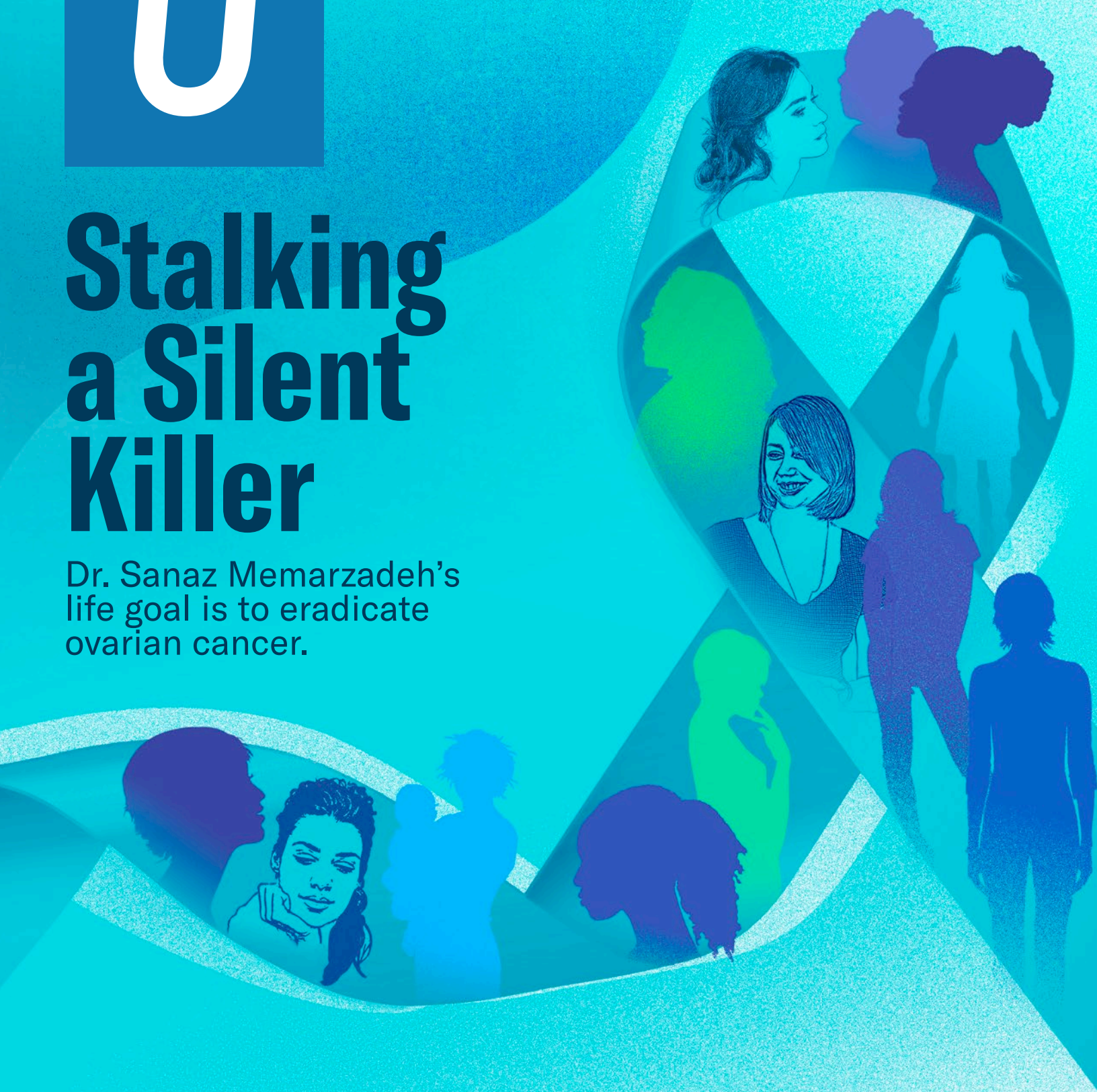
Stalking a Silent Killer

Dr. Sanaz Memarzadeh's life goal is to eradicate ovarian cancer.



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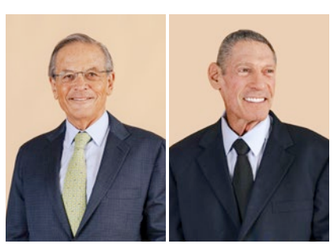
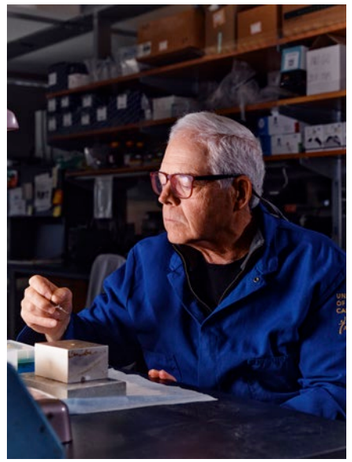


JESSICA PONS

Two founders of the California Institute for Immunology and Immunotherapy talk about its potential to reshape the future.

FEATURES

JESSICA PONS



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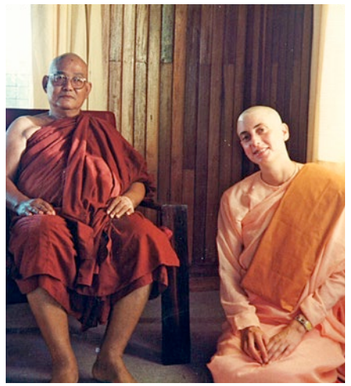

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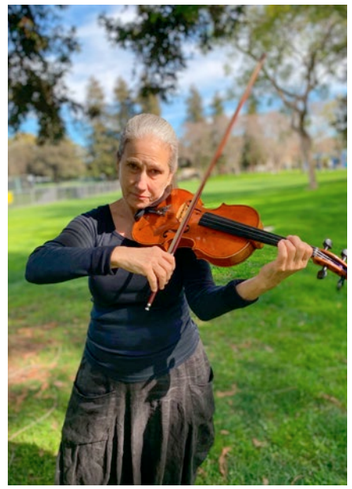

COURTESY OF CONSTANCE MEYER

> "I'm trying to solve ovarian cancer. I'm not going to quit until we do."
>
> *Dr. Sanaz Memarzadeh*

BREAKTHROUGHS AND NEWS FROM UCLA HEALTH.

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Summer 2025
Volume 45 · Issue 2

Patients, or the families of patients, quoted and/or photographed or pictured in this publication have given their consent to have their names and/or images used and their stories told.

Printed on recycled paper

UCLA Health Leads in AI Innovation

Artificial intelligence (AI) has captured the world's attention for its ability to analyze vast amounts of data, recognize patterns and support decision-making. These tools are rapidly shaping the medical field, offering new opportunities to improve patient health outcomes and enhance the patient experience. At UCLA Health, our world-renowned researchers and clinicians have been involved in AI research for decades and are leaders in developing and adopting innovative medical diagnostics, treatments and technologies.

We are committed to leading innovation in health AI research and applying AI solutions to drive advancements in medical research and care. UCLA Health maintains a portfolio of more than 30 active AI models that function across the spectrum of health care, from improving patient care and experience to alleviating clinician burnout and solving operational inefficiencies. We develop AI solutions internally, collaborate with industry leaders and cutting-edge vendors and leverage new offerings from Epic, the electronic health record software. Above all, we are committed to the principles and practices of responsible AI, and rigorously evaluate model performance, fairness and safety.

Our Office of Population Health & Accountable Care, which focuses on improving patient health outcomes across the care continuum, has developed two innovative AI models that drive proactive patient outreach. One model predicts a patient's risk of hospital readmission or emergency department visits, facilitating timely interventions that prevent unnecessary hospitalizations. Another model forecasts a patient's future health care needs, allowing us to allocate resources efficiently and personalize care plans. Together, these models help address barriers to care, such as access and treatment gaps, while also improving patient outcomes and reducing health care costs.


JEFF SCHNEPP

AI also plays a critical role in personalized medicine. By analyzing individual patient data — genomic, lifestyle and environmental factors — AI systems can help tailor treatments that are uniquely suited to each person. At the UCLA Institute for Precision Health, AI helps our experts more efficiently find solutions that improve the effectiveness of therapies, reduce side effects and enhance the quality of life for patients undergoing treatment.

As we incorporate AI into our practices, we remain mindful of the ethical considerations this involves. We must ensure transparency, fairness and accountability in AI systems, while also training and supporting our staff to work with these tools effectively and safely. AI is not meant to replace the critical role of health care professionals, but, rather, to empower them to make more informed, data-driven decisions that ultimately benefit our patients. The expertise and compassion of our workforce will continue to be prioritized to maintain the highest standards of care for our patients and their families.

UCLA Health is proud to be at the forefront of this transformation in health care delivery. Together, we are forging a path toward a future where AI enhances our ability to deliver the highest quality care while preserving the compassionate, patient-centered approach that is the hallmark of UCLA Health.

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

SOPHIA AND THE WONDERFUL, AMAZING, GOOD, VERY GREAT DAY

By Eric Glassner

IRINA VASILEITSKAYA

Sophia Roybal Anderson is filled with joy on her special day as a Laker Girl.

WHEN SOPHIA ROYBAL ANDERSON AND HER MOMS ARRIVE at Crypto.com Arena, home of the Los Angeles Lakers, on the morning of February 8, the not-quite-yet-7-year-old from New Mexico is a little shy but still eager to enter the mostly empty building and meet the Laker Girls, who already are on the court preparing their dance routines for this afternoon's game. By the time she gets inside, however, it is like the sugar from her breakfast has just kicked in and she is running in circles and giggling with a nervous excitement that pours out of her.

Today, Sophia will be a Laker Girl, too.

