UCLA Health | David Geffen School of Medicine

AMARA YAD:
ERASING THE STAIN OF A DARK LEGACY

A UCLA Health physician and his colleagues undertake a decade-long mission to right a historic wrong.

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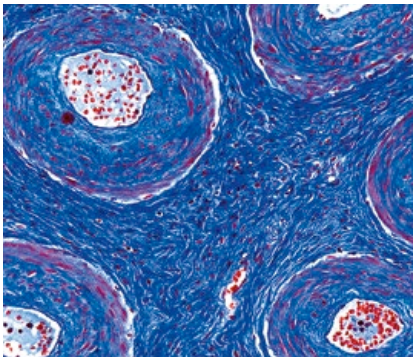

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"When you discover that the foundation of what you thought of as a beautiful building is rotten, you don't keep building on it."

Dr. Kalyanam Shivkumar

BREAKTHROUGHS AND NEWS FROM UCLA HEALTH.

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A Year of Commitment to Care

UCLA Health has a clear and ambitious mission: to deliver leading-edge, compassionate patient care; conduct multi-disciplinary research that leads to innovative medical breakthroughs; and educate the next generation of health care leaders. Over the past year, our dedicated team of faculty, staff and trainees has achieved several noteworthy awards and recognitions that I'm proud to share with you. These accolades serve as a testament to our unwavering commitment to our mission and delivering the highest standards of excellence in all that we do.

One of the most recognized and prestigious awards we received this past year was from *U.S. News & World Report*, which placed us as a #1 hospital in California and in Los Angeles for 2023. We were also included on the prestigious national honor roll of best hospitals for the 34th consecutive year. The award recognizes us as a leader in outstanding patient care outcomes and patient experience.

In addition to the *U.S. News* evaluation, UCLA Health also consistently performs well in a variety of assessments of quality and safety conducted by independent publications, accreditation bodies, advocacy groups and disease-specific organizations, using a wide range of methodologies. These awards affirm that we are delivering on our mission and upholding our values of integrity, compassion, respect, teamwork, excellence and discovery.

What do these awards mean for our patients and the communities we serve?

Assurance of excellence: We pride ourselves on being leaders in our field, and recognitions from this year underscore our commitment to patient safety, quality and access. The LeapFrog Group awarded UCLA Health the highest level of achievement across all four of our hospitals for quality and safety. Additionally, the Centers for Medicaid Services (CMS) awarded UCLA Health's hospitals a five-star rating for quality, a feat achieved by only a handful of hospitals in the country. In addition, more than 100 UCLA Health physicians were named to *Los Angeles Magazine*'s 2023 list of "Top Doctors" in Los Angeles. The results are based on a *Los Angeles Magazine* survey that asked physicians throughout Los Angeles County to identify doctors they considered to be at the top of their fields. This consistency in various rankings demonstrates UCLA Health's ongoing commitment to delivering high-quality care and safety. Whether you are seeking out preventative care or treatment for an illness, you can expect the highest standard of compassionate medical care.

Employees devoted to world-class care: *Forbes* listed UCLA Health among the 2023 America's Best Employers by State, America's Best Large Employers, America's Best Employers for Diversity, America's Best Employers for Women and America's Best Employers for New Grads. We were also selected by *Newsweek* as one of "America's Most Loved Workplaces." These awards are crucial for recruitment and retention of talented healthcare professionals. We are proud of our dedicated staff and appreciate that they feel positive about our organizational values, shared sense of mission and their future at UCLA Health.

Continuous improvement: We are committed to consistently improving and adapting to the ever-changing landscape of health care. Last year, we launched several new programs, including the opening of a newly expanded Rosenfeld Hall facility that consolidates the latest technology under one roof to enhance continuous training for future and practicing physicians and other health care professionals. We also continue to make strides in the development of a state-of-the-art behavioral health campus in the mid-Wilshire area of Los Angeles to help address the regional need for behavioral health services. The new hospital will meet the state's highest standards for acute psychiatric hospital buildings and will include comprehensive behavioral health care services for adult, geriatric, pediatric, adolescent and intensive care patients, as well as crisis care. In addition, an adjacent medical office building will be renovated to expand, relocate and optimize outpatient behavioral health programs and clinical research and education programs associated with the licensed neuropsychiatric hospital and dedicated psychiatric emergency services.

I want to extend my gratitude to our patients and the communities we serve for putting their trust in us for their health care needs. Their feedback and experiences play a pivotal role in shaping the care we provide, so we continue to listen, learn and evolve to meet their expectations and needs. As we embark on 2024, we are committed to being a beacon of health and healing for our patients, their families and the communities we serve.

Johnese Spisso, MPA
President, UCLA Health
CEO, UCLA Hospital System
Associate Vice Chancellor, UCLA Health Sciences

UCLA Health

Exceptional Health Care

#1 in California and Los Angeles*

"Best Hospitals" National Honor Roll
34 consecutive years

*Tied for #1 ranking

I TREAT SCHIZOPHRENIA. IT'S GETTING HARD TO DISTINGUISH ITS DELUSIONS FROM OUR CURRENT DIGITAL REALITY

By Alaina V. Burns, MD (RES '16)

I HAVE BEEN RUNNING A DAY TREAT-ment program for individuals with schizophrenia for nearly seven years. Schizophrenia is an often life-altering psychiatric condition that is characterized by profound changes in cognition, perception and emotional expression. Among the core symptoms are delusional thoughts, currently defined by the *Diagnostic and Statistical Manual of Mental Disorders*, or *DSM-5*, as "fixed beliefs that are not amenable to change in light of conflicting evidence."

To try to determine the extent to which my patients feel monitored, persecuted or invaded, I ask them variations on the same questions each week. Over the past several years, as the insidious impact of the digital world on the psyche has become more obvious to me, I have had to modify my questions to reflect our current reality.

Are you able to use the internet? Do you avoid it for any reason? Have you changed your cellphone number or replaced your mobile device over the past year? Do you receive strange messages through social media? Are famous people posting about you? Are there any online conspiracies that are targeting you?

The first reported case of "systematized delusions involving the internet" was published in 1997. It contained a description of a "Mr. D" who was "brought to the hospital because he believed that his life was controlled by the internet." He spent "long intervals on the computer" and had become concerned that he was seeing evidence of "double-talk" in what he read and that a neighbor was "putting information about his life" online.

Reading the tale of Mr. D now is like peering through a long, narrow tunnel back to the retrospectively quaint last decade of the 20th century. He is "patient zero," the first in what is now a large and growing body of literature documenting delusions involving the internet and supporting technologies. This is unsurprising, given the decades of research showing how emerging cultural, social and political themes — the rise of rock 'n' roll, the fall of the Berlin Wall, North Korea's development of nuclear weapons — repeatedly become incorporated into delusional frameworks.

A person who develops delusional thoughts may find confirmation of these thoughts online. If I believe that I am being secretly recruited by the Central Intelligence Agency, I may then determine that unsolicited marketing emails are in fact coded messages. If I believe my neighbors are plotting against me, I may start to suspect they have hacked my Wi-Fi network.

A PERSON WHO DEVELOPS DELUSIONAL THOUGHTS MAY FIND CONFIRMATION OF THESE THOUGHTS ONLINE.

Conversely, the internet can serve as the source of a delusional framework. I may begin to see that celebrities on my social media feed are publishing posts that seem created just for me, leading me to believe that I have special powers. An advertisement that appears in my search engine results may have been placed there by a government agency.

More and more I find myself twisting into cognitive and linguistic pretzels, trying to help my patients (and myself) determine where we draw the line between psychosis and reality. In response to my query about whether he uses the internet, one patient responded, "Do I use the internet, or does the internet use me?" Well, there is truth in both statements, and one would need a more sophisticated knowledge of government and corporate monitoring, surveillance capitalism and artificial intelligence to determine the extent to which we humans still retain our agency over computers.

When we are discussing social media platforms and my patients tell me that "the algorithm is hacked," I cannot help but agree. Yes, it is true: Your phone is listening to you, the camera on your laptop is watching you and the advertisements you see online are predicting what you will buy and the websites you will want to browse.

I have met patients who have fallen deeply down the rabbit hole of online conspiracy theories, and eventually these theories bleed into their nonvirtual lives and cause them to take actions they otherwise would not have taken. I try to help them return to regular life, with a job and relationships that are not based on a digital platform.

Psychiatrists used to distinguish between delusions that were "bizarre," or impossible, and those that were "non-bizarre," or possible but false. The *DSM-5* no longer makes this distinction, in part because people do not reliably agree with each other when it comes to determining what is possible or impossible. And as our technology advances at an astonishing pace, what was unthinkable yesterday may in fact be plausible today.

Defining a delusion as a belief that is not amenable to change in light of conflicting evidence requires that we have a shared understanding of what is "truth" and how it is determined. As the internet makes our collective truth harder and harder to define, I find myself increasingly lost in the shifting boundary between my patients' reality and my own.

Dr. Alaina V. Burns *is assistant clinical professor of psychiatry and behavioral sciences in the Jane and Terry Semel Institute for Neuroscience and Human Behavior. This essay was first published as an op-ed in the* Los Angeles Times.

MIKE ELLIS

CELEBRATION OF LIFE — AT THE END OF LIFE

By Maanasi Kademani

OPENING WITH THE RHYTHM OF A STEADY HEARTBEAT, and then a guitar's gentle strumming, the song begins with the words, "You gave us love and you gave us life, wild woman with sparkling eyes."

The song — embedded with a recording of her actual heartbeat — was written especially for Stacy Estrella, 51, who was admitted to the ICU of Ronald Reagan UCLA Medical Center with a sudden, aggressive fungal infection that was rapidly spreading to her brain. The infection left her drifting in and out of consciousness, unable to speak. The vibrant woman who loved to garden and was always singing and dancing now had only a few days to live. As her family faced the news, the nurses told them about a special program that might help ease their pain.

Five years ago, critical care specialist Thanh Neville, MD '05 (RES '08, FEL '11), started the 3 Wishes Program at UCLA Health, an initiative to provide dignity and compassion to patients as they face the end of their lives. From setting up date nights to organizing a mariachi band serenade to officiating weddings at the bedside, the range of wishes have been varied.

The program is introduced to patients and their families when it is clear that the patient will die in the intensive care

COURTESY OF THE ESTRELLA FAMILY

Fulfilling the third of her 3 Wishes, Stacy Estrella was surrounded by her family: (from left) husband Ryan, son Ethan and daughters Chloe and Emily, and her beloved dog, Riley.

unit. Patients and their families are invited to make requests for wishes that would help to honor the patient's last moments, and for wishes that help families remember their loved ones. Requests are not limited and are often made in collaboration with the nurses and care staff.

Estrella's first wish came in the form of music. "'Landslide,' by Fleetwood Mac, was one of her favorite songs that we would always sing as a family," says Emily Leiva, Estrella's daughter. The nurses introduced the family to music therapist Jenna Bollard, who worked with Leiva and her family to pen a cover of the song to the rhythm of Estrella's heartbeat. "My mom was just a wonderful personality," Leiva says. "For the doctors to honor who she was, and listen and really care about our story, was so meaningful."

Since it was launched, the 3 Wishes Program has fulfilled more than 5,000 wishes for more than 1,600 patients. Especially through the pandemic, the program has made the dying process more compassionate, kind and personally meaningful to families. "It is so rewarding to be able to offer something at the end of life, when medical treatment has reached its limitations," Dr. Neville says.

Dr. Neville began the program with $10,000 in seed funding to conduct a research study inspired by a similar initiative at a Canadian hospital. "UCLA treats a myriad of critically ill patients. To provide wishes for all of those who met the program's criteria, I projected that the study — and the money — would last about six months." she says.

When she presented her findings at a meeting at the end of the six months, she assumed the program was at its end. The next day, she received a phone call notifying her that a member of the audience was so moved, they donated $10,000 more to keep the initiative going. "It's thanks to philanthropy and the support we have received from the administration at UCLA Health that we have been able to continue and grow the program to where it is today," she says.

The program now operates in six adult ICU units across UCLA Health's two hospitals — Ronald Reagan UCLA Medical Center and UCLA Santa Monica Medical Center. As the first hospital system to offer the program in the U.S., UCLA Health has led the way for numerous hospitals across the nation to follow suit.

The program has made a difference not only for patients, but also for caregiving staff. This was especially true during the pandemic, during which the program represented a glimmer of hope for patients and providers separated from their families. Nursing staff came up with creative ways to make the program possible during the pandemic, creating keepsakes of patients' fingerprints to integrate into paintings and keychains to send to families after careful UV sterilizing treatment. "They become a part of our families, we cry with them, we pray with them, and we allow them to tell their stories," says Mayra Cruz Rivas, RN.

Estrella's second wish was to see the sun again. Her nurses worked together to transport her bed outdoors, bringing extra oxygen tanks and ventilators to make sure she had as much time as possible in the sunshine. "The effort everybody put in was amazing. The empathy I felt from the care team in that moment felt like something out of a movie," Leiva says.

"IT IS SO REWARDING TO BE ABLE TO OFFER SOMETHING AT THE END OF LIFE, WHEN MEDICAL TREATMENT HAS REACHED ITS LIMITATIONS."

Estrella's third wish reunited her with her pet dog, Riley, who spent Estrella's final night curled up with her in her bed.

When Leiva's mother died, Dr. Neville and her care staff were present in the room with the family. "I looked up, and Dr. Neville was standing there, crying with us, and feeling our grief with us," Leiva said.

As the 3 Wishes Program moves into its sixth year, "Our goal is to continue this culture of compassion," Dr. Neville says. With support from the National Institutes of Health, she is working to expand and implement the program at three safety-net hospitals in Los Angeles that cater primarily to underserved communities. "This end-of-life program makes a difference to our patients and families," Dr. Neville says. "In a way, it grants the wish of providers in the ICU as well — the wish to provide the best family-centered care possible for every person, which sometimes means helping people leave this life with dignity and compassion." ●

Maanasi Kademani *is an intern in UCLA Health Communications and a fourth-year UCLA undergraduate studying human biology & society and entrepreneurship.*

For more information about the 3 Wishes Program, go to: ***uclahealth.org/programs/3wishes***
To hear Stacy Estrella's song, go to: ***ucla.in/stacysong*** or scan the QR code

Rosenfeld Hall opens as new hub for leading-edge training, technology and collaboration

A NEWLY EXPANDED FACILITY that consolidates the latest technology under one roof will enhance continuous training for future and practicing physicians and other health care professionals. Rosenfeld Hall is the new home for the UCLA Simulation Center and the UCLA Health Center for Advanced Surgical & Interventional Technology (CASIT). The 30,000-square-foot facility also houses simulation training programs in partnership with the UCLA School of Nursing, the UCLA Health Center for Nursing Excellence and the UCLA Center for Prehospital Care.

"This modern facility capitalizes on UCLA's longstanding interdisciplinary strengths to advance training for a wide range of health care professionals and underscores a commitment to the highest quality care informed by cutting-edge technology and collaborative research," says Steven M. Dubinett, MD (RES '84), dean of the David Geffen School of Medicine at UCLA.

REED HUTCHINSON

Third-year medical student Amulya Vadlakonda uses robotic surgery simulator at Rosenfeld Hall opening event. The system is compatible with platforms used in operating rooms at Ronald Reagan UCLA Medical Center.

Rosenfeld Hall, previously called the Learning Resource Center, expands by one-third the UCLA Simulation Center's square footage and brings its standardized patient program to the same site as the technology-based programs. CASIT, previously located on the basement level of Ronald Reagan UCLA Medical Center, with a research and development lab in the UCLA Center for Health Sciences, now has three times more space. All floors are wired with a modern audio-visual system that facilitates live streaming of simulation training sessions and links with operating rooms at the medical center across the street.

Rosenfeld Hall provides a state-of-the-art facility to prepare trainees and clinicians for patient care challenges through the use of pioneering simulation-based techniques in such areas as surgical interventions, extended reality (XR) and artificial intelligence (AI). Simulation-based training provided by the UCLA Simulation Center and CASIT is integrated into every year of the medical school's curriculum, and in the majority of residency programs, including anesthesiology, general and orthopaedic surgery, pediatrics, interventional radiology and obstetrics and gynecology, as well as emergency, family and internal medicine.

"This new facility markedly enhances CASIT's ability to continue pushing the boundaries of health care technology and training with our partners in support of our overarching objective — to provide the highest quality care for all patients," says Peyman Benharash, MD '02 (RES '08, FEL '10), CASIT's executive director.

Yue-Ming Huang, executive director of the simulation center and adjunct professor of anesthesiology and perioperative medicine, notes that simulation training was offered many years ago by individual departments operating independently. "We are bringing together clinicians, educators, engineers and other disciplines in teams united with a common goal — to develop competent, compassionate and collaborative physician leaders, health care professionals and researchers," she says.

— Evelyn Tokuyama

"This modern facility capitalizes on UCLA's longstanding interdisciplinary strengths to advance training for a wide range of health care professionals."

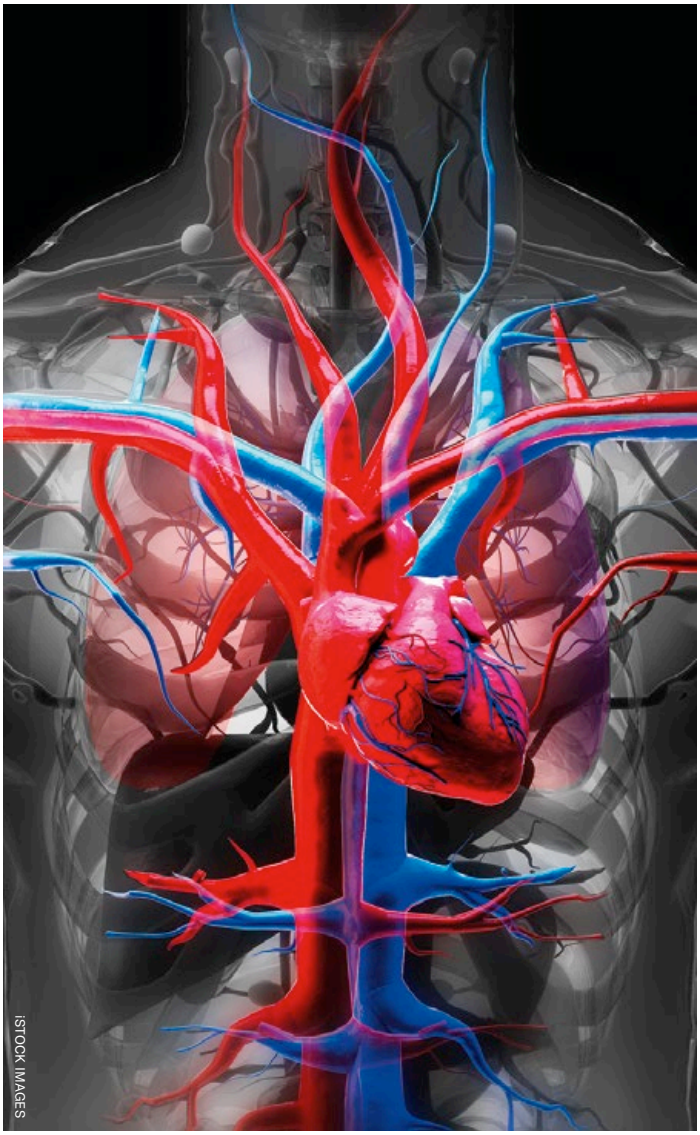
Stem-cell derived mechanism could lead to regenerative therapies for heart damage

A UCLA-LED TEAM HAS identified an essential internal-control mechanism that can promote the maturation of human stem cell-derived heart muscle cells, offering a deeper understanding of how heart muscle cells develop from their immature fetal stage to their mature adult form.

The findings could lead to new therapies for heart disease and cardiac damage.

The collaborative effort with Duke-NUS Medical School in Singapore and other institutions identified an RNA splicing regulator named RBFox1, which was considerably more prevalent in adult heart cells than in those of newborns, based on a preclinical model. The sharp rise in RBFox1 during the maturation of heart cells was also confirmed through analyses of existing single-cell data.

> "For the first time, we've shown that by merely altering RNA splicing, we can encourage the significant maturation of heart cells derived from human stem cells."



