone receptor to the abnormal cholesterol synthesis in TNBC.

The receptor protein also has a unique shape that makes it an attractive target. For these and other reasons, ROR- γ has been targeted by pharmaceutical companies, mostly for its role inside a group of immune T cells, to treat autoimmune conditions, like psoriasis. There have been a number of clinical trials but no FDA approvals yet. Still,

research by the Chen lab has shown ROR- γ could be a good protein to target for other conditions, including TNBC.

Developing an inhibitor

While much is known about ROR- γ , there’s still work to do. The Chen lab hopes to leverage the NCI grant to learn more about ROR- γ and how it contributes to TNBC. That means dissecting the protein’s biology to better understand which genes get turned on and how that might drive tumor growth, metastasis and treatment resistance.

The NCI wants to close the survival gap between TNBC and other breast cancers, and hitting ROR- γ may be a path forward.

Ultimately, they want to test molecules that shut down ROR- γ in the same way Herceptin turns off HER2 and Tamoxifen controls estrogen receptors.

“The grant will allow us to more deeply study the protein function and how it controls essential pathways in TNBC,” says Chen. “Beyond that, we want to test small molecule inhibitors in different models, including patient-derived xenografts, and see whether they can have a strong anti-tumor effect.”

An ankle becomes a knee for child with sarcoma

Childhood is typically filled with adventure and joy. Kids run and play with reckless abandon at recess and fill their minds with new concepts in the classroom. For 9-year-old Jorge Portugal-Herrera, a Green Bay Packers fanatic and aspiring football player, all that stopped when he was diagnosed with cancer.

“It began with knee pain in December 2015,” says Jorge’s mother, Alma Portugal. “Every month, there were emergencies because of the pain, but doctors couldn’t find anything wrong. We were told it was inflammation and to go home and ice his knee.”

Thanks to a multidisciplinary team of sarcoma experts at UC Davis Health, Jorge received comprehensive care





ORDINARY K E E

Surgery
delivers hope
for future
in sports

to treat the cancer and save his leg. That involved an extraordinary procedure to replace his diseased knee with his own healthy ankle. UC Davis Health is the only Sacramento-area health system to offer the complex surgery, called a rotationplasty.

The Portugal-Herrera family, originally from Michoacán, Mexico, lives in Acampo, a 600-acre town near Lodi, California. Jorge Herrera, Sr. is a farmworker in the area, and Alma pruned grape vines before becoming Jorge’s full-time caregiver. Their home also includes 11-year-old Gaby, 18-year-old Sarai and her 18-month-old son, Ernan. The eldest, 23-year-old U.S. Marine Francisco, stays in touch with his family via FaceTime.

From unexplained pain to a sarcoma diagnosis and treatment plan

Jorge endured six months of intense knee pain and missed a lot of school

IT WAS NOT AN EASY DECISION. IT GAVE US A LOT OF ANGUISH, BUT IN THE END IT WAS THE BEST OPTION FOR HIM.

