

SYNTHESIS

THE MAGAZINE OF UC DAVIS COMPREHENSIVE CANCER CENTER

VOL 20 | NO 2 | WINTER 2017

A detailed microscopic image of tissue, likely stained with hematoxylin and eosin (H&E). The image shows numerous cells with prominent, dark blue nuclei and lighter, yellowish cytoplasm and extracellular matrix. The cells are arranged in clusters and some show signs of atypia, such as irregular shapes and sizes. The overall appearance is that of a histological section, possibly from a tumor or a specific organ like the liver or pancreas.

Fast-tracking pathology

PAGE 22

Banking on life

PAGE 4

Young cancer patients tackle challenges together

PAGE 8

From grief, a gift

PAGE 18

Dear Reader,

People affected by cancer are at the center of what we do. In our research laboratories, clinics, hospital and even pharmacies our scientists, clinicians and staff are laser-focused on either preventing cancer from developing, detecting cancer early or working to help patients live longer and better after a cancer diagnosis.

In this issue of *Synthesis* you will learn about several examples of this mission, ranging from highly specialized imaging tools to better detect pancreatic cancer to a program that supports adolescents and young adults with cancer and connects them through our annual Pushing Past Cancer conference.

You will be amazed at the stunning images captured by the MUSE microscope, a technology developed by UC Davis and other scientists. These images represent what we hope will be a huge advance in the ability to analyze tissue specimens immediately after a biopsy, enabling a rapid diagnosis and sparing patients the anxiety caused by waiting days for pathology results — and expediting treatment.

For patients on clinical trials, our Investigational Drug Service does far more than dispense experimental cancer medications. Our story describes how these specialty pharmacists are an essential part of the care team, ensuring that patients are safe as they travel through their cancer treatment journey.

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



Primo “Lucky” Lara | ACTING DIRECTOR, UC DAVIS COMPREHENSIVE CANCER CENTER

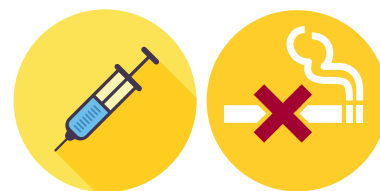
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Breaking Barriers to Beat CancerSM

PUSHING PAST CANCER 8



MOONSHOT GRANT PROJECTS 3



CANCER DISPARITIES 12

BITS & PIECES

2 Moonshot grant for canine cancer study, Neuropathy after chemotherapy, Smart immune cell research, and more...

PROVING GROUND

4 **BANKING ON LIFE**
Lung cancer survivor grateful for comprehensive care

OUTREACH

8 **PUSHING PAST CANCER**
Young patients connect

Q&A

12 **CANCER DISPARITIES**
Looking through a long lens

IN TRANSLATION

14 **IMAGING**
A new way to see cancer

BENEFACTORS

18 **FROM GRIEF, A GIFT**
Donation accelerates drug development

PATIENT FOCUS

20 **LONG-DISTANCE DONOR**
Meets her match

FIRST STEPS

22 **THE MUSE MICROSCOPE**
Fast-tracking pathology

ON THE COVER An image of normal breast tissue, blood vessels and fat cells by the MUSE microscope, which uses ultraviolet light. See story on page 22.

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Moonshot grant advances immune therapy for dogs — and one day people — with cancer

UC Davis has received its **first National Cancer Institute (NCI) Moonshot grant** — \$2.5 million over five years — to explore immunotherapy treatments for dogs who develop melanoma and osteosarcoma and that may one day benefit humans, as well.

“These are two cancers that dogs get which are similar to human cancers, and we need new therapies for both of them,” said **Robert Canter**, a surgical oncologist at the UC Davis Comprehensive Cancer Center and the study’s co-principal investigator. “Both of these diseases often go right to the lungs and have extremely high mortality rates.”

Canter and co-principal investigator **Robert Rebhun**, a veterinary oncologist and researcher at the UC Davis School of Veterinary Medicine, will combine natural killer cells with cytokines to boost



Robert Rebhun and patient

the immune system against cancer cells in 70 dogs with naturally occurring melanoma or osteosarcoma.

“Through Moonshot, the NCI is betting that canine studies will directly translate, inform and improve immunotherapy for human cancer patients,” he said. “This is a ‘win-win’ in that we can investigate promising immunotherapies for pet dogs with cancer that otherwise may be out of treatment options.”

In addition to Canter and Rebhun, investigators include **Arta Monjazeb, Michael Kent, William Murphy, Ellen Sparger, Titus Brown, Susan Stewart** and **William Culp**.

Neuropathy after chemotherapy an understudied problem

In two papers published in the *Journal of the National Cancer Institute*, researchers from UC Davis, UCLA and other institutions found that peripheral neuropathy, which causes pain, numbness, and tingling in hands and/or feet, can bother early-stage breast cancer patients years after completing chemotherapy. In addition, a systematic literature review found only a handful of studies that tracked long-term peripheral neuropathy, leaving little data for patients and clinicians to make informed decisions.

“Until recently, the really strong focus has been to identify treatments to reduce breast cancer recurrence and mortality,” said **Joy Melnikow**, a co-author who directs the Center for Healthcare Policy and Research at UC Davis. “I think we’ve reached the point now where we need to ask

questions about the adverse effects that come along after curative treatments. **We need to balance what are sometimes small therapeutic benefits with the risk of long-term adverse events.**”

After a systematic review of the literature, researchers found only five papers on studies that followed patients for a year or more. In addition, the research produced widely variable results.

“**The most striking finding from the review was how little data was out there,**” Melnikow said. “And these studies report a wide range of frequency for peripheral neuropathy, from as low as 11 percent to more than 80 percent of patients at one to three years after treatment.”

The second study was launched to help remedy this scarcity of information. The team looked at 1,512 early-stage

breast cancer patients from a large clinical trial that investigated the effectiveness of various combinations of chemotherapies. Overall, two years after the start of treatment, 42 percent of patients experienced neuropathy symptoms and 10 percent reported severe discomfort. In addition, women experiencing more severe neuropathy symptoms reported much worse quality of life.

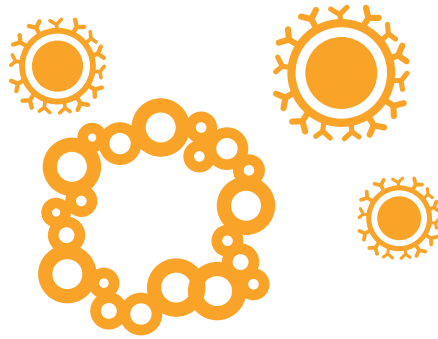
Oncologists have encouraged patients to receive adjuvant chemotherapy to guard against breast cancer recurrence. However, given the potential for side effects, and the effectiveness of other treatments, the authors concluded that the choice of adjuvant chemotherapy drugs or their avoidance should include consideration of long-term effects of breast cancer treatment.