ISTOCK IMAGES

"This is the first piece of evidence suggesting that RNA splicing control plays a vital role in postnatal heart cell maturation," says Jijun Huang, PhD, who conducted this research during his postdoctoral training in anesthesiology at UCLA. "While RBFox1 alone may not be sufficient to push mature fetal heart muscle cells all the way to fully matured adult cells, our findings uncover a new RNA-based internal network that can substantially drive this maturation process beyond other available approaches."

The transformation of heart muscle cells from birth until they reach full maturity involves significant shifts in their structure, functionality, and physiological properties. The mechanisms overseeing this comprehensive maturation have been poorly understood thus far.

Although the precise mechanics associating RBFox1-mediated RNA splicing with ensuing maturation processes still require further exploration, the study provides proof of concept that modulating RNA splicing can profoundly affect cardiomyocyte maturation. This newfound knowledge hints at future therapeutic applications, pending additional research to expand upon these initial findings.

"For the first time, we've shown that by merely altering RNA splicing, we can encourage the significant maturation of heart cells derived from human stem cells," says Yibin Wang, PhD, professor emeritus of physiology at the David Geffen School of Medicine at UCLA and director of the Cardiovascular & Metabolic Disorders Program at Duke-NUS. "These findings present a potential molecular approach to enhance heart cell maturation, which could address a major challenge in the domains of cardiac regenerative therapy and disease modeling."

— Enrique Rivero

"Regulation of Postnatal Cardiomyocyte Maturation by an RNA Splicing Regulator RBFox1," *Circulation*, October 16, 2023

Childhood trauma linked to criminal legal involvement in next generation

A STUDY LED BY UCLA RESEARCHERS found that the children whose parents had adverse childhood experiences (ACEs) such as abuse, neglect, violence in the home or loss of a parent are at increased risk of arrests and convictions by young adulthood. The authors report that their findings suggest that there is a crucial need for prevention of ACE exposure in the first place, as well as efforts to mitigate the impact of ACEs before they have downstream impacts on the next generation of children who are not yet born.

"The study is based on a nationally representative dataset and is the first to show an intergenerational relationship between parental ACE exposure and a young person's involvement in the criminal legal system. This suggests that there may be an intergenerational transmission of risk," says UCLA Health pediatrician and researcher Elizabeth Barnert, MD (FEL '14).

The research team analyzed data from the Panel Study of Income Dynamics (PSID), the world's longest-running panel survey, and its 2014 Childhood Retrospective Circumstances Study (CRCS). Adults 18-to-97 years old retrospectively reported on their childhood experiences. Having four or more parental ACEs was associated with a near twofold increase in adjusted odds of arrest before age 26, and more than a threefold increase in adjusted odds of conviction before that age, compared with children of parents with ACEs.

ISTOCK IMAGES

"Our results suggest that it is not only important to prevent childhood adversity, but also to find ways to effectively mitigate the impact of ACEs when they do happen — because the effects may last even more than one or two generations," Dr. Barnert says.

The findings are important for pediatricians, who often identify and address instances of childhood trauma and other forms of adversity. The results also are applicable for policymakers, who must set guidelines on how society deals with young people who come to the attention of law enforcement.

> "We wanted to begin to paint a picture of who these young people are because we think there needs to be a switch from a paradigm of blame to one of empathy."

Dr. Barnert and colleagues launched this study to better understand the issues facing children and families in the United States, and, in particular, to understand how childhood adversity might transmit through generations. "It can be frustrating to see that the carceral system often doesn't solve problems for young people, and in some ways, it can traumatize them even further. It alienates parents instead of engaging them," Dr. Barnert says. "We wanted to begin to paint a picture of who these young people are because we think there needs to be a switch from a paradigm of blame to one of empathy and public health problem-solving."

— Kevin McClanahan

"Parents' Adverse and Positive Childhood Experiences and Offspring Involvement with the Criminal Legal System," *JAMA Network Open*, October 25, 2023

Accuracy of genetically based disease predictions vary from individual to individual


UNSPLASH/ANIRUDH

POLYGENIC SCORES — ESTIMATES of an individual's predisposition for complex traits and diseases — hold promise for identifying patients at risk of disease and guiding early, personalized treatments, but UCLA Health experts found the scores fail to account for the wide range of genetic diversity across individuals of all ancestries.

"Polygenic scores can estimate the likelihood of an individual having a certain trait by analyzing the small effects of thousands to millions of common genetic variants into a single score, but their performance among individuals from diverse genetic backgrounds is limited," said Bogdan Pasaniuc, PhD, a researcher at the UCLA Health Institute for Precision Health and an expert in statistical and computational methods for understanding genetic risk factors for common diseases.

The researchers' analysis shows that the accuracy of polygenic scores (PGSs) varies among individuals across a continuum of genetic ancestry. This is true even in populations that are traditionally considered homogeneous, Dr. Pasaniuc says.

Assessing PGS performance has commonly been done at the "population" level, such as in "Europeans," clumping individuals of similar ancestries in a genetic-ancestry cluster. "Ignoring the diversity, or 'heterogeneity,' within clusters can obscure variation within a group, conceal the similarities that may exist in individuals in different groups and leave out individuals who do not fit neatly into a particular genetic ancestry," says Yi Ding, a UCLA graduate student in bioinformatics and the paper's first author.

To provide a more precise estimate of PGS accuracy, the researchers developed a method to evaluate it at the individual level. They applied PGSs for 84 complex traits to data from more than 35,000 individuals in the UCLA ATLAS Precision Health Biobank, one of the most diverse biobanks in the world. (Los Angeles is home to one of the most ancestrally diverse populations globally.)

The new tool's "training" data came from a subset of individuals in the UK Biobank in the United Kingdom. As a substitute for discrete genetic ancestries, a continuous metric of "genetic distance" was used to establish the position of each individual in the ATLAS database on the genetic-ancestry continuum, essentially showing how similar or dissimilar a target (ATLAS) individual's genome was to that from the UK training population.

"We found that the more dissimilar — or genetically 'distant' — a target individual's genome was from the UK Biobank training data, the lower the accuracy of the PGS," Ding says.

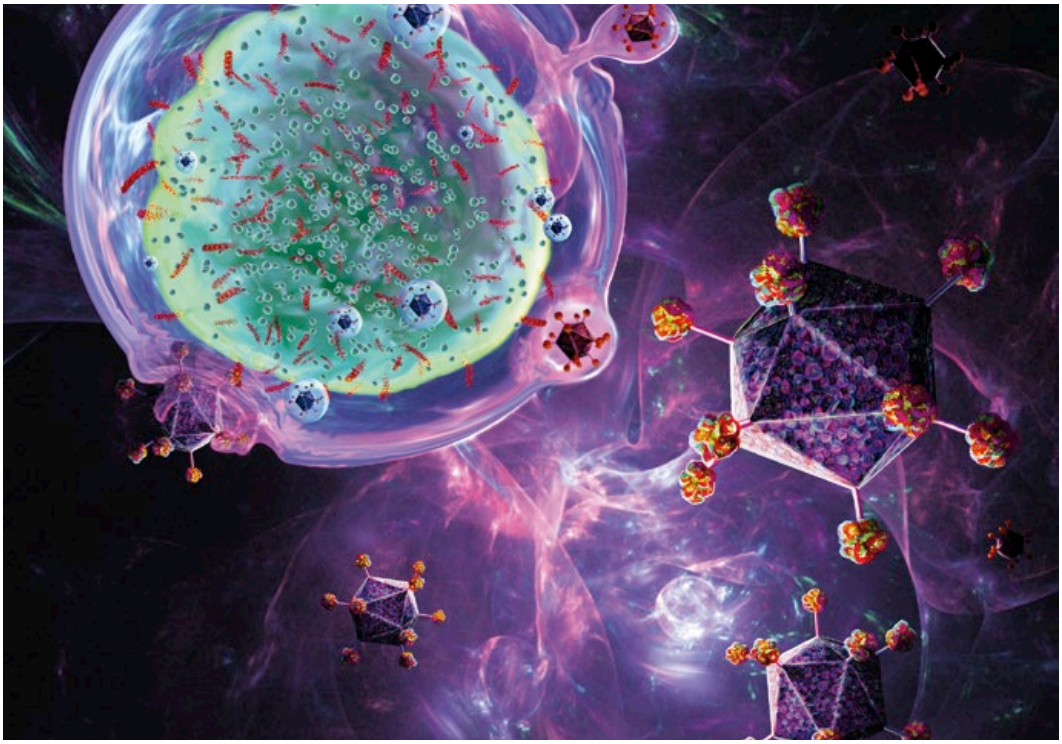
The accuracy of PGSs declined as genetic distance became greater even when the researchers looked specifically at genetic-ancestry groupings that have been considered homogeneous, such as among individuals of European genetic ancestries. Conversely, some individuals could have higher levels of genetic similarity with those outside their own genetic-ancestry group, showing that PGS performance could differ between two individuals from the same ancestry but be comparable for two people from different ancestries — depending on their genetic similarity. "Our genetic-distance metric outperformed discrete clustering in identifying individuals who could benefit from PGSs," Dr. Pasaniuc says.

The research team identified several factors that could affect PGS accuracy and usefulness, especially in people with recent ancestry from two or more continental sources, such as African Americans and Latinos. These individuals have "mosaic" genomes, with segments of different continental ancestries at every region. It is difficult to accurately classify these individuals using conventional ancestry labels, Dr. Pasaniuc says. "For PGSs to be equitably used, the assessment of PGS accuracy should account for the full spectrum of genetic diversity."

— Kevin McClanahan

"Polygenic Scoring Accuracy Varies Across the Genetic Ancestry Continuum," *Nature*, May 17, 2023

Scientists engineer potent immune cells for 'off-the-shelf' cancer immunotherapy



SCIENCESOURCE

UCLA SCIENTISTS HAVE developed a new method to engineer more powerful immune cells that can potentially be used for "off-the-shelf" cell therapy to treat challenging cancers. Also known as allogenic therapy, this type of cell therapy uses immune cells derived from healthy donors instead of patients. The approach can bring cell therapies, like chimeric antigen receptor (CAR) T cell therapy, to more patients in a timelier manner.

"Time is often of the essence when it comes to treating people with advanced cancers," says Lili Yang, PhD, associate professor of microbiology, immunology and molecular genetics and a member of the UCLA Health Jonsson Comprehensive Cancer Center. Using the standard approach, "we have to extract white blood cells from a patient, genetically engineer the cells and then re-infuse them back into the patient. This process can take weeks to months and can cost hundreds of thousands of dollars."

The new approach is a crucial step toward developing more effective cell therapies that can be mass-produced at lower cost and shipped to hospitals around the world, making CAR-T cell therapy more affordable and accessible to a broader range of patients.

For the study, Dr. Yang and her team focused on gamma delta T cells, an immune cell known for its ability to target a wide array of cancers — including solid tumors — without causing graft-versus-host disease, a common complication in allogeneic cell therapies.

While gamma delta T cell-based treatments have been studied before, they have had limited clinical success due to donor variability, short-lived persistence and cancer cells' ability to escape or avoid the body's immune response. However, Dr. Yang and her team found that donor gamma delta T cells with high expression of a CD16 surface marker had a greater ability to kill cancer cells.

"These CD16-high gamma delta T cells exhibit unique characteristics that increases their ability to recognize a tumor," says Dr. Yang, who is also a member of the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA. "We found by using CD16 as a biomarker for donor selection we can improve their anti-cancer properties."

Dr. Yang and her team also engineered the cells so they were equipped with CAR and IL-15, two essential components that help enhance gamma delta T cells' cancer-fighting capabilities. The team of scientists were then able to efficiently produce the more potent engineered cells in large quantities, which they then tested on two different preclinical ovarian cancer models. They found the cells could attack tumors and remained in the models for a long period of time, enabling them to continue their anti-tumor effects. Additionally, there were no signs of complications such as graft-versus-host disease.

"The results of this research shed light on the promising feasibility, therapeutic potential and remarkable safety profile of these engineered CD16-high gamma delta T cells," Dr. Yang says. "We hope this can be a viable therapeutic option for cancer treatment in the future."

— Denise Heady

"We found by using CD16 as a biomarker for donor selection we can improve their anti-cancer properties."

"Unlocking the Potential of Allogeneic Vδ2 T Cells for Ovarian Cancer Therapy through CD16 Biomarker Selection and CAR/IL-15 Engineering," *Nature Communications*, November 8, 2023

Hospitals serving large Black, Latino populations have fewer resources for cancer care

AMONG THE NATION'S HOSPITALS, those that serve high numbers of Black and Hispanic patients are far less likely to have advanced medical equipment and critical services that have been shown to boost the quality and effectiveness of cancer care, according to a study led by investigators at the UCLA Health Jonsson Comprehensive Cancer Center.

The findings highlight the importance of ensuring accessibility across diverse health care facilities to equitable, high-quality care for all patients diagnosed with cancer. "When it comes to treating people with cancer, we know adequate resources are essential for quality care," says Gracie Himmelstein, MD, PhD, a resident physician in the Department of Medicine. "And we know what hospital you go to has a big impact on what care you get. A big piece of why that is has to do with the resources that are available at those hospitals."

The researchers analyzed patient data from hospitals across the U.S. that accept Medicare and Medicaid, and they obtained hospital-reported data from the 2020 American Hospital Association Survey. Their analysis included 4,373 hospitals, 432 of which serve high numbers of Black patients and 432 that serve a large population of Hispanic patients (with 62 of these also serving a high number of Black patients).

The team looked at the availability of 34 cancer-related services at these facilities, including core services, and found that hospitals serving high numbers of Black, Hispanic and other racial and ethnic minority patients were significantly less likely to offer all the core services. Among these core services, 13 significant disparities emerged. These included access to PET/CT scanners, palliative care, esophageal cancer ablation services, several radiotherapy techniques, diagnostic radiology services, treatments like chemotherapy and robotic surgery, tobacco treatment programs, support groups and acute inpatient psychiatric consultations.

MIKE ELLIS

"Many of these services are indispensable for offering top-quality cancer treatment," says Patricia Ganz, MD '73 (RES '76, FEL '78), director of the Center for Cancer Prevention and Control Research at the Jonsson Cancer Center.

"The study's findings shed light on the uneven distribution of crucial resources in different health care settings, which can alter access to timely and appropriate screening, treatment planning, cancer care delivery and outcomes," Dr. Himmelstein says.

The researchers say that further work is needed to understand the interplay between these disparities and the role of geographic, linguistic and cost barriers, as well as cultural beliefs and discrimination.

— Denise Heady

"Distribution of Cancer Care Resources Across U.S. Hospitals by Patient Race and Ethnicity," *JAMA Oncology*, November 16, 2023

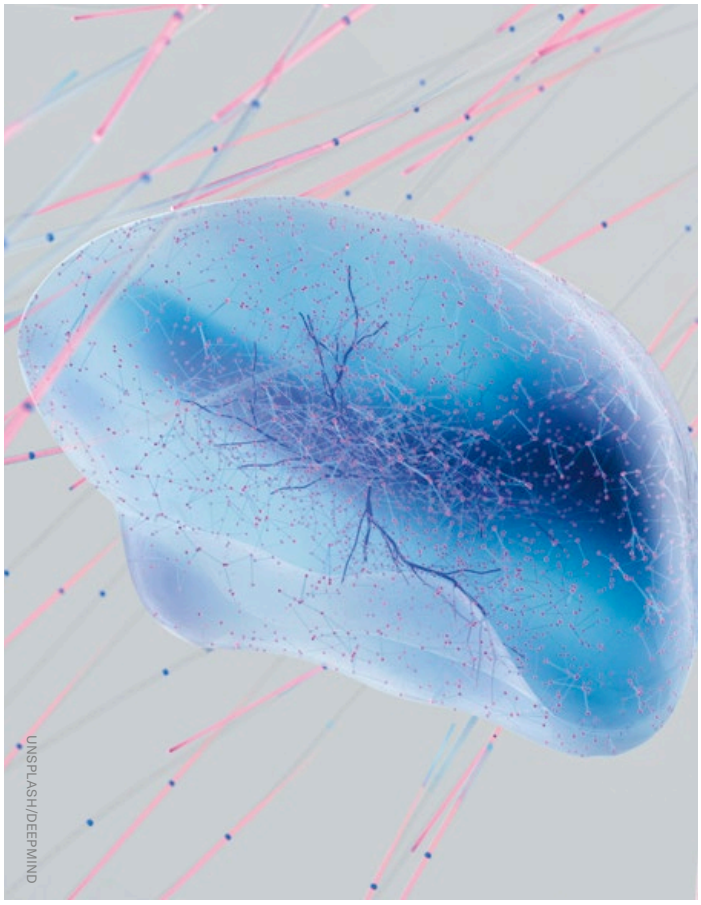
Sets of neurons work in sync to track 'time' and 'place'

A PAIR OF STUDIES LED BY UCLA researchers offer new insights into the way neurons in the human brain represent time and space — the most basic ingredients of consciousness of human existence and the primary dimensions of experience that allow us to reconstruct the past and envision the future.

The new findings are based on recordings of the activity of single neurons in the brain, from studies led by Itzhak Fried, MD, PhD '97, director of epilepsy surgery. Patients who had undergone surgical placement of special depth electrodes developed and implanted by Dr. Fried for surgical treatment of intractable epilepsy agreed to perform cognitive tasks while their brain cell activity was recorded for these studies.

In one study, researchers sought to determine how the brain keeps track of both space and time simultaneously. "To provide an answer, our patients played a timed navigation game where they alternated between searching for and retrieving gold in a virtual gold mine," Dr. Fried says.

The researchers first identified "time cells" that activated during waiting periods between the patients' searching periods and retrieval periods. These "at-rest" time cells would activate one after another, as if each was responsible for counting a single second, throughout the waiting period.


UNSPLASH/DEEPMIND

During game navigation, separate "place cells" appeared as participants navigated to specific locations in the virtual mine, with a new set of "time cells" appearing at particular points during navigation.

"This is the first study to demonstrate the coexistence of time and place cells in the human brain," Dr. Fried says. "Together, they constitute a biological basis for the cognitive map of spatiotemporal context that we propose comprises the scaffolding onto which memories are written."

In the second study, researchers wanted to understand how the brain keeps track of time during an extended period, such as when people are watching a movie with no interruptions. They wondered if neurons would activate periodically — at recurring time intervals — similar to the way certain spatial neurons fire at spatial intervals when a rodent or human moves through an environment.

The researchers showed 14 neurosurgical patients an hourlong movie while recording single-neuron activity from multiple brain regions. Examination of the firing rates revealed that some units exhibited striking periodicity in their firing over the course of the movie, and the time scale of this periodicity varied from unit to unit, ranging from tens of seconds to several minutes.

Dr. Fried says the researchers were surprised to find this unique set of neurons, mostly in the entorhinal cortex, that modulated their activity in such a strikingly periodic manner across time scales that extended to minutes.

The researchers observed that when the video was presented at two different speeds – regular and sped up – a significant percentage of these temporally periodic cells, or TPCs, maintained their dominant time scales, suggesting a degree of regularity regardless of the audiovisual content. "Our results suggest that TPCs' temporal periodicity may complement the spatial periodicity of grid cells, together providing scalable metrics for both space and time and enabling the encoding and retrieval of human experience," Dr. Fried says.

— David Sampson

"Our results suggest that TPCs' temporal periodicity may complement the spatial periodicity of grid cells, together providing scalable metrics for both space and time and enabling the encoding and retrieval of human experience."