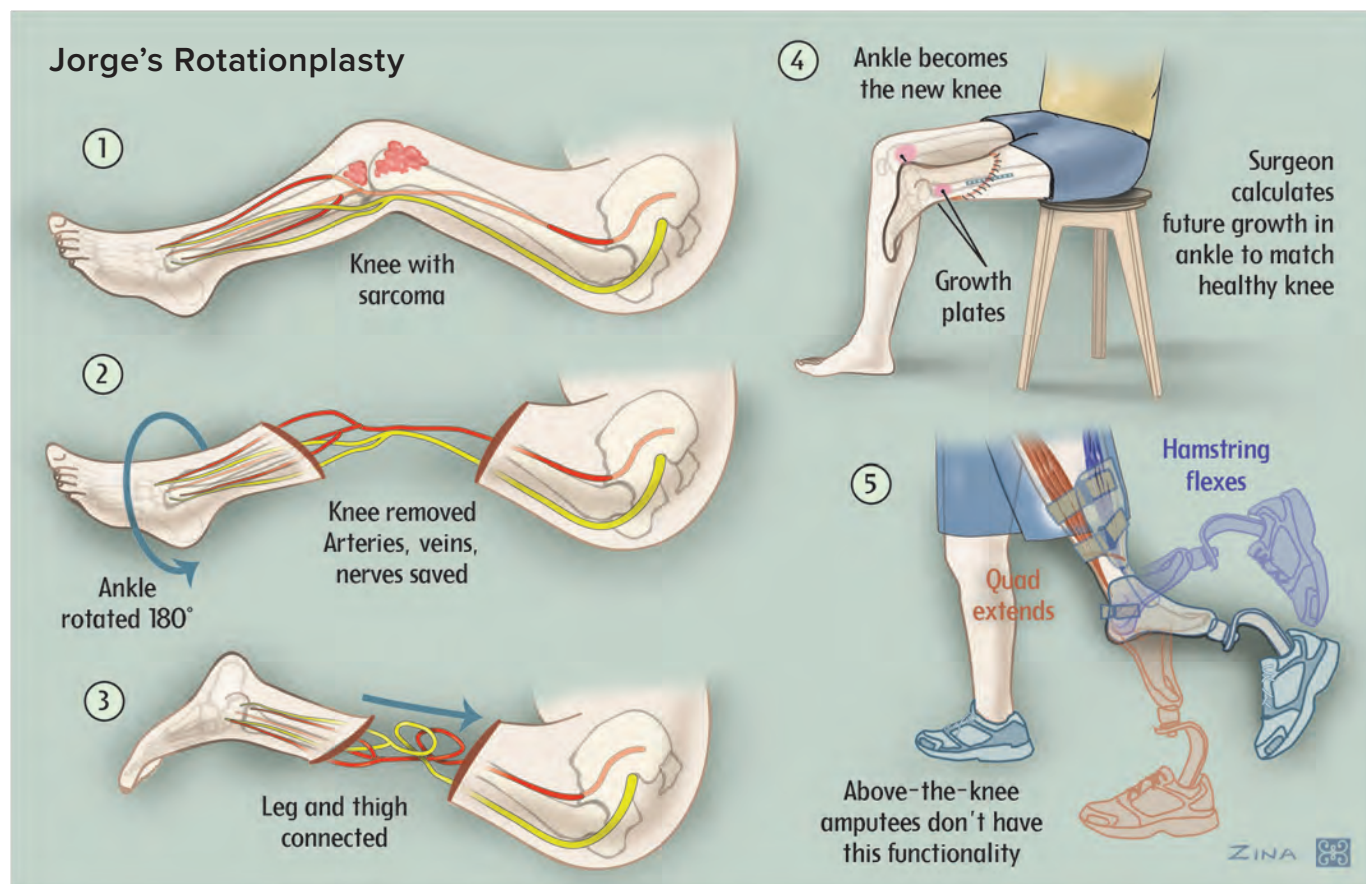
before his doctor discovered something new on an X-ray. Physicians in Lodi quickly referred the family to UC Davis Health, where specialists diagnosed Jorge with Ewing’s sarcoma and devised a treatment plan.

“We worked as a multidisciplinary team,” says pediatric oncologist Marcio Malogolowkin. “Steven Thorpe, his orthopaedic oncology surgeon, and I were involved from the very beginning, from patient referral to evaluation to confirmation of diagnosis and start of therapy.”

Collaboration is fundamental to the mission of the Cancer Center’s Pediatric and Adolescent and Young Adult Sarcoma Clinic, where families get care from oncologists, surgeons, nurse navigators, physical therapists and child life specialists.

“The best way to provide care to our patients in a timely manner is this kind of approach,” says Malogolowkin. “Families leave the clinic with a full assessment and agreement among the team. They have an individualized plan, and we go through the process with them so they don’t feel alone.”

Jorge’s tumor was in his left distal femur and proximal tibia — or inside his left knee — and surrounding soft tissues. To help shrink the mass before surgery he would receive several weeks of chemotherapy. The next phase of treatment would be far more complex.



The doctors presented three options to the Portugal-Herrera family — all were daunting: amputation of the leg from above the knee; limb-sparing surgery with a custom-implanted, expandable metal prosthesis; and rotationplasty, using Jorge’s ankle joint to make a new knee.

Thorpe explained that amputation above the knee would drastically limit Jorge’s mobility. An implanted prosthesis would require multiple surgeries to accommodate his growing body and would be a difficult procedure because the cancer involved both sides of his knee. Rotationplasty, although cosmetically challenging, would give Jorge a new knee joint after tumor removal and better mobility for an active life without the need for additional surgeries.

Convincing him and his parents, however, was another matter. After the operation, Jorge’s foot would extend out backwards from where his knee would normally be — an anomaly that keeps many people from choosing to do it.