“Smart” immune cell research gets boost with Innovator Award

UC Davis Assistant Professor **Sean Collins** received a \$1.5 million award from the National Institutes of Health to advance the development of “smart” immune cells for therapies to treat cancer and other diseases. The five-year NIH Director’s New Innovator Award aims to provide new insight into how to engineer immune cells to control their recruitment and response to tumors.

“Immune cells are emerging as major tools for the next generation of cancer therapies,” said Collins, of the Department of Microbiology and Molecular Genetics and the UC Davis Comprehensive Cancer Center. “Our project is aimed at understanding how immune cells channel information downstream of inputs from the cell surface to control different behaviors.”

One challenge in developing immune cell therapies is to strike a balance between the beneficial anti-tumor responses and negative side effects caused by an amplification of the immune response, such as



fever, difficulty breathing, seizures and other problems.

By targeting smart cells to respond in a specific and controlled manner and limiting their ability to amplify the attack signal, Collins hopes the cells will be able to work more effectively to fight tumors and avoid damaging the body’s healthy cells. Taking a systematic, genome-wide approach, Collins’ team will break down the complexity of an immune cell’s signaling network, developing maps that reveal the different response pathways within the cell.

Collins’ award is one of 55 “High Risk, High Reward” New Innovator Awards announced by the NIH in October.

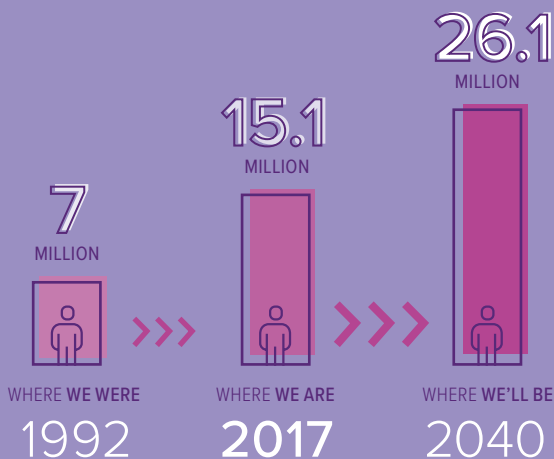
Gandara named ‘Giant of Cancer Care’

David R. Gandara, professor and director of thoracic oncology at UC Davis Comprehensive Cancer Center, was named a “**Giant of Cancer Care**” in lung cancer by OnLive in recognition of his work to advance the field of oncology through his contributions in research and clinical practice. Gandara was one of 12 inductees at the Chicago History Museum on the first day of the 2017 meeting of the American Society of Clinical Oncology (ASCO) in June, which brings together more than 30,000 oncology professionals from around the world.



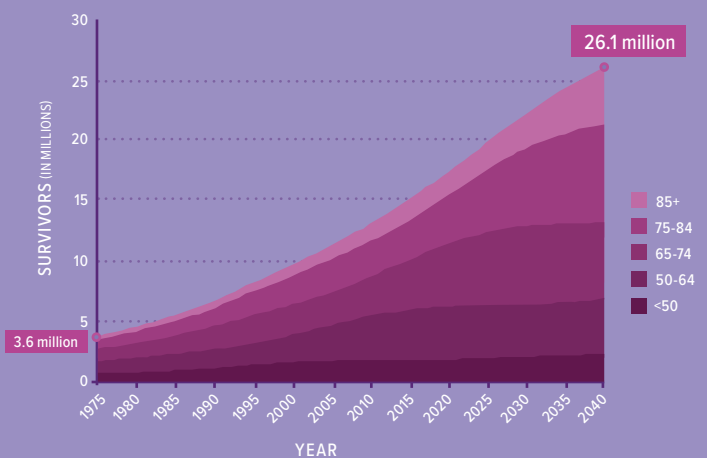
CANCER SURVIVORS

Cancer survivorship is on the rise; by 2040 the number will reach more than 26 million.



A Surge in Older Survivors:

Estimated Number of U.S. Cancer Survivors by Age Group



Source: Bluethmann SM et al. Cancer Epidemiol Biomarkers Prev. 2016 Jul;25(7):1029-36. Courtesy of NCI

'They care about you'

Banking on life

PATIENT JOE BANKS THANKFUL FOR CARE THAT'S 'JUST RIGHT'

IN 2011, TWO DAYS BEFORE Joe and Barbara Banks were to leave for Tahiti to celebrate their 40th wedding anniversary, the retired Air Force colonel found out the lung cancer that had been in remission four years was back, it had spread, and he likely had six months to live, at best.

The non-smoker and self-described gym rat accepted that he would never meet his expected grandchild, and he said goodbye to family, including his pregnant daughter-in-law. But he also took the advice of his cancer

It turned out that Banks had a genetic mutation that made him eligible for a study led by oncologist Tianhong Li, associate professor of internal medicine.

center doctors and made an appointment to be evaluated for ongoing clinical trials. When he did, he entered a comprehensive system of care in which

the cancer center's Investigational Drug Service pharmacists play an essential role and for which he is grateful.

It turned out that Banks had a genetic mutation that made him eligible for a study led by oncologist Tianhong Li, associate professor of internal medicine. Li was the first to study the possible benefits of combining the chemotherapy drug, Alimta (pemetrexed), given intravenously, and the targeted anti-cancer therapy, Tarceva (erlotinib), taken orally.



“I began the treatment in April of 2011 and, by the fall of 2011, all the cancer was gone,” Banks says. “For me, it worked.”

Banks, who lives in Rescue, Calif., has since been taken off of the Alimta, but remains on a 21-day cycle of Tarceva. The drug can cause miserable side effects. Banks experiences some of them — nausea, diarrhea, and rashes — but he insists they are a small price to pay for getting to spend time with his wife, Barbara, and meeting and enjoying his two grandsons.

“Tarceva is my miracle drug,” Banks says. “It allows me to lead an almost normal life.”

Recently, Banks had a brief scare when an anomaly appeared on a PET scan of his lungs. Thankfully, it was

The drug can cause miserable side effects. Banks experiences some of them — nausea, diarrhea, and rashes — but he insists they are a small price to pay for getting to spend time with his wife, Barbara, and meeting and enjoying his two grandsons.

nothing. Banks and his wife later flew to Hawaii to celebrate the clean scan and his 70th birthday.

Upon their return, the couple headed for one of Banks’ regular visits to the Investigational Drug Service where he received his next dose of Tarceva.