"A Neural Code for Time and Space in the Human Brain," *Cell Reports*, October 30, 2023

Fine-tuning 3D lab-grown mini-tumors may help to predict patient response to cancer therapies

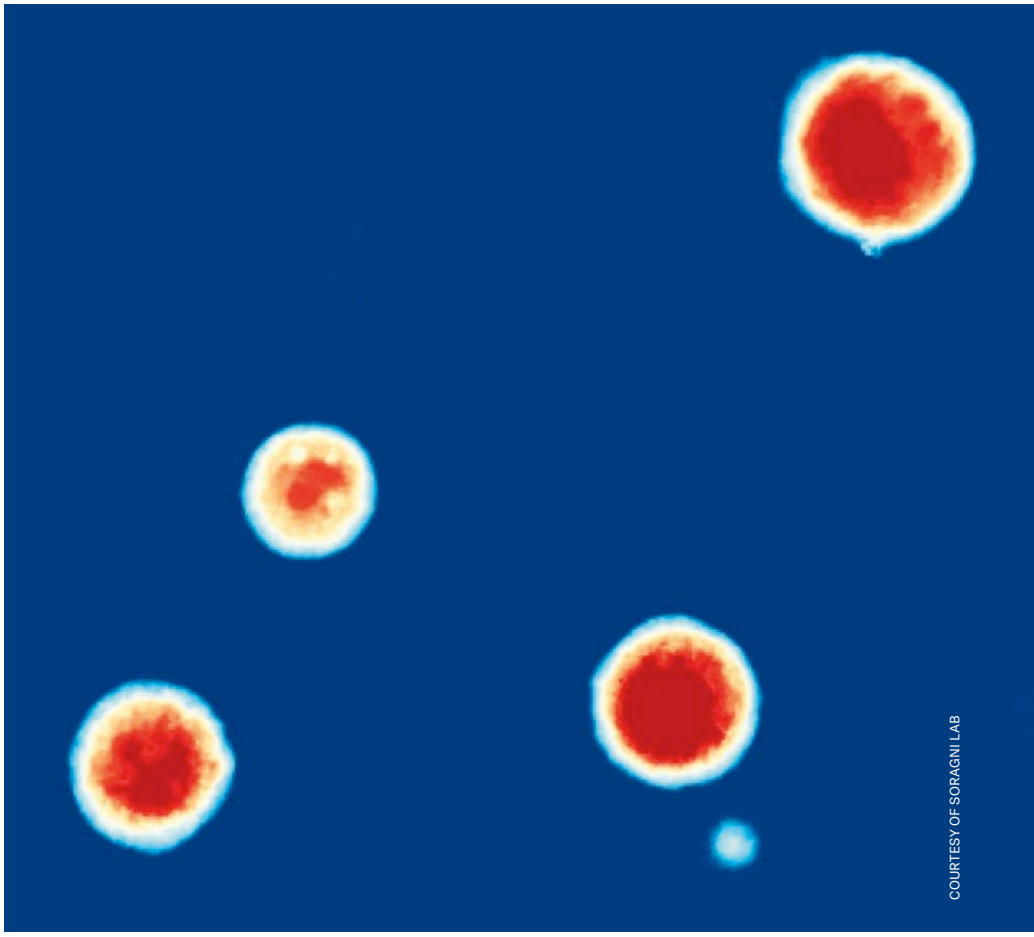
SCIENTISTS FROM THE UCLA HEALTH Jonsson Comprehensive Cancer Center have developed a new method to bioprint miniature tumor organoids designed to mimic the function and architecture of real tumors. The improved process allows researchers to study individual organoids in great detail, which can help them identify personalized treatments for people with rare or hard-to-treat cancers.

"Tumor organoids have become fundamental tools to investigate tumor biology and highlight drug sensitivities of individual patients," says Alice Soragni, PhD, assistant professor of orthopaedic surgery and a member of the UCLA Jonsson Comprehensive Cancer Center. "However, we still need better ways to anticipate if resistance could be arising in a small population of cells, which we may not detect using conventional screening approaches."

Organoids can be grown in a lab using cell lines or patients' own cells to better understand human biology and diseases. By recreating patient tumors, researchers can test different drugs to see if the tumor will respond well or poorly to the treatment. This can make it easier for physicians to choose the best therapies for their patients.

While these mini-tumors have helped improve drug modeling and are becoming invaluable tools for testing the efficacy and safety of potential drugs, it is challenging for current models to capture underlying tumor heterogeneity, which may be responsible for the resistance to therapy observed in clinical settings.

To overcome these challenges, the team of researchers created a method that uses a bioprinting technique to print cells in a thin layer of support extra-cellular proteins to give rise to 3D mini-tumors without altering the tissue histology and gene expressions. The team combined bioprinted cells with high-speed live-cell interferometry (HSLCI), an imaging system that is a non-destructive approach to measuring the weight of living cells in real-time. These methods are then combined with machine-learning algorithms to analyze and measure individual organoids.



Improved process allows researchers to use an advanced imaging method to study and analyze individual organoids in great detail.

"We are able to accurately measure the masses of thousands of organoids simultaneously," says Michael Teitell, MD '93, PhD '93, director of the UCLA Jonsson Comprehensive Cancer Center. "This information helps identify which organoids are sensitive or resistant to specific therapies, which can be used to quickly select the most effective treatment options for patients."

With the new method, researchers confirmed that they could measure the growth patterns of the bioprinted tumor cells over time to see how they responded to different drugs or treatments. The researchers were able to identify an effect of certain drugs on cells as soon as six hours from adding the therapies. The team also identified small groups of cells that did not respond to the drugs, even within very homogeneous cell line samples consisting mostly of cells that were responsive to the treatment.

"This new pipeline has enhanced the quality and depth of information we can get from drug screening of 3D models of disease," Dr. Soragni says. "We are now applying the same approach to organoids established from hard-to-treat, rare cancers."

— Denise Heady

"Drug Screening at Single-Organoid Resolution via Bioprinting and Interferometry," *Nature Communications*, June 6, 2023

25 years *of* Herceptin

Millions of lives have been saved since a UCLA Health oncologist and his team brought forward the first FDA-approved gene-based drug to fight cancer.

Dennis J. Slamon, MD (FEL '82), PhD
Director, Clinical and Translational Research, UCLA Health Jonsson Comprehensive Cancer Center
Chief, Hematology/Oncology, David Geffen School of Medicine at UCLA

In the early 1990s, women who were diagnosed with the HER2-positive subtype of breast cancer weren't expected to live more than three-to-five years after diagnosis. Now, depending on the stage of the cancer at diagnosis, women with HER2-positive breast cancer have among the highest survival rates of all women with breast cancer. That is thanks to the revolutionary breast cancer drug Herceptin, which was developed by a team of scientists led by oncologist Dennis J. Slamon, MD (FEL '82), PhD, director of clinical and translational research at the UCLA Health Jonsson Comprehensive Cancer Center and chief of hematology/oncology at the David Geffen School of Medicine at UCLA. Deemed the "drug that changed the breast cancer treatment landscape," Herceptin has saved millions of women's lives by targeting cancer at its genetic roots. Dr. Slamon spoke with Denise Heady, science communications and media relations manager for the UCLA Health Jonsson Comprehensive Cancer Center, about the paradigm-shifting approach to cancer treatment and how the discovery has opened up an entirely new area of research.

MILO MITCHELL

Dr. Dennis J. Slamon.

Since its introduction in 1998, Herceptin has saved the lives of nearly 3 million women by targeting a specific genetic alteration. This was an entirely new way of treating cancer. How did you come up with the rationale for developing this drug?

Dr. Slamon: The rationale for developing Herceptin, and for all the things that have come after it in terms of this class of targeted therapy, was relatively simple. It was an approach that was based on trying to change what we were doing in cancer medicine, which was throwing in a bomb and hoping that would kill more bad cells than good cells. Instead, we wanted to try to study the cancer cell at a molecular level and identify what was broken and find out if we could target that specifically. The hope would be if we could target that specifically, we'd come up with something that was, hopefully, more effective and safer because normal cells wouldn't have what was broken, only the cancer cells. So, that was really the rationale behind looking for things that might be broken and unique to cancer cells.

"Today, we're using lessons learned from the HER2 story to really chase a number of other cancers, including some of the most difficult cancers to treat like pancreatic cancer, ovarian cancer, lung cancer and colorectal cancer. We're doing the same thing with more sophisticated technology than we had 25 years ago."

How does Herceptin work?

Dr. Slamon: Herceptin is an antibody that works by attaching itself to the HER2 protein. The HER2 alteration occurs when there are too many copies of the HER2 gene in the tumor cells. The normal cells do not have that mistake. It's a genetic mistake that occurs; it's not inherited. When I use the word genetic, it means it happens at the gene level, not that it's inherited from your parents or somewhere along your family line. It means that when the body's Xerox machinery is copying your DNA, a mistake gets made in these breast cells that then become malignant. The Xerox machinery makes too many copies of a particular region of a chromosome that contains the HER2 gene. The HER2 gene makes a protein that regulates growth; it actually stimulates growth. So, it makes sense that whenever there are too many copies and there's too much of the protein, you get abnormal growth, which develops into this very aggressive HER2-positive breast cancer. The Herceptin antibody attaches to this protein and stops its functioning, and the antibody also identifies the protein to the immune system more effectively to allow the immune cells to come in and do their work to destroy those malignant cells.

What was your reaction when you saw the initial results from the phase 3 clinical trial?

Dr. Slamon: It was pretty exhilarating to see that what we had thought about in theory and what we were able to show in models really worked in patients. It was sort of a vindication, that the approach we were taking was correct. But it was also validation that we could continue this approach and find other targets that were driving cancers to help us develop new and novel therapies. And that's really one of the exciting things about the HER2 story. It was an early research process that helped define what happened afterward in a lot of different fields of cancer. And that's been pretty exciting to see, as well.

You often say the women who participated in the clinical trial for Herceptin are the real heroes of this story. Can you explain?

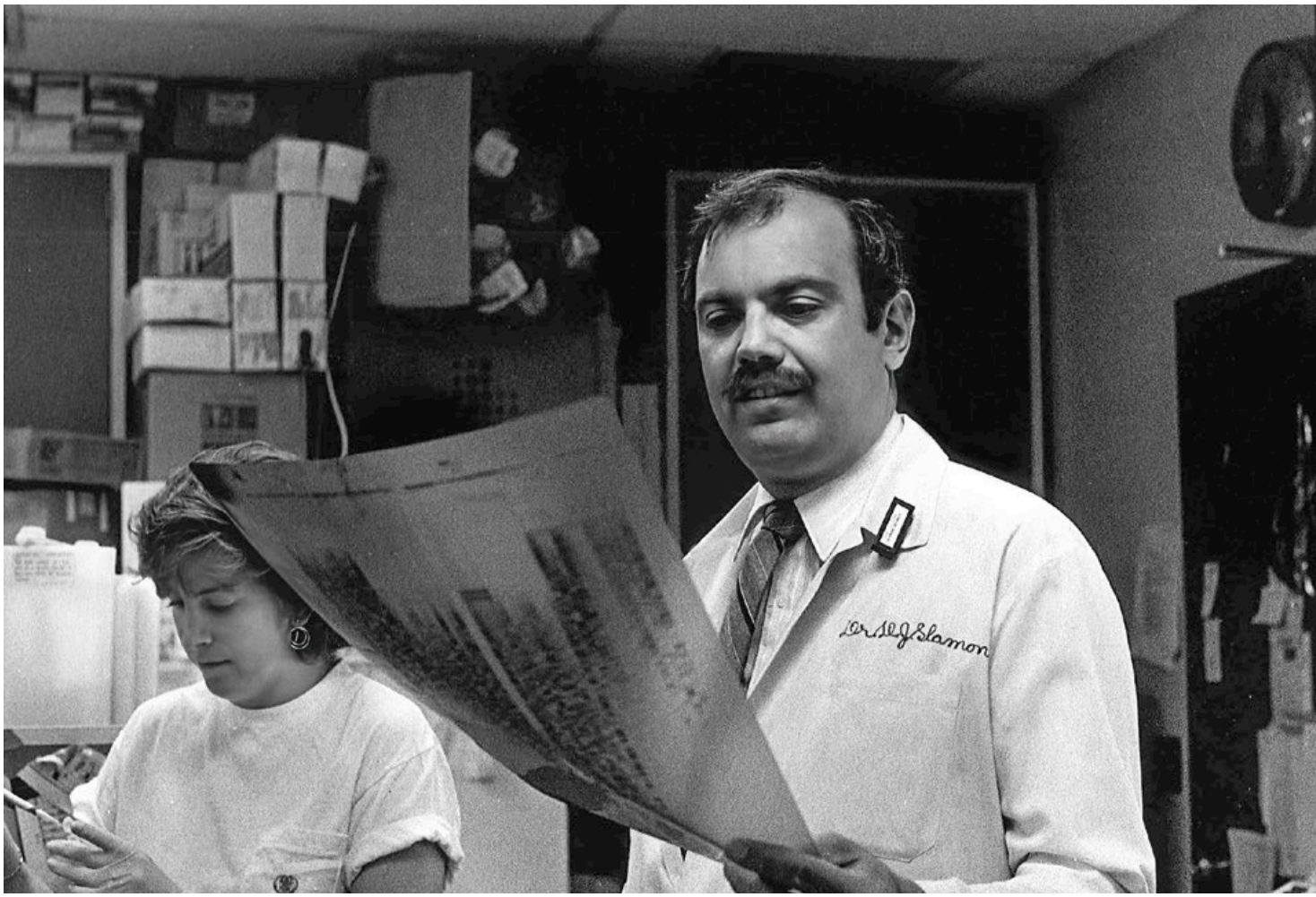
Dr. Slamon: These are women who had other options. They could go on to other kinds of therapies or they could go into other clinical trials. They looked at our clinical trials as something that made sense to them in terms of a treatment approach. They volunteered to participate in a clinical trial, and in that sense, they weren't just subjects, they were active colleagues. They were partners in the clinical trial. And I believe that they deserve as much credit as any of us who were involved in the research work, because they were very much a part of this research.

You gave scientists a new way of understanding and treating one of the most dreaded diseases. How has this breakthrough guided your research today?

Dr. Slamon: Today, we're using lessons learned from the HER2 story to really chase a number of other cancers, including some of the most difficult cancers to treat like pancreatic cancer, ovarian cancer, lung cancer and

Louise Cooper was among the first patients to receive treatment with Herceptin afer the drug was approved by the FDA.

UCLA HEALTH JONSSON COMPREHENSIVE CANCER CENTER ARCHIVE



UCLA HEALTH JONSSON COMPREHENSIVE CANCER CENTER ARCHIVE

"It was pretty exhilarating to see that what we had thought about in theory and what we were able to show in models really worked in patients," Dr. Dennis J. Slamon recalls of his earlier years conducting research to develop the groundbreaking breast cancer drug Herceptin.

colorectal cancer, just to name a few. We're doing the same thing with more sophisticated technology than we had 25 years ago. But we're able to do the same sort of thing: Take a cancer cell and really dissect it at a molecular level, identify what's broken and see how we can effectively treat it. We also have more treatment tools — not only traditional medications like pills or chemotherapy, but also targeted therapies like antibodies. Or new pills that only affect abnormal proteins that are playing a role in the cancer process, and, thus, don't have an effect on normal cells, so they are safer. All of that has opened up incredible vistas in cancer research and cancer therapy that I think are only going to improve over time. What we're doing now is trying to really exploit the lessons learned and expand those into other cancers.

What new research are you working on that you are most excited about?

Dr. Slamon: We have some really exciting things that are going on right now for ovarian cancer, which is a particularly deadly disease. While we have some therapies for it, these patients frequently have recurrences and over the long haul, many of them don't do well. We have some developments that have already made it into the clinic that are showing early results that are positive.

What advice do you give to the next generation of physician-scientists?

Dr. Slamon: I think the best advice I can give the next generation of scientists is the same thing that sort of drove us with the HER2 story. And that's to be your own worst critic. If your data keeps telling you the same thing, stick with it, no matter if people are saying that can't be right or it doesn't fit with what we've seen previously. If your data consistently tells you the same thing and you've really critiqued it carefully, then stick to your guns and pursue it. And I think that really helped us with the HER2 story, and it helped convince a small core of other people in the industry who believed this approach might work, that it was a valid approach to take, as well. ●

In 2019, Dr. Dennis Slamon won the prestigious Lasker-DeBakey Clinical Medical Research Award for his work on the development of Herceptin. To read about it, go to: : **ucla.in/Slamon-Lasker** or scan the QR code

DR. RAMIN SALEHI-RAD

STEPS INTO THE *U* MAGAZINE SPOTLIGHT

Within two years of leaving his native Iran as a teenager, Ramin Salehi-Rad, MD '11 (RES '14, FEL '17), PhD '09, assistant professor of medicine, was enrolled at UCLA, where he earned his undergraduate, MD and PhD degrees. "I came from an environment where questioning and discourse was not possible — there was one narrative that was forced on people. I came to UCLA, and I was challenged by my professors and exposed to diverse thought, and it really forced me to think and become a better person," he says. Today, as a physician-scientist, Dr. Salehi-Rad is focused on basic and translational research to understand mechanisms that lead to development of lung cancer and create new immunotherapies to overcome resistance to treatment, as well as studies to improve early detection and increase chances to disrupt disease progression.

WHEN DID YOU FIRST START TO THINK ABOUT SCIENCE?

As a kid, I always asked a lot of questions and I had a lot of curiosity about why things happen. Thinking about science broadly, it asks questions about why things happen, so I think I've always been drawn to science.

WHAT WAS YOUR FIRST EXPERIMENT?

I grew up in Iran, and we didn't really have laboratory resources in school to conduct our own experiments. But in high school, our teacher demonstrated a chemistry experiment with hydrogen peroxide to create a foam, and I was fascinated by that. It wasn't until I came to the United States that I had a chance to work in a lab and do my own experiments. I was drawn to chemistry, specifically organic chemistry — generating new molecules that never existed before, breaking bonds, making new bonds — and that is why I got my PhD at UCLA.

WHAT HAS BEEN THE GREATEST CHALLENGE IN YOUR WORK?

The greatest challenge in doing research in lung cancer is the complexity and heterogeneity of disease within individual patients, as well as in between patients, which makes it very difficult to develop treatments that can apply broadly.

WHERE DOES YOUR INSPIRATION COME FROM?

I have a drive and a passion to try to understand why things happen, which has drawn me to research. And I have a strong desire to help people, and that is what has drawn me to medicine. The combination of the two has led to my career as a physician-scientist.

WHAT HAS BEEN YOUR BIGGEST "AHA!" MOMENT?

The biggest "aha" moment was when I first recognized my inner voice. Before that, I was very driven by goals. I came to the United States and had to learn English and was focused on doing well in school, and I don't think I had the necessary time or space to be introspective. But as I got older and settled into this new society, I became fascinated as an undergraduate with free will, and I read a lot about that and about meditation and mindfulness. I think that's been really transformative for me, both for my personal life and my professional life. It has made me a better, kinder person.

WHAT IS YOUR GREATEST VIRTUE?

I think I'm pretty focused on trying to make sure people around me are okay and happy. I've been fortunate in my life to have a lot of friends, and that extends to work, as well. There is a lot of goodwill, and as a result I've had a lot of collaborations that have been very fruitful.

WHAT IS YOUR GREATEST FAULT?

Distractibility, and not being able to say no to things that take my focus away from the things that matter the most.

WHOM DO YOU MOST ADMIRE?

Dr. Steven Dubinett [RES '84, former chief of pulmonary medicine and current dean of the David Geffen School of Medicine at UCLA]. The greatest decision I've made in my academic career was to join his lab. He is a world-renowned scientist with many collaborations, and, as chief of pulmonary medicine at UCLA, he led so many important research projects related to lung cancer. But more importantly, for me, just watching him as a leader and seeing his kindness, his generosity and his commitment to the people he works with has been so important. I've learned so much from him about how to create a work environment that's not just productive, but also happy.

IF NOT A SCIENTIST, WHAT WOULD YOU BE?

An economist. I really admire economists, and I gravitate toward those like Glenn Loury at Brown who apply economic methodologies to social issues. I would love to be an economist.

WHAT IS YOUR MOST TREASURED POSSESSION?

It is a painting that my uncle in Iran drew of a village in Iran. He passed away two years ago, and I framed it, and I really like it.

TO WHICH SUPERHERO DO YOU MOST RELATE?

Friends, my nieces and different independent sources who have ascribed to me a superhero persona all say it's Rocket Raccoon from *Guardians of the Galaxy*. And I will say that I relate to this character. He is very loyal to his friends, and he's also defined by his humor and his ability to make light of challenging situations. That feels like it somewhat mimics my life.

WHAT ARE YOU MOST COMPULSIVE ABOUT?

I'm pretty compulsive about a lot of things, that's the problem.

JONATHAN BARTLETT

HOW DO YOU WANT TO CHANGE THE WORLD?