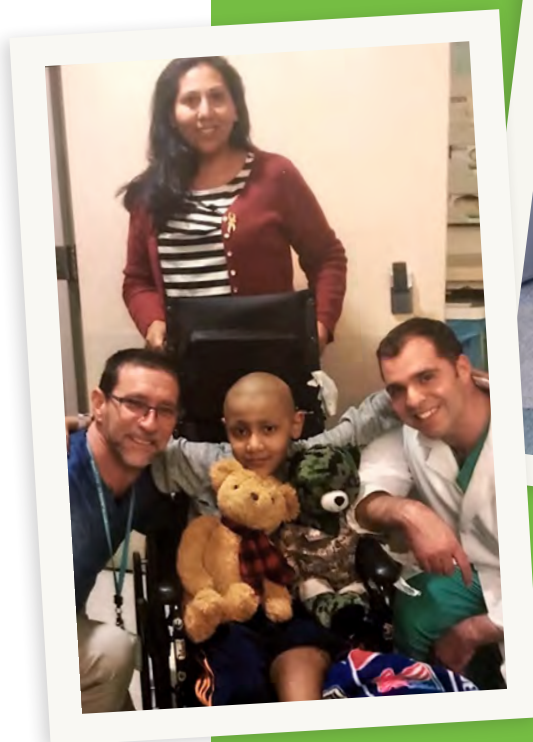
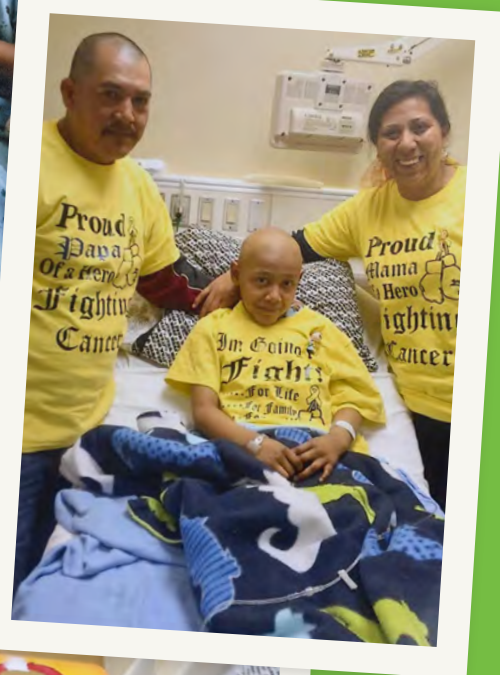
“It was not an easy decision,” says Portugal-Herrera. “It gave us a lot of anguish, but in the end it was the best option for him. The doctors told him he had to know everything because his body was going to change.”

Preparing then 7-year-old Jorge was critical. Part of that included watching a video, which showed Jorge what his new leg would look like. Throughout, Jorge was quiet, but seemed to understand.

A long day of surgery and waiting

At 6 a.m. on Nov. 29, 2016, hospital staff admitted Jorge, and the Portugal-Herrera family waited anxiously for the life-saving surgery to end.

In the operating room, Thorpe worked to remove the tumor which involved resecting the knee, including the top of the tibia and the bottom of the femur. Separation and isolation of the blood vessels and nerves from the tumor



PATIENT FOCUS

resection required six hands — those of Thorpe and his assisting surgeons to safeguard against damage or clotting.

“What takes a meticulous amount of time is that the blood vessels and nerves extending from the thigh to supply the leg and foot have to be dissected away from the tumor, bone,

and surrounding soft tissue you are taking out,” says Thorpe. “If a vessel clots off, the rotationplasty can fail. If you stretch a nerve too much, you can cause injury to it.”

Four hours later, the team quickly set to work on the next phase of surgery: reconstructing the leg. First, the team

rotated the leg 180 degrees so that the preserved shin bone and femur were aligned and could be affixed.

“This can be difficult because of the difference in the anatomy of the two bones,” says Thorpe. “You have to get the rotation just right so it can heal in appropriate limb rotation so that the



eventual prosthetic and leg can function.”

The surgeons next stitched the quadriceps muscles in the thigh to the calf muscle to create knee extension, and the hamstrings to the long muscles on the front of the shin to create knee flexion. To protect the spared nerves and vessels, now much longer than needed for the length of the shorter leg, the surgeons carefully coiled them and tucked them into space to protect them from damage or potential clots.

When reconstruction was complete, Thorpe carefully closed the skin of the calf to the thigh, completing the operation. All told, with anesthesia and surgery Jorge was in the operating room nearly 12 hours.

Post-op recovery another long ordeal

Jorge could feel his foot immediately and was soon wiggling his toes. He was able to move his new knee within two months of the surgery. But the healing took time. He needed postoperative chemotherapy which, while important to curing his cancer, can impair healing. Jorge also fell and broke his ankle (new knee), which in turn delayed his getting a prosthesis.

JORGE COULD FEEL HIS FOOT IMMEDIATELY AND WAS SOON WIGGLING HIS TOES. HE WAS ABLE TO MOVE HIS NEW KNEE WITHIN TWO MONTHS OF THE SURGERY. BUT THE HEALING TOOK TIME.

Happily, his family, friends and school personnel were there throughout to help him pull through. While he was hospitalized, for example, his mother performed “surgery” on his stuffed toys, including several Teddy bears his brother had given him so that now all of them had the same procedure Jorge had.



Jorge prepares to put on his prosthesis.

It was a year before Jorge finally had the prosthesis, and he experienced another setback when he broke the ankle (new knee) again trying to kick a soccer ball. Today, however, he easily pulls the prosthesis on and off and can

climb, run and dive for the football, albeit with some happy tumbles along the way.

The Portugal-Herrera family is pleased with the collective decision to reconstruct Jorge’s leg, which they believe will give him the best chance to be a regular kid with few physical limitations.

“I told his family, ‘I hope he’s so physically active he wears the prosthesis out,’” says Thorpe. “I love taking care of kids with sarcoma like Jorge. Their resilience always amazes me.”