Sophia's journey to this day began not long after she was born, on March 13, 2018, in Albuquerque, with a hole in her heart. Two holes, actually, a large one in the bottom chambers and a medium-size one in the top chambers, UCLA Health pediatric cardiologist Gary Satou, MD (RES '96), informed her mothers, Hope Anderson and Yvette Roybal. After five years of trying to get pregnant, Anderson and Roybal were determined to seek the best care possible for their child, and they found their way to UCLA and Dr. Satou — driving 13 hours to see him because the baby was too frail to travel by air. Several months later, Sophia underwent surgery at UCLA to repair the defects.

Sophia has come a long way since then. Today, she is sweet, spunky, sassy, driven and "just awesome," her moms say. "She loves acting and performing — that's her zone." Sophia plays soccer and is starting gymnastics. And she is an especially empathetic child. When another child in school falls down, Sophia is the first one to come help them up, her teachers report.

The family continues to make annual trips from their home in Santa Fe to Westwood for checkups with Dr. Satou.

Which brings us to this day. For this year's visit, Sophia was selected to participate in the UCLA Health Laker for a Day program, which recognizes UCLA Health patients who face serious illnesses with courage, strength and determination with a behind-the-scenes experience during a Lakers home game.

The Laker Girls are in the middle of rehearsing a routine as Sophia and her moms are brought onto the floor and seated courtside — where celebrities typically sit during games — to watch the practice. The dance team's coaches come over and introduce themselves, making Sophia feel at ease with questions like, "What's your favorite music?" and "Are you ready to learn some dances?"

Soon, the entire team is wrapping Sophia in the warmth of their smiles, and bursting with their own excitement at the surprise they are about to give her — that she will join them as a special Laker Girl for the day. After showing her a few simple routines, which Sophia quickly picks up, she shows the team a move of her own: a hop-and-twirl combination that earned cheers from the Laker Girls.

Now for the big reveal. Two of the team members present Sophia with her own custom Laker Girl outfit — the same one that the team members will wear for the game. The sparkle of her smile is reflected in the glitter of the team jersey. Holding tight to her new team uniform and a pair of new sneakers, Sophia's excitement can hardly be contained as she sprints over to her moms to show them off.

The day progresses, and in a suite overlooking the court Sophia and her moms are joined by other members of their family — her aunt, grandparents and 3-year-old brother. Sophia can't wait to show off her Laker Girl outfit and quickly changes. Before the game starts, two team members come to the suite to spend time with her, braiding her hair and (with moms' approval) giving her some light makeup.

Then it is time to go down to the floor so Sophia can join the rest of the team. In the tunnel leading to the court, the other members of the team are thrilled to see Sophia in her matching outfit — the littlest Laker Girl — and she joins them for warm-ups and demonstrates her own flexibility before learning the basics of the Laker Girls' signature "catwalk" entrance. Sophia then steps into the packed arena holding the hands of two of her new teammates.

As the game is about to start and the Laker Girls go to work, Sophia returns to the suite to watch the first half with her family. But there is another surprise: Dr. Satou is in the house, and he pays her a special visit, along with other members of her care team — pediatric cardiac surgeon Peyman Benharash, MD '02 (RES '08, FEL '10), and Patricia Roderick, director of special projects for UCLA Health and the David Geffen School of Medicine at UCLA, who has become a family friend.

At halftime, Sophia and her family are escorted down to the floor to prepare for her big moment. They are seated on the bench courtside with the Laker Girls, and during a timeout in the third quarter, Sophia and the entire squad make their way to center court where a video montage of Sophia's journey, from her birth to today, plays on the big scoreboard and the PA announcer tells the assembled fans about her life. As the video finishes, the announcer calls on the audience to celebrate Sophia, and the crowd erupts with thunderous applause. To cap off the celebration, Sophia performs a routine with the Laker Girls. Then it is back to the suite to watch the rest of the game.

And that is Sophia's wonderful, amazing, good, very great day as the ultimate Laker Girl. ●

***Eric Glassner** is associate director for UCLA Health Corporate Partnerships. UCLA Health Marketing Communications senior writer Sandy Cohen contributed reporting.*

IRINA VASILEITSKAYA

Sophia is surrounded by love from (from left) Dr. Gary Satou, mothers Yvette Roybal and Hope Anderson, and Dr. Peyman Benharash on her special day.

ANTICIPATING OVERCROWDING RISK IN THE ICU

By Monika Brown

THE INTENSIVE CARE UNIT PROVIDES a sanctuary for the most critically ill or injured patients in a hospital, representing the height of specialized medical care and monitoring. But a surge in new patients can jeopardize the delicate balance between staffing, resources and bed turnover required for high-quality treatment and can lead to suboptimal health outcomes.

The task of preventing overcrowding, also known as "congestion," is a complex operational challenge. Patients admitted to an ICU come from various areas of the hospital, including surgical, emergency and inpatient departments. Not only do these patients have different diagnoses, but they also have different recovery times. So, to control congestion, the ICU must monitor other units in the hospital for the likelihood of patients needing to move into the ICU and consider the potential length of stay for current and future ICU patients to know when beds will be available.

Many ICUs currently use reactive strategies under which decisions on patient admissions and discharges are simply based on the level of occupancy and demand for care at any particular moment in time. This means that efforts to reduce overcrowding are only made once occupany levels are high. In a paper published last year, researchers from the UCLA Anderson School of Management provided a method to predict days in advance when an ICU is likely to face a high risk of congestion. Armed with this advance warning, an ICU can alleviate congestion and keep a high standard of care by implementing timely measures, such as increasing staffing levels, reducing service times and diverting or postponing arriving patients.

MANY ICUs CURRENTLY USE REACTIVE STRATEGIES UNDER WHICH DECISIONS ON PATIENT ADMISSIONS AND DISCHARGES ARE SIMPLY BASED ON THE LEVEL OF OCCUPANCY AND DEMAND FOR CARE AT ANY PARTICULAR MOMENT IN TIME.

The researchers propose a model-based approach to develop simple rules to predict the status of the ICU. The role of interpretability is paramount in practical settings: The approach provides health care workers with clear, easy-to-understand-and-communicate rules to make predictions about the risk of ICU congestion in the near future. They show that their method outperforms data-driven methods, which depend on historical data to identify patterns. Data-driven methods often only provide the end-user with a black box prediction. This manifests in the difference between health care workers having a laminated card with interpretable rules versus only being able to see a computer output with a predicted congestion risk and no context as to how the prediction was made.

The researchers' approach combines queueing theory (which predicts queue lengths and wait times) with simulation and machine learning methods to devise interpretable rules. Their methodology involves several steps.

First a queueing model of the ICU is created to simulate its dynamics and patient flow. This model is used to simulate a large number of scenarios that an ICU can face — labeled as either "high risk" or "not high risk" for congestion. Next, several features are created to summarize the status of the unit. A key predictor of risk is the remaining length-of-stay profile for patients in a hospital's units. Using an intermediate machine learning model, the method identifies patients' profiles based on remaining length-of-stay. The unit utilization status is then summarized according to the number of patients within each length-of-stay profile. These engineered features, plus the knowledge about likelihood of ICU transfers from each profile, are then used to train a linear machine learning model to predict the ICU congestion risk.

The approach outputs simple linear rules based on the status of the unit (i.e., number of patients within each length-of-stay profile).

More precisely, the researchers illustrated their approach using a realistic queuing model of a hospital with several units. Using the simulation model, they generated 1,000 sample Saturdays as their starting scenarios and, with these, predicted the risk for the most congested days in the ICU, which are Tuesday through Friday. They compared their results with the results of other variants of model-based methods and data-driven methods.

The error rate for their model-driven method was below 5%, while the error rate for the data-driven methods was roughly six times higher. A reason for the outperformance of the researchers' model-based approach, over data-driven approaches, is that they can generate unlimited amounts of data simulated by their queueing model and better estimate congestion risk with this larger amount of data.

In the end, the researchers' method provides the ICU with rules to determine congestion risk based on the number of patients in the hospital system and their expected remaining time in the different units. They believe other service operations could benefit from additional research on the combination of queueing theory and simulation with interpretable machine learning algorithms. ●

***Monika Brown** is a freelance writer specializing in data visualization. This article originally was published online in UCLA Anderson Review (anderson-review-ucla.edu). It is reprinted with permission.*

iSTOCK IMAGES

Against the odds: Patient continues to thrive despite terminal cancer diagnosis

ON HALLOWEEN NIGHT IN 2021, BONNIE WHAM-PRUtow and her family faced a real-life nightmare. The emergency room doctor on the Big Island of Hawaii had just told her that she had metastatic brain cancer, and they believed she only had a couple of weeks to live. Bonnie and her husband, David, were completely taken by surprise. Wham-Prutow had previously visited her primary care doctor for headaches and balance issues, and she was told she had vertigo.

To say they were devastated would be an understatement.

"We were really caught off guard," says Wham-Prutow, 69. "We went from getting ready to go trick-or-treating with our grandkids to being told I had maybe weeks to live."

It turns out the breast cancer Wham-Prutow thought she had beaten years ago had returned, but this time it was in her brain. Her MRI showed an extensive number of inoperable tumors.

Her doctor in Hawaii gave her one option: hospice.

Bonnie, David and their two daughters, Lauren and Erin, didn't accept the prognosis and began searching for the best medical team and care available. That search led them to UCLA Health. Wham-Prutow's first step was to consult with neurosurgeon Won Kim, MD '09 (RES '16, FEL '16), associate professor of neurosurgery and co-director of the Stereotactic Radiosurgery and Brain Metastasis Program at UCLA. After reviewing Wham-Prutow's scans, Dr. Kim recommended whole-brain radiation therapy as the best course of action, as surgery was not an option due to the number and location of the metastases. In addition, Wham-Prutow had developed leptomeningeal disease, a condition that occurs when cancer cells spread to the cerebrospinal fluid that surrounds the brain and spinal cord.

> Wham-Prutow's latest scans showed remarkable progress. Her lesions had either shrunk significantly or nearly disappeared, and all her organs were clear.