I've been doing science long enough to be humbled by it and to know it is a very slow and incremental process, and one can only hope to contribute a little bit. Ideally, maybe, I hope that the discoveries we make can contribute pieces to the puzzle that in the future will come into view and lead to new therapies or prevent development of cancer. I don't have a grand vision of how I want to change the world; it's the cumulation of individual, small achievements.

WHAT IS YOUR DEFINITION OF HAPPINESS?

That's been a question I think I've struggled with my whole life. I think it is when I'm able to align my life with my values.

WHAT IS YOUR DEFINITION OF MISERY?

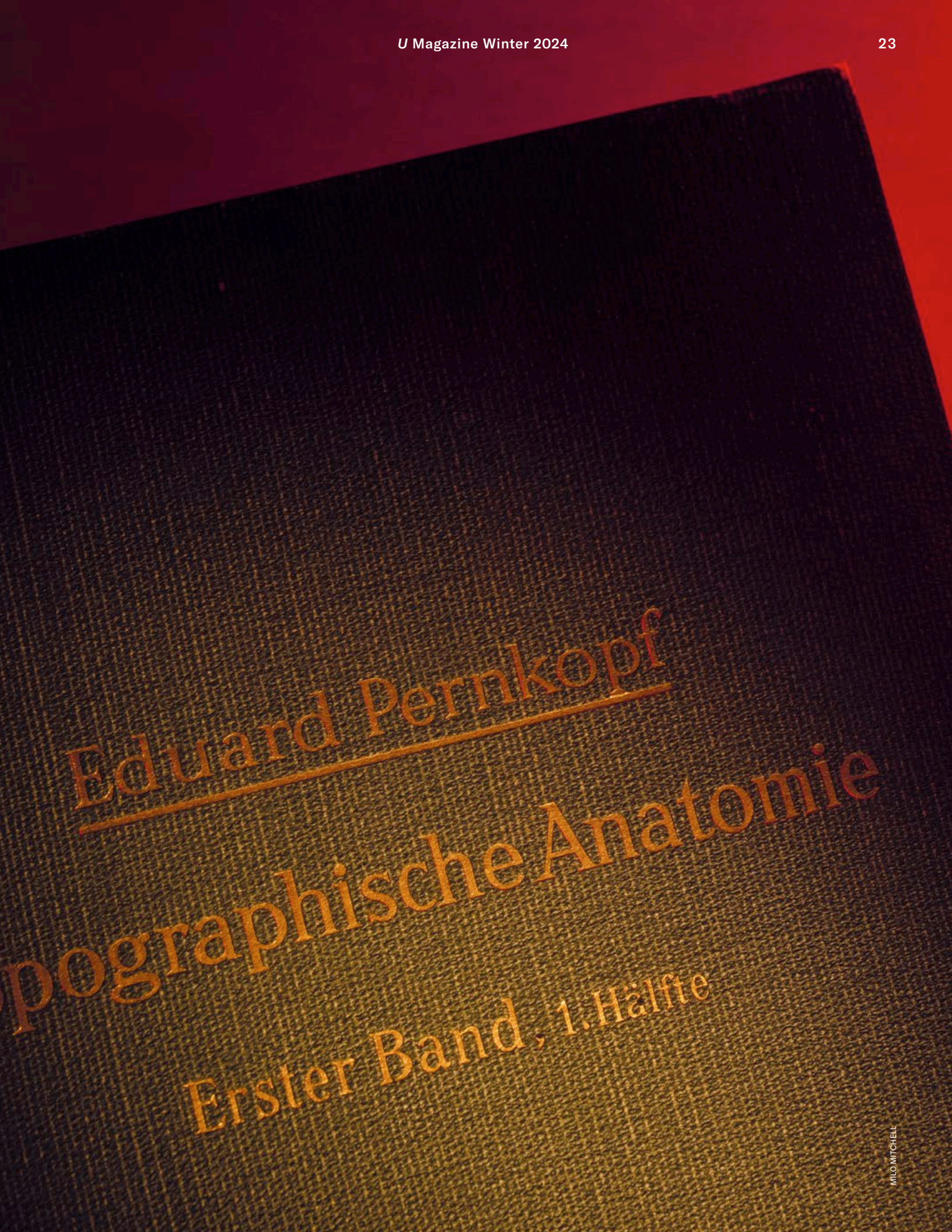
When I feel restricted or don't have the freedom to do or say what I really want to do or say. ●

AMARA YAD:
ERASING THE STAIN OF A DARK LEGACY

A UCLA Health physician and his colleagues undertake a decade-long mission to right a historic wrong.

By Dan Gordon

This is the first of two parts. Part 2 will be published in the next issue of U *Magazine.*



MILO MITCHELL

AS THE OLDEST SCIENTIFIC DISCIPLINE IN MEDICINE, anatomy dates at least as far back as the ancient Egyptians, whose elaborate embalming methods necessitated a familiarity with organs and body parts. Hippocrates described the heart and blood vessels in establishing medicine as a scientific field in the 5th century BC. In modern times, generations of aspiring doctors have learned about anatomy in their first year of medical school, in part by dissecting human cadavers in the lab.

But this is not a story about anatomy, per se.

It is a story about an avowed Nazi physician, Dr. Eduard Pernkopf, during the time of the Holocaust, who ascended to the highest post at one of Europe's most prestigious medical schools and violated the Hippocratic Oath in the most egregious way — exploiting the bodies of executed victims of Nazi terror to create a multivolume series of atlases of the human anatomy. For decades, those atlases were held up as preeminent resources, guiding complex surgeries and teaching medical students. Even after the shameful history was revealed, many considered the information in these tainted volumes too valuable to discard.

And it is a story of a UCLA Health physician who, revolted by the origins of the atlas, has made it his mission to right what he sees as an abhorrent historical wrong. Kalyanam Shivkumar, MD (FEL '99), PhD '00 — "Shiv" to those who know him — has built an internationally renowned program as director of the UCLA Cardiac Arrhythmia Center. A leading innovator of heart procedures with a penchant for quoting Sanskrit and legendary UCLA basketball coach John Wooden, Dr. Shivkumar found himself unable to let go of his disgust upon learning of the story behind the atlases in 2012. So, he channeled his indignation into a 10-year effort, with the help of UCLA colleagues, to create a new and better resource and make it freely available to anyone.

"What Shiv has done is inspiring," says Barbara Natterson-Horowitz, MD (RES '90, '92, FEL '95), a UCLA professor in the Division of Cariology and codirector of the UCLA Evolutionary Medicine Program. "In contrast to Pernkopf's documents of death, his anatomic atlases will be powerful tools for saving lives."

"EVEN IN A PROFESSION THAT IS SWORN TO PROTECT AND HEAL, HUMAN BEHAVIOR CAN SINK INTO VERY LOW AND DIABOLICAL PLACES."

And lastly, this is the story of an undertaking much larger than that ambitious initial act. Shortly before the release of the first of six planned volumes of the *Atlas of Cardiac Anatomy*, Drs. Shivkumar and Natterson-Horowitz established Amara Yad — a combination of Sanskrit and Hebrew translating to "The Immortal Hand." The project has set out to produce as many as 40 open-access anatomic atlases, leveraging scientific and technological advances to map the entire human body as a resource for future clinicians and researchers. More than that, the Amara Yad Project will educate medical students, trainees and others on past and present moral stains on the profession while supporting corrective measures that address the damage, restore trust and educate a new generation of physicians on their sacred duty to ethically serve their patients.

"Even in a profession that is sworn to protect and heal, human behavior can sink into very low and diabolical places," says Liebe Geft, who, just before her retirement as director of the Museum of Tolerance in October, hosted an event at the Los Angeles venue in honor of the Amara Yad launch. "We can never condone abuse of the power, authority and privilege placed in the hands of the medical practitioner for the sake of some spurious notion of scientific advance."

The Amara Yad Project epitomizes a central element of the mission of the David Geffen School of Medicine at UCLA, says Steven M. Dubinett, MD (RES '84), the school's dean. "We spend a lot of time on technical education, but there is a moral imperative to our jobs as well. We must clearly articulate our values in a way that lets our community of patients, as well as our students, trainees and physicians, understand that we are in health care because we're about healing — and that the best way to demonstrate that is not only through compassionate care, but also attention to our history," he says. "It makes me proud that we have faculty who have taken this on."

FOR DECADES, ANATOMISTS AND SURGEONS regarded *Topographische Anatomie des Menschen* (*Atlas of Topographical and Applied Human Anatomy*) with awe. Published in seven volumes from 1937 to 1960, the series — best known as the "Pernkopf atlas," after Dr. Pernkopf, the Austrian anatomist who oversaw the work — used hand-drawn illustrations to display human bones, muscles, nerves, tendons and tissue in vivid color and graphic, annotated detail. As both an artistic work and a clinical resource, the Pernkopf atlas was viewed as unsurpassable — lauded as late as 1990 by a *New England Journal of Medicine* review as "in a class of its own." *The Journal of the American Medical Association* declared it a "classic among atlases," calling its illustrations "truly works of art."

Only later would the source of the endless supply of cadaver subjects featured in the atlas' pages become clear.

In 1933, the year Dr. Pernkopf was appointed chair of anatomy at the University of Vienna, he joined the Nazi party. Weeks after the Anschluss, when Nazi Germany invaded and annexed Austria into the Third Reich in 1938, Dr. Pernkopf was appointed dean of the medical school. He proceeded to dismiss nearly 80% of the school's faculty, including all Jews and other Nazi opponents, three Nobel laureates among them. The remaining professors were required to swear an oath of loyalty to Hitler. In

MILO MITCHELL

Dr. Kalyanam Shivkumar (left) and Dr. Barbara Natterson-Horowitz established Amara Yad to not only produce a series of new anatomic atlases, but also to educate future generations of physicians about moral stains on the medical profession and train them to ethically serve their patients.

a chilling photograph taken just days after he assumed the leadership post, Dr. Pernkopf, dressed in full Nazi regalia with a portrait of Hitler behind him, stands at the lectern for his inaugural address to faculty, who greet him with the Nazi salute.

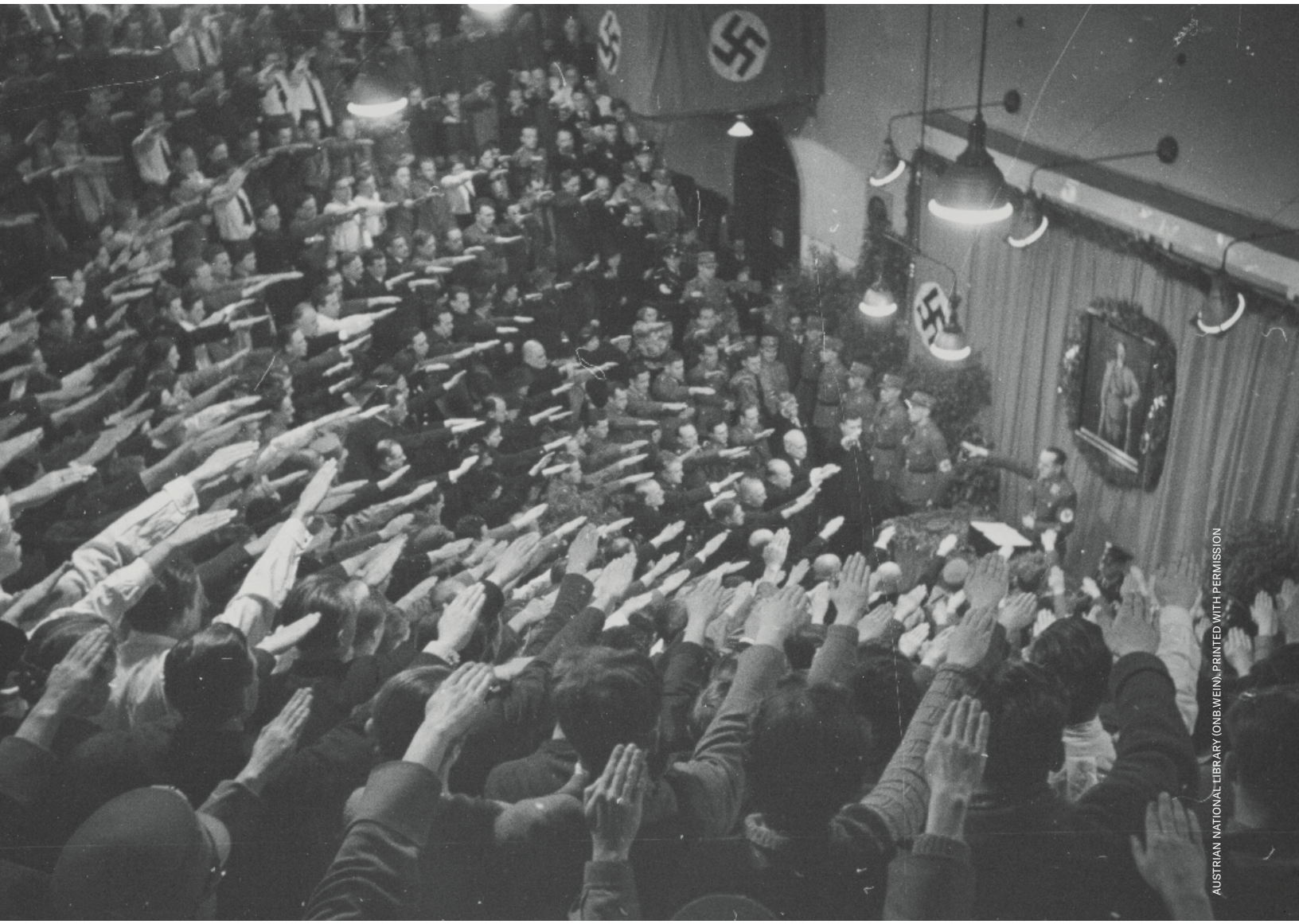
Although Dr. Pernkopf's vile past wasn't entirely a secret, decades passed during which his works remained widely used while their source was barely discussed. That began to change in the 1980s through revelations and disturbing questions raised in a series of journal articles and letters. Among other things, the four main medical artists employed by Dr. Pernkopf were themselves proud Nazis who, in the early editions of the atlas, signed their illustrations with swastikas and other Nazi symbols — crudely airbrushed out in later editions.

By the mid-1990s, new published papers questioned the source of the cadavers Dr. Pernkopf's team had used. After prodding from Yad Vashem, the World Holocaust Remembrance Center based in Jerusalem, the University of Vienna launched an investigation. The university's report confirmed the suspicions: From 1938 to 1945, the anatomy department under Dr. Pernkopf received at least 1,377 bodies of executed people, the majority of them political prisoners targeted by the Nazi regime. In all likelihood, the report concluded, images of the dissected bodies of these individuals were strewn across the atlas' pages.

"It became quite obvious that there was this extremely distressing suppressed history," Dr. Shivkumar says. "Pernkopf received the bodies of people imprisoned and murdered for trivial crimes — and these murders were timed for when it was convenient to the team that was using the bodies to make the atlases."

In the preface to the first edition, Dr. Pernkopf credits the vivid images in part to the access his group had to an endless supply of bodies. "He owns it, and not in an apologetic way," Dr. Natterson-Horowitz says. "Here is a physician, leader of a top medical school, with a total lack of awareness or shame about using these victims."

DR. SHIVKUMAR WAS UNFAMILIAR WITH THE PERNKOPF HISTORY in 2002, the year he established the UCLA Cardiac Arrhythmia Center. As an electrophysiologist, his focus is on abnormal heart rhythms. Although most arrhythmias are benign, an improperly beating heart can negatively affect blood



Dr. Eduard Pernkopf, at lectern dressed in a Nazi uniform, was greeted with a Nazi salute from faculty during his inaugural lecture as dean of the medical school of the University of Vienna.

flow to vital organs. As many as 6 million Americans have atrial fibrillation, which can produce palpitations, chronic fatigue and shortness of breath that severely impede quality of life. In the most lethal cases, untreated arrhythmias can lead to cardiac arrest or stroke.

Under Dr. Shivkumar's leadership, the UCLA Cardiac Arrhythmia Center has risen to international prominence, drawing referrals and consultations for some of the most complicated cases. Among other innovations, his group has developed new techniques for treating ventricular tachycardia, a potentially life-threatening arrhythmia in which the heart's lower chambers beat too quickly. Dr. Shivkumar is also a leader in the field of neurocardiology — the complex interplay between the nervous and cardiovascular systems and how targeting certain nerves can effectively treat ventricular arrhythmias. In September 2023, his group received an $11.5 million National Institutes of Health grant to study the use of nervous system modulation to prevent fatal arrhythmias.

It was Dr. Shivkumar's determination to venture outside the heart and into the body's nervous system that led him to Dr. Pernkopf.

In 1975, Wallace A. McAlpine, MD, a cardiac surgeon in Toledo, Ohio, published an anatomic atlas of the heart and coronary arteries, featuring highly detailed photographic images of the cardiac anatomy. "He converted the basement of his house into a studio to take pictures using Kodachrome film," Dr. Shivkumar says. "The result was a work of art."

Dr. Shivkumar came across that atlas not long after Dr. McAlpine's death in 2005, then went hunting for the original images. Ultimately, he found the collection of approximately 4,000 slides in the basement of the Cleveland Clinic Library, acquired them and digitized Dr. McAlpine's work, making it freely available.

But by 2010, Dr. Shivkumar recognized that nerve modulation was becoming a key to treating conditions involving the cardiovascular system, and as valuable as the McAlpine atlas was for mapping the heart, it was confined to that organ. So, Dr. Shivkumar began to inquire about anatomic resources that provided a detailed map of the peripheral nerves to assist his group in developing new procedures. And among those in the know, the definitive

resource was clear. "All roads led to Pernkopf," Dr. Shivkumar says.

In 2012, a Canadian colleague gifted Dr. Shivkumar an entire set of the Pernkopf atlas, but in doing so shared the painful history. "Shiv was shaken by this," Dr. Natterson-Horowitz recalls of her friend and colleague. "He was offended by what happened, and by the fact that so many generations of physicians had used either Pernkopf or a newer atlas informed by the Pernkopf work, without knowledge of the history. He became fixated with getting to the bottom of this. I would come into his office to find him meeting with rabbis, trying to learn more."

More than a decade later, Dr. Shivkumar still becomes emotional when the subject is raised. "It's an insult to humanity," he says. "How can medicine have such a stain?"

KALYANAM SHIVKUMAR WAS BORN IN 1968 IN CHENNAI (then called Madras), located on the Bay of Bengal in southeastern India. His father was a mathematician, his mother a chemistry teacher. His grandfather had been a journalist who spent eight years in prison after being charged with sedition for publishing a newspaper directed by Mahatma Gandhi; he was released after India achieved independence in 1947 and went on to serve as a member of parliament.

Dr. Shivkumar still recalls his first exposure to the horrors of the Holocaust, when he was about 12. His grandfather brought in a friend, a British war photographer, to show pictures from the concentration camps. "You have to understand, in the part of the world I'm from, for millennia people from all religions, cultures and ethnic groups have coexisted," Dr. Shivkumar says. "I'll never forget seeing those photos and having my dad and grandfather tell me, quoting Primo Levi, 'This happened, it could happen again, and it could happen anywhere.'"

Dr. Shivkumar describes his own family as Hindu Brahmin, and he was raised reading Sanskrit. But, while he remains rooted in Hindu values, he dismisses the suggestion that his moral outrage at Dr. Pernkopf and other atrocities associated with the Holocaust is informed by his faith. "It's basic humanity," Dr. Shivkumar says. "Which faith would contradict this? Gandhi, when asked if he was a Hindu, said 'Yes, I am. I am also a Muslim, a Christian, a Sikh, a Buddhist and a Jew.'"

KNOWING THE SORDID ORIGIN STORY BEHIND THE PERNKOPF ATLAS RAISED A MORAL DILEMMA.

Dr. Shivkumar immigrated to the U.S. after graduating from medical school. He came to UCLA in 1995 as a cardiology and electrophysiology fellow. One of Dr. Shivkumar's first attending physicians was Dr. Natterson-Horowitz, then a first-year faculty member. She remembers him standing out for more than his technical skills. "Shiv had an unusual fund of knowledge," she says, "which included the ability to quote from wide-ranging sources — Maimonides and Osler, Ramakrishna and Shalihotra, and, after a few months at UCLA, John Wooden."