The pharmacy is a critical part of the care of clinical trials patients like Banks. Staff members dispense all oral medications, keeping patients safe by carefully tracking the other medications they take. They follow-up with patients within one to two business days to make sure there are no side effects

PROVING GROUND

of trial drugs, triage any symptoms, and make sure the medications are being taken correctly.

“Cancer treatment can be overwhelming,” says Jennifer Murphy,

an oncology pharmacist. “We want to make sure patients leave us knowing what they need to know to be

successful. We also remind them we are here for them.”

Brian Jonas, a cancer center oncologist, appreciates the work the investigational drug pharmacists do to ensure patient safety, and stresses that they are important members of the cancer care team.

“You need personal commitment to do high-quality research and provide leading-edge treatment for patients,” he says. “The investigational drug staff exemplifies that dedication to both research and patient care.”

For Banks, perhaps the greatest benefit of the pharmacists’ role in his care is the friendships he has formed — relationships unique in the world of clinical trials.

“I really do feel like cancer is a struggle,” he says. “A lot of times you can feel alone, especially on the hospital end. But they take the time to establish a personal relationship with you and care about you.”

As they have done for other patients, the pharmacy staff threw Banks a party recently to celebrate his 100th round of treatment.

“My wife says it’s like the TV show *Cheers* — everybody knows my name.”

Banks made thank-you gifts and wrote letters of gratitude to about 15 cancer center staff members, including those in the pharmacy whom he affectionately calls the “drug mafia” and “some of the friendliest people on the planet.” He knows each by name, the latest news about their children, and major events in their lives.

“It’s really meant a lot to me,” he says. “I hope I get to celebrate number 200 with them.”

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TO THE CLINICAL TRIAL DRUG MAFIA

Ladies...what can I say...I couldn't ask for more wonderful pill pushers! Thank you so much for all that you do for me and for all those in the many clinical trials. Your medications give us something very precious...the gift of hope.

Just as important to me, is the friendly personable way you issue my meds and I am sure you do the same for everybody else.

The fight against cancer is a tough one and it is so uplifting to share a few light moments with your care givers. Please never change the way you treat your patients...you guys have it just right!!

Sincerely,


Joe M. Banks, Colonel, USAF (Ret)

PS: I hope you were standing at attention when you read this! If not do it over!



Banks is examined by Christine Teklehaimanote



Jennifer Murphy



“We want to make sure patients leave us **knowing what they need to know** to be successful. We also remind them **we are here** for them.”

— JENNIFER MURPHY

PUSHING PAST
CANCER

Young cancer patients
tackle challenges together

Amun Bains always thought she'd be a doctor. **That was before she got cancer.** Suddenly, at 22, she faced ovarian cancer — and the uncertainty that came with it.

Even as a young woman, Bains was no stranger to pain, fatigue and problems most women her age never deal with, including anemia, ovarian cysts and blood transfusions. But this time was different.

"I couldn't say it out loud," she said of her surprising diagnosis. "It was unfair."

Only a year from completing a chemistry degree, and her medical school dream derailed, cancer forced her on a stressful detour.





Amun Bains

Thankfully, she discovered peers with similar issues — **fellow young cancer patients, people who “got it.”** Not only did they understand her experience, but with them she could turn her struggles into action.

Thankfully, she discovered peers with similar issues — young cancer patients, people who “got it.” Not only did they understand her experience, but with them she could turn her struggles into action. She did that through the Young Adult Cancer Advisory Board and the group’s annual, day-long event for adolescents and young adults affected by cancer, Pushing Past Cancer.

On Nov. 4, more than 100 people — patients undergoing treatment, survivors, caregivers and family members — attended the fifth annual event, co-hosted by the UC Davis Comprehensive Cancer Center. Speakers delivered talks on legal rights, health insurance concerns, pain management and cannabis use, coping with chemo brain, skincare during

chemotherapy, meditation and yoga as stress relief, and career counseling.

“Adolescents and young adults with cancer have very unique needs that are not addressed by most oncology programs,” says Marcie Ellis, the event coordinator and a member of the cancer center’s Supportive Oncology Program. “Fertility, employment issues, poor health insurance, body image, fear of recurrence and isolation are a few examples.”

Jamie Ledezma, a cancer survivor, patient rights attorney, and professor with the Southwestern Community College District, emphasized the importance of understanding the Americans with Disabilities Act (ADA). The ADA covers more than parking or wheelchair ramp access — from

telecommuting to temperature adjustments — but each patient’s case is unique. States and counties may also have their own regulations; for example, patients in California are protected by a law that prevents universities or employers from requiring their social media account information.

Small, volunteer-led talks delved into sex and relationships, including intimacy challenges and how cancer can complicate committed partnerships. Dina Hankin, a mental health and child development specialist at UCSF Benioff Children’s Hospital, shared tips for managing cognitive issues such as forgetfulness at school or work.

Ellis says peer-to-peer interaction is essential for young cancer patients — many of whom have never met another young person affected by cancer and may feel like they no longer fit in with their friends. Pushing Past Cancer allows them to meet others with similar experiences, and welcomes cancer patients from any health system, regardless of where they get their care.

OUTREACH

Randi Benton was only 18 when she was diagnosed with ovarian cancer. She was referred to the UC Davis Comprehensive Cancer Center after having surgery to remove a tumor on one of her ovaries. Now 25, Benton still battles the disease with regular chemotherapy treatments. She makes an effort to attend the event with her mother every year to network and make friends.

“Because I am a young adult, I don’t get to speak to people (my age) who’ve had this (disease),” Benton says.

“I’ve often felt alone. I’ve had to internalize my emotions.”

Like many others in attendance, cancer shattered Benton’s life. She’d been accepted to several colleges, including Fordham University, where she’d planned to study law. Despite deferring admission, she worries the “dark cloud” that is

cancer will prevent her from ever achieving her larger goals.

While she suffers from chemo brain, Benton remains ambitious. “I want to do everything,” she says. “I’m trying to challenge myself.”

While law school may be off the table, learning French is on her to-do list, she says, smiling.

Luckily, a classmate introduced her to Ellis and members of the Adolescent and Young Adult Cancer Advisory Board a few months after her surgery. Bains has served on the board ever since. It has given her a purpose, boosted her confidence and provided a support system outside of family.



Adolescent and Young Adult Cancer Advisory Board members Azadea Afkhami and Amun Bains

Reimagining life

DeeDee Kindley, a career counselor and event speaker, has volunteered with cancer patients and their families for years. She says that young people who experience something traumatic such as cancer and must change their life plans often approach them with new clarity.

“They might not know exactly what they want to do, but they sure know what they don’t want to do,” she says. “And they know who and what they want in their life and what they don’t want in their life.”