But before they could start treatment, they had to get Wham-Prutow out to Los Angeles, which carried some potential health risks. "Flying, where there is less atmospheric pressure, can cause brain swelling," says Dr. Kim, an investigator at the UCLA Health Jonsson Comprehensive Cancer Center. "Normally, this isn't a big issue, but in Bonnie's case, if she had experienced a bleed, seizure or additional swelling during the flight, it could have led to a stroke or coma."

But Wham-Prutow and her family decided it was worth the risk, and she and her husband arrived at UCLA Health the next day, and she soon began radiation therapy to shrink the tumors and slow progression. After completing radiation, Wham-Prutow's symptoms started to improve. The next step would to be revaluate in three months to determine the effectiveness of the radiation. "At this time, we were now more optimistic about Bonnie being able to enjoy her days outside of the hospital," says David. "We didn't think three more months of life was in the forecast, and now we finally felt like there was hope."

Chemotherapy would follow to treat the HER2-positive breast cancer that had spread to a lymph node in Wham-Prutow's left armpit. Because she was handling the treatment well, Bonnie and David were given the green light to go home to Hawaii for Thanksgiving. They returned to UCLA at the end of February for a three-month follow-up with the team.

The news was better than they could have hoped. Wham-Prutow's latest scans showed remarkable progress. Her lesions had either shrunk significantly or nearly disappeared, and all of her organs were clear. A brain MRI revealed a 70-to-80% reduction in lesions, with the remaining ones continuing to shrink. A subsequent scan three months later showed no lesions. Additionally, her tumor markers, which were dangerously high in November 2021, had returned to normal levels.

What was originally thought to be a prognosis of just weeks was now uncertain. "We were told Bonnie was doing spectacular and this was the best response to treatment possible," David says.

This improvement underscores the importance of a skilled, collaborative approach.

"Having the breadth of experience from multidisciplinary teams allows us to find creative answers or find hope where others might not be able to see it," Dr. Kim says. "With tumors that respond well to targeted therapies, the prognosis is not as grim as it once seemed."

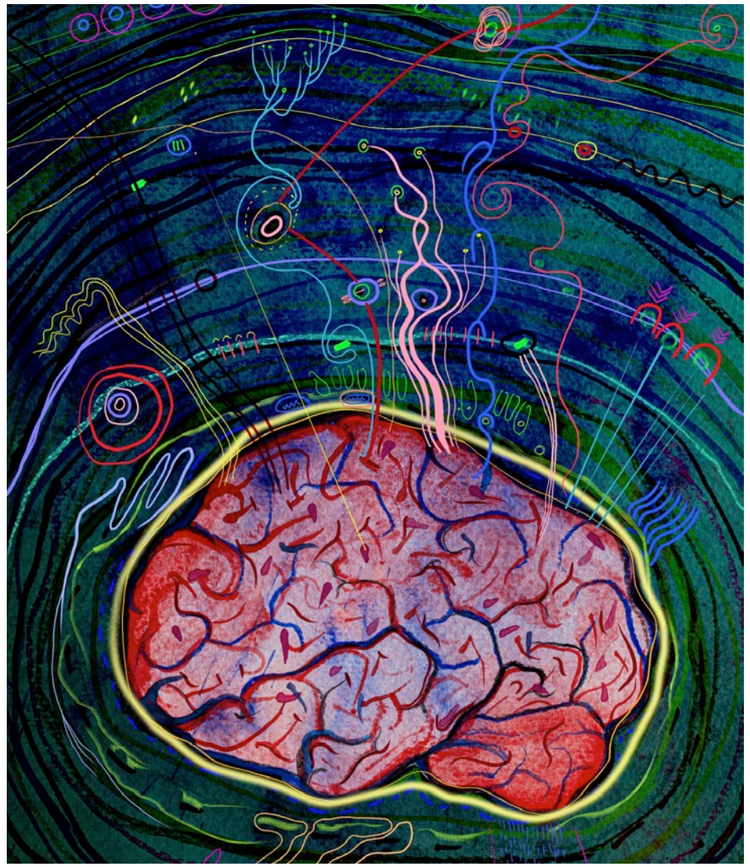
Now, more than three years after her diagnosis, Wham-Prutow remains progression free, with no evidence of disease. She continues to receive infusions and is monitored by her team for any signs of recurrence. "It was a blessing from God to lead us to this incredible UCLA team," she says. "They saved my life."

"Bonnie is not just surviving," says David. "She's thriving."

— Denise Heady

Bonnie Wham-Prutow (in hat), surrounded by her family, cherishes every moment after defying the odds. More than three years after being told she had only weeks to live, she continues to embrace life to the fullest.

COURTESY OF THE WHAM-PRUTOW FAMILY



ISTOCK IMAGES

Brain rhythms can predict seizure risk of patients with Alzheimer's disease

A UCLA HEALTH RESEARCH TEAM has identified changes in brain rhythms that indicate seizure activity in patients with Alzheimer's disease. The findings build on pioneering work by Keith Vossel, MD, director of the Katherine and Benjamin Kagan Alzheimer's Disease Treatment Development Program, that first linked silent epileptic activity to cognitive decline in Alzheimer's disease.

Dr. Vossel's previous studies showed that silent seizures, detected through overnight electroencephalography (EEG) and one-hour magnetoencephalography (MEG), occur in more than 40% of Alzheimer's patients — beyond the 20% who experience overt seizures. His research has demonstrated that both silent and overt seizures accelerate cognitive decline.

In this latest study, the team analyzed MEG and EEG recordings for high-frequency oscillations (HFOs) — fast bursts of rhythmic activity first discovered by Anatol Bragin, PhD, a researcher in neurology at UCLA's Brain Research Institute, as markers of epilepsy. While HFOs are widely studied in epilepsy, this study is the first time they have been examined in neurodegenerative diseases. The researchers found that HFOs occur at rates two-to-three times higher in Alzheimer's patients than in cognitively normal individuals. MEG proved more effective than EEG at detecting these signals due to its superior signal-to-noise properties.

> "MEG screening for HFOs takes just 10 minutes, offering a practical and efficient way to identify Alzheimer's patients at higher risk of epileptic activity."

The study also found that HFOs were more asymmetric (appearing more on the right side) in Alzheimer's patients with epileptic activity. Notably, HFOs that coincided with epileptic spikes were suppressed by the antiseizure medication levetiracetam, based on data from Dr. Vossel's Phase 2a clinical trial. These findings suggest that HFOs could serve as a critical biomarker for identifying Alzheimer's patients at the highest risk for seizures. "Encouragingly, MEG screening for HFOs takes just 10 minutes, offering a practical and efficient way to identify Alzheimer's patients at higher risk of epileptic activity," Dr. Vossel says.

Dr. Vossel's prior research has shown that low doses of levetiracetam can improve spatial memory and problem-solving abilities in Alzheimer's patients with epileptic activity. A quick MEG exam could therefore provide a valuable tool for early intervention — enhancing patient care while reducing health care costs.

— Will Houston

"High-frequency Oscillations in Epileptic and Non-epileptic Alzheimer's Disease Patients and the Differential Effect of Levetiracetam on the Oscillations," *Brain Communications*, February 13, 2025

How our neighborhoods contribute to infant-health disparities

RACIAL DISPARITIES IN INFANT health have persisted for decades, with people of color at increased risk for poor health outcomes, including preterm birth (born before 37 weeks) and low birth weight (less than 5.5 pounds). Both have long-term effects on neurodevelopment, and preterm birth is a leading cause of infant mortality.

In 2019, nearly 450,000 babies were born in California. Some of these new lives were already touched by inequity: preterm birth rates were 67% higher for Black parents than white parents. Latino and Asian rates were 36% and 11% higher, respectively. Rates were also higher for low birth weight at term: 150% higher for Blacks; 38% for Latinos and 81% for Asians.

In a new study, scientists examined how neighborhood environments accounted for disparities in infant health outcomes in California's 2019 birth records data. They measured the impacts of air pollution, drinking-water contamination, green space (tree canopy coverage), heat vulnerability and noise. They also looked at the "area deprivation" factor — an aggregate measure of neighborhood income, education, employment and housing quality.

Highlights of their findings included:

Black/Latino vs. white disparities were due to area deprivation

Air pollution was a significant factor in the Latino vs. white disparity in low birth weight at term

Lack of greenspace was a factor in Black, Latino and Asian disparities

MAJA MODEN

The study noted that Black and Latino parents generally lived in the most disadvantaged neighborhoods compared to white and Asian counterparts.

"I'm always interested in the mechanisms of racism and how different racial groups get differential treatment because of the distribution of green space, industrial power plants or road construction," says Shiwen "Sherlock" Li, PhD, who was a UCLA doctoral student in the Department of Neurology during the study. "There is ritualized policy that's behind all these mechanisms, creating these health disparities down the road."

"This study supports the call for further improvements in cleaning our air and drinking water and increasing access to green space in urban environments, especially in neighborhoods where Black and Latino communities reside," says Beate Ritz, MD, PhD, professor of epidemiology at the UCLA Fielding School of Public Health and in the Department of Neurology at the David Geffen School of Medicine at UCLA.

Infant health outcomes result from a wide range of elements, so the researchers' analysis had to parse out non-environmental risks, including adequacy of prenatal care, public or no health insurance, smoking during pregnancy, chronic or gestational diabetes and hypertension.

The researchers developed complex computational models that controlled for all the individual risks and focused just on the pathway of race to neighborhood environment to birth outcome. "I wanted to look at taking some of the blame and responsibilities off the individual level and more on improving environments," Dr. Li says. "In my opinion, it's more approachable to address health disparities through policy changes."