In June 2018, Jorge celebrated one year cancer-free with his family and friends with a party and a “Krabby Patty” cake inspired by SpongeBob SquarePants. He still works to get caught up with his studies, and still struggles from time to time getting accustomed to his new normal at home and at school.

But when he’s strong enough, he hopes to acquire a state-of-the-art prosthesis like the ones disabled athletes use, and lights up when he imagines it.

“What motivates us to keep moving forward is that he always smiles,” says Portugal-Herrera. “Even through things that are really hard, he smiles.”

First CAR T therapy patient hopeful

Treatment targets stubborn lymphoma

Bobby Hughes doesn't complain much, but truth be told he's been clobbered, as his wife, Jerri, says. The first hit was an aggressive lymphoma.

Then he had blood poisoning, bowel surgery, a cancer recurrence, and finally kidney failure, from which he recovered.

But on Jan. 31, as he lay in a bed in the UC Davis Medical Center groggy but smiling, there was hope. Hughes had just become the first patient at UC Davis Health to receive a revolutionary new kind of treatment for diffuse large B-cell lymphoma — a one-time therapy that could put him into remission for good.

The treatment? His own white blood cells, engineered to become lethal weapons against the stubborn lymphoma that threatened his life. Called CAR T therapy (short for chimeric antigen receptor T-cell therapy), the approach is a new immunotherapy option for patients who have failed on chemotherapy and can't have a stem cell transplant.

With Jerri at his side and son Bobby Jr. at the foot of the bed, nurse Mike

Chan slipped the precious little bag of opaque liquid onto the IV pole, and slowly it dripped through a line and into his bloodstream.

"I feel good," he said. "I'm glad the time is here."

CAR T treatment program targets patients with stubborn disease

The health system's preparation for this day began more than a year ago, as UC Davis Health was building its cellular therapy program. Accreditation, inspections, protocols and procedures, contingency plans, and staff and physician training all needed to occur before the first patient received the treatment.

UC Davis Health is the only system in the region that offers FDA-approved CAR T therapy for lymphoma, according to Kite Pharma, the Santa Monica-based company that developed the treatment.

For 61-year-old Hughes, the journey began in May 2017 when a trip to a Bay Area hospital emergency room for stomach pain ended with a cancer diagnosis and six rounds of chemotherapy. A scan shortly afterward showed the tumors had vanished, but two months later the pain — and the tumors — were back.

This time, the chemotherapy treatment made Hughes very sick, and a subsequent Bay Area hospitalization resulted in a blood infection, kidney failure and surgery to remove more than a foot of intestine.

Hughes, who lives in El Sobrante, then transferred to the UC Davis Comprehensive Cancer Center under the care of oncologist and blood cancer specialist Joe Tuscano.

Tuscano says Hughes is one of a minority of patients whose lymphoma is “refractory,” or resistant to treatment, and also unlikely to respond to stem cell transplantation.

“You can cure as many as 50 to 60 percent of patients with standard chemo,” he says. “And among those you can’t cure with chemo, some can be cured with a stem cell transplant. But some patients are either not good candidates for transplant or their disease is not amenable to transplant. Those are patients considered for CAR T.”

The CAR T cells are kept on dry ice at minus 190 degrees Celsius then thawed in a bath of water before being infused into the patient.

Patients are closely monitored

With the prospect of a totally different approach to his unrelenting disease, Hughes’ outlook brightened.

“This is the last treatment,” he said. “Even if it doesn’t work for me, maybe they will find something out that will help someone else.”

CAR T therapy begins with collection of a blood sample from the patient and use of a machine to separate the T cells from other blood cells. The T cells are then sent to a laboratory where they are made into CAR T cells. That process, which takes two to three weeks, involves inserting the gene for the chimeric antigen receptor (CAR) into the T cells. The cells multiply in the



lab and are then returned to UC Davis for treatment of the patient. Patients may be given low-dose chemotherapy prior to the treatment, which occurs with a single intravenous infusion of the modified T cells.

Hughes was monitored very closely in the hospital for any adverse effects of the treatment and continues to have frequent outpatient checkups.

Although the CAR T therapy is commercially available, reimbursement for the treatment can vary depending on a patient’s third-party insurance provider. That said, Tuscano says use of the therapy will grow for lymphoma and eventually other diseases.

“There will be many more indications for the treatment right around the corner — many kinds of blood cancers, and maybe even for solid tumors,” he says.

For Bobby and Jerri Hughes, their children and grandchildren, the future already is brighter.

“I just know that everything that could have been done has been done,” says Jerri Hughes. “That makes me feel good.”

“I just know that everything that could have been done has been done...that makes me feel good.”

—Jerri Hughes

*Of note, as with any treatment or therapy, CAR T therapy requires prior authorization and approval by the patient’s insurance to ensure patient eligibility and coverage prior to administering treatment.



GAMING A CURE



Crowdsourced computer challenge tackles deadly toxin

Imagine this choice: You're hungry, and there's enough to eat, but the food increases your long-term risk for cancer. That's the dilemma facing billions of people whose food supplies are infected by aflatoxins, the most prevalent carcinogen most people have never heard of.