Kindley helps her clients unlock their passions by asking the right questions. She shares her personal mantra, “I know I can,” with people like Bains, who need help being resilient and focusing on new professional goals.

Moving beyond challenges

In July 2013, a month before she began her senior year at Sacramento State University, Bains had surgery to remove a juvenile granulosa cell tumor on her ovary. She assumed she could jump right back into her academics and progress toward medical school.

“I didn’t even think to defer,” she says, “I thought I could rest after graduation.”

Her first week of class was rough. She leaned on classmates during lab, felt anxious about exposure to chemicals, and feared her cancer would come back. Walking to class took mental preparation — sometimes she instead napped in her car after the drive to campus.

It was hard to keep her grades up. And it strained her social life. She says part of having cancer is grieving



Marcio Malogolowkin, Pediatric Hematology and Oncology Division Chief, talks with event participant

aspects of life that change, including the loss of beloved activities like soccer, and some friendships, too. Bains spent a lot of time alone reading, knitting and playing with her loyal Pomeranian-Chihuahua mix, Riley.

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Ellis says peer-to-peer interaction is essential for young cancer patients — **many of whom have never met another young person affected by cancer** and may feel like they no longer fit in with their friends.

“So much has changed after cancer,” she says. “You need people who are going to stick around.”

Bains took copious notes and

felt empowered by the speakers at this year’s Pushing Past Cancer event. She still wants to pursue a career somewhere in the medical field and is hopeful she’ll get a shot at a meaningful job where she can care for others.

“After what I’ve been through,” she says, “I know I could do it.”



Pushing Past Cancer 2017 participants

LOOKING AT CANCER DISPARITIES

with a long lens

ROBERT CROYLE, DIRECTOR OF THE DIVISION OF CANCER CONTROL & POPULATION SCIENCES AT THE NATIONAL CANCER INSTITUTE, sat down with *Synthesis* editor Dorsey Griffith during a recent visit to Sacramento. They discussed challenges and opportunities in addressing cancer health disparities. This is an excerpt of their conversation.



In this era of “personalized” cancer treatment based on genetic profiles, you oversee a program that supports population-based strategies to tackle cancer on a grand scale. How do you reconcile the two approaches?

A. Linking the individual to the population as a whole is a huge and complex challenge both scientifically and from the perspective of policy. The way that we engage with the public is at the individual level. But a lot of the most powerful levers to improve individual health are through macro, population-level policies. It’s a challenge to explain that a population-based strategy can be incredibly cost effective and have a broader impact.

Is tobacco control a good example of that given its relationship to cancer death rates?

A. Yes. We are about to embark on a new strategy, utilizing the FDA’s legal authority to regulate nicotine levels in cigarettes. NCI-supported research shows that when you provide smokers with a lower-nicotine cigarette, people reduce consumption. This has the potential to be a real game-changer in making cigarettes a lot less appealing and less addictive for teenagers.

What are the thorniest challenges in controlling cancer?

A. The scientific advances are outstripping our capacity to pay for care. Compelling new treatments that are very expensive increase the risk of exacerbating the gap between rich and poor in terms of what cancer care you get. It’s one reason we are developing a new focus on rural populations.

In today’s political climate are you concerned about our ability to ensure cancer care for all?

A. We can prioritize research that examines the impact of economic factors on cancer care. You want good evidence to drive policy, and we

need more direct, comprehensive and compelling evidence on what many refer to as “financial toxicity,” and that is cancer patients who go bankrupt as a result of their diagnosis and treatment, or who don’t adhere to their medication regimen and don’t fill their prescription or come to follow-up visits because the financial burden is too extreme. When you look at maps of cancer incidence and mortality you see substantial geographic disparities.



With the aging population, we anticipate more cancer patients and survivors. Are we prepared?

A. We call it the “silver tsunami,” an aging population and a growing number of cancer survivors. This is an area where we are kind of playing catch-up. We have good knowledge acquired about late effects of cancer, but we are still developing strategies about what is appropriate in terms of monitoring and surveillance about cancer survivors. We have developed a lot of tools, but getting those used in the entire population is challenging, and we don’t know the degree to which providers are providing state-of-the-art, evidence-based (survivor) care.



What is the role of former Vice President Joe Biden’s Moonshot initiative?

A. It reflects passionate leadership from Vice President Biden. But it also coincided with remarkable advances in immunotherapy and other modalities. A lot of Moonshot initiatives are focused on translational research to accelerate progress in treatment, but the Moonshot also serves to increase visibility of cancer as a problem and cancer research as part of the solution. One aspect of the Moonshot is increasing capacity and incentives for data sharing.



What are the realistic achievable goals to reducing cancer health disparities?

A. One way is to really build and expand on what we have. The nation has a tremendous cancer research infrastructure and capacity in basic, clinical and population-level research. But what we haven’t fully done is exploited that to improve cancer care for the entire population. Caring for cancer is not a direct responsibility of NCI, but the NCI absolutely has a responsibility to make sure our research enterprise serves the public as a whole, and there are many, many ways we can leverage our research to improve care.

For more information on the work of the Division of Cancer Control & Population Sciences, please visit <https://cancercontrol.cancer.gov/>.

Moonshot grant funds HPV vaccination and tobacco cessation research

The NCI Division of Cancer Control and Population Sciences and Office of Cancer Centers have funded two Moonshot initiatives to be carried out at the UC Davis Comprehensive Cancer Center.

One will examine barriers to use of the human papilloma virus (HPV) vaccine, which may prevent cervical and many oral cancers, and a second will examine ways to better integrate tobacco treatment into cancer center services.

A one-year grant led by Moon Chen Jr. and **Julie Dang of the cancer center’s Population Sciences & Health Disparities Program, will examine how to accelerate uptake of the HPV vaccine among adolescents**, with plans to use the information collected to develop strategies to increase vaccination rates. The funds are the result of the Cancer Moonshot Blue Ribbon Panel Report on expansion of the use of proven prevention strategies.

The initiative led by Elisa Tong, UC Davis internist and cancer center researcher, builds on a strong, UC-wide effort launched at UC Davis to address tobacco usage at every clinical encounter. The new funding will help researchers work with cancer providers and staff, including pharmacists, to refine and evaluate how clinicians and other cancer center staff identify and treat patients who smoke. **This effort will continue to enhance how electronic medical record tools can be leveraged to help cancer care providers offer and refer patients for evidence-based cessation treatment.**



A NEW WAY TO SEE CANCER

Technique spares patients unnecessary surgery

Pancreatic ductal adenocarcinoma (PDAC) may be the deadliest cancer.