— Mary-Rose Abraham

"Contributions of Neighborhood Physical and Social Environments to Racial and Ethnic Disparities in Birth Outcomes in California: A Mediation Analysis," *Environmental Research*, November 1, 2024

Cardiac surgery consortium leverages data for improved clinical outcomes

FOR MORE THAN A DECADE, THE University of California's five health centers have pooled data from their cardiac surgery procedures to share best practices and markedly improve patient care.

Advanced analytics on 200 data elements from each patient have provided significant insights into local and systemwide performance, allowing the University of California Cardiac Surgery Consortium (UCCSC) to build standardized and sustainable quality improvements. Importantly, the metrics are vetted, audited and aligned to those of the Society of Thoracic Surgeons (STS), a national database. "Benchmarking ourselves against national data allows us to be sure that we are among the best quality among elite institutions performing cardiac surgery, not only in California and in our local markets, but nationally," says Richard J. Shemin, MD, chief of the Division of Cardiac Surgery.

The consortium's health centers perform about 4,000 cardiac operations annually. Clinical outcomes in isolated coronary artery bypass grafting (CABG), the most common cardiac procedure, showed improved early extubation, reduced blood utilization and reduced readmissions between 2015 and 2023. Overall, they resulted in 132 bed days saved and a financial margin improvement of about $15 million.

Dr. Shemin founded UCCSC in 2012, bringing together University of California health centers in Los Angeles, San Diego, Irvine, Davis and San Francisco. Each health center uploads its clinical data every quarter. Biome Analytics, a cardiovascular technology firm, then performs multivariable regression analyses on single-site and systemwide outcomes.

The health centers' 4,880 CABG procedures between 2015 and 2023 demonstrated improvement in several markers:

Any blood product utilization decreased by 8.26%

Rate of early extubation (less than six hours) increased by 22%

Average initial ventilator hours decreased by 1.5 hours

Median length of stay in the ICU decreased by 0.38 days

30-day readmissions decreased by 3.96%

New onset atrial fibrillation, at 25.4%, was below STS benchmark

Associated cost savings were also analyzed. For example, early extubation resulted in a margin improvement of about $6.7 million and decreased ventilation in about $3.6 million. The 132 bed days saved equaled a cost savings of about $486,000.

In a further bid to reduce complications and readmissions, UCLA Health uses advanced technologies to monitor patients at home, including wearables and tablets with Bluetooth to assess vital signs such as blood pressure, heart rhythm and blood oxygen levels. "We've been able to reduce our readmission rates from the 20% range down to single digits," Dr. Shemin says. "Patients' satisfaction levels go up, and they feel cared for."

— Mary-Rose Abraham

ISTOCK IMAGES

ISTOCK IMAGES

People from some racial and ethnic groups may face barriers to obtaining obesity medications

ASIANS, NON-HISPANIC BLACKS and Hispanics were significantly less likely than whites to use obesity-management medications to lower their weight, new research suggests. The differences could not be fully explained by income or education level, health insurance coverage or clinical need.

The study is one of the few to compare the use of obesity-management medications across racial and ethnic groups, and the first to consider how socioeconomic status might contribute to these disparities, says Kimberly Narain, MD (FEL '13), PhD '16, assistant professor-in-residence of medicine and a researcher in the Division of General Internal Medicine and Health Services Research.

The findings suggest that more research is needed to explain these differences, she says.

The researchers used data from the Medical Expenditure Panel Survey for the years 2011-2016, 2018 and 2020, controlling them for a number of demographic, socioeconomic and medical factors. The study sample contained 91,100 adults who were eligible for obesity-management drugs. Of those, 68% were classified as obese and 32% were classified as overweight with at least one weight-related condition. Broken down by race and ethnicity, about 3% were Asian, 14% were Black, just under 16% were Hispanic and about 68% were white.

The researchers focused on all FDA-approved medications to treat obesity available during the time period of the study. They also conducted an analysis that considered potential off-label use of GLP-1 receptor agonists FDA-approved for the treatment of diabetes, which also may lead to weight loss.

The researchers found that Asians were 64% less likely, Blacks 49% less likely and Hispanics 30% less likely than whites to use obesity-management medications, after taking level of obesity, number of clinical conditions, diabetes status, insurance type, demographics, socioeconomic status and census region into account.

While income, education, health insurance type and clinical need did not fully account for these disparities, the researchers suggest that lower education and either a lack of insurance, reliance on public health insurance or inadequate health insurance coverage may at least partially explain the disparities among Blacks and Hispanics, while lower body mass index (BMI) may explain some of it among Asians.

In addition, there may be cultural differences in the acceptance of larger body types and the acceptability of medications to treat obesity that may underlie some of these differences. Lastly, differences in how medical providers communicate with individuals across race and ethnicity may be playing a role in these differences.

There are limitations to the findings. The researchers could not determine causality in the relationships between race, ethnicity and use; they had to rely on BMI, which is a flawed measure among some groups, for eligibility for the medications; and the medications they considered did not include newer FDA-approved obesity medications.

But a full understanding of the factors that drive, or prevent, use of these medications among racially and ethnically diverse populations is crucial to ensuring that everyone has equal access to these medications, Dr. Narain says.

— Enrique Rivero

"Exploring Racial and Ethnic Differences in Utilization of Medications for Obesity Management in a Nationally Representative Survey," *Journal of Racial and Ethnic Health Disparities*, December 17, 2024

UCLA researchers find high levels of industrial chemical in fentanyl

ISTOCK IMAGES

A UCLA RESEARCH TEAM HAS found that drugs being sold as fentanyl contain high amounts of the industrial chemical bis(2,2,6,6-tetramethyl-4-piperidyl) sebacate, or BTMPS. This new substance of concern emerged in the illicit drug supply nearly simultaneously in multiple U.S. locations from coast to coast.

From June through October 2024, the team quantitatively tested samples of drugs sold as fentanyl that had high levels of the chemical, which belongs to a class of compounds called hindered amine light stabilizers and has a variety of applications, including as a sealant, adhesive and additive to plastics. "The emergence of BTMPS is much more sudden than previous changes in the illicit drug supply, and the geographic range where it was detected nearly simultaneously suggests it may be added at a high level in the supply chain," says Chelsea Shover, PhD, assistant professor-in-residence of medicine. "This is concerning because BTMPS is not approved for human consumption, and animal studies have shown serious health effects such as cardiotoxicity and ocular damage, and sudden death at certain doses."

In drug-product testing where the team was able to quantify different components by mass, samples contained an average of seven times more BTMPS than fentanyl, with BTMPS sometimes accounting for more than 50% of a drug sold as "fentanyl."

BTMPS is not a controlled substance, and though studies in rats have shown action on nicotinic receptors, it has not been commonly understood as a "drug." The reasons for its addition to fentanyl remain unknown, and traditional testing methods such as clinical testing or postmortem toxicology for criminal investigations would be unlikely to detect it. The effects on human health are also unknown, but the researchers are concerned.

Testing was performed by the National Institute of Standards and Technology and included drug product samples from Los Angeles and Philadelphia and residue testing of samples from Delaware, Maryland, Nevada, Washington and Puerto Rico, along with two other California sites.

— Enrique Rivero

"UV Stabilizer BTMPS in the Illicit Fentanyl Supply in 9 U.S. Locations," *JAMA*, February 5, 2025

Treatment strategy reprograms brain cancer cells to combat glioblastoma

UCLA SCIENTISTS HAVE IDENTIfied a new potential strategy for treating glioblastoma, the deadliest form of brain cancer, by reprogramming aggressive cancer cells into harmless ones. The findings demonstrate that combining radiation therapy with a plant-derived compound called forskolin can force glioblastoma cells into a dormant state, making them incapable of dividing or spreading.

When tested in mice, the addition of forskolin to radiation prolonged survival, offering a new potential avenue for combating glioblastoma, a disease with limited treatment options and a median survival time of just 15-to-18 months after diagnosis. "Radiation therapy, while effective in killing many cancer cells, also induces a temporary state of cellular flexibility," says Frank Pajonk, MD, PhD, professor of radiation oncology. "We found a way to exploit this flexibility by using forskolin to push these cells into a non-dividing, neuron-like or microglia-like state."

Glioblastoma is notoriously difficult to treat, largely due to the cancer cells' ability to divide uncontrollably and the protective blood-brain barrier that limits the effectiveness of drug therapies. Current standard treatments — surgery followed by chemotherapy and radiation — have remained unchanged for two decades. A key cause of treatment failure is the ability of glioma stem cells to regenerate tumors after treatment and to resist conventional therapies.

Recent discoveries suggest that radiation not only kills some glioblastoma cells, but also temporarily makes the glioma stem cells more flexible, or adaptable, providing an opportunity to alter their identity. Building on this concept, the UCLA researchers decided to look at the combination of radiation and forskolin, a drug compound known to influence cell differentiation by promoting the maturation of cells into neurons, which do not divide uncontrollably like cancer cells. "Our approach is unique because it leverages the timing and effects of radiation," says Ling He, PhD, an assistant project scientist in the Department of Radiation Oncology. "Unlike traditional therapies that force cancer cells to mature, we use radiation to create a temporary, flexible state, making glioma cells easier to guide into specialized, less harmful types. By adding forskolin at the right moment, we push these cells to become neuron-like or microglia-like, reducing their potential to regrow into tumors."

To test whether forskolin could reprogram these cells, the team of scientists examined the combined treatment's effects on cellular behavior, including the expression of neuronal markers, cell cycle distribution and proliferation. Gene expression changes were analyzed using RNA sequencing, while single-cell RNA sequencing revealed how individual glioblastoma cells transitioned into new phenotypes. The impact on glioma stem cells was assessed through limiting dilution assays. The approach was then tested in mouse models to assess its ability to improve survival.

> "Our approach is unique because it leverages the timing and effects of radiation."

The researchers found that the forskolin was able to cross the blood-brain barrier, significantly depleting glioma stem cells and slowing tumor proliferation. This approach also significantly slowed tumor growth in mice and, in some cases, led to long-term tumor control.