"It doesn't really exist here, so people don't think about it, but this is a major problem worldwide, almost an epidemic," says associate professor Justin Siegel, who directs the UC Davis Innovation Institute for Food and Health. "In certain parts of the world, it affects corn, sorghum, casaba, millet — essentially everything has aflatoxin in it."

Aflatoxin is produced by the fungus *Aspergillus flavus*, which loves hot, humid climates. The poisonous molecule mutates DNA, has been linked to stunting and anemia, and is a major cause of liver cancer. Though it hasn't been a problem in the United States since stringent regulations were imposed decades ago, climate change could alter that calculus. For people in India, Africa and parts of China, aflatoxin is a constant danger.

"There are fields of molding crops that people will eat," says Siegel, "that are chockful of these toxins, because otherwise they have nothing."

Siegel is helping lead a novel project to overcome aflatoxin. Working with the University of Washington, Northeastern University, Thermo Fisher Scientific, Mars Inc. and others, he is trying to

reengineer promising enzymes to break down aflatoxin and create a much safer food supply. But there's a problem: the number of potential enzyme shapes is virtually infinite.

"There are more potential structures than stars in the universe," says Siegel.

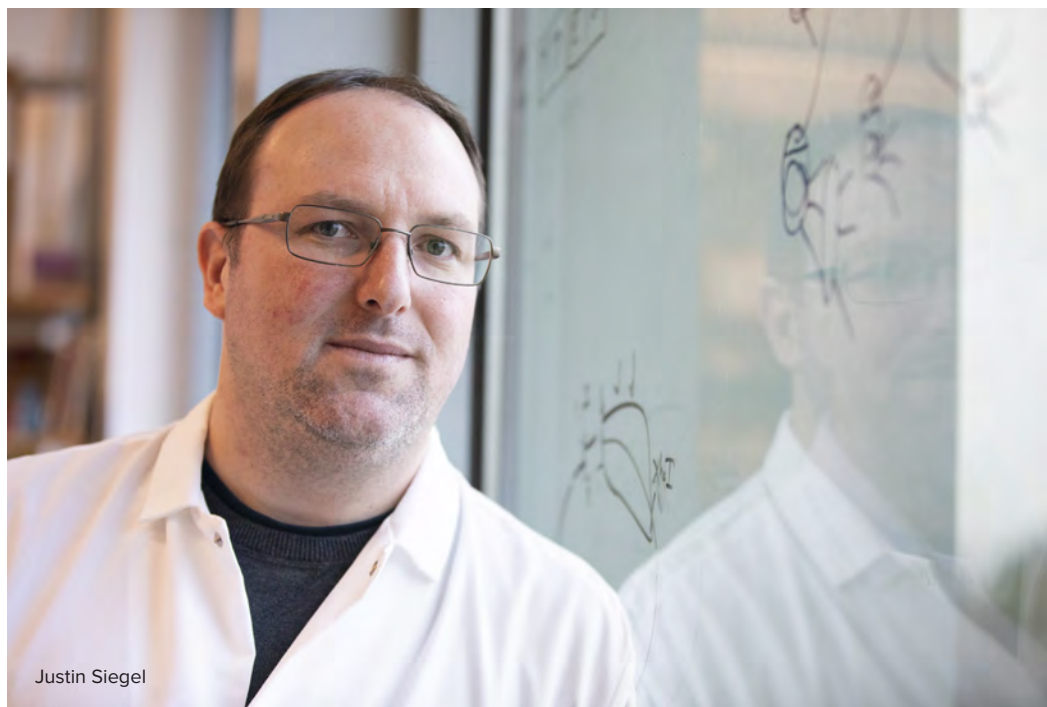
What they needed was a way to distribute the workload and cover more ground. They found it in a crowdsourcing game called FoldIt.

Bring on the gamers

Developed by researchers at the University of Washington, FoldIt is not an ordinary computer game. Participants don't look for treasure or conquer Wales, they experiment with different protein shapes to find

"It doesn't really exist here, so people don't think about it, but this is a major problem worldwide, almost an epidemic."

Associate Professor Justin Siegel,
UC Davis Director, Innovation Institute
for Food and Health



Justin Siegel



Graduate student Alex Schaffer, Justin Siegel and Ryan Caster with a FoldIt protein design.

For the Aflatoxin Challenge, players are given enzymes that could potentially break down the molecule and make it nontoxic — they only have to redesign it in just the right way.

the best structures. With proteins, form dictates function, so harnessing thousands of creative people to generate novel structures can really move the science.

“A human mind can come up with ideas for shapes and structures that look interesting,” says Siegel. “FoldIt takes this human intuition and applies a biophysical metric to ask: How realistic is it for this to happen? While you can imagine this structure, is it likely to occur or is it extremely unlikely? It couples the human imagination with physical reality.”