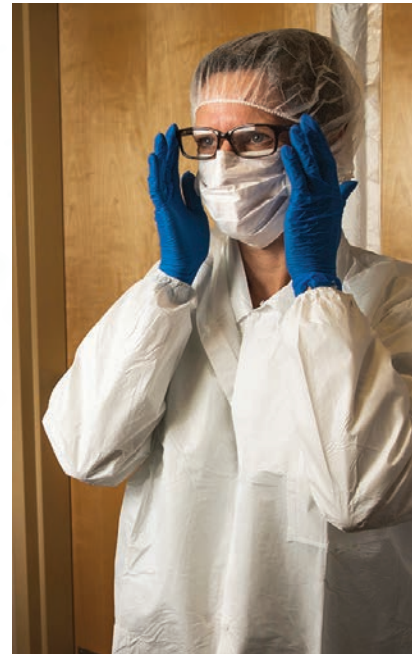
The five-year survival rate for patients diagnosed at stage III is 3 percent; those with stage IV disease

have a 1 percent chance.

Because it is so challenging, physicians take an aggressive approach. Surgery is often indicated to eliminate the disease before it metastasizes. But these procedures move forward with limited information. In some cases, the cancer has already spread to other organs, making surgery useless. Other times, patients don't have cancer at all.

A marker-based imaging test could profoundly impact the ability to detect pancreatic cancer before it metastasizes. In particular, this technique could benefit patients with familial pancreatic cancer or cystic lesions.

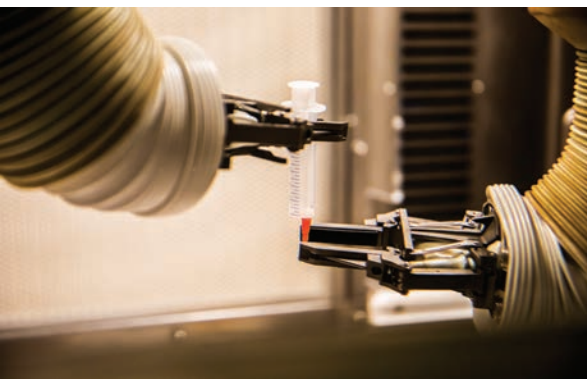
"People with familial pancreatic cancer are at higher risk, but there's no way to tell unless you biopsy them," says Julie Sutcliffe, professor in the UC Davis departments of Internal Medicine and Biomedical Engineering. "But you're not going to randomly biopsy people who have not been diagnosed. Also, some patients come in with cystic lesions. These lesions may or may not become cancer, but right now we can't tell the difference. We have to treat them like cancer, and that can lead to extra surgeries."



No one knows this better than Richard Bold, chief of surgical oncology, who has conducted his share of PDAC procedures.

"The surgery can have significant risks," says Bold. "Unfortunately, we convert some people to diabetics, and some of these patients might never have needed this operation. The biology of what they have is something that never would have become cancer, never would have impacted their life."

What's been missing is a non-invasive technique to definitively identify pancreatic tumors and gauge their spread. UC Davis researchers



What's been missing is a **noninvasive technique to definitively identify pancreatic tumors** and gauge their spread. UC Davis researchers recently received a **\$3.3 million grant** from the National Cancer Institute to help solve this problem.

recently received a \$3.3 million grant from the National Cancer Institute to help solve this problem. The funding will support efforts to develop advanced imaging to pinpoint pancreatic and possibly other cancers, giving clinicians more information to help patients.

Partnering to improve PET

Sutcliffe is the principal investigator on this project, but her participation highlights how circumstance can play a major role in science.

“My entry into the PDAC world was not scientific, it was personal,” says Sutcliffe. “I was diagnosed 12 years ago with breast cancer. Richard Bold was my surgeon; now he’s my collaborator.”

Along with their UC Davis colleagues, they are developing better ways to use positron emission tomography (PET) to image pancreatic tumors. PET has been a workhorse in oncology, although less successfully in pancreatic cancer. Patients receive an injection — glucose molecules attached to the

radioactive isotope, fluorine 18. The idea is that cancer cells are hungrier than normal cells and will eat more glucose/fluorine molecules and light up on the scan.

That’s the theory. Unfortunately, the reality is more complicated. Normal cells and inflamed areas also can consume more glucose, and some cancers lack the protein transporters that take in blood sugar, keeping them dark in PET images.

“In a cancer patient, they may have simultaneous things going on, and we’ll have a hard time sorting out which cells are cancerous and which are not,” says Bold. “We get false positives and false negatives that really leave us in a quandary. If we could develop something that’s more specific to cancer, we could eliminate those false readings.”

Building a better target

The key to improved imaging is finding ways to get cancer cells — and only

cancer cells — to take up the radioactive fluorine. This way, clinicians can be confident that the bright images on PET scans are tumors. Having this kind of specific information could be a tremendous benefit for patients.

“If the cancer has metastasized, the tumor cannot be surgically removed,” Sutcliffe says. “Unfortunately, current imaging is frequently inaccurate, and patients undergo needless exploratory surgery to identify the metastatic disease. If we could image this, we could see if the patient has disease in the pancreas, liver, lungs — wherever it has spread. We could determine if surgery will actually help the patient.”

For more than a decade Sutcliffe’s lab has been studying a molecule called $\alpha\beta6$. This protein receptor lives on the invasive parts of tumors — the

areas that are infiltrating healthy tissue. While $\alpha\beta6$ may not be driving metastasis, it’s certainly along for the ride.

“The receptor we are targeting is expressed on pancreatic cancer cells,” says Sutcliffe. “It’s a marker for cancer aggression and not just in pancreatic cancer. There are applications in ovarian, head and neck, breast, colon, cervical and other cancers.”