In the highly aggressive and fast-growing model, the combination therapy extended the median survival from 34 days to 48 days. Similarly, in the less aggressive glioma mouse model, median survival increased to 129 days with the combination treatment, compared to 43.5 days in mice treated with radiation alone. Importantly, the sublethal radiation doses used have minimal effects on their own, noted the researchers. "These findings highlight the potential of this dual therapy to substantially improve survival in glioblastoma models," Dr. He says.

Researchers were surprised to find that glioma cells can change into microglia-like cells, a type of immune cell in the brain. Normally, these two cell types come from completely different origins during development. Microglia come from mesoderm, a layer that forms things like blood and immune cells, while glioma cells are thought to come from ectoderm, a layer that forms brain and nerve cells. However, in the unique environment of a tumor, these cancer cells can adapt and "switch identities" between different types of cell. "Our ultimate goal is to one day transform the standard of care for glioblastoma," says Dr. Pajonk, who is a member of the UCLA Health Jonsson Comprehensive Cancer Center and the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research at UCLA. "By targeting glioma cell plasticity and leveraging the multipotent state induced by radiation, this research offers a promising strategy to disrupt tumor progression and enhance patient survival."

Although the study shows promising results, the researchers observed that some mice eventually experienced a recurrence, emphasizing the need to refine dosing and explore alternative dosing strategies to improve the long-term durability of tumor response.

— Denise Heady

"Radiation-induced Cellular Plasticity Primes Glioblastoma for Forskolin-mediated Differentiation," *Proceedings of the National Academy of Sciences*, February 26, 2025

DR. DAVID A. NATHANSON

STEPS INTO THE *U* MAGAZINE SPOTLIGHT

As a kid growing up in Alaska, David A. Nathanson, PhD ’11 (FEL ’13), aspired to become a doctor, like his father, and a bush pilot, flying planes to remote areas of the state to treat patients, and maybe also get in a little fishing. A chance encounter with a former UCLA faculty member — Dr. Michael E. Phelps, inventor of the PET scanner — while casting on the Nushagak River in southwest Alaska changed that course and ultimately led him to UCLA to pursue a PhD. “He opened my eyes to this whole new world,” Dr. Nathanson says. Today, Dr. Nathanson, professor of molecular and medical pharmacology, is casting for improved therapies to treat patients with glioblastoma, the deadliest form of brain cancer. His work took a dramatic turn in 2022 when he and UCLA colleagues received FDA approval for clinical trials of a new drug to evaluate its safety and preliminary efficacy in treating patients. “It is still very early, but we are seeing some patients who are living 16 months, 20 months, when they otherwise might not have lived six months,” Dr. Nathanson says. “We have a ways to go before we can talk about curing this disease, but if we can give patients the opportunity to be with their families for those extra months, that gives me hope that we are moving in the right direction.”

WHEN DID YOU FIRST START TO THINK ABOUT SCIENCE?

I was born and raised in Alaska, where you grow up around moose and bears and have a real awareness of the natural world. I thought of myself as being an explorer, collecting bugs and fish. That was the spark for my scientific interest, teaching me to explore my curiosities. But it wasn’t until I came to UCLA, where I got to add drugs to cancer cells and watch them die, that I became addicted to science.

WHAT WAS YOUR FIRST EXPERIMENT?

This is more of a science project than an experiment, but I made an insect zoo when I was around 7 or 8 years old. Unfortunately, it didn’t last long because while trying to cook hamburgers and hot dogs for potential “patrons,” I accidently set the forest on fire. Despite a well-deserved scolding from the fire department, I didn’t stop being curious, though through much safer experiments.

WHAT HAS BEEN THE GREATEST CHALLENGE IN YOUR WORK?

Having the patience, and the will, to keep going. In science it’s inevitable — it’s actually expected — that you fail. The greatest challenge is accepting that failures need to happen for you to ultimately succeed.

WHERE DOES YOUR INSPIRATION COME FROM?

Primarily from patients with brain tumors. I get the opportunity to meet many of them, and their courage and perseverance inspires me and reinforces my determination to pursue this path. Even so, it can be a difficult balancing act. When I first started, I would get overwhelmed with emotion when meeting patients with an incurable disease. Now, though, this motivates my focus on developing therapies that could one day improve their lives.

WHO IS YOUR SCIENCE HERO?

Dr. Charles Sawyers. What makes him very special and inspiring for me is that he not only uncovered important mechanisms and drivers of cancer, but also that he contributed to the development of drugs that directly impact patient care. That is the path I am trying to emulate. He is on the Mount Rushmore of scientists.

WHERE ARE YOU HAPPIEST?

Right here in this office or my lab talking to students about science. Flying my plane or fishing would be second or third — there is a tremendous sense of peace and a lack of constraints in both those activities — but I am, by far, happiest when I am with students and sharing ideas.

WHAT HAS BEEN YOUR BIGGEST “AHA!” MOMENT?

Getting the drug we’ve been developing to pass into the brain. Around 99% of anti-cancer drugs can’t get past the blood-brain barrier, so if a drug can’t get into the brain to treat the tumor, we don’t stand a chance. But when we made a drug that can actually reach the brain to directly attack the tumor, we finally nicked the armor of glioblastoma. We’ve landed a significant first punch that we can build on and improve.

WHAT DO YOU CONSIDER TO BE YOUR FINEST ACHIEVEMENT?

Being able to train PhD students. I hope that work that I do with them will lead to important discoveries that impact the lives of patients with brain cancer. I think we are on that path, but my goal is for the people that I train to take the baton and do it better than me.

WHAT ARE THE QUALITIES OF A GREAT SCIENTIST?

Perseverance, grit, creativity, determination and a short-term memory because you have so many failures. There are days when I go home upset, but the next day it’s forgotten. I think the great scientists are the ones who just keep going despite the adversity and the obstacles.

WHAT CHARACTERISTIC MOST DEFINES YOU?

I am passionate about what I do.

WHAT IS YOUR GREATEST VIRTUE?

My integrity.

WHAT’S YOUR GREATEST FAULT?

I’m temperamental and can be impatient.

WHAT IS YOUR MOTTO?

“Let’s do this!”

WHAT DO YOU VALUE MOST IN YOUR COLLEAGUES/STUDENTS?

Having a strong sense of collaboration. You can’t solve big problems alone, and the willingness to set aside your own personal goals and ambitions to be able to work together as a team is tremendously valuable.

WHO DO YOU MOST ADMIRE?

My parents. I wasn’t an angel growing up, and I got into quite a bit of trouble as I figured out who I was and what I wanted to become. I credit my parents with having the patience and the faith and the willingness to support me as I tried to determine what my path would be.

WHEN DO YOU NOT THINK ABOUT SCIENCE?

Never, never, never, never. It doesn’t matter what I’m doing, it creeps in.

IF NOT A SCIENTIST, WHAT WOULD YOU BE?

A bush pilot, obviously!

WHAT IS YOUR MOST TREASURED POSSESSION?

My plane. That’s my baby.

WHAT ARE YOU MOST COMPULSIVE ABOUT?

Making sure the door is locked. I will check that the door is locked three or four times at night before I go to bed.

WHAT IS THE BEST MOMENT OF YOUR DAY?

Between 4 and 7 am. It’s quiet; the city is asleep. I get a coffee. I read. It is the best time to think and be creative.

HOW DO YOU WANT TO CHANGE THE WORLD?

I’d love to be able to improve on the outcomes for patients with brain cancer. The website for my lab says: “To cure glioblastoma.” I did that intentionally because I want that pressure. If we are able to make an impact on patients’ lives during my career, I’d feel very good about having a part in making that happen.

WHAT IS YOUR DEFINITION OF HAPPINESS?

Observing something that has never been observed before.

WHAT IS YOUR DEFINITION OF MISERY?

Giving up on something.

WHAT MUSIC DO YOU LISTEN TO WHILE YOU WORK?

Tupac, Led Zeppelin, and my go-to is “Drop the World” from Lil Wayne. ●

The Research Engine that Can

The newly established California Institute for Immunology and Immunotherapy has the potential to reshape the future of science and medicine.

Arie S. Belldegrun, MD
Research Professor and Founder, UCLA Institute of Urologic Oncology
Co-founder and Board Member, California Institute for Immunology and Immunotherapy
Founder, Chairman and CEO, Kite Pharma
Co-Founder and Chairman, Bellco Capital

Gary K. Michelson, MD
Chairman of the Board, California Institute for Immunology and Immunotherapy
Founder and Co-chair, Michelson Philanthropies and Michelson Medical Research Foundation

There was a time, Arie S. Belldegrun, MD, recalls, when immunotherapy was considered a backwater of cancer research. “People didn’t even know how to spell it,” he says. Not anymore. Today, immunotherapy — the prevention or treatment of disease by stimulating the body’s immune response — is at the forefront of modern biomedical research. Powered by advances in genetic engineering, gene editing and gene therapy, it touches on areas of medicine ranging from cancer to heart disease to Alzheimer’s.

Now, the push to further advance this leading-edge research is gaining momentum with the establishment of the California Institute for Immunology and Immunotherapy (CIII), a public-private partnership with the State of California to be operated as a non-profit medical research organization governed by an independent board that includes UCLA Health representatives. Its aim is multifold: to understand the human immune system and to deploy it to treat, cure and prevent disease, advancing human health, while also catalyzing economic growth and innovation in Southern California. “UCLA’s goal is to build the immunology equivalent of Silicon Valley in Los Angeles,” said John C. Mazziotta, MD (RES ’81, FEL ’83), PhD, vice chancellor of UCLA Health Sciences and CEO of UCLA Health, when announcing establishment of the institute, which will be housed in the newly acquired UCLA Research Park.

“Our vision for this institute is for it to be a ‘field of dreams,’” says Gary K. Michelson, MD, “and the world’s leading center for the study of the immune system to develop advanced immunotherapies to prevent, treat and cure all of the diseases that afflict people today and to end these diseases.”