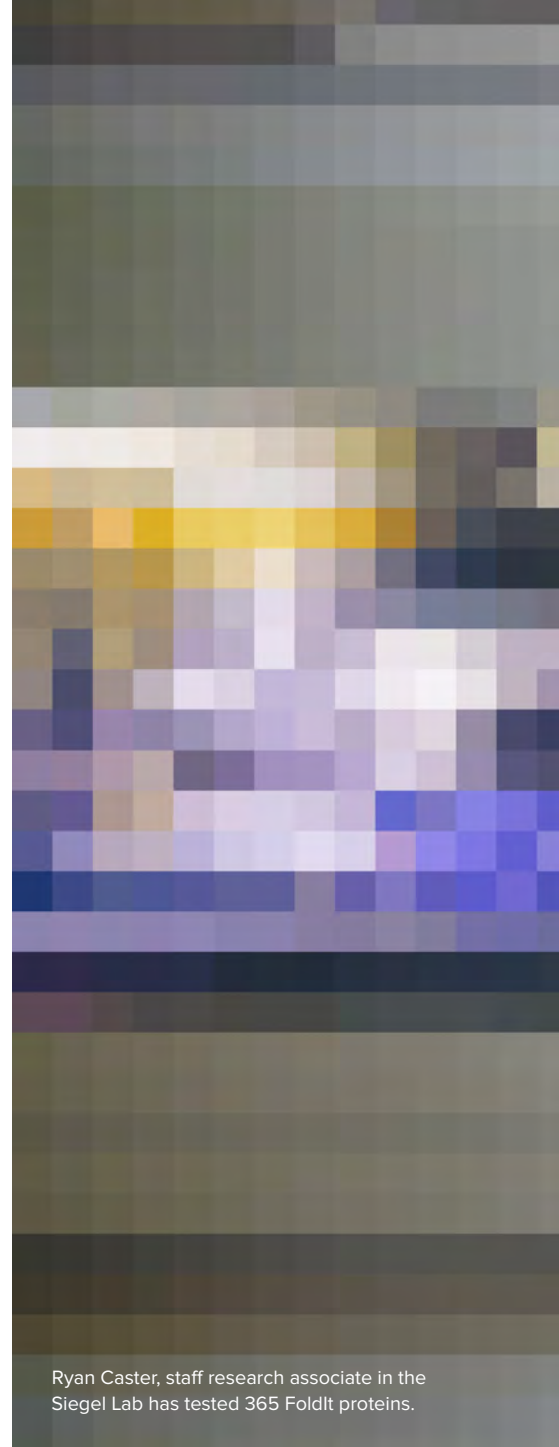
For the Aflatoxin Challenge, players are given enzymes that could potentially break down the molecule and make it nontoxic — they only have to redesign it in just the right way.

“We thought it would be a good way to get people engaged in this problem, which a lot of FoldIt players have never heard of,” says Siegel. “Around 4.5 billion people are eating this toxin on a daily basis, and we’re trying to eliminate it without destroying their food.”

There have been a number of design cycles, each one lasting several months, giving thousands the opportunity to play. Patrick Camarador was a pharmaceutical chemistry major at UC Davis when he joined in.

Camarador had tried playing FoldIt in high school, but it didn’t resonate with him. But after taking a biochemistry class, he rediscovered the game and even started livestreaming his play on Twitch.

He had never heard of aflatoxin before the challenge, but embraced



Ryan Caster, staff research associate in the Siegel Lab has tested 365 FoldIt proteins.

the opportunity to take on a deadly poison. He liked that it was contributing to good science, and it didn’t hurt his studies either.

“FoldIt helps me memorize the 20 amino acids just by visual shape alone,” says Camarador. “The more I played the game and designed my own proteins, the more I got familiar with which amino acid is which.”

Camarador is now a PharmD candidate at California Northstate University.



He still plays FoldIt, as his studies allow.

“It’s cool for me,” he says, “because I get to apply concepts I’ve learned in pharmaceutical chemistry and design classes.”

The continuing journey

The Aflatoxin Challenge is a unique partnership between universities, an international consumer company and life sciences giant Thermo Fisher, and each group brings important

talents to the project.

“Thermo is providing DNA at a scale that normally wouldn’t be possible to let us really explore what these players are making,” says Siegel. “Mars is providing social, financial and translational support. It took this uncommon collaboration to really drive this project forward.”

Once they solve this enzymatic puzzle, Siegel envisions spraying the enzyme on crops or even

engineering it into the plants themselves. The group has been testing some of the better designs in the lab to see how they work against aflatoxin, but it’s a trial and error process and could take a while.

“No hits yet, but it’s early days,” says Siegel. “We’ve learned a lot about how much you can change these enzymes before they break. We haven’t had a breakthrough, but we’re making progress.”

*In honor of
a man with a
generous spirit,
a generous gift*

Donation
supports
innovative
robotic
treatment



Ellen Kwong

Ellen Kwong uses a lot of positive words to describe her late son, Glenn: loving, caring, humorous and upbeat. But the word Mrs. Kwong uses most is “generous.”