Whether he's delivering a professional talk or engaged in one-on-one conversation, Dr. Shivkumar is more likely than not to reference the legendary UCLA basketball coach. In his office at the UCLA Cardiac Arrhythmia Center, he proudly displays an autographed, framed poster of Wooden's oft-cited Pyramid of Success, the universal road map for team and individual excellence. "Wooden said it very beautifully — that he deeply cared about what is right, not who is right," Dr. Shivkumar says.

Another favorite Wooden quote spoke to Dr. Shivkumar as he began to ponder an effort to render Dr. Pernkopf's work irrelevant. The quote was about basketball but, like so many credited to the Wizard of Westwood, it applied to life: "It's not so important who starts the game, but who finishes it."

AFTER ITS CONTEMPTIBLE HISTORY WAS EXPOSED, the Pernkopf atlas remained highly influential — seen as an irreplaceable resource that could save lives, even if its authors shamefully disregarded them. It was published in five languages from 1960 to 1990. Although it went out of print after the history was revealed, secondhand copies — fetching, in some cases, thousands of dollars — can still be found, including on Amazon.

But if few copies of the originals remain in circulation, many Pernkopf images have appeared, in some form, in other publications. "For any anatomist who was creating an atlas following Pernkopf, it would be surprising if they had not consulted the Pernkopf atlas, and you can see the influences," Dr. Natterson-Horowitz says.

Knowing the sordid origin story behind the Pernkopf atlas raised a moral dilemma. If the books contained critical information that could be used for the benefit of patients, should they nonetheless be disregarded given that the information came from the exploitation of Nazi victims? On the one hand, some have argued, the knowledge derived from the Pernkopf work — and from other incidents of unethically produced science throughout history — can't simply be erased and applying the knowledge to improving lives honors the victims. Others counter that the evil doings can't be separated from the work and condoning the atlas' continued use opens the door to future moral and ethical transgressions that rely on the ends to justify the means.

In particular, the Pernkopf work was viewed as peerless when it came to its utility for peripheral-nerve surgeons. In 2015, Susan E. Mackinnon, MD, a leading nerve surgeon at Washington University in St. Louis who had long leaned on the illustrations to guide complex pain operations, approached Sabine Hildebrandt, MD, a pediatrician and lecturer in global health at Harvard Medical School and an expert in the history of anatomy during the Third Reich,

about her misgivings. They consulted leading scholars in Jewish medical ethics — including Rabbi Joseph Polak, who survived the Westerbork and Bergen-Belsen concentration camps as a child while losing his father and 30 other family members in the Holocaust.

The scholars issued a document on the case, known as the Vienna Protocol, that was formally adopted in 2017 by a group of experts at Yad Vashem. It concluded, based on Jewish law, that the Pernkopf images should be utilized if they were helping to save a life, as long as the patient was aware of the history and consented: "In this way, the dead are accorded at least some of the dignity to which they are entitled."

While Dr. Shivkumar found the conclusion "touching, and it shows how noble people can be," he had other ideas. "I was repulsed" at the thought of the Pernkopf works continuing to find circulation, he says. "It didn't sit with me very well."

AS DR. SHIVKUMAR SAW IT, ALL OF THE WRESTLING with how and whether the Pernkopf atlas should continue to serve as a resource was based on the premise that replacing Dr. Pernkopf's work was insurmountable. For decades, no serious effort had been undertaken to surpass it. Now, fueled by his moral outrage, Dr. Shivkumar was ready to summon his team to take up the challenge. "Why should we have to choose?" he says. There would be no ethical quandary if the product of Dr. Pernkopf's evil became obsolete.

Among the rabbinic scholars he consulted was Michael Berenbaum, an author and professor at American Jewish University in Los Angeles, where he is director of the Sigi Ziering Institute: Exploring the Ethical and Religious Implications of the Holocaust.

After several meetings with Dr. Shivkumar and his team, Rabbi Berenbaum says, "we were profoundly impressed by their commitment to providing an ethically normative means by which to guide surgeons and others grappling with the structure and nature of the heart."

Rabbi Berenbaum likens knowledge stemming from Dr. Pernkopf's atlas to fruit from a poisonous tree. "These are ill-gotten gains," he explains. "Even though the information is essential, we would not want to be the beneficiary of those medical crimes. We want to find that knowledge in a manner that doesn't violate ethical decency, norms and propriety."

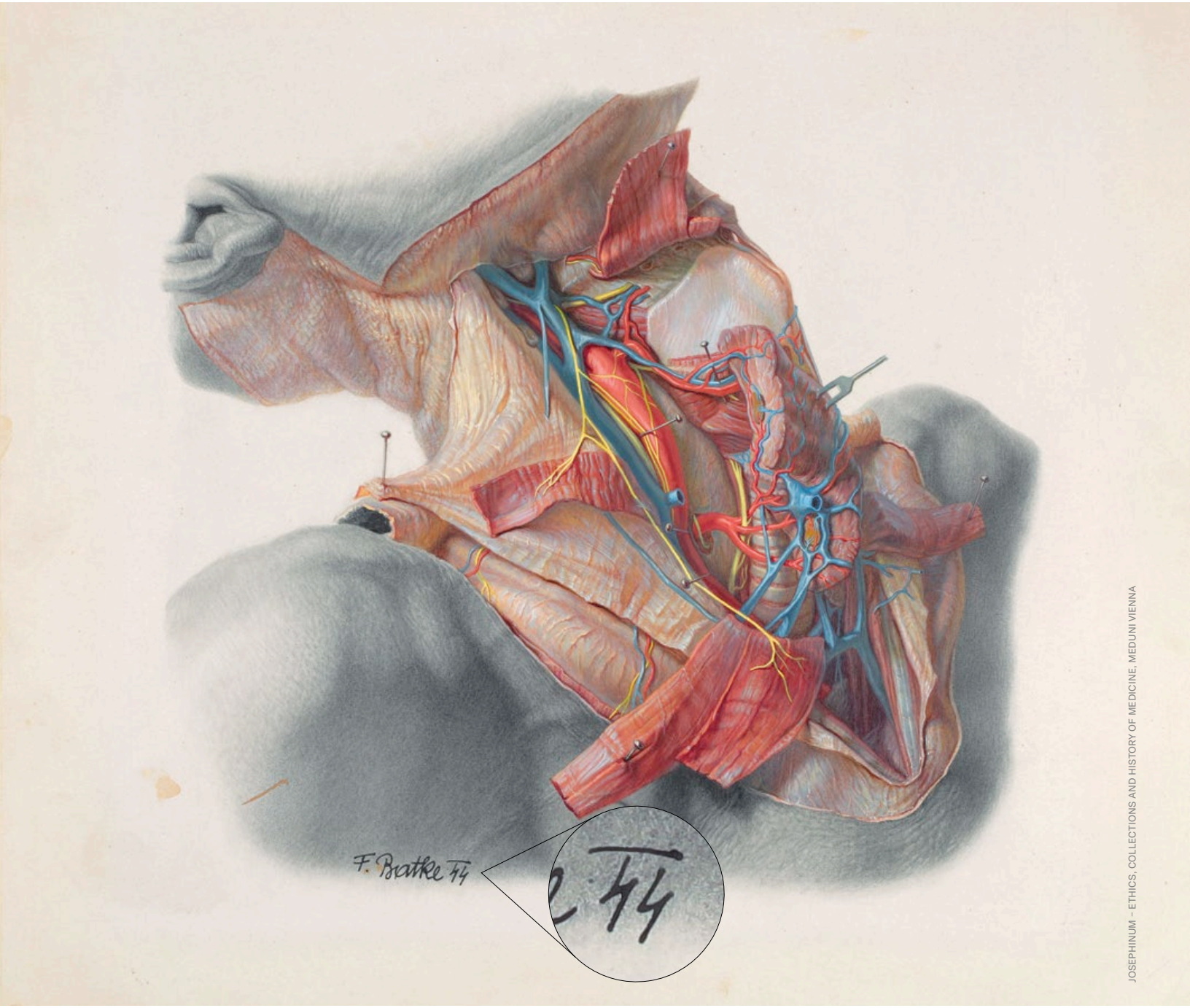
Dr. Shivkumar also reached out to Richard S. Panush, MD, a rheumatologist who had taken a public stand against the Pernkopf atlas after a 1995 *Annals of Internal Medicine* article set off the chain of events that led to the University of Vienna investigation. Dr. Panush, then at St. Barnabus Medical Center in Livingston, New Jersey, was deeply disturbed by the recollections of Edzard Ernst, MD, PhD, a former Vienna Medical School faculty member who wrote of the Nazi takeover of the university and raised the likelihood that Nazi victims were used as research subjects.

When Dr. Panush found the atlas in his hospital's library, he recoiled. He wrote a letter in response to the *Annals* article, detailing the actions he took following that discovery — including getting his institution to remove the atlas from circulation, place it in a case with a historical explanation and offer the display in a cautionary context.

Dr. Shivkumar struck up a friendship with Dr. Panush, who is now an emeritus professor at USC, and has used his sentiments as a call to action. "Dr. Panush said our obligation is to repudiate Pernkopf and all he stood for," Dr. Shivkumar says. "He said we cannot forget that Pernkopf's character and actions were so abhorrent

MILO MITCHELL

Drs. Shivkumar and Natterson-Horowitz display the first volume of the new atlas created by the Amara Yad project.



JOSEPHINUM – ETHICS, COLLECTIONS AND HISTORY OF MEDICINE, MEDUNI VIENNA

An original illustration for the Pernkopf atlas displays the double lightning bolt *Siegrune* of the SS in the illustrator's signature.

as to irrevocably taint this work. I share that belief."

So, in 2012, Dr. Shivkumar set out to surpass Dr. Pernkopf. He vowed that he and his team would create an anatomic atlas of the entire body, starting with the heart. They would make it open access, so that all members of the medical and surgical community could benefit. And they would remove the need for anyone to consult the work of Dr. Pernkopf — the fruit from the poisonous tree. "When you discover that the foundation of what you thought of as a beautiful building is rotten, you don't keep building on it," Dr. Shivkumar says.

"What Shiv is doing is absolutely heroic," Dr. Panush asserts. "He has totally changed the conversation. If the atlas becomes obsolete, all of these other issues become moot."

Of course, there was a reason no one had tried to surpass the Pernkopf atlas before. "When I told the anatomists we were doing this, they said it was impossible," Dr. Shivkumar says. "But as electrophysiologists, we have not come across any arrhythmia we're not able to manage. So, I said, 'We have done harder things. This is doable.'" ●

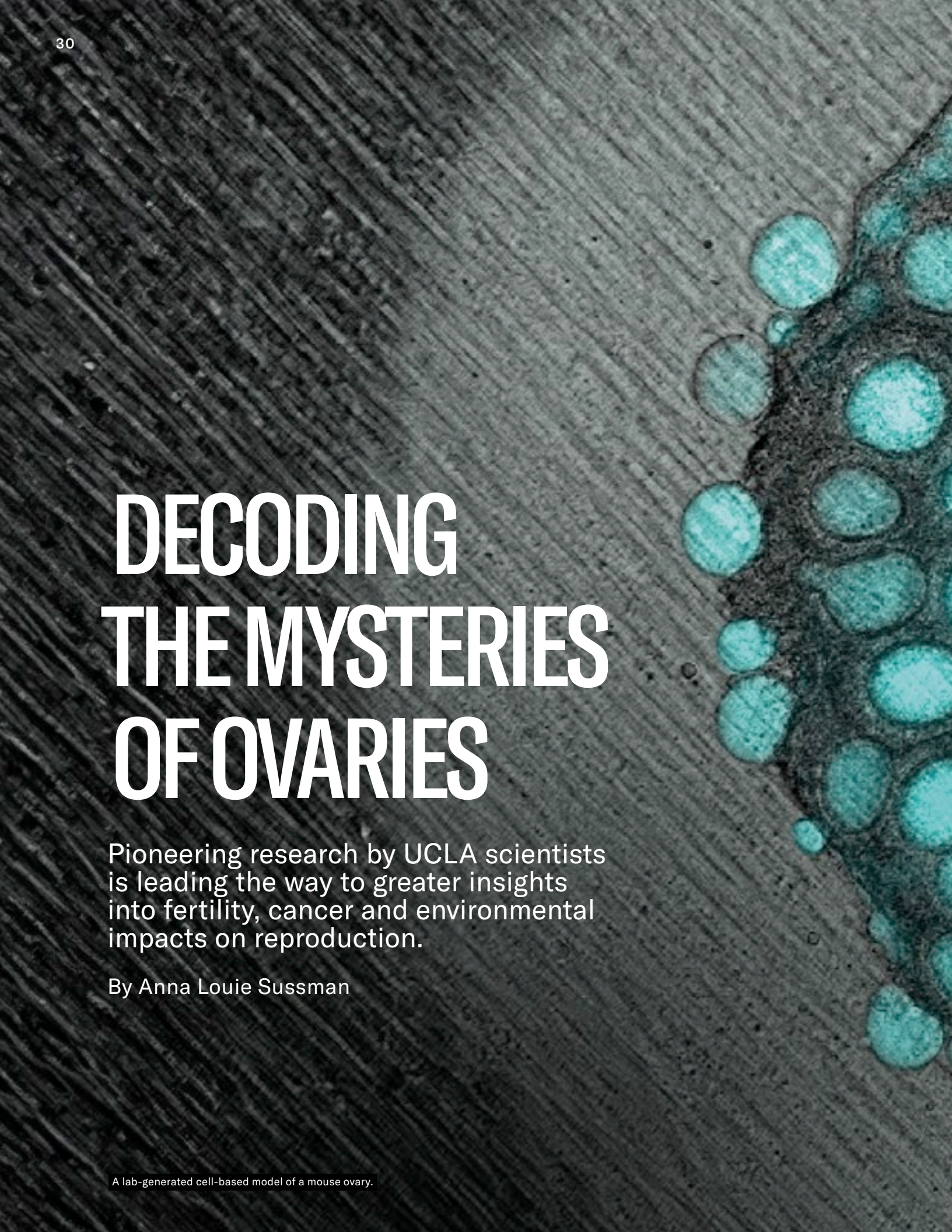
***Dan Gordon** is a frequent contributor to* U *Magazine. His two-part story, "UCLA In the Time of AIDS," received the Robert G. Fenley Gold Award for Excellence in Writing and "Best of Show" from the Association of American Medical Colleges.*

Part 2 of this article will chronicle how the UCLA team surpassed the Pernkopf atlas and the larger ambitions of the Amara Yad Project to honor the victims of medical exploitation through corrective action.

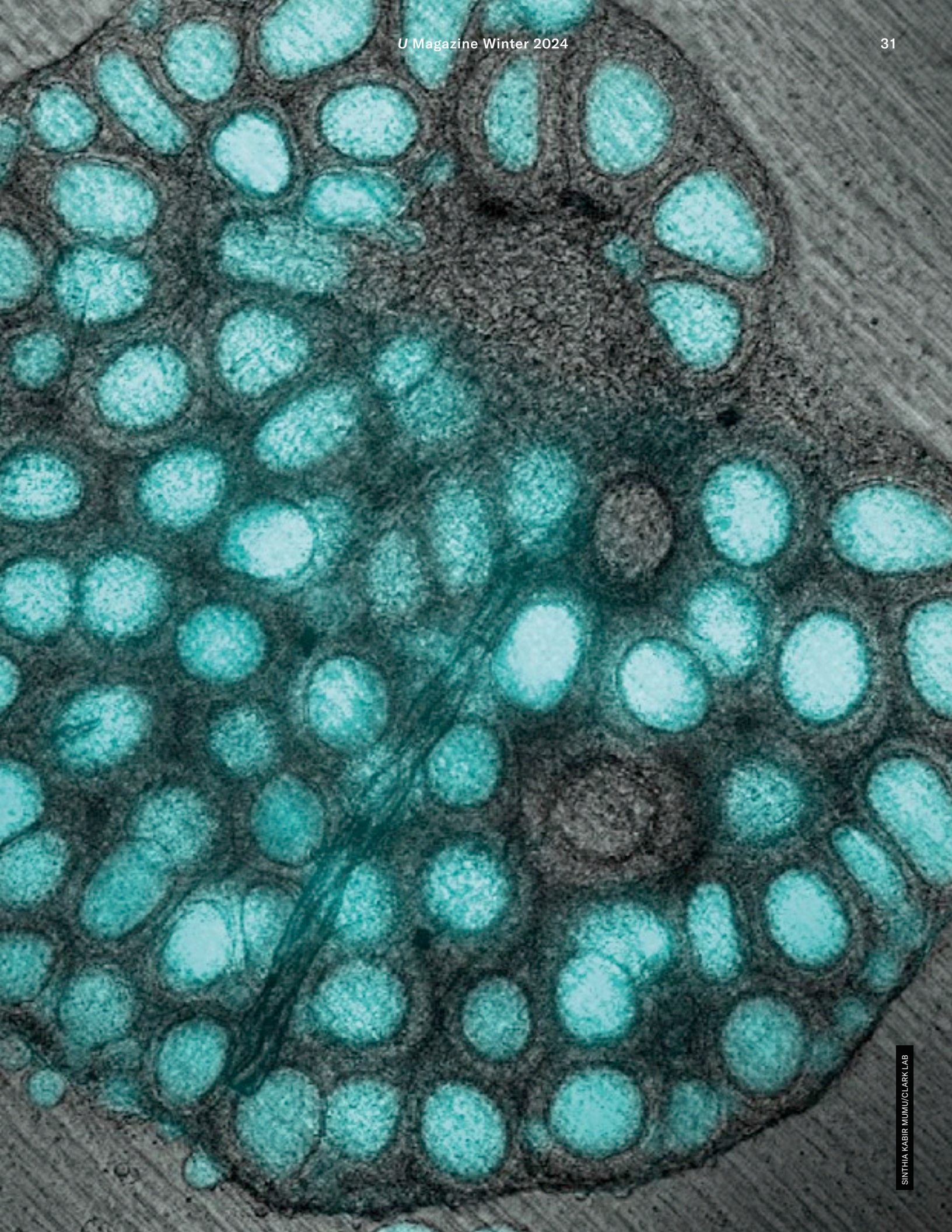
DECODING THE MYSTERIES OF OVARIES

Pioneering research by UCLA scientists is leading the way to greater insights into fertility, cancer and environmental impacts on reproduction.

By Anna Louie Sussman



A lab-generated cell-based model of a mouse ovary.



SINTHIA KABIR MUMU/CLARK LAB

ADAM AMENGUAL

"Ovaries," says Dr. Beth Karlan (right), with colleague Dr. Amander Clark, "are fascinating organs. I always say they look like little brains."

"Sinthia, can you please grab the little ovaries," Amander Clark, PhD, calls out to a lab technician in a long blue coat. The "little ovaries" aren't genuine ovaries, of course — those would be difficult to grab, given their location inside the mammalian body — but a small tray of organ models engineered from different types of mouse stem and progenitor cells. By providing them with nutrients and a collagen-coated scaffolding on which to grow, Dr. Clark, a stem cell scientist and developmental biologist who is director of the UCLA Center for Reproductive Science, Health and Education and professor of molecular, cell and developmental biology in the UCLA College Division of Life Sciences, coaxes them to undergo a process of self-organization into a model of an organ that will eventually be capable of the ovary's chief function: production of eggs and hormones.

"We're trying to create folliculogenesis [creation of an egg], hormone production and ovulation in culture," Dr. Clark says. This complex process takes 23 days. It begins with the creation of germ cells from stem cells, which are combined with somatic progenitor cells derived from fetal mouse ovarian tissue. Then, Dr. Clark says, "The magic happens: They self-assemble and form what we call 'reconstituted ovaries.'" There are several cohorts of reconstituted ovaries underway, some of them eight days into the developmental process, some at 21 days. They are growing in wells in covered plastic dishes, labeled with the date and lot number. Under the right circumstances, they will form follicles containing oocytes, which, once they mature, become ova — i.e., eggs.