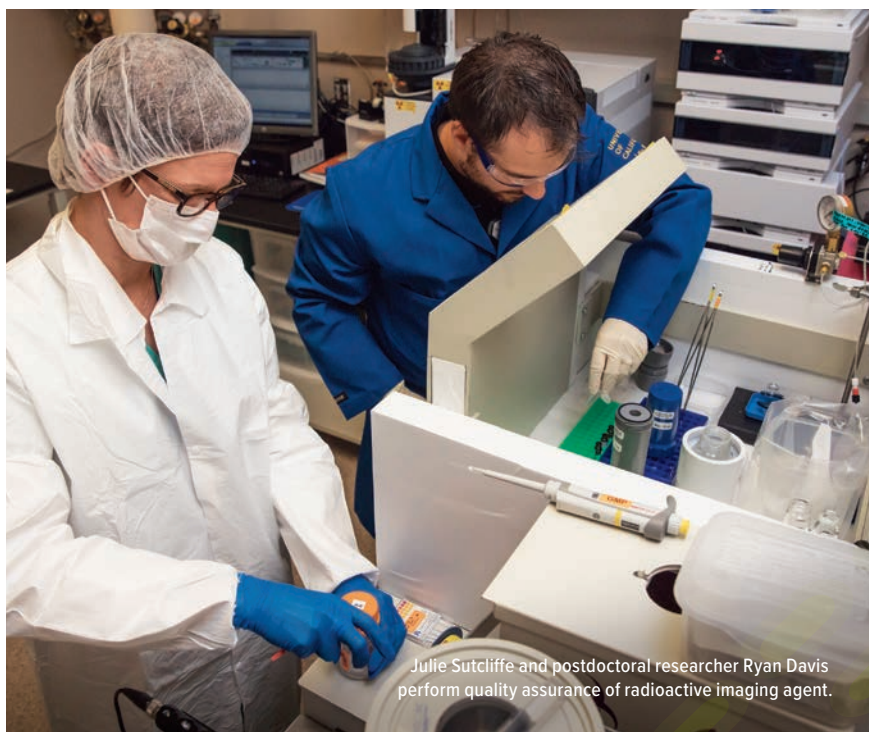
The key to improved imaging is finding ways to get cancer cells — and only cancer cells — to take up the radioactive fluorine. This way, clinicians can be confident that the bright images on PET scans are tumors.

Because it’s a cell surface receptor, $\alpha\beta6$ offers relatively easy access to cancer cells. To take advantage, the team synthesized a peptide (a piece of a protein) that binds to the receptor. Eventually the peptide, and whatever is attached to it, is brought inside the cancer cell.

The end result is a combo molecule called ^{18}F - $\alpha\beta6$ -BP, which carries a radioactive fluorine payload and binds exclusively to $\alpha\beta6$. It wasn’t easy. Working with radioactive molecules requires extra care and ratchets up the difficulty level.

“Fluorine has a two-hour half-life, so you have to work fast,” says Sutcliffe. “It’s manufactured in the lab particle accelerator, a cyclotron, and you have to make it the day you’re using it. You can’t touch it, plus the clock is ticking.”

The process also has to meet good manufacturing practice (GMP) guidelines to ensure the quality of each batch. Still, even with these challenges, ^{18}F - $\alpha\beta6$ -BP could solve a lot of problems, allowing clinicians to better assess a patient’s needs without surgery.



Julie Sutcliffe and postdoctoral researcher Ryan Davis perform quality assurance of radioactive imaging agent.



Post-doctoral researcher Sven Hausner performs remote synthesis of radioactive imaging agent.

Working with radioactive molecules **requires extra care** and ratchets up the difficulty level.

Joining the consortium

Sutcliffe and colleagues are excited by the prospect of helping patients with pancreatic cancer, but that's just a start. Because $\alpha v\beta 6$ is so common in many cancers, their new imaging molecule could be used widely to assess tumor progression.

In addition, the grant does more than fund their work; it gives UC Davis researchers access to the Pancreatic Cancer Detection Consortium (PCDC),

which includes Mayo Clinic, Johns Hopkins University, Dana Farber Cancer Institute and other institutions.

"We become the major imaging site and can recruit patients from the other sites," said Sutcliffe. "This is a really dynamic group of investigators, and we believe we can make a lot of progress toward an effective early-detection method."



"We get false positives and false negatives that really leave us in a quandary. If we could develop something that's more specific to cancer, **we could eliminate those false readings.**"

— RICHARD BOLD

FROM GRIEF, A GIFT

Donation accelerates drug development

NO ONE ever expected that Sue Jane Leung would ever be diagnosed with lung cancer.

“When my mom found out she had cancer in 2006, the news exploded like a bomb in our family,” says Lucinda Hsu, Leung’s daughter. “She didn’t smoke, but she still got lung cancer. Later we

Although Leung died from the disease in 2011, Hsu says **her mother’s tenacity played an important role in her relatively long survival with lung cancer.**

found out that lung cancer occurs more often in Asian women, even those who don’t smoke.”

After her diagnosis, Hsu says her mother lived courageously.

“She was an incredible example of bravery and courage to her family and friends in her determination and

will to fight the disease,” Hsu says. “Her oncologist often remarked how hard my mom worked and how disciplined she was about her health. She was his model patient.”

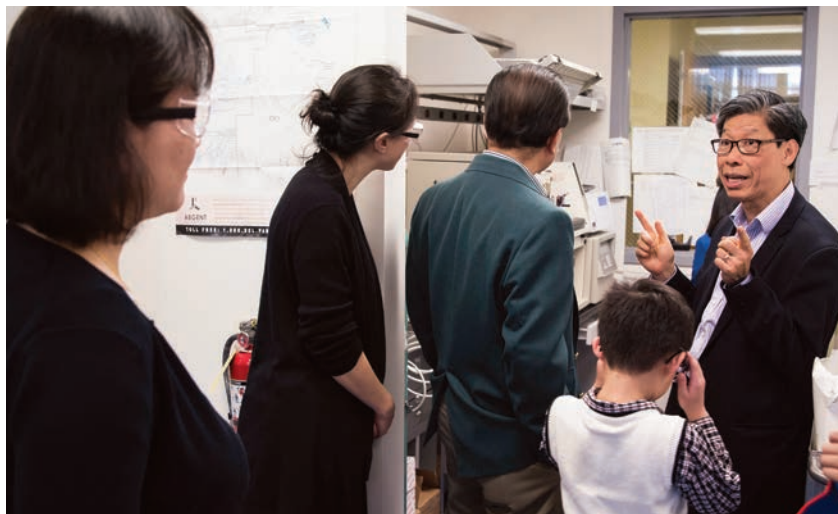
Although Leung died from the disease in 2011, Hsu says her mother’s tenacity played an important role in her relatively long survival with lung cancer.

“She survived with cancer for over five years,” she says. “This is an incredible feat when the five-year survival rate for lung cancer is so low. During this time she endured numerous procedures, surgeries, radiation and two years of continuous chemotherapy.”

Hsu says it was her mother’s strength and determination that led the family to make a gift to UC Davis. A UC Berkeley alumna, Hsu and her father James Leung, a UC Davis engineering graduate, have given \$1.5 million to establish the Sue Jane Leung Presidential Chair in Cancer Research for the UC Davis Comprehensive Cancer Center and the Department of Biochemistry and Molecular Medicine.

This is the first presidential chair for the cancer center, and it will be held by an individual who shows excellence in cancer research and with expertise in cancer drug development and delivery.