“That was Glenn,” she says as a smile washes over her face. “He reached out to help people he didn’t even know.”

Glenn Kwong, the youngest of three, died in 2015 from esophageal cancer, more than two years after his diagnosis at UC Davis Health. In honor of Glenn’s generous spirit, Mrs. Kwong made a financial gift to his surgeon, Gregory Farwell, who researches and treats head and neck cancers. The gift helped Farwell hire coordinators for an important clinical research project in multidisciplinary collaboration with colleagues from the UC Davis Department of Biomedical Engineering (see page 4).

The project involves a tool developed by biomedical engineer Laura Marcu that can distinguish between cancerous and benign tissue and can be used by the surgeon during a procedure. Farwell, who does robot-assisted head and neck cancer surgeries, worked with Marcu to integrate the tool with the robot so that he can more precisely remove cancer tumors and spare healthy surrounding tissue identified with the new tool.

“The donation was humbling because what Glenn and his mom went through was intense,” says Farwell. “Thanks to the Kwong family and other grateful patients, we can apply additional resources to our studies.”

Keeman Wong, executive director of development for the Cancer Center, says gifts made in memory of a loved one or in honor of a care provider are very special.

“It warms our hearts to know that these gifts are usually made as a way to say ‘thank you’ or that ‘this person meant a lot to me and I want to pay tribute to them,’” he says. “In this case, Mrs. Kwong did both — to honor her son and recognize Dr. Farwell and his team for their care.”

The best course of treatment for Glenn was surgery to remove his larynx, or voice box, and the cancerous section of his esophagus. Once Farwell removed the malignant tissue, another surgeon, Richard Bold, performed a gastric pull-up, in which the remainder of Glenn’s esophagus was attached to his stomach to preserve his ability to eat normally.

“Head and neck tumors create problems with things we take for granted, like eating, drinking and talking — the things that connect us as humans and are among the greatest joys in life,” Farwell says. “Glenn displayed such strength while undergoing treatment and had wonderful family support. I can’t overemphasize how important that is.”

Mrs. Kwong described her son’s resilience throughout his ordeal.

“I knew Glenn was in pain, but he never complained,” she says. “He never said a negative word. No matter how tired he was.”

Despite months of chemotherapy and radiation before and after his surgery, Glenn maintained a positive attitude and sense of humor. Before he got sick, Glenn managed an apartment building and volunteered his time helping others, which he continued as long as he could.

“Once, after his surgery, Glenn asked, ‘Mom, can you drive me to this house?’ I had no idea where we were going,” says Mrs. Kwong. “We got to the house, he went inside, and he came back out with an old man. Glenn said, ‘I ran into

Thanks to the Kwong family and other grateful patients, we can apply additional resources to our studies.

DR. GREGORY FARWELL



Dr. Gregory Farwell with Ellen Kwong

him on the street the other day walking home with groceries.’ The next week, we gave the man a ride to the store.”

Glenn and his mother were always close, and their special bond grew stronger during his cancer treatment. They had spent years before his diagnosis traveling throughout the world — Russia, Italy, Taiwan, Greece — and stuck together during his sickest days at home or at the hospital.

“The human body is resilient even after such aggressive treatment,” says Farwell. “Glenn was still able to enjoy life.”

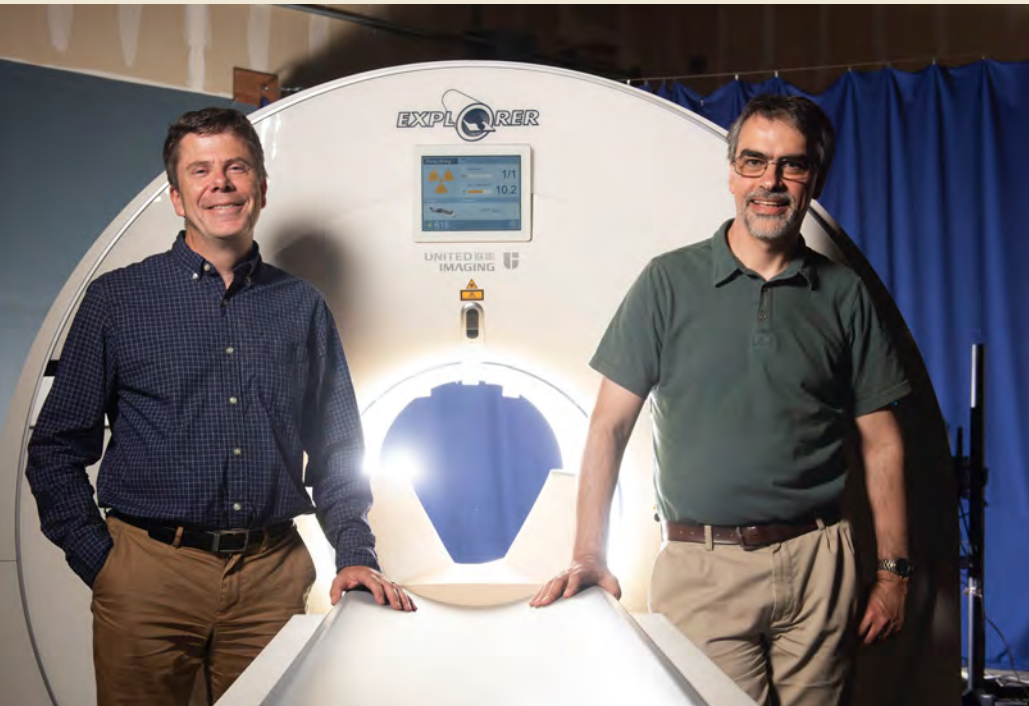
Although he lost his ability to speak, Glenn communicated by writing. He and Mrs. Kwong scribbled notes to one another on yellow legal pads scattered throughout their home. They wrote about his care and upcoming appointments, vacations and events, and especially about food. Mrs. Kwong still treasures the last piece of paper they wrote on with the words “seafood soup” in huge letters.