They are barely visible to the naked eye, but under a microscope, Dr. Clark watches the eight-day-old ovary at work. A bit like a half-painted landscape, in which one can see the forms starting to take shape, the immature reconstituted ovary is a work in progress. Dr. Clark points to the stem-cell derived germ cells that have been marked with blue fluorescence. "You can see some of them down here, these little circles — they're tiny, tiny oocytes that are starting to form." In the same reconstituted ovary, she grows both stem-cell derived oocytes and oocytes carried through with the ovarian somatic progenitors, allowing her to compare how the lab-grown oocytes compare to ones that had already started to develop in the ovary. That's "the beautiful thing about this system," she says. "What we want to see is how similar are the blue ones, the stem-cell derived ones, within the same organ to the wild type ones?"

The 21-day-old reconstituted ovaries have formed follicles, each of which contains a single oocyte, as well as granulosa cells, which release hormones, including estrogen, progesterone and testosterone. The estrogen released in the initial phase of the ovulatory cycle tells the oocyte to keep growing. Eventually, a clutch of these immature follicles will activate, a process caused by mechanisms that, Dr. Clark says, "are not well understood." In humans, one follicle becomes the dominant one, released by the ovary into the fallopian tube during ovulation. By studying every step of this process under a microscope, Dr. Clark and her colleagues hope to better understand this basic reproductive function. Her insights could help people increase their reproductive success, particularly by improving costly and too-often unsuccessful fertility treatments.

Ovaries play an essential role in the perpetuation of our species, but they don't always function as they should. The World Health Organization recently estimated that infertility affects one-in-six couples globally. The common reproductive disorder polycystic ovary syndrome is associated with metabolic disease, mood disorders and difficulty getting pregnant. The ovaries also play host to one of the deadliest known cancers, which has proven especially difficult to screen for and treat. Armed with a wide range of methodologies, such

OVARIES PLAY AN ESSENTIAL ROLE IN THE PERPETUATION OF OUR SPECIES, BUT THEY DON'T ALWAYS FUNCTION AS THEY SHOULD. THE WORLD HEALTH ORGANIZATION RECENTLY ESTIMATED THAT INFERTILITY AFFECTS ONE-IN-SIX COUPLES GLOBALLY.

as stem-cell-derived ovaries, genetic databases and animal models, researchers and clinicians at UCLA are unlocking the secrets of this mysterious, complex and powerful organ.

"Ovaries are fascinating organs. I always say they look like little brains," says Beth Karlan, MD (FEL '89), the Nancy Marks Endowed Chair in Women's Health Research in the David Geffen School of Medicine at UCLA and director of cancer population genetics in the UCLA Health Jonsson Comprehensive Cancer Center. "They are not only responsible for the ongoing of our race and society as humans, but also for all the hormones that lead women through life and longevity, whether it's through puberty, through menopause or beyond."

FOR PEOPLE HOPING TO GET PREGNANT, ONE OF THE most important factors is "oocyte competency," that is, the oocyte's capacity to mature, fertilize, implant and grow into a healthy baby. About one-third of infertility cases are attributed to female-factor infertility (another third is male-factor, and the remaining third of cases are unexplained or related to multiple factors). Today, there is still no reliable way to assess oocyte competency before conception.

Moreover, humans are born with all the oocytes they'll ever have, a number estimated at 700,000-to-1 million. That number declines with age until menopause, and the quality of the eggs deteriorates, too. As women age, the oocyte maturation process is more error-prone, resulting in more chromosomal abnormalities that lower the chances of pregnancy. "What's really missing in this field is non-invasive ways to test oocyte competence," Dr. Clark says. "If a woman is going through IVF, and there are a lot of eggs retrieved at once, how do we tell which egg is competent?"

Without insight into the health of the egg, fertility doctors are left with no option but to fertilize all the eggs retrieved and then choose the best embryo based on its appearance or the results of genetic testing, a practice that can result in an excess of embryos, unsuccessful embryo transfers or both. Similarly, a patient undergoing oocyte cryopreservation (also known as "egg freezing") cannot know if those eggs are healthy until she chooses to fertilize them, at which point the patient may be significantly older or no longer ovulating.

Lab-grown human eggs are still, in all likelihood, in the distant future. But with her reconstituted ovaries, Dr. Clark can study minute aspects of oocyte development in order to pinpoint where the process goes awry. Although they are not exact replicas of a human ovary — for starters, they are made from mice cells — they are built from cells similar to those that make up a human ovary. Her team can set up about 10-to-12 ovaries every two weeks, and each one will typically yield about 50 oocytes, giving Dr. Clark many data points to study.

This is fortunate, as there are many aspects of oocyte development that remain shrouded in mystery. How, for example, does energy metabolism function to help or hinder the growth of an egg? It is known that fertilized oocytes must use a lot of mitochondria, which provide the energy that powers a cell's biochemical reactions, in order to be able to support early embryo development. Another key part of oocyte development is germinal vesicle breakdown, in which the oocyte's nucleus dissolves during the luteinizing hormone surge in order to resume meiosis, the special type of cell division that creates sperm and eggs. "What does it take to break down that nucleus?" Dr. Clark muses. "This model might be able to teach us something about germinal vesicle breakdown and the resumption of meiosis, which is so important for healthy, competent oocytes."

There is a growing body of science linking rising rates of infertility to environmental factors, from the ubiquity of endocrine-disrupting chemicals to temperature fluctuations associated with climate change. Grasping the basic underlying processes underlying ovarian function through the reconstituted ovary model will allow Dr. Clark and her team to unpack this connection between environmental change and impaired reproduction. "The temperature is going up, we live in an increasingly plasticized world — how does that affect our reproductive tissues and the germline cells?" she asks.

INDEED, RAPID HUMAN-MADE ENVIRONMENTAL CHANGES MAY CONTRIBUTE to the rise in polycystic ovary syndrome, or PCOS, in which the body accumulates excess fat around the midsection. While this was once a clever evolutionary adaptation, the current obesogenic environment has turned it maladaptive, causing metabolic and reproductive

dysfunction. This is the theory put forth by Daniel A. Dumesic, MD, professor of reproductive endocrinology and infertility, and an insight that garnered him recognition this year as a Distinguished Researcher by the Androgen Excess and PCOS Society.

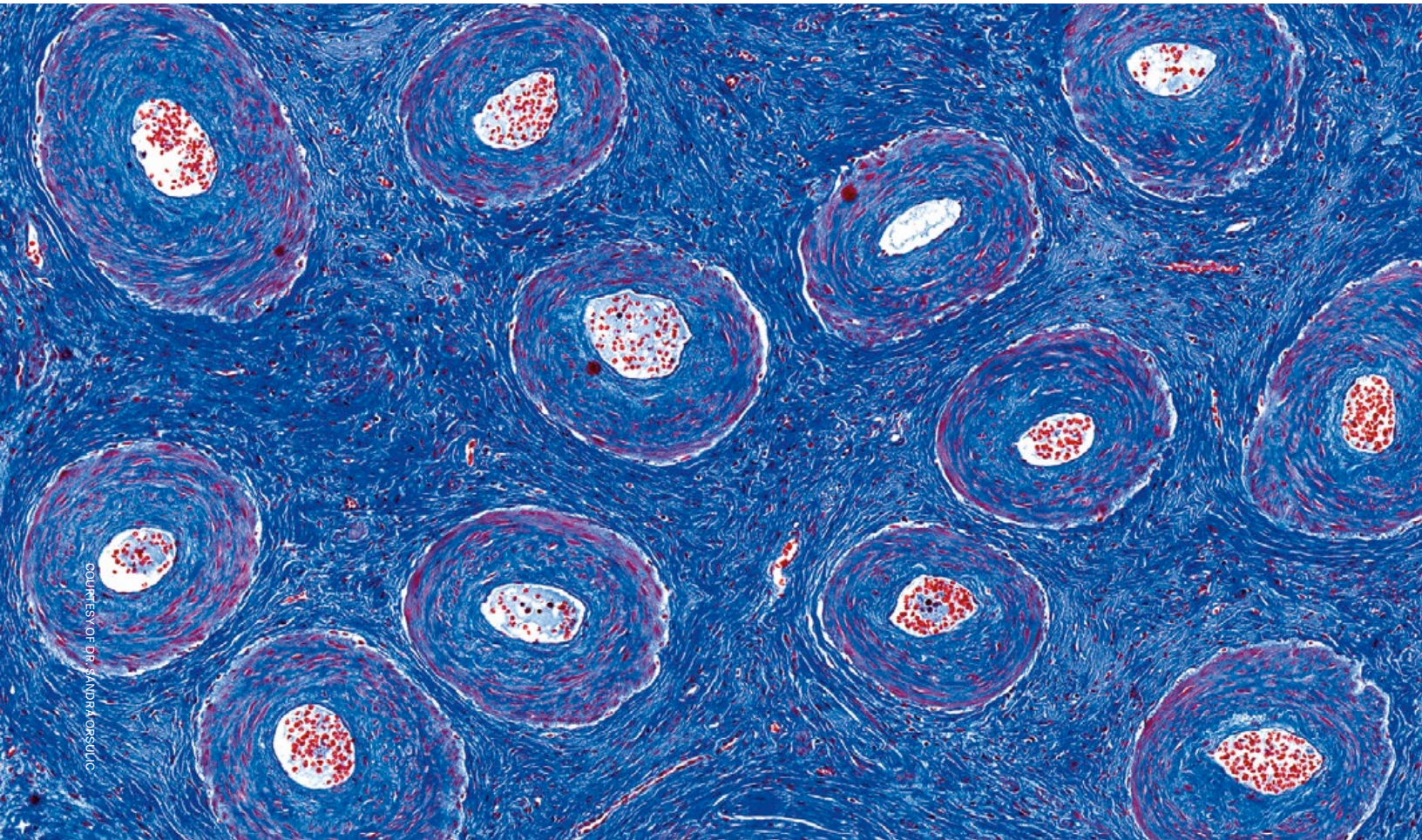
Despite affecting an estimated 10-to-15% of pre-menopausal women, PCOS is still poorly understood and underdiagnosed. There are also important subtleties within PCOS, which has multiple manifestations. This confusion and lack of familiarity means that women with PCOS spend an average of more than two years undergoing clinical exams and visiting multiple doctors before being diagnosed.

PCOS wasn't always such a downer. In fact, Dr. Dumesic notes, millennia ago, extra abdominal fat and infrequent ovulation were valuable evolutionary adaptations. "In times of famine, when we were hunter-gatherers, these women were storing fat, and simultaneously providing glucose and free fatty acids for energy as they hunted," he explains. "And if they ovulated infrequently, they had less chance of becoming pregnant or dying in childbirth," giving them and their children a higher chance of survival, albeit within a smaller family. "PCOS, at least in the androgen-excess form [involving elevated levels of testosterone] as we now commonly see, is likely an evolutionary metabolic adaptation." Unfortunately, Dr. Dumesic adds, in industrialized countries, obesity is far more common than famine, and this predisposition to weight gain no longer serves us. "Our genes can't keep up with it," he says.

To buttress this explanation, he and coauthors have documented reports in medical literature of PCOS-like disorders stretching back two millennia, including by illustrious ancient physicians such as Hippocrates and the Middle Ages sage Moses Maimonides. They also cite more modern work on PCOS, such as large genome-wide association studies (GWAS), which allow researchers to scan entire sets of genetic data from across populations to identify genetic variations linked to a specific disease. For PCOS, these genome-wide association studies have examined women with and without PCOS to pinpoint genes that are involved with many reproductive and metabolic functions. Notably, the genes that put women at risk for PCOS are expressed in women found all over the world, pointing to "the ancient human origins of PCOS, potentially dating back before the migration of humans out of sub-Saharan Africa 300,000-50,000 years ago or earlier," as Dr. Dumesic has written.

Depending on the type of PCOS they have, women can have difficulty getting pregnant or can be highly responsive to the medications used in fertility treatment, including in vitro fertilization (IVF). Younger and leaner women with PCOS can still have good reproductive outcomes because their elevated testosterone level stimulates excess follicle growth. But older PCOS women, or those who've already experienced weight gain, will have a harder time, since obesity can pose a risk to oocyte quality.

Knowing this, Dr. Dumesic hopes that patients at risk for PCOS, or for transmitting it to their offspring, can take a more proactive approach to a disease that begins to manifest around the time of puberty. For girls born to mothers with PCOS, this



Laboratory image of a stained human ovary highlights the intricate network of blood vessels interwoven with structures of connective tissue.

COURTESY OF DR. SANDRA ORSULIC

"THERE ARE LOTS OF ADVOCATES LOBBYING FOR BREAST CANCER, AND THEY CAN DO IT BECAUSE THEY'RE USUALLY HEALTHY. WOMEN WITH OVARIAN CANCER, THEY ARE TYPICALLY NOT OUTSIDE LOBBYING BECAUSE THEY'RE TOO SICK."

could mean a nutrition and exercise regimen that can help prevent the preferential fat storage that would predispose them to health risks or reproductive issues. For women of reproductive age, especially those who are already at an elevated body-mass index, this could mean prioritizing weight loss long before planning to attempt pregnancy.

CANCER PREVENTION IS THE HOLY GRAIL FOR CANCER GENETICIST DR. KARLAN, who has been treating patients with ovarian cancer for more than three decades. To date, this goal has proved elusive. "I've always viewed ovarian cancer as an albatross around the neck of ob-gyns," says Dr. Karlan. She was initially inspired to study ovarian cancer as a fourth-year medical student in the 1980s when she encountered a patient perhaps five years older than herself who had an advanced case. As Dr. Karlan recalls, the patient asked her a "very basic question: 'Why am I here in the hospital dying from ovarian cancer while you are pursuing your dreams to become a doctor?'"

Dr. Karlan took this question to heart, and she has spent her career trying to answer it. At the time, "there was no screening test for ovarian cancer like we have the pap smear for cervical cancer or a mammogram for breast cancer." Fast forward to today, "and we still don't have a screening test for ovarian cancer," she says.

To understand why, it helps to know a few things about this type of cancer, sometimes called "the silent killer." There are no specific symptoms of ovarian cancer. Its most-common symptoms include abdominal bloating, pelvic pain, feeling full quickly and urinary frequency — symptoms that are so common and vague that they are often ignored or misdiagnosed. In addition, there are many types of ovarian cancer, with distinct characteristics. The most common type, epithelial ovarian cancer, accounts for about 90% of cases, and within that category there are five subtypes. Recognizing that ovarian cancer is not one monolithic disease is helping drive the development of more targeted therapies.

Despite the name, most ovarian cancers are now recognized as originating in the fallopian tubes and not the ovaries. It is believed that very early on the malignant cells from the fallopian tubes migrate to the ovarian surface, where they further grow and metastasize. If physicians were able to catch ovarian cancer at this early stage, survival rates might be closer to 90-to-95%, as they are with early-stage breast cancer. "Part of the problem is a catch-22," Dr. Karlan says. "Most ovarian cancer presents when it's already metastatic, at stage 3 or stage 4, and to screen you want to find the disease at stage 1, before it spreads." (At stage 3, survival rates drop to 35%.) "For us to discover effective screening tests, we need to have access to more early cases."

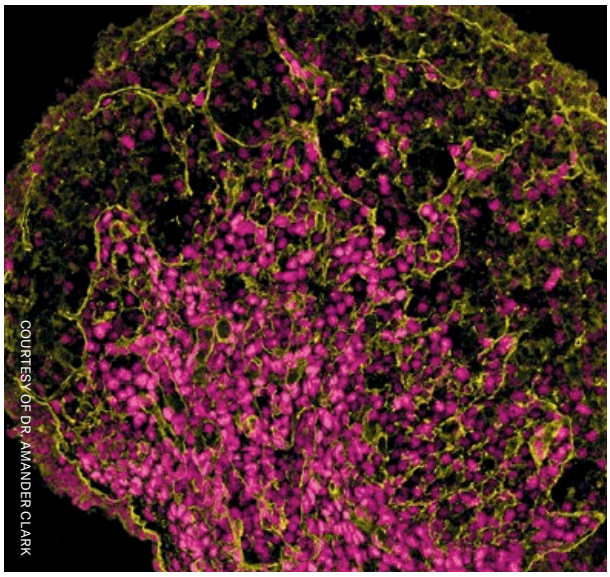
This creates another catch-22: The lower survival rate may partially explain why less funding has been allocated toward its study than to breast cancer or prostate cancer. (Ovarian cancer is also less common than breast cancer, affecting about one-in-80 women versus breast cancer's one-in-eight.) "There are lots of advocates lobbying for breast cancer, and they can do it because they're usually healthy," says Sandra Orsulic, PhD, a molecular pathologist in the David Geffen School of Medicine at UCLA and longtime collaborator with Dr. Karlan. "Women with ovarian cancer, they are typically not outside lobbying because they're too sick."

Dr. Karlan's work as a clinician informs the research questions she brings into her laboratory work. Just as she could not explain to her patient why she could pursue her dream to become a doctor while the young woman was dying, Dr. Karlan struggled to account for the wide range of clinical outcomes she observed among her patients, even those who had undergone the same surgery on the same day. Why would one be dead within two years while another would be alive and thriving for another 20?

The answers, she thought, lay in the tissues. In 1990, she began a biorepository, a library of human tissues and other samples such as blood, tumor tissue, DNA and urine, annotated with correlative data such as family history of cancer, which treatments they'd undergone and how they'd responded, whether or not they smoked and other potentially relevant information. As time went on, she and colleagues grew the biorepository to include samples of frozen tumors, as well as information about the genetic changes in the tumor and inherited genetic alterations in the patients. It eventually expanded to include more than 100,000 samples. This extensive web of data, alongside daily work with patients, allowed them to test additional hypotheses and identify more connections, and then bring potential insights into the lab to investigate on a molecular basis. "What's the impact of antibiotics on response to chemotherapy? Did blood pressure medicine or statins impact clinical outcomes? Novel questions that come from clinical observation could be taken back to the laboratory to explore further," Dr. Karlan says.

When Dr. Karlan began this research in the 1980s, the tools available for laboratory work were far less advanced. But by the early 2000s, geneticists had succeeded in mapping the human genome. As the field of genetics advanced, so did cancer researchers' understanding of how genes and gene expression contributed to an individual's susceptibility to cancer, especially with the completion in 2018 of the Cancer Genome Atlas Project, which sequenced samples from more than 11,000 patients with ovarian cancer.

The familial clustering of ovarian cancer that Dr. Karlan and her colleagues had observed was traced to the BRCA1 and BRCA2 genes, which also puts carriers at risk for breast, prostate, pancreatic and other cancers. Interestingly, she and her colleagues found that women with the BRCA mutations tended to have better survival rates from ovarian cancer. "By knowing their genetics, by having their tissues, by knowing the outcomes, we were able to show that women who have these germline mutations in genes that have to do with DNA repair have a better survival rate," she says.



Developing human ovary.

In BRCA carriers, the mutated gene makes it more difficult for their cells to repair damaged DNA, which leads them to accumulate more defects that can eventually allow cells to transform into cancer cells. However, that same quality makes BRCA carriers more responsive to chemotherapy, which works by causing DNA breaks in the cancer cells themselves. "It's why they get cancer, but it's also why it's easy to kill the cancer cells with therapy," Dr. Karlan explains.

RESEARCHERS USED THIS SAME INSIGHT TO IDENTIFY A CLASS OF DRUGS CALLED PARP INHIBITORS that are now used to treat ovarian cancer. These drugs block a cell-repairing protein from doing its job, which causes cancer cells with a BRCA mutation to die out. Dr. Karlan noticed that over time, some of her patients were no longer responding to the drugs. Because she had been sampling patients' tissues longitudinally — for as long as a decade in some cases — she could use genetic sequencing to show how the patients' cells had mutated over time. This led her and her collaborators to identify "reversion mutations" — changes that occur when the cells become so stressed by chemotherapy and PARP inhibitors that they actually accumulate new mutations that functionally repair the original BRCA mutation, rendering them less sensitive to treatment.

To gain an even deeper understanding of how these changes unfold, Dr. Karlan and Dr. Orsulic turned to mouse models of ovarian cancer, which allow researchers to perform controlled experiments that could not ethically be carried out in humans. When Dr. Orsulic was beginning her career, she also saw that ovarian cancer was under-studied, especially through the use of animal models. Creating one was not a straightforward task. She first attempted to make one as a post-doctoral fellow using mice, long before the Cancer Genome Atlas Project had helped identify relevant genes for ovarian cancer. "We didn't know what genes to start with," she says. "It was all pretty anecdotal."