“This generous gift from the Leung family will allow us to build a world-class





Back Row: Lucky Lara, Kit Lam, James Leung, Sabina Chang, Lucinda Hsu
Front Row: Jackson Chang, Matthew Hsu

cancer drug development and drug delivery program at UC Davis, and accelerate the development of novel targeting nanotherapeutics and nanoimmunotherapeutics that can save lives,” says Kit Lam, professor and chair of the Department of Biochemistry and Molecular Medicine, and co-director of the cancer center’s Cancer Therapeutics Program.

Before deciding to make the gift, Hsu’s father, who lives in Vacaville, Calif., met with Lam to understand the scope of the work under way to improve cancer treatment. “My father wanted to find out more about the cancer research being done and what the doctors are trying to accomplish,” Hsu says. “He wanted to make sure it fit with what he wanted to accomplish with his gift.”

Making the gift to UC Davis has involved the entire extended family.

**This is a way to bring
something positive
out of a tragedy.
This is our way to
do something to
honor our mom.**

— LUCINDA HSU

Hsu, who lives in San Diego with her husband and son, has two siblings who also felt it was important to support cancer research. Her brother Lawrence lives in San Francisco and has three children. Her sister Sabina lives in Mercer Island, Wash., and also has three children.

“My mother believed a cure for cancer will be found and hoped that at least one

of her grandchildren would someday pursue a career in cancer research or the practice of medicine,” Hsu says. “This is something that will help other families, people we may never know.”

Hsu says establishing the presidential chair is also a way her family can honor the memory of her mother.

“This is a way to bring something positive out of a tragedy,” she says. “This is our way to do something to honor our mom. Her fear was that her grandchildren wouldn’t get a chance to know her. But this is something that we can point to that honors her legacy. It’s important for her grandchildren to see something that she cared deeply about.”

To learn how you can help support cancer research, education and patient care, contact Keeman Wong, senior director of development, at kmwong@ucdavis.edu or 916-734-9322.

LONG-DISTANCE DONOR meets her match

WHEN DIANA von der Heyde learned that a former classmate needed a bone marrow transplant, the 25-year-old joined a bone marrow registry, never thinking she would one day save the life of a man more than 5,500 miles away — or that they would meet during an emotional reunion five years later.

Rick Little of Merced, Calif., was diagnosed with acute myeloid leukemia

the blood-forming system in his bone marrow, changing his red blood cell type from his original A-positive to his donor's O-positive.

Although Little hoped he and his donor might one day connect, their meeting almost never happened. Five months after the transplant, his blood counts had dropped and he had just 50 percent of his donor's cells. Within

Although Little hoped he and his donor might one day connect, their meeting almost never happened.

in 2011. Doctors referred him to UC Davis, where he learned he would need a

stem cell transplant. Unaware of the donor's identity, he was nevertheless grateful for the stranger's selfless act.

After treatment to destroy cancer cells in his body and suppress his immune system, he received his transplant under the care of oncologists Carol Richman, Joseph Tuscano and Mehrdad Abedi. After a month in the hospital, the donor's cells replaced





Stem cell recipient Rick Little meets his donor, Diana von der Heyde, face to face for the first time.

a month, he had none — and relapsed. Doctors first gave him an additional course of anti-leukemia therapy, which removed the abnormal cells. Then he received a donor leukocyte infusion using separately collected T cells from von der Heyde to stimulate the graft-versus-leukemia effect.

Little developed a common side effect called graft-versus-host disease, or GVHD. The disease occurs when the donor's immune cells mistakenly attack the recipient's normal cells. The problem can occur even when the patient is taking drugs to suppress the immune system, as Little was and continues to take today to combat GVHD. Despite the complications, the transplant and immunosuppressive therapy worked.

Curious about his donor, Little supplied his contact information to the National Marrow Donation Program. In February 2014 von der Heyde responded in an email from her home in Holzwickede, Germany.

Little's spirit lifted. Their friendship was instant. They shared details about

Curious about his donor, Little supplied his contact information to the National Marrow Donation Program. In February 2014 von der Heyde responded in an email from her home in Holzwickede, Germany. Little's spirit lifted. Their friendship was instant.

their families, exchanged photos. After months of emailing, they initiated weekly Skype chats on Sunday evenings.

"It lights me up," Little said of his calls with von der Heyde. "I can't get the smile off my face."

In October — five years after Little's transplant — von der Heyde flew to California with her boyfriend, Tim Mester, to meet Little, Little's adult children and grandchildren and his medical team at the Cancer Center and hospital.

"It was unreal, like meeting a family member," said von der Heyde, still surprised to have had such a lasting impact on someone and with so little effort. "It's no big deal because it's just

like donating blood. It can have such a big effect."

Little guided his visitors through the hospital and cancer center, sharing stories of his treatments and reminiscing with staff. The recipient introduced his donor to his nurses and bone marrow transplant team, who held back tears as they embraced them both.

"I truly love this woman," he said after the reunion.

The two have agreed to meet again in five years — when Little is 75 and von der Heyde, 35. The age gap, language barrier and thousands of miles are only minor hurdles for these friends, who share much more now than an O-positive blood type.

THE MUSE MICROSCOPE: Fast-tracking pathology

For patients who may face a cancer diagnosis, waits can be agonizing.

More than 80 percent of the time, patient biopsies will come back normal. Meanwhile, the patient is waiting for results for a potentially lethal disease. They live with a great deal of anxiety.

— RICHARD LEVENSON

Biopsied tissue is routed to pathology, where it is sliced, stained and scrutinized. At best, the results will come back the next day. Depending on where the lab is, the process can take a week or longer.

“More than 80 percent of the time, patient biopsies will come back normal,” says Richard Levenson, professor and vice chair for strategic technologies in the UC Davis Department of Pathology and Laboratory Medicine. “Meanwhile, the patient is waiting for results for a potentially lethal disease. They live with a great deal of anxiety.”