Dr. Belldegrun, director of the UCLA Institute of Urologic Oncology and the founder of several successful biotechnology companies, and Dr. Michelson, an orthopaedic surgeon, prolific inventor and philanthropist, are among the six philanthropic co-founders of the CIII. (The others are Michael Milken, Meyer Luskin, Sean Parker and Eric Esrailian, MD [FEL ’06], chief of the Vatche and Tamar Manoukian Division of Digestive Diseases at UCLA.) Dr. Belldegrun and Dr. Michelson spoke about the institute and its mission with Dr. Esrailian. Their conversation has been edited for length and clarity.

Drs. Gary K. Michelson and Arie S. Belldegrun.

JESSICA PONS

DAVID ESQUIVEL/UCLA

Five of the six philanthropic founders of the California Institute for Immunology and Immunotherapy (from left), Dr. Gary K. Michelson, Meyer Luskin, Dr. Eric Esrailian, Dr. Arie S. Belldegrun and Michael Milken.

Both of you trained and practiced as surgeons. How did you transition from practicing medicine to entrepreneurship?

Dr. Arie Belldegrun: I always wanted to be on the cutting edge of science and clinical medicine. I started pursuing a PhD in immunology, trained as a urological surgeon and pursued a post-doctorate fellowship in cancer immunotherapy at the National Institute of Health's National Cancer Institute, under the leadership of Dr. Steven Rosenberg, considered to be the father of modern immunotherapy. I practiced as a cancer surgeon and an academic physician-scientist at UCLA, where I was involved in immunotherapy and gene-therapy translational research and conducted innovative clinical trials in cancer. That is how I was introduced to the pharmaceutical world of drug development. It was, therefore, a natural progression for my colleagues and me to try to create our own innovations and our own products, with the hope of helping thousands, or hundreds of thousands, of patients rather than treating or operating on one patient at a time. With the help of professors at UCLA's Anderson School of Management, we were able to come up with our first business plan, and were ready to launch our first biotech company, UroGenesys, which we later renamed Agensys.

Gary, what was your path?

Dr. Gary K. Michelson: There is a story: A boy is walking along a beach after a storm, and there are thousands of starfish washed up on the sand. As he walks, the boy stops, picks one up and throws it back into the water. Then he walks a little more, picks up another and does the same thing, over and over. A man walks up to him and says, "There's so many starfish, you can't save them all. What you are doing isn't going to make a difference." With that, the boy bends over, picks up another starfish and throws it back into the ocean. "Well," he says to the man, "it's going to make a difference to that one." As surgeons, we treat patients one at a time. We are that boy; we will make a difference to that one. Which is wonderful. But if I can invent a device that enables me to do this operation faster, safer and better, and that invention gets into the hands of 10,000 other surgeons, it can help so many more people. Through entrepreneurship, I realized that this was an opportunity to do what I was doing on a much grander scale.

Those are wonderful responses, thank you. Let's segue to the California Institute for Immunology and Immunotherapy. Why are immunology and immunotherapy two fields that are worth this massive investment of time and money?

Dr. Belldegrun: Immunology and immunotherapy are not two different areas: Immunology is the parent and immunotherapy is the child. Immunotherapy is the translation of immunology into an immune-based therapy and creating a product or a drug to treat a multitude of diseases. The CIII is not meant to be an institute that just studies immunology. And it is not about research per se. It is about translating the latest and best research into therapies to help patients. I strongly believe that immunology and immunotherapy is the most exciting and rewarding science today because it is rapidly transforming all areas of medicine and how we can treat almost all diseases. It has already become a multibillion-dollar industry, and it's still in its infancy. It is bringing together researchers, genetic scientists, cell-therapy manufacturing experts, clinicians, translational scientists, AI and quantum engineers to solve a single problem. Nothing is more exciting than that.

Dr. Michelson: I believe in basic research, but I do not believe in science for science's sake alone. I believe in science for our sake, for people's sake. In my view, the purpose of science and research is to have discoveries manifest in the world, to change the world, to help people and to make the world a better place. When you look at human suffering and all the chronic diseases that afflict and kill people, the one thing they have in common is that it is our own immune system that is the mediator of every one of those diseases. Rather than what I call "reductive research," which drills way down to get to the bottom of a specific problem but really has no application beyond that, we need science that looks for big answers to solve a lot of problems. That is what the CIII will do.

Something like the CIII has not existed for Los Angeles before. We are not like Boston, the Bay Area or San Diego. What will this mean for the city?

Dr. Michelson: The County of Los Angeles has a population that is greater than the combined populations of the seven smallest U.S. states, so it is remarkable that we have not had the gravitational mass to hold on to all of the brilliant graduate students who go off to other places to pursue their careers. It's not as if L.A. doesn't have its share of billionaires who can invest in biotech; the problem is that there's been no biotech to invest in here. Until now. We need an iron core at the center of our city to provide the gravitational mass to bring everything together and provide an attractive environment for these brilliant scientists.

Dr. Belldegrun: As a UCLA professor involved with the pharmaceutical industry, I often found myself traveling to San Diego, to Irvine, to San Francisco, to Seattle, and then to Boston and New York. It became clear to me that, other than Amgen, which was in Thousand Oaks, Los Angeles was like a "fly-over city" for biotech and pharma. I believe we have been able to change that image somewhat in the past decade with companies like Astellas, Gilead and AstraZeneca establishing a presence here. We are making progress, but it's just the beginning and not good enough. We have all the right components here in Los Angeles to create a world-class powerhouse: outstanding academic research institutions — UCLA, Caltech, USC, Cedars, City of Hope — with brilliant scientist, clinicians, graduate students and plenty of access to venture capital money. The missing link has been the right location for a biotech campus and an entrepreneurial ecosystem that will breed more biotech companies. Pharma, as always, will then follow. Establishing the CIII on the Westside of Los Angeles, close to the freeway and the airport and adjacent to, but not on, the UCLA campus is a dream come true and will provide a highly desirable location for biotech entrepreneurs. Our aim is to establish a world-class California translational institute, not limited to UCLA — hence the California name. We have, therefore, reserved a seat on our board of directors for a member from one of our neighboring institutions.

Dr. Michelson: Another thing that makes this institute radically different is that we're going to invest in young researchers. The CIII will have its own embedded, self-funded incubator/accelerator. A graduate student can come in saying, "I've got this great idea," and we can hear it — kind of like Shark Tank — and determine if it is valuable and worth funding. Who better to judge an idea about immunology than the world's leading immunologists?

We've touched on the fact that this is the California Institute for Immunology and Immunotherapy, but as founders, we chose UCLA as the strategic partner. Why is UCLA the ideal partner?

Dr. Michelson: UCLA is an incredible university with great scientists. Most importantly, it has a fabulous network of doctors and hospital beds. One of the big problems that universities have had is the so-called Valley of Death. They come up with a discovery, and unless they can get pharma to do something with it, it dies. So, they're at the mercy of the pharmas, and often they don't get great value for what they've discovered. One of the things that makes UCLA really unique is that it has access to GMP (good manufacturing practice, to ensure that products are consistently produced and controlled according to quality standards) to create our own experimental drugs and run our own trials, without being at the mercy of pharma. That makes UCLA a wonderful partner.

Dr. Belldegrun: UCLA has been a recognized powerhouse of immunology and immunotherapy for decades, making it an ideal partner for the CIII. Generations of students have been trained in the field here, and many of them are now UCLA professors. Multiple faculty members have assumed leadership roles in the academic immunotherapy societies, were active participants in the development of the most successful immunotherapy drugs and were founders and partners in transformative immunotherapy biotech companies. I have travelled the world and can assert with confidence that the culture of immunology and gene therapy ingrained at UCLA is unique and well-recognized globally. That unique culture provides an excellent draw to attract the best and brightest to join us.

We've covered a lot of ground. What is your long-term vision and hope for the legacy of this institute?

Dr. Michelson: When the State of California agreed to give us several hundred million dollars for the CIII, Gov. Gavin Newsom asked me a question: "Why do I need you when I've got 10 other universities?" And the best response was to ask, "So how come they haven't done it?" Because they can't. It's not in their DNA. And I think now people are starting to get it. We need to be product oriented. We need to be building a complete ecosystem of biotech startups. One of them will be the next Amgen or Genentech. It's going to take a while, but we'll get there.

Dr. Belldegrun: For me, the CIII legacy should be a world-class entrepreneurial and well-funded institute that combines top immunology science and the brightest scientists dedicated to rapid translation to immunotherapy drugs, products and companies. It needs to function as a profitable business operation, governed by an independent and experienced board of directors, with a single goal of taking advantage of its own intellectual property to create the most successful biotech companies. Academia is important, research is important, and the institute will have all of that, but it needs to be differentiated as a well-oiled business machine. The board's mission should be to create a vision for the CIII of how to secure the future of the institute as a financially successful enterprise, independent of outside pressures, an evergreen operation that continues to attract the most entrepreneurial brains in the industry. It will take some time, but once we have proven our success and the technology developed enters the market, this unique approach will start returning capital to the institute, its scientists and to the university, as well. Success will breed success. ●

For more information about the California Institute for Immunology and Immunotherapy, scan the QR code or go to: calimmunology.org

STALKING A SILENT KILLER

By Anna Louie Sussman
Photos by Jessica Pons

Dr. Sanaz Memarzadeh puts ovarian cancer in her sights, and she's not giving up until she solves the mysteries of this too-often-fatal diagnosis.

Dr. Sanaz Memarzadeh.