Furthermore, the mechanics of ensuring that the cancer genes affected only the mouse's ovaries were incredibly difficult, due to the inaccessibility of the fallopian tube and the sheer tininess of a mouse ovary. Eventually, she removed the mouse's ovaries, transformed them in a tissue-culture dish with different combinations of mutated genes and put them back into mice to identify which combinations of genetic alterations will lead to cancer development.

Today, she and her colleagues study ovarian cancer tumors on more refined versions of these mouse models, which have been engineered with different mutated genes to exhibit many of the same genetic alterations found in human ovarian cancer. Mice recapitulate many of the aspects of human pathophysiology, including the formation of the tumor microenvironment in reaction to the cancer cells. For example, by examining the microenvironment of tumors, they discovered that following a tumor's removal, the subsequent wound healing actually attracts remaining free-floating cancer cells to the inflamed tissue where the tumor was cut away. This raises a question: When exactly is the tissue most vulnerable to the re-implantation of these cancer cells? Drs. Karlan and Orsulic have identified the period one-to-five days after surgery as a critical period for intervening to inhibit inflammation, a finding that could help reduce the recurrence of cancer after surgery.

The sheer complexity of the ovary — its role in producing mature, healthy oocytes and preparing the body for reproduction; its vulnerability to dysfunction, whether that be cancer, premature menopause or PCOS; its evolutionary role — means it "needs to be looked at by many different investigators," Dr. Karlan says. She points to a number of still-unsolved mysteries whose answers may lie within the ovary. Why do some women with a BRCA mutation go through premature menopause? Why do some BRCA carriers get breast cancer at early ages while others get ovarian cancer at a late age? Why does endometriosis increase the risk of ovarian cancer? What's the role of inflammation?

"There is very, very complex biology at play," she says. "The ovaries are an extraordinary organ." With all their mystery and wonder, "the world is a better place because of ovaries." ●

Anna Louie Sussman *is a freelance journalist based in New York. A former staff reporter at* Reuters *and* The Wall Street Journal*, her writing has been published in* The New Yorker, The New York Review of Books *and* The New York Times.

Un-Tattoo You

By Sandy Cohen

JOHN MCCOY

Dr. Robert Reiss removes a tattoo from Reyna Garcia at Homeboy Industries.

"SNAP! SNAP! SNAP!" GOES THE machine and Reyna Garcia winces in pain. A faint smell of something burning rises in the small room in the offices of Homeboy Industries, where a UCLA Health physician is using a laser wand to remove two five-inch-long cursive tattoos — remnants of a life she is leaving behind — from Garcia's face.

When Garcia first started coming to Homeboy Industries near downtown Los Angeles, she had a lot more ink, including clown markings on her face: diamond shapes above and below her eyes and a black circle on her nose. After many visits, those tattoos are gone. Now, the script on either side of her face is growing more faint — practically illegible — after a series of treatments so painful that she cries during the procedure.

Robert Reiss, MD, a UCLA Health internal medicine specialist, is administering Garcia's treatment. He began volunteering with Homeboy in 2019 and has been treating Garcia for more than a year.

"We're almost done, kiddo," he tells Garcia, as the red light from the three-pronged laser wand he's holding traces the fading black ink on her face.

He and Garcia meet every eight weeks. Each time, Dr. Reiss takes a photo so Garcia can see the progression as her tattoos gradually disappear from her skin. "I'm going to have an anxiety attack!" Garcia says, only half-kidding, as she blows air out in quick exhalations, like a woman giving birth.

After her face, Dr. Reiss moves onto Garcia's hand, where he's removing the large '20' inked there. Garcia decides not to treat the tattoo on her stomach today. Things have been painful enough already.

"See you in eight weeks," Dr. Reiss tells her as she leaves. "I'll email you."

Dr. Reiss is no fan of tattoos, generally considering them to be "regrets in the making." "I've joked that when I retire, I'll open a tattoo-removal business right next to an ink parlor," he says. "I'd call it, 'What Was I ThINKing?'"

He volunteered with Homeboy Industries after hearing a talk by Father Gregory Boyle, the nonprofit's founder. Established in 1988, when Father Boyle was pastor of Dolores Mission Church in East Los Angeles, Homeboy today is the largest program in the country dedicated to rehabilitation of former gang members. During the talk, Father Boyle

— or Father G, as he is commonly known around the Homeboy offices — told the audience, "We need people to remove tattoos. We want you."

"I looked at my wife, and she looked at me, and the die was cast," Dr. Reiss says.

Since he started volunteering, Dr. Reiss has spent every Tuesday — except for a brief period during the pandemic — at Homeboy Industries. He learned tattoo removal by observing another volunteer physician and went to conferences to further hone his skills. Finally, he started treating patients himself.

He has developed close relationships with many of the men and women he treats. "The process we're going through together, it's been amazing," Garcia says. "I'm very grateful for him. He loves his job, and it comes out of him naturally. At the end of the road, it's going to be a success because I'm going to be able to see myself with my clear face," she says, adding she hopes her 4-year-old son won't remember her with facial tattoos.

For Christopher Aviles, having the tattoos on his forearms removed is key to the new life he's trying to create. The 30-year-old just graduated from college and completed Emergency Medical Technician training. "Getting my tattoos removed is giving me that clean-cut image that the L.A. County Fire Department wants," he says. "It means so much to me, and I'm just very glad Dr. Reiss is doing this work."

On a recent Tuesday, Dr. Reiss sees a new patient, a young man in his early 20s with a full sleeve of tattoos on his right arm, a large rose on the side of his neck and the word "Family" in cursive on the side of his face. That's the one he wants gone. Dr. Reiss explains the two laser machines he will use in the process. "They don't remove the ink," he says. "What they do is break up the ink into smaller particles so your white cells can sweep them away."

The stronger of the two machines will be used first, when the ink is most dense, Dr. Reiss says. The treatment can sometimes — though not usually — cause blistering, he explains. It makes the skin extra sensitive to the sun, so it's important to cover the treated area with sunblock several times a day, he adds.

Reyna Garcia checks out her new look after a session with Dr. Reiss.

The patient doesn't have any questions, so Dr. Reiss hands him a pair of protective glasses, puts a pair on himself and fires up the machine. "It's going to hurt, buddy," he says, patting the young man on the shoulder. Then he turns on the laser and the "SNAP! SNAP! SNAP!" begins.

***Sandy Cohen** is a senior writer in UCLA Health Communications and a former national writer for* The Associated Press*. Her article, "The Price," received the Robert G. Fenley Gold Award for Excellence in Writing and the COVID Pivot Award from the Association of American Medical Colleges.*

AWARDS & HONORS

Dr. Carol Bennett, Henry E. Singleton Professor of Urology, received the Lifetime Achievement Award from the Association of Black Women Physicians.

Dr. Suzanne McDiarmid (FEL '88), Distinguished Professor of Pediatrics and Surgery and division chief of pediatric gastroenterology and hepatology, received the Lifetime Achievement Award from the Liver Health Foundation.

Dr. Gerardo Moreno (MD '04), chair of the UCLA Department of Family Medicine, was elected to the National Academy of Medicine.

Dr. Paul Vespa (FEL '96), Gary L. Brinderson Family Professor of Neurointensive Care, was elected president of the Neurocritical Care Society.

Dr. Rhonda Voskuhl, Jack H. Skirball Professor of Multiple Sclerosis Research, received the inaugural Rachel Horne Prize for Women's Research in MS.

Twenty-two UCLA Health and David Geffen School of Medicine at UCLA faculty are named on the Clarivate Analytics Highly Cited Researchers list as among those who have authored studies that rank in the top 1% in the number of scholarly citations worldwide. They are: **Dr. Carrie Bearden**, professor of psychiatry and biobehavioral sciences; **Dr. Matthew Budoff**, professor-in-residence of medicine; **Dr. Genhong Cheng**, professor of microbiology, immunology and molecular genetics; **Dr. Bartosz Chmielowski (FEL '08)**, associate clinical professor of medicine; **Dr. Timothy Cloughesy (RES '91, FEL '92)**, professor of clinical neurology; **Dr. Giovanni Coppola**, professor-in-residence of psychiatry and biobehavioral sciences; **Dr. Richard Finn (RES '00, FEL '03)**, professor of medicine; **Dr. Gregg Fonarow (MD '87, RES '90, FEL '93)**, Eliot Corday Chair in Cardiovascular Medicine; **Dr. Edward Garon (FEL '06)**, professor of medicine; **Dr. Daniel Geschwind (RES '95, FEL '97)**, Gordon and Virginia MacDonald Distinguished Professor of Human Genetics, Neurology and Psychiatry; **Dr. Jonathan Goldman (FEL '08)**, associate professor of medicine; **Dr. Michael Green**, professor-in-residence of psychiatry and biobehavioral sciences; **Dr. Steve Horvath**, professor of biostatistics and human genetics; **Dr. Elaine Hsiao**, De Logi Endowed Chair in Biological Sciences; **Dr. Baljit Khakh**, professor of physiology and neurobiology; **Dr. Aldons Lusis**, Distinguished Professor of Medicine, Human Genetics, Microbiology, Immunology & Molecular Genetics; **Dr. Carol Mangione**, Barbara A. Levey, MD, and Gerald S. Levey, MD, Endowed Chair in Medicine; **Dr. Antoni Ribas (FEL '02)**, professor of medicine, surgery and molecular and medical pharmacology; **Dr. Jeffrey Saver**, professor of neurology; **Dr. Michael Sawaya**, molecular biology researcher; **Dr. Michael Sofroniew**, professor of neurobiology; and **Dr. Marc Suchard, (MD '04)**, professor of human genetics and computational medicine.

A Successful Return of the Visionary Ball

After a hiatus due to the COVID-19 pandemic, the Department of Neurosurgery in the David Geffen School of Medicine at UCLA hosted the 2023 Visionary Ball on October 11, 2023, at the Beverly Hilton Hotel. The celebration brought together more than 400 grateful patients, philanthropists, physicians, business leaders and community partners to support the UCLA Department of Neurosurgery and raise vital funds to advance research and the education of the next generation of neurosurgeons and neuroscientists. The event also raised awareness to support patients who face complex neurological disorders.

The evening began with a reception and technology showcases of the ExcelsiusGPS, a multifunctional robotic navigation platform designed for spine surgery from Globus Medical, and an interactive presentation on robotic 3D imaging from Brainlab, followed by dinner.

Howie Mandel, award-winning comedian, television personality, actor and producer, emceed the evening's program that acknowledged the accomplishments of three honorees and began with a video that highlighted the faculty and research innovations of the UCLA Department of Neurosurgery.

Dr. Linda M. Liau (RES '97, FEL '98, PhD '99, MBA), chair and executive medical director of the UCLA Department of Neurosurgery and W. Eugene Stern Chair in Neurosurgery, shared, "I have been a part of UCLA Neurosurgery for over 30 years. In this time, I have seen the field evolve in countless ways. Novel imaging technologies and advanced therapies have transformed our approach to the

TODD CHENEY/UCLA HEALTH

(From left) Dr. Linda Liau, Medical Visionary honoree Johnese Spisso, Smokey Robinson, Courage Award honoree Erika Kort, Jeffrey Katzenberg, Dr. Eric Esrailian, Visionary Award honoree Byron Allen, Howie Mandel and Jay Leno.

most difficult diagnoses. We have a more diverse pool of neurosurgeon trainees than ever before. Above all, patients with conditions that were once considered untreatable are enjoying longer, healthier lives. What hasn't changed is the dedication and innovation that has defined UCLA Neurosurgery through its entire history."

Dr. Liau then introduced a video from 2016 Courage Award Honoree Don Bellisario, who sent his regards and announced the establishment of the Donald and Vivienne Bellisario Chair to support a researcher who will study neurological disorders caused by an abnormal buildup of cerebrospinal fluid in the ventricles deep within the brain.

Dr. Liau introduced Shenell Malloy, Brad Silver and Lauren Miller Rogen, patients who shared their stories with "Points of Light" speeches. These patient testimonials underscored the important and life-changing work happening every day in the UCLA Department of Neurosurgery.

Dr. Eric Esrailian (FEL '06), chief of the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases and The Lincy Foundation Chair in Clinical Gastroenterology, introduced Johnese Spisso, MPA, president of UCLA Health, CEO of the UCLA Hospital System and associate vice chancellor of UCLA Health Sciences. Honored with the Medical Visionary Award, Spisso led UCLA Health through unprecedented times during the COVID-19 pandemic and was instrumental in expanding collaborations with regional hospitals.

Spisso thanked everyone who had made the evening possible and accepted the award on behalf of all the team members at UCLA Health. "It is humbling to accept the Medical Visionary Award, and I am grateful to have our collective work recognized in this meaningful way," she said. "These honors are not something that one achieves on their own. As a leader in health care, I know firsthand that the success of an organization is a team effort."

Jeffrey Katzenberg, co-founder of Hollywood Pictures, DreamWorks Pictures and DreamWorks Animation, introduced Visionary Award recipient Byron Allen, comedian, producer, philanthropist and founder, chairman and CEO of Allen Media Group. Allen was recognized for his career achievements, contributions to society and philanthropic support. In describing the profound effect that his mother's undergraduate education at UCLA had on his family, Allen said, "I want to thank UCLA for changing our lives for the better, forever." He inspired the crowd with a speech about his philosophy for making an impact, and concluded by thanking UCLA Neurosurgery for honoring him with the Visionary Award.

Erika Kort, who received the Courage Award, came to UCLA under difficult circumstances and received care from UCLA neurosurgeon Dr. Daniel C. Lu. Kort was honored for her strength and resilience in the face of a rare cavernous angioma in her spinal cord. Accepting the award, she thanked her family, UCLA staff and those in attendance for their presence, which supports advances in neurosurgical research and clinical care that changes the lives of patients, such as herself, and countless others. "Thank you for investing in our futures, and thank you for this incredible honor," Kort said. "Thanks especially to Dr. Lu — you were my family's rock when we felt like everything was falling apart, and we will be forever grateful for your kindness, patience and expertise."

TODD CHENEY/UCLA HEALTH

Motown legend Smokey Robinson.

A highlight was a comedy set performed by Jay Leno, Emmy Award-winning television host, writer and comedian. The Visionary Ball — a celebration of life, a tribute to courage and a recognition of achievements — concluded with a musical performance by Motown legend, Grammy Award-winner, Rock and Roll Hall of Fame inductee, singer, songwriter and record producer Smokey Robinson. ●

For more information, contact Nora McCarl at: 310-210-5795

Turning a Cancer Diagnosis into Life-Affirming Giving

By Marina Dundjerski

KYLE MIYAMOTO

Dr. Deborah Wong (left) with Jimmy and Julie Sanders, founders of Jimmy Swims.

Four years ago, Jimmy Sanders challenged himself to swim across Lake Arrowhead. Diagnosed in 2012 with stage 4 papillary thyroid cancer, by 2014 his cancer had metastasized to his lungs and, over the next few years, he went through three rounds of radioactive iodine therapy. In 2020, he was preparing for a grueling fourth round of the therapy and wanted a way to strengthen his body for the treatment. Sanders, now 67, was a competitive swimmer in his youth and decided the swim was "just something I needed to do," he said.

Sanders and his wife, Julie, who first met as teens at a Culver City swim club and have a second home in Lake Arrowhead, approached the Arrowhead Lake Association in 2020 to obtain permission to swim across the lake and make the swim a fundraiser for UCLA cancer research. The association agreed, and the couple contacted the UCLA Health Jonsson Cancer Center Foundation (JCCF). After hearing of the plan, JCCF helped Sanders and his wife create a donor website for "Jimmy Swims."

That first year, Sanders swam alone, with his wife nearby in a patrol boat and a few friends on paddleboards. "Although I had never done this before, I had a feeling that this was more than just for me," he said.

What began as a personal goal has "taken on a life of its own," said Sanders, who graduated Phi Beta Kappa and summa cum laude from UCLA. Each year, the swim has gained more support from the community. The 2023 annual fundraiser, held on September 4, included more than 100 participants, including swimmers, paddleboarders and kayakers — ranging from 10 to 84 years of age — and brought in more than $168,000 for the UCLA JCCF. Sanders's UCLA oncologist, Dr. Deborah J. Wong (RES '09, FEL '13), and her husband brought their daughter and two sons, both of whom swam with their mom. Olympic gold medalist swimmer Kaitlin Sandeno participated with her sister, a breast cancer survivor and a former UCLA Health Jonsson Comprehensive Cancer Center (JCCC) patient. To date, the Sanderses have raised close to $350,000 for cancer research.

Right before the 2023 swim, Sanders was hospitalized and was advised to undergo radiation therapy; he had his first treatment the day before the swim. Motivated by the outpouring of support, he wanted to make sure he attended, although he was unsure he would be able to join in. He watched as participants entered the water and felt compelled to swim. "I still don't know what got me from point A to point B, but when I swam, there was this serenity and calmness. Everything stood still, and I saw all these people supporting Jimmy Swims. How could I not?" he asked. "I put my head down and kept on swimming, thinking not only of the accomplishment, but also what it would and could mean. The participants inspire me, and I wanted to inspire people to keep going, to not give up and keep fighting. If there's a will, there's a way."

Proceeds from the annual event help fund research conducted by Dr. Wong and Dr. Christiaan Schiepers (FEL '90) to advance therapies at the JCCC for head and neck cancers, including metastatic thyroid cancer. "We thought you needed millions of dollars to do something like this, to make a difference," Julie Sanders said. "It was surprising and made our hearts full to know that just $25,000 can make a huge difference."

Sanders noted that when he and his wife started the event, it was a way to recognize and show gratitude to his own team of doctors at UCLA, and to shine a light on cancer, especially thyroid cancer, which does not receive a lot of attention. "But raising money that's substantial and making an impact on future generations, it's something that we would have never imagined," Sanders said. "The ability to give back is our motivation to move forward. It means a lot emotionally. It means the world actually." ●

***Marina Dundjerski** is a freelance writer in Los Angeles.*

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UCLA Honors Laurie and Steven Gordon with Fiat Lux Award

By Mary Goodstein

Laurie and Steven C. Gordon, whose philanthropic support and volunteer leadership have enriched UCLA for more than two decades, were honored September 11, 2023, with the Fiat Lux Award. The award, which recognizes distinguished or extraordinary service to the campus, was presented by UCLA Chancellor Gene D. Block during a ceremony at the chancellor's residence.

"It gives me great pleasure to honor Laurie and Steven Gordon, two people who have been thoughtful and dedicated supporters of UCLA and our health system," Chancellor Block said. "We are fortunate to count the Gordons among our friends, and we thank them deeply for their leadership, advocacy and generosity."

The couple's philanthropic relationship with UCLA began in earnest in 2010, when they were determined to turn the pain of losing a family member into a positive contribution. Steven's father had suffered from Parkinson's disease, and the couple wanted to support research that might help prevent others from experiencing Parkinson's and other debilitating neurological conditions. The Gordons began learning about neuroscience research at UCLA, getting to know faculty members and discovering where their support could make a difference.

Then, after Laurie's son, Max, died in 2013, finding a meaningful way to honor him became a priority for the couple. In Max's memory, the Gordons made a gift to UCLA in 2014 to create the Max Gray Fellowships in the Child and Adolescent Mood Disorders Program in the Jane and Terry Semel Institute for Neuroscience and Human Behavior at UCLA. The gift has enabled the program to fund 29 fellows to date and expand patient capacity.


TODD CHENEY/UCLA PHOTOGRAPHY

Laurie and Steven Gordon with Chancellor Gene D. Block (left) and Beverly Hills Mayor Julian A. Gold (right).

In 2018, with another gift from the Gordons, the David Geffen School of Medicine at UCLA established the UCLA Laurie and Steven Gordon Commitment to Cure Parkinson's Disease, and the UCLA Neuroscience Research Building was renamed the Laurie and Steven C. Gordon Neuroscience Research Building. The gift also enabled UCLA to establish, in 2022, the Laurie and Steven C. Gordon Chair in Neurosciences; the endowed chair is currently held by Dr. Ming Guo.

Steven Gordon, the chairman and principal owner of Domino Realty since 1970, is a UCLA alumnus. He is chairman of the Ronald Reagan UCLA Medical Center board of advisors, a member of the board of the UCLA Health System and a founding member of the UCLA Ziman Center for Real Estate. He was co-chair of the UCLA Centennial Campaign Cabinet and currently is a member of the UCLA Second Century Council.