To remedy this, researchers at UC Davis are working on a new way to view tissue. They’ve created the MUSE microscope, which uses ultraviolet rather than visible light. MUSE samples do not require the rigorous preparation that can slow down analysis of conventional slides. This new workflow could speed diagnosis and treatment, making cancer patients’ lives a little better. The researchers recently introduced the technology and its

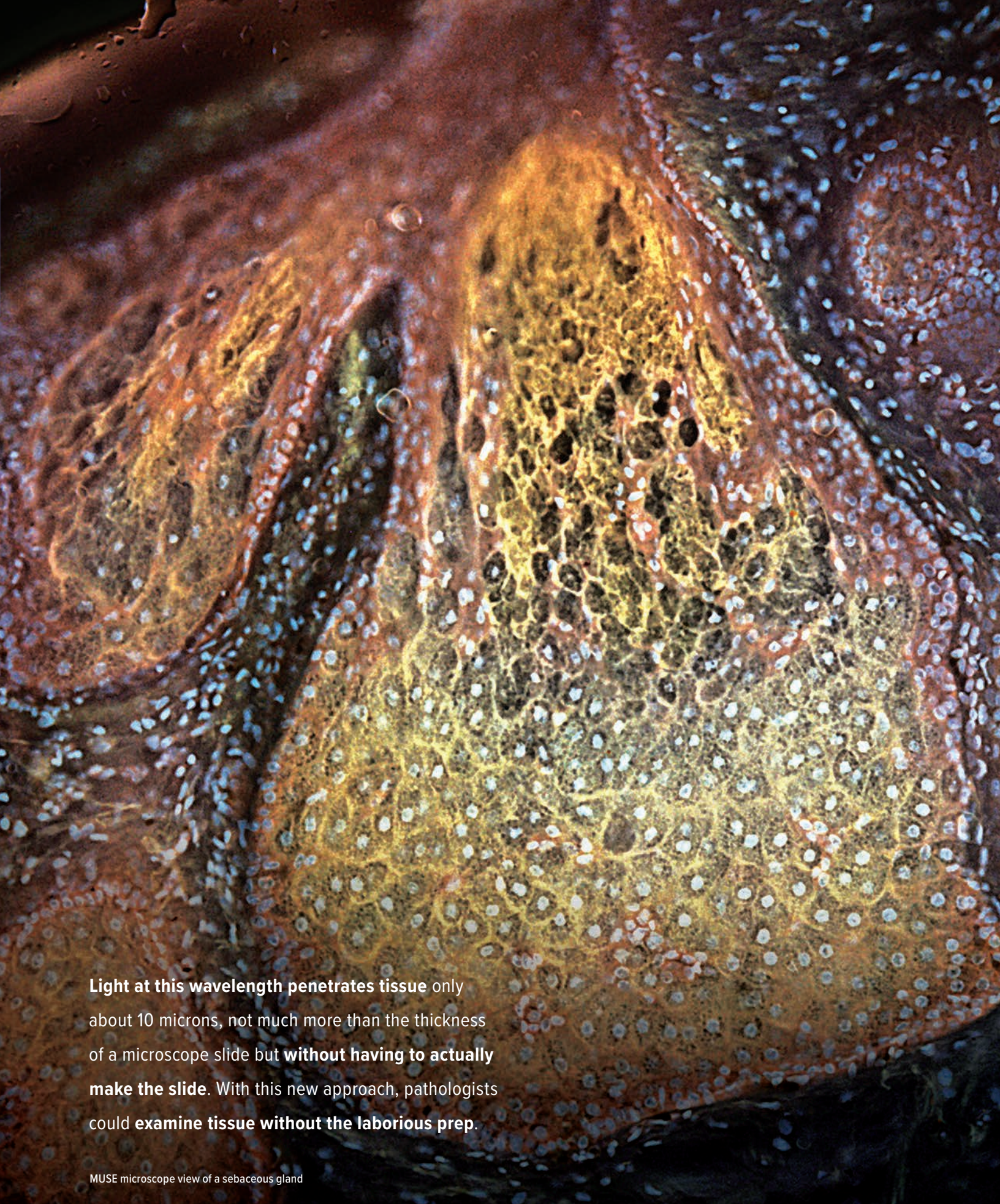


Richard Levenson

many potential uses in an article in the journal *Nature Biomedical Engineering*.

MUSE (microscopy with ultraviolet sectioning excitation) started in the laboratory of Stavros Demos, now at the University of Rochester. Demos was using a tunable laser to examine intact tissue. By adjusting wavelengths, he could change what he saw.

Pay dirt came around 280 nanometers (far below the visible range). Light at this wavelength penetrates tissue only about 10 microns, not much



Light at this wavelength penetrates tissue only about 10 microns, not much more than the thickness of a microscope slide but **without having to actually make the slide**. With this new approach, pathologists could **examine tissue without the laborious prep**.

MUSE microscope view of a sebaceous gland

more than the thickness of a microscope slide but without having to actually make the slide. With this new approach, pathologists could examine tissue without the laborious prep.

“It takes a tremendous amount of effort, labor and reagents to make a slide,” says Levenson. “You have to physically cut the tissue. MUSE gets rid of that logistical problem by going straight from tissue to diagnosis.”

While the diagnostic advantages are obvious, MUSE could offer other benefits. Surgical oncologists often send



“The standard processing is formalin fixation, and the formalin really damages DNA. **We’re moving into a precision medicine world**, using this genetic material to help make a diagnosis. It would be nice if it were in a little better shape.”

— JOHN MCPHERSON

samples to the lab mid-procedure to make sure they get the entire tumor. A fast technique like MUSE could mean less time on the operating table.

Interventional radiologists conducting core needle biopsies could get tissue assessed rapidly to ensure the sample is actually tumor and not healthy tissue or dead cells. Currently, if they don’t get what they need, the patient may need to return for a repeat procedure.

John McPherson, deputy cancer center director and professor in the Department of Biochemistry and Molecular Medicine, is excited because less prep could mean better samples.

“I look at the DNA and RNA from tumors,” says McPherson.

“The standard processing is formalin fixation, and the formalin really damages DNA. We’re moving into a precision medicine world, using this genetic material to help make a diagnosis. It would be nice if it were in a little better shape.”

Clinicians like the technology, but first MUSE must be used in clinical trials to prove it’s at least as effective as current methods.

“We have to show that it gives the equivalent diagnosis,” says McPherson. “We’re going to do side-by-side tests, a bake-off, if you like. Once we get preliminary data, we can move on to larger trials.”

Synthesis is published twice each year by the UC Davis Comprehensive Cancer Center.

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Long-time prostate cancer patient **Rollie Swingle** joined his oncologist **Primo “Lucky” Lara** in late November for a UC Davis Comprehensive Cancer Center Facebook Live discussion about Swingle’s late-stage prostate cancer diagnosis and his long-time survival, thanks to new treatments available through clinical trials. Visit our Facebook page at www.facebook.com/UCDavisCancer.

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Synthesis – the art of bringing together distinct elements

in a way that makes them whole— is a particularly

relevant name for the magazine of UC Davis Comprehensive Cancer Center, which is distinct in its commitment to team science.

Our research program unites clinical physicians, laboratory scientists, population specialists and public-health experts from

throughout UC Davis and Lawrence Livermore National Laboratory

with the goals of making cancer discoveries and delivering

these advances to patients as quickly as possible. We are

also dedicated to sharing our expertise throughout the region,

eliminating cancer disparities and ensuring all Californians have

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