The twenty-teens were rough years for Flower Miller. In 2013, one of her twin daughters was diagnosed with type 1 diabetes. Miller, then in her early 40s and the mother of three girls (her eldest daughter would also be diagnosed with diabetes two years later), was still riding the steep learning curve of understanding how to manage her child's illness when, nearly a year after the diagnosis, she started experiencing troubling symptoms of her own. She was often bloated, and she found herself waking up more frequently at night to use the bathroom. After just a few bites of food, she felt full. Given what she was going through with her daughter, Miller chalked it up to stress.

Flower Miller (second from left) with daughters (from left) Malia, Violet and Maile.

"I was so high-stress, and so I had some symptoms that were vague," Miller says. "I'm a woman — we just brush them off."

When she saw her gynecologist in January 2014, everything, including her pap smear, was normal. But by April, her stomach was bloated and hard, as if she were pregnant, even though a pregnancy test indicated she was not. "That's when I was, like, 'Hey, this is not normal,'" she says.

Miller's gynecologist initially suspected irritable bowel syndrome. But when she pressed on Miller's abdomen, the doctor could feel her ovaries were swollen, and she immediately ordered a CT scan. The results showed spots throughout Miller's abdomen. The diagnosis: ovarian cancer.

"I asked her what the outcome might be — I thought maybe she would tell me it's treatable and we can do A and B and C — but she just took my hand and said, 'Well, there's hope.' And I thought, 'She's telling me that I'm dying.' I was terrified," Miller says.

> "I was so high-stress, and so I had some symptoms that were vague. I'm a woman — we just brush them off."
> — Flower Miller

The doctor referred Miller's case to the UCLA Health tumor board, a group of oncologists and other specialists who collectively discuss and make decisions about a patient's care. Sanaz Memarzadeh, MD (RES '00, FEL '03), PhD '08, a gynecologic-oncology surgeon, was on the panel and took her as a patient. Miller knew little about ovarian cancer, only that it typically is deadly, and she spent the days before her first meeting with Dr. Memarzadeh preparing for the worst. As much as it distressed her to consider the possibility that she might die, she invited a group of moms to her home to show them how to treat her daughter's diabetes — if she were no longer around to do it.

But Dr. Memarzadeh had a completely different vision. She laid out her plan for Miller's treatment: surgery, chemotherapy, another surgery, additional chemotherapy and, finally, remission. "You really think I can get to remission?" Miller remembers asking. "And Dr. Memarzadeh said, 'That's what we do.'"

That positive attitude, and the attentive care she received at Dr. Memarzadeh's hands, shifted Miller's own attitude toward survival. "I just thought, OK, that's a total game changer. It flipped," she says.

Miller, now moving toward her 11th year of remission, knows she is one of the lucky ones. The majority of women diagnosed with ovarian cancer — 80% — eventually succumb to it. More

than 300,000 women worldwide are diagnosed with the disease annually, and it kills approximately 13,000 American women each year. It is patients like these who drive Dr. Memarzadeh, a physician-scientist and director of the G.O. Discovery Lab (its motto: "Engineering hope for women with cancer") in the UCLA Broad Stem Cell Research Center, to assemble a team of world-class researchers from UCLA and beyond. Together, they are harnessing insights, tools and technologies from a multiplicity of disciplines in order to focus the most leading-edge science on this particularly deadly scourge.

"My life's goal is to make sure that when we treat a patient with ovarian cancer, we eradicate the cancer," Dr. Memarzadeh says. "And if a woman is facing relapse, we provide treatments that can eliminate the cancer so that it does not come back again."

Ovarian cancer is difficult to treat for reasons that range from the subcellular to the social. Some of its unique biological features — its location in the peritoneal cavity and the microenvironment around its tumor cells — make it highly resistant to treatment. Its status as, in Dr. Memarzadeh's words, a "below-the-belt" cancer means research on it has historically been underfunded. In fact, Dr. Memarzadeh says, ovarian cancer has one of the lowest funding-to-fatality ratios of all cancers.

Aaron Meyer, associate professor of bioengineering: "By recruiting cells and changing the activities of cells, they can drive things like killing cells, such as a tumor cell."

This also makes it difficult for Dr. Memarzadeh to trace family histories of the disease with her patients, since people may be reluctant to discuss gynecological issues with family members. And as Miller experienced, its symptoms are vague enough that many women don't recognize it, or they brush them off, so it often is not diagnosed until it's at an advanced stage. All of these factors compel Dr. Memarzadeh to bring every scientific resource she can muster to the fight against it.

The most essential of these are her colleagues. "A major effort of mine has been to talk to my colleagues, who I think are brilliant, and try to get them excited to work with us on ovarian cancer," she says. Through collaborations with researchers from different backgrounds, she is bringing a multidisciplinary and pan-cancer approach to finding new ways to treat her patients, creating a vital link between the worlds of clinical practice and research.

To foster camaraderie, she has hosted many of her scientific collaborators at her home for group dinners, providing food and drinks and then inviting them to discuss studies on ovarian cancer that she's selected in advance. "My colleagues in science are acutely aware of the importance of clinical translation of the work, and equally are passionate about making an impact," she adds.

Since she was a young girl growing up in Iran, Dr. Memarzadeh had an interest in science. Instead of playing with dolls, she was fascinated by the workings of nature. "I loved taking a seed and watching it

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For the love of Robin

Following the death of her daughter, Robin, from ovarian cancer at age 20, Paulinda Schimmel Babbini turned her grief into action to found The Ovarian Cancer Circle/Inspired by Robin Babbini.

By Sandy Cohen

PAULINDA SCHIMMEL BABBINI'S NAILS are always painted a vivid teal. Teal is the official color of ovarian cancer awareness, and Babbini is committed to spreading the word. The color draws attention, and the moment someone remarks on her nails, she takes the opportunity to tell them about her daughter, Robin, who died of ovarian cancer in 2006, when she was just 20 years old.

Babbini has made it her mission to educate women and girls of all ages about ovarian cancer, which is among the leading causes of cancer-related death among women, according to the American Cancer Society. "People just don't know enough about this cancer," she says, "especially because its symptoms are so elusive."

In the four years after Robin's death, Babbini slowly emerged from her mourning to take a huge step outside of her comfort zone. Describing herself as a private woman unaccustomed to public speaking, Babbini, with the help of a small group of volunteers, launched her nonprofit, The Ovarian Cancer Circle/Inspired by Robin Babbini, in 2010. Since its inception, The Circle, as many know it, has raised and donated more than $1 million to support gynecologic oncology research at UCLA Health.

"Either I could have crawled into a cave and become the most depressed person imaginable, or I could take a new path and move beyond my loss, turning grief into something positive and productive," Babbini says. "The Circle is a vigorous, positive outlet to do good. It has saved me, and it will, I hope, save many, many lives."

Robin was in high school when she started to complain about nausea, back pain and indigestion. Nonetheless, the spirited teenager kept up her fast-paced life as a cheerleader, editor of the school newspaper and member of the drama club.

When the pain didn't subside, Babbini took her daughter to see a gynecologist. But he didn't connect a high-school-age girl with the potential of a gynecologic cancer and failed to ask the right questions, she says. "He really misunderstood it all and, sadly, shrugged it off."

On her own, Robin began thumbing through a medical reference book they had at home. "Mom," Babbini recalls her daughter saying to her, "I have ovarian cancer." "No!" Babbini responded. "You're too young. You're only 17."

Within a few months, Robin's pain was so severe, she went to the emergency room, where a CT scan revealed four large tumors. Robin would need surgery right away.

The diagnosis was stage 3 ovarian cancer, which had spread to her colon. Robin underwent a hysterectomy, colon resection and six rounds of chemotherapy. She recovered enough to graduate from high school and start her freshman year at UC Santa Barbara, where she pledged to the Kappa Kappa Gamma sorority.

But ovarian cancer has a high recurrence rate; for stage 3 disease, it is 80%, according to the American Cancer Institute.

Babbini prayed: "God, let us be on the side that it doesn't recur."

The cancer returned during her freshman year. Robin did her best to balance college life with frequent trips back to L.A. for tests, treatments and chemotherapy, Babbini says.

Still, the cancer advanced, and Robin succumbed to the disease that same year.

IN THE EARLIEST DAYS OF THE OVARIAN Cancer Circle, Babbini was introduced to Sanaz Memarzadeh, MD (RES '00, FEL '03), PhD '08, a gynecologic oncologist and researcher at UCLA Health. Babbini was impressed by a presentation Dr. Memarzadeh made during a conference, and she knew at that moment that she wanted to support her work.

For Dr. Memarzadeh, The Circle's support transcends its annual donations. A 2020 study found that funding for ovarian cancer research is about 5% of the amount allocated for prostate cancer, though ovarian cancer is far more deadly. Researchers concluded that national funding for ovarian cancer research doesn't correspond with the lethality of the disease.

"For underfunded diseases like gynecologic cancers, philanthropic support is essential," Dr. Memarzadeh says. It allows her lab to conduct experiments with few restrictions, exploring novel, breakthrough ideas and generating preliminary data that can lead to subsequent support from larger agencies such as the National Institutes of Health.

But funding is only part of the partnership between the physician-scientist and The Circle. "Paulinda has created a community of women who are passionate about women's-cancer research," Dr. Memarzadeh says. "Some are survivors themselves; some are in treatment; some have lost loved ones to this cancer. The Circle has become an invaluable communications resource, tethering our research goals to increased public awareness."

That has extended to engagement with such civic resources as the City of West Hollywood, the Los Angeles City Council and other women's groups. "So, yes, the funding is important, but their work also brings heightened awareness to cancers that are understudied and triggers conversations about the signs and symptoms and the need for more research that leads to better treatments," Dr. Memarzadeh says.

Dr. Memarzadeh is often the guest of honor at The Ovarian Cancer Circle's fundraising events, where she presents the latest research being conducted in the G.O. [Gynecologic Oncology] Discovery Lab that she runs. "Sanaz communicates the science of her work so clearly, and with such inspiration, that our guests often walk out of there donating even more money than they'd planned," Babbini says.