Laurie Gordon, a former attorney for United Artists Communications and former vice president of Warner Bros. International Theatres, was president of the board of advisors of the Stewart and Lynda Resnick Neuropsychiatric Hospital at UCLA from July 2020 through June 2023.

During the award presentation, Dr. John C. Mazziotta (RES '81, FEL '83), vice chancellor of UCLA Health Sciences and CEO of UCLA Health, saluted the couple, saying, "From personal tragedy, you've created hope, and from suffering, you've created solutions."

The Gordons are the fourth recipients of the Fiat Lux Award, following Renee and Meyer Luskin in 2012, Arline and Henry Gluck in 2021 and Jane Semel in August 2023. ●

Mary Goodstein *is the senior creative director, principal gifts for UCLA Health Sciences Development.*

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Distinguished Alumnus Receives Highest UCLA Honor

By Mary Goodstein

UCLA alumnus Ronald A. Katz, an inventor and entrepreneur who for more than 50 years has helped advance UCLA's mission through his wide-ranging philanthropic giving and volunteer service, was honored September 27, 2023, with the Fiat Lux Award, which recognizes distinguished or extraordinary service to the university. Katz, the driving force behind the founding of UCLA Health Operation Mend, received the award from UCLA Chancellor Gene D. Block during a private dinner at the chancellor's residence.

"We thank Ron Katz, his late wife, Maddie, and their family for their visionary leadership, advocacy and generosity, not only to military medicine, including Operation Mend, but across the UCLA campus," Chancellor Block said.

Ron and Madelyn "Maddie" Katz, both UCLA undergraduates, envisioned Operation Mend in 2006 after seeing a young Marine interviewed on the news who had been severely disfigured by an improvised explosive device while serving in Iraq. Maddie Katz thought UCLA Health had the expertise to help, and the couple brought UCLA and military leadership together to form a partnership.

The Katzes soon made a lead gift to UCLA to launch the program, which provides free specialty medical, surgical and psychological treatment, including transportation and accommodations, to post-9/11 veterans and service members injured in the line of duty.

"Quite simply, the generosity of Ron Katz through the creation of Operation Mend has made an indelible mark on UCLA Health and forever changed it for the better," said Dr. John C. Mazziotta (RES '81, FEL '83), vice chancellor of UCLA Health Sciences and CEO of UCLA Health.

Dr. Mazziotta noted that the Katzes' generosity has extended far and wide, with the Katz family having opened their homes to hundreds of veteran families and inspired other individuals and organizations to support UCLA.

Among Maddie and Ron Katz's other contributions to UCLA was a gift for a reimagined surgical waiting room at Ronald Reagan UCLA Medical Center. "Maddie's Room" provides a welcoming, warm and comfortable space for families hoping for good news about a loved one in surgery.

Following Maddie's death from pancreatic cancer in 2009, Katz made a donation to establish the UCLA Maddie Katz Endowed Chair in Palliative Care Research and Education. Later, his lead gift helped launch the 3 Wishes Project at UCLA, which provides personalized, end-of-life comfort to patients and families.

Over the years, the Katzes have given to numerous programs and areas across campus, including the Herb Alpert School of Music to establish the Mickey Katz Endowed Chair in Jewish Music at UCLA in honor of Ron Katz's late father, the master musician and performer.

After graduating from UCLA in 1958 with a bachelor's degree in business administration, Katz had a successful career as an inventor and entrepreneur.

"I am humbled to receive the Fiat Lux Award, joining the distinguished company of some of the very best people I know," Katz said at the award reception. "Everyone in this room is someone special to me. I have had the joy of working with so many of you on projects across this great UCLA campus and have been blessed by the loving support of my family and friends in these endeavors."

Katz is the fifth recipient of the Fiat Lux Award, following Renee and Meyer Luskin in 2012, Arline and Henry Gluck in 2021, Jane Semel in August 2023 and Laurie and Steven C. Gordon in September 2023. ●

(Front row, from left) Rhea Turteltaub, UCLA vice chancellor for external affairs; Ronald Katz; Chancellor Gene D. Block. (Back row, from left) Dr. Kodi Azari (FEL '04), medical co-director of Operation Mend; and Johnese Spisso, MPA, president of UCLA Health, CEO of the UCLA Hospital System and associate vice chancellor of UCLA Health Sciences.

TODD CHENEY/UCLA PHOTOGRAPHY

Mary Goodstein *is the senior creative director, principal gifts for UCLA Health Sciences Development.*

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Ralph and Shirley Shapiro Honor Retinal Health Pioneer

Longtime UCLA philanthropic partners Shirley and Ralph Shapiro have donated $100,000 to establish the Kreiger Retinal Support of Medically Underserved Populations Fund. The contribution honors Dr. Allan Kreiger (MD '63), founding retina division chief in the Department of Ophthalmology at UCLA Stein Eye Institute, and will provide resources for the screening and treatment of retinal diseases in medically under-resourced populations.

"WHEN YOU HAVE AN OPPORTUNITY, IT'S WONDERFUL TO BE ABLE TO GET A PROJECT STARTED AND GIVE PEOPLE A CHANCE TO JOIN TOGETHER TO FULFILL THE MOST PRESSING NEEDS THAT COME TO OUR ATTENTION."

When Dr. Steven Schwartz (RES '92), chief of the retina division and The Ahmanson Chair in Ophthalmology, first discussed the project with Ralph Shapiro, the exact purpose had yet to be determined, beyond honoring Dr. Kreiger. However, Shapiro did not wait for further details before lending his support.

"Years ago, I discovered that no one knows more about what needs to get done than the person you're trying to help," said Ralph Shapiro.

Stein Eye will continue fundraising efforts, with plans to raise $1 million, then repurpose the fund to establish an endowed term chair named in Dr. Kreiger's honor. The chair will benefit a faculty member whose research and patient care advances retinal health, with a continued focus on underserved populations.

Dr. Kreiger taught and mentored the majority of retina specialists trained at Stein Eye. He received his medical degree from UCLA and completed his residency at the Wadsworth Veterans Administration Hospital in Los Angeles. Dr. Kreiger started his career at Stein Eye in 1967 as a clinical instructor and became a professor in 1977. Over the past five decades, he made many significant contributions to the field, notably in the areas of ocular manifestation of AIDS and acute retinal necrosis syndrome. He received the prestigious S. Rodman Irvine Prize from the UCLA Department of Ophthalmology and the Sherman M. Mellinkoff Faculty Award from the David Geffen School of Medicine at UCLA.

Shirley Shapiro earned a bachelor's degree in education from UCLA in 1959; Ralph Shapiro earned a bachelor's degree in business administration from UCLA in 1953 and a juris doctorate from the UCLA School of Law in 1958. He is chairman of Avondale Investment Partners and an investor and commercial real estate holder.

The Shapiros have generously given to UCLA for six decades and are among the school's most steadfast partners. The family has made more gifts to UCLA than any other individual donors, having given more than 1,600 across 100 departments. They have helped establish more than 20 endowed chairs and have contributed to medical research, environmental law, disability studies, education, the arts, children's welfare programs and many other areas.

Ralph Shapiro notes the importance of collective giving and bringing awareness to efforts such as the Kreiger Retinal Support fund. "None of us alone have the resources to fulfill all the unmet needs," he said. "When you have an opportunity, it's wonderful to be able to get a project started and give people a chance to join together to fulfill the most pressing needs that come to our attention." ●

COURTESY OF THE SHAPIRO FAMILY

Ralph and Shirley Shapiro with their son, Peter Shapiro.

For more information, contact Susan DeRemer at: 310-825-3381

UCLA Health System Board Meeting Focuses on Healthy Aging

TODD CHENEY/UCLA PHOTOGRAPHY

Halle Berry and Henry Gluck.

The UCLA Health System Board held its 11th annual meeting on October 9, 2023, at the UCLA Meyer and Renee Luskin Conference Center. UCLA Health System Board chairman Henry Gluck opened the meeting with a warm welcome for guests and event speakers. The evening featured presentations centered on the theme, "Longevity: Tools for Healthy Aging."

A person's lifespan and quality of life can be influenced by changes the body experiences, either naturally through aging or due to disease. UCLA Health clinicians and scientists work to develop strategies that empower people to live healthier lives. Presentations explored aging disorders and the integrated approaches grounded in research and high-quality, evidence-based care that can improve quality of life.

Dr. Mark S. Litwin (FEL '93), chair of the Department of Urology and The Fran and Ray Stark Foundation Chair in Urology, and Dr. Jesse N. Mills, director of the Men's Clinic at UCLA, gave presentations on men's health and aging disorders. Dr. Litwin began by showcasing the new virtual reality system used when removing tumors that allows surgeons to rotate the image in three dimensions and delete organ images that may be in the way. This enables the team to view how the tumor interacts with veins and arteries, leading to more successful tumor removals.

Dr. Mills then presented his "longevity elevator pitch," which emphasized each person's role in making the most of their time with tips such as limiting the intake of red meat and having a purpose in life. He concluded by saying that no matter the approach to longevity, one had to enjoy the ride.

Dr. Beth Y. Karlan, vice chair and professor in the Department of Obstetrics and Gynecology and Nancy Marks Endowed Chair in Women's Health Research, and Dr. Deborah Krakow, chair of the Department of Obstetrics and Gynecology, followed with their presentations on women's health and menopause. Dr. Karlan described menopause and highlighted that "aging is not a bad thing," as the later years could be some of the best in a person's life. Dr. Karlan, who is also director of cancer population genetics in the UCLA Health Jonsson Comprehensive Cancer Center, highlighted the fact that it is important "to think about it holistically," and that cancer is not all about DNA, giving the example that only 10% of cancer risk is inherited. "A lot of living long is how you live," she said.

This year's special guest speaker was award-winning actress, director, producer and advocate Halle Berry. Health and wellness are topics close to her heart, and her rē•spin health and wellness platform aims to shift the way people view their health journey. Berry spoke about her own menopause experience and the journey that led her to the state's capitol to lobby for a bill on menopausal care. She encouraged women to speak up and advocate for more medical attention directed to menopause. Following her talk, the female physicians and Johnese Spisso, MPA, president of UCLA Health, CEO of the UCLA Hospital System and associate vice chancellor of UCLA Health Sciences, joined Berry on stage for a panel discussion covering women's health, aging, menopause and taboos around such subjects.

Gluck closed the evening by thanking board members for their continued partnership and contributions as UCLA Health ambassadors. Following the meeting, guests enjoyed a reception and interacted with members of the Integrative Medicine Collaborative, which addresses the physical, emotional, mental, social, spiritual and environmental aspects that influence health. Also on hand were therapy animals from the UCLA Health People-Animal Connection. ●

For more information, contact Danielle Barr at: 310-267-0050

DONATIONS & GIFTS

HELPING STUDENTS BECOME MEDICAL ASSISTANTS

The Change Reaction recently made a gift of $159,750 to help fund scholarships for 30 students in the UCLA Health Medical Assistant Program. This intensive, 12-month program is offered through a partnership between UCLA Health and UCLA Extension, combining theory and practical experience to prepare students to transition successfully into a career as a medical assistant. Medical assistants care for patients by administering medications, taking vital signs and undertaking other vital tasks. This contribution will address a crucial personnel shortage in the local community.

For more information, contact Ellen Haddigan-Durgun at: 310-321-8366

PHILANTHROPIC GIFT NAMES THE GEFFEN HALL COURTYARD

On September 18, 2023, the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases hosted a celebration to dedicate the Donald & Andrea Goodman/Meyer & Renee Luskin courtyard at Geffen Hall. The reception commemorated the launch of the UCLA Goodman-Luskin Microbiome Center and honored the philanthropists — Andrea and Donald Goodman and Renee and Meyer Luskin — whose $20 million

TODD CHENEY /UCLA PHOTOGRAPHY

Andrea and Donald Goodman (left) and Renee and Meyer Luskin (fifth and sixth from left) with UCLA faculty from the Goodman-Luskin Microbiome Center.

philanthropic investment helped establish the center. The evening attendees included Dr. John C. Mazziotta (RES ’81, FEL ’83), vice chancellor of UCLA Health Sciences and CEO of UCLA Health, and Johnese Spisso, MPA, president of UCLA Health, CEO of the UCLA Hospital System and associate vice chancellor of UCLA Health Sciences. Dr. Eric Esrailian (FEL ’06), chief of the UCLA Vatche and Tamar Manoukian Division of Digestive Diseases and The Lincy Foundation Chair in Clinical Gastroenterology in the David Geffen School of Medicine at UCLA; Dr. Steven M. Dubinett (RES ’84), dean of the David Geffen School of Medicine at UCLA and associate vice chancellor for research; and Dr. Elaine Hsiao, the center’s inaugural director, all addressed the gathering.

For more information, contact Laurel Zeno at: 310-418-2364

5K WALK/RUN SUPPORTS PANCREATIC CANCER RESEARCH

On October 22, 2023, the 26th Annual L.A. Cancer Challenge (LACC), held on the UCLA campus, raised more than $561,000 to benefit pancreatic cancer research. Dr. Miklos Sahin-Toth, professor of surgery in the David Geffen School of Medicine at UCLA, Garry

ANGELA DAVES HALE PHOTOGRAPHY

Dr. Miklos Sahin-Toth with Agi Hirshberg, director of the Hirshberg Foundation, and the UCLA Spirit Squad.

Shandling Chair in Pancreatic Diseases and chair of the Scientific Advisory Board of the Hirshberg Foundation for Pancreatic Cancer Research, served as the LACC Honorary Medical Chair 2023. A world-renowned expert in the area of the pancreas disorders, Dr. Sahin-Toth also oversees the Hirshberg Foundation Seed Grant Program.

For more information, contact Gretchen McGarry at: 310-794-4746

EXPANDING INTEGRATIVE HEALTH TRAINING

Linda and Dr. Carl Moy have pledged $250,000 to benefit the UCLA Health Center for East-West Medicine, under the guidance of Dr. Ka-Kit Hui (MD ’75, RES ’78), founder and director of the center and Wallis Annenberg Endowed Chair in Integrative East-West Medicine. Inspired by Dr. Hui and his team, the couple

COURTESY OF THE MOY FAMILY

Linda and Dr. Carl Moy.

established the Linda and Carl Moy Fund to Enhance and Innovate Healthcare Professional and Student Education Programs in Integrative Health. This meaningful gift will train scholars and clinicians in the practice of integrative medicine through expanded online courses, increased training opportunities for medical students and new continuing education courses for health professionals.

For more information, contact Emily McLaughlin at: 310-794-4763

AWARD FOR CANCER AND AUTOIMMUNE DISORDERS

Dr. Keriann Backus, assistant professor of biological chemistry and the Alexander and Renee Kolin Endowed Professorship of Molecular Biology and Biophysics Term Chair in the David Geffen School of Medicine at UCLA, has received $1 million from the Ono Pharma Foundation as part of the Ono Pharma Breakthrough Science Initiative Awards Program. The three-year award will help advance her research developing new methods to identify potential drug targets for cancer and autoimmune disorders.

For more information, contact Reshma Anvekar at: 310-567-0746

GRATEFUL FAMILY THANKS UCLA WITH A PLANNED GIFT

Through a charitable remainder trust, Karen and Henry Somers have made a contribution to equally benefit the UCLA Divisions of Cardiology and Liver and Pancreas Transplantation. Deeply grateful for the lifesaving care he received, Henry Somers said, “Karen and I feel fortunate to be able to give gifts to the hospital. I owe my life to UCLA, because they have saved me multiple times!” Both the Divisions of Cardiology and Liver and Pancreas Transplantation have been instrumental in Henry Somers’ care at UCLA.

For more information, contact Lindsey Walton at: 424-468-7588

Climbing for a Cause

By H. Albin Gritsch, MD (RES '91)

TOM RACEK

Members of Living Donor Adventures, with whom Dr. H. Albin Gritsch climbed on Mt. Kilimanjaro, celebrate reaching the summit.

THE FIRST TIME I CLIMBED TANZANIA'S Mt. Kilimanjaro was in 2015. It is one of the Seven Summits — the highest peaks on each continent — and because its base starts at a lower elevation than Mt. Everest's, it actually is, at 19,341 feet above sea level, the highest freestanding mountain on Earth.

I went back in March of 2023 with a group of living organ donors who created an organization called Living Donor Adventures to demonstrate that you can still be active and adventurous after donating an organ. When I asked one of the climbers why he donated a kidney, he said, "I have two and only need one. Why wouldn't I share the extra one?"

It is an important and urgent message. As surgical director of the UCLA Health Kidney Transplant Program, I know the statistics all too well. There are roughly 500,000 people in the United States on dialysis, with more than 100,000 waiting for a transplant. Every month, another 3,000 or so new patients are added to the transplant waiting list, and roughly 13 people die each day while waiting for a donor organ.

The need for donor kidneys is acute and wait times for deceased-donor kidneys are long — the national median is upwards of 3½ years, and up to 10 years in Los Angeles. More living donors, which now account for less than half of all kidney transplants in the United States, could help to alleviate this bottleneck.

But many people believe that if they donate an organ like a kidney, their life will be forever altered, and their activities limited.

And here was this group of living organ donors preparing to climb Kilimanjaro, setting out to prove them wrong.

When I learned of this endeavor, I wanted to be a part of it. I reached out to the guide who led my climb eight years ago, Stanley Mariki, with whom I'd stayed in contact over the years. "Would you organize a parallel climb with the Living Donors Adventure Group?" I asked him. There were seven of us, including two UCLA Health nurses, who joined 32 living kidney and liver donors, along with almost 100 porters and guides.

The plan was to reach the summit on March 9, World Kidney Day. We took the longer, eight-day route up the mountain, to better adjust to the altitude. When I made the trek in 2015, I nearly ran out of gas by the time we reached the rim — Kilimanjaro is a dormant volcano — at 18,500 feet, but I was able to press on to the true summit. I'm older now, and this time when we got to the rim, I really felt the effects of altitude and decided not to push myself further.

Obviously, I wanted to make it to the summit — everybody else got there — but for me, the mission this time was to promote the fact that living organ donors can have an active and adventurous life after giving a piece of themselves to help another human being.

And, also, to help support Stanley.

I knew that with the COVID-19 pandemic he'd been struggling to make a living, and I'd told him that since we were coming all the way to Africa, my friends and I also wanted to do a safari, which he organized for us, as well.

Dr. H. Albin Gritsch (second from right) with members of his safari group after the climb on Mt. Kilimanjaro, including guide Stanley Mariki (third from right) and his children and wife, Einoth (left).

COURTESY OF DR. H. ALBIN GRITSCH

Stanley has three children — an 8-year-old daughter, a boy who is 7 and a toddler of 2. I asked if his kids had ever been on a safari. They had not, so I told him that I'd pay for them to come along.

For them, it was an experience of many firsts: their first safari, the first time they stayed in a hotel, the first time they used binoculars, the first time they took pictures with a 35-millimeter camera with a zoom lens. They were in heaven.

There was the impact of meeting so many living organ donors and seeing their motivation to not only give a life-saving gift, but also to promote the fact that as individuals we each can make a difference.

Me, too. I learned so much from Stanley on this trip, about his family history and life in Tanzania. I found it all fascinating and moving. That he shared his life with me in this way was eye opening, showing me how we really are a global village and that what we do in the United States ripples out to peoples around the world, for better or worse.

As citizens of a wealthy nation, we in the U.S. have opportunities to help people in other parts of the world. It is easy to send a check, but another impactful way is to directly support their livelihood. By engaging Stanley, it provided him with the resources to buy some land and build a foundation for his house.

For me, the greatest impact was bringing my friends to meet Stanley and his family, and for them to hear stories about his life and the history of Tanzania. And there was the impact of meeting so many living organ donors and seeing their motivation to not only give a life-saving gift, but also to promote the fact that as individuals we each can make a difference.

Sure, getting to the summit would have been a personal victory, but having the opportunity to bring all these people together was the real win.

Dr. H. Albin Gritsch *is the John Jergens Chair in Kidney Transplantation in the David Geffen School of Medicine at UCLA, and he would happily speak with anyone interested in visiting Tanzania (HGritsch@mednet.ucla.edu).*

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