“He liked food and he liked people,” Mrs. Kwong says, giggling. “His favorite meal was a steak.”

The Kwong family appreciates the care Glenn received at UC Davis Health. Three years after Glenn’s passing, his 94-year-old mother took the time to visit Farwell to personally say thank you for all of his efforts. Making a gift to support Farwell’s research felt natural.

“All along,” says Mrs. Kwong, “I really wanted to come in to say thank you for everything they (his care team) did for my son.”

First-of-its-kind total-body PET scanner arrives at UC Davis



EXPLORER, the world's first medical imaging scanner that can capture a 3-D picture of the whole human body at once, will be operational this summer. The EXPLORER Imaging Center occupies leased space on Folsom Boulevard.

The brainchild of UC Davis scientists Simon Cherry and Ramsey Badawi, EXPLORER is a combined positron emission tomography (PET) and X-ray computed tomography (CT) scanner. Because the machine captures radiation far more efficiently than other scanners, EXPLORER can produce an image in as little as one second and, over time, produce movies that can track specially tagged drugs as they move around the entire body.

The developers expect the technology will have countless applications,

from improving diagnostics and tracking disease progression to researching new drug therapies.

The scanner was developed in partnership with Shanghai-based United Imaging Healthcare (UIH), which built the system based on its latest technology platform and will eventually manufacture the devices for the broader healthcare market.

The first human scans from EXPLORER were made public in November 2018. They quickly circulated widely online, stunning radiologists and other imaging experts worldwide. The FDA approved the technology in December.

Badawi and Cherry first conceptualized a total-body scanner 13 years ago. Their idea was kick-started in 2011 with

a \$1.5 million grant from the National Cancer Institute and boosted in 2015 with a \$15.5 million grant from the NIH.

Cherry, distinguished professor in the UC Davis Department of Biomedical Engineering, says he expects EXPLORER will have a profound impact on clinical research and patient care because it produces higher-quality diagnostic PET scans than have ever been possible. EXPLORER also scans up to 40 times faster than current PET scans and can produce a diagnostic scan of the whole body in as little as 20 to 30 seconds.

Alternatively, EXPLORER can scan with a radiation dose up to 40 times lower than a current PET scan, opening new avenues of research and making it feasible to conduct many repeated studies in an individual, or dramatically reduce the dose in pediatric studies, where cumulative radiation dose is particularly important.

For the first time, an imaging scanner will be able to evaluate what is happening in all the organs and tissues of the body simultaneously. For example, it could quantitatively measure blood flow or how the body takes up glucose everywhere in the body. Researchers envision using the scanner to study cancer that has spread beyond a single tumor site, inflammation, infection, immunological or metabolic disorders and many other diseases.

"I don't think it will be long before we see a number of EXPLORER systems around the world," Cherry says. "But that depends on demonstrating the benefits of the system, both clinically and for research. Now, our focus turns to planning the studies that will demonstrate how EXPLORER will benefit our patients and contribute to our knowledge of the whole human body in health and disease."

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Synthesis — the art of bringing distinct elements together to form a cohesive whole — is the name of our magazine and our strategy as the Central Valley’s only National Cancer Institute-designated comprehensive cancer center. Leveraging UC Davis strengths in innovative cancer models and technologies, precision therapeutics, transformative imaging and mitigation of cancer risks and disparities, we aim to reduce the cancer burden in our region and beyond. Uniting physicians, scientists and public health experts, we are committed to making cancer discoveries and delivering them quickly to patients so they have the best possible outcomes.

Synthesis — linking the best in cancer science to improve patients’ lives — is our promise.

More than 40 people braved the shave at Rock the Bald, the Cancer Center’s inaugural head-shaving event in March, including **Christine McKay** from the Division of Hematology and Oncology, who raised \$2,500 of the nearly \$50,000 in total contributions for St. Baldrick’s Foundation and pediatric cancer research.