EVERY YEAR SINCE SHE FOUNDED THE Circle, Babbini visits UC Santa Barbara to speak to the current members of Robin's sorority. She encourages the young women to be vigilant about symptoms such as bloating, difficulty eating, nausea or pain in the pelvis or abdomen, and to seek screening with a gynecologic oncologist. "I can talk about Robin and with all my heart keep her memory bright, but I must educate these young women that ovarian cancer is not just an older woman's disease — anybody can get it," Babbini says.

Babbini also lobbies year-round with city officials to raise awareness. During national Ovarian Cancer Awareness Month in September, both L.A. City Hall and West Hollywood's City Hall are lit up nightly in teal. The 11 LAX Gateway pylons have also glowed teal for ovarian cancer awareness.

It is estimated that ovarian cancer will take the lives of some 13,000 women in the United States in 2025. Babbini wants to save as many of those lives as she can. "The more women who learn about the symptoms, the more proactive they can be," she says. "I often think that if I had known then what I know now, Robin would be here today."

Helping save women from her daughter's fate gives lasting purpose and meaning to Babbini's life. Wherever she goes, Robin's mother talks about ovarian cancer and hands out informational bookmarks, which include a smiling photograph of Robin.

And every day, Babbini looks at the candle that she lights in her home in memory of Robin. "She's not here with me physically," Babbini says, "but she's here with me in spirit every single day. My motto forever will be, 'No more Robin stories!'"

***Sandy Cohen** is a senior writer for UCLA Health Marketing Communications and a former national writer for* The Associated Press.

For more information about The Ovarian Cancer Circle, scan the QR code or go to: theovariancancercircle.org

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grow to become a plant," she says. "Most of the girls would play with Barbies and other toys, but I was more interested in doing experiments."

Her mother was a nurse and her father an anesthesiologist, so it wasn't long before she first visited a hospital. Dr. Memarzadeh's family emigrated to the United States when she was a teenager, and she majored in neuroscience at the University of Pittsburgh, completing her studies in just three years. She jumped immediately into medical training there, where her omnivorously curious mind latched onto several specialties. At one point, she landed with a group of surgeons who were also researching immunology related to pancreatic cell clusters called islets, and she became fascinated by immunology and the practice of surgery. She was also intrigued by the scientific aspects of reproductive biology, and for a time thought she would become an infertility doctor.

But during her residency at UCLA, she spent time on the gynecologic oncology floor, where she cared for a young woman whose ovarian cancer recurred over and over, despite undergoing surgery after surgery. When Dr. Memarzadeh attended conferences seeking new research and answers, she was frustrated to see doctors recommending the same old courses of treatment that she knew were not working for her patients. "There was not enough knowledge about the disease," she says. "I think the knowledge base, still, for gynecologic cancers is not where it should be."

She knew that, if given the opportunity, she could make a scientific contribution. Dr. Memarzadeh entered the David Geffen School of Medicine at UCLA's prestigious Specialty Training and Advanced Research (STAR) Program, earning a PhD in molecular biology while training under Owen Witte, MD, a renowned researcher and University Professor of microbiology, immunology and molecular genetics, who has made groundbreaking contributions to understanding of human leukemias, immune disorders and epithelial cancers, with whom she continues to collaborate.

Today, as she divides her time between the laboratory and the operating room, her work, in every sense, begins and ends with her patients. It is their health and well-being that motivates her — "My patients are my inspiration; I am struck by the bravery of the women who are facing these diagnoses," she says — but it is also their generosity that enables her to do the research she does. As part of her clinical work, she has built a biobank of hundreds of tumor samples, as well as other biological material and health data from patients she has treated over the years.

This invaluable resource, and the passion for patient care that underpins it, has attracted collaborators from outside the school of medicine. Aaron Meyer, PhD, an associate professor of bioengineering in the UCLA Samueli School of Engineering, is among them. Dr. Meyer's area of expertise is systems biology; he describes himself as someone who gets "very excited by understanding how the body works — the intellectual exercise of it."

One of Dr. Meyer's longtime interests has been antibodies, a part of the body's immune response that, in cancer research, at least, has been overshadowed by advances in understanding and using T cells to fight cancers. But, Dr. Meyer notes, although antibodies are just proteins, they may hold important clues to harnessing the body's immune system.

"Unlike a T cell, they're not living — they can't really do a whole lot on their own," he explains. But, he continues, in their interaction with immune cells, these proteins can trigger important responses. "By recruiting cells and changing the activities of cells, they can drive things like killing cells, such as a tumor cell."

> "My patients are my inspiration. I am struck by the bravery of the women who are facing this diagnosis."
> — Dr. Sanaz Memarzadeh

One question that researchers in the 1990s had begun asking was, "Do cancer patients make antibodies against their cancer?" The answer is yes, but there was little known about it beyond that. Dr. Meyer thought that, given the advances since then in understanding the body's immune response to cancer, he might be able to dig deeper into how antibodies fit in. But to study this, he needed access to patient samples. Colleagues at UCLA told him that Dr. Memarzadeh was very collaborative, and he knew that ovarian cancer, in particular, produced a lot of antibodies. What's more, ovarian cancer has not been as responsive to T-cell therapies, which are more effective against other types of cancer such as leukemia and lymphoma.

"Cancer patients have these antibodies, but do they actually interact with the immune cells in the right way?" Dr. Meyer asks. In 2021, he approached Dr. Memarzadeh and explained his interests. "Sanaz has a very patient-focused perspective, so I think one of the first questions she had was, 'OK, this is a lot of cool science, but how is this going to help my patients?'" he recalls with a laugh.

Her question prompted him to think about how he might actually apply this idea, and together they secured funding from the Mark Foundation for Cancer Research. Today, they are exploring how the antibodies produced by ovarian tumors interact with the immune system, knowledge they hope will point toward a viable therapy.

Dr. Memarzadeh had many tumor tissue samples. For her research project with Dr. Meyer, she expanded her biobank to start collecting peritoneal cavity fluid from ascites, a condition in which fluid builds up in the abdomen, and which is responsible for the bloating that is one symptom of ovarian cancer. This fluid is also rich in the antibodies they wanted to study. The scientists incubate the tumor cells with the antibody-rich fluid, wait for the antibodies to bind to the tumor cells, and then isolate those particular antibodies and tumor cells from the rest of the fluid. They then add immune-cell receptors and observe whether or not the antibodies react with those receptors to trigger an immune response.

Dr. Meyer and Dr. Memarzadeh found that these antibodies produced by tumor cells fail to interact with an important receptor known as CD16, commonly found on natural killer (NK)

Dr. Lili Yang: "There's something special about this cancer."

cells that can destroy cancer cells, and which are an important tool in cancer immunotherapy. While viruses and diseases such as COVID-19 or Epstein Barr produce antibodies that do interact with CD16, "tumor antibodies have completely lost that ability for some reason," Dr. Meyer explains. "We're trying to figure out how you turn that back on."

The mechanism that makes or breaks that interaction appears to relate to a specific sugar on the bottom of the antibody, and the scientists' next step is figuring out how to convert or modify the sugar to restore the interaction. Dr. Meyer is excited to publish this research and see if others in their field can move the science forward to a viable therapy. "There's a lot of very creative people out there, and there's probably going to be other labs and groups that have creative ways of developing therapies using this observation," he says.

Another challenging aspect of treating patients with ovarian cancer is the tendency for traditional treatments, such as platinum-based chemotherapy, to lose their effectiveness. One explanation for this is that cancer cells, under pressure from therapeutic treatment, change and evolve, a quality known as "lineage plasticity." This quality has been documented in aggressive forms of prostate and lung cancer, but when Dr. Memarzadeh saw a colleague presenting about it, she was struck by the similarity to the same pattern with high-grade serous ovarian cancer, the most common type of ovarian cancer. Working with UCLA colleagues including Thomas Graeber, PhD, professor of medical and molecular pharmacology, Dr. Memarzadeh is taking what she calls a "pan-cancer approach," thanks to a $1.2 million grant from the U.S. Department of Veterans Affairs. "We're taking lessons learned from other cancers and applying them to gynecologic cancers," she says.

Another way Dr. Memarzadeh examines this resistance to treatment is by tackling it at the peptide level. Peptides are the groups of amino acids that, in combination, form proteins. They are assembled using instructions given by ribonucleic acid, or RNA, the class of molecules that essentially act as messengers between our DNA, or genetic material, and the proteins that are the building blocks of our cells, tissues, hormones and enzymes. Cancer cells, Dr. Memarzadeh notes, use these proteins to generate unique antigens, the biological signs that alert the immune system to send help. These cancer-specific proteins can emerge through a process called alternative splicing, which affects how a cell processes its RNA. Identifying these antigens, she says, would "provide a unique opportunity for targeting the cancer cells using immunotherapy approaches, while sparing the normal cells."

Her partner in this research is Yi Xing, PhD '06, a computational biologist and executive director of the Department of Biomedical and Health Informatics at Children's Hospital of Philadelphia, whose work illuminates how RNA is transcribed and translated into the relevant proteins. Together, they're using advanced computing technologies Dr. Xing and his colleagues develop in their lab to analyze a large cohort of platinum-resistant ovarian cancers, hoping to identify cancer-specific proteins by mapping out the cells' RNA.

"Historically, and even to this day, large-scale analysis of RNA is still much more tractable than large-scale analysis of proteins," explains Dr. Xing, who also is a professor of pathology and laboratory medicine in the University of Pennsylvania's Perelman School of Medicine and founding director of the Center for Computational and Genomic Medicine at Children's Hospital of Philadelphia. "By analyzing RNA, we can infer what proteins are present. It's not a one-to-one correspondence, but the pool of RNA gives you a very good indication about the pool of proteins in the cell."

In collaboration with hematologist-oncologist Christopher S. Seet, MD (FEL '14), PhD '18, and Dr. Witte, who is founding director of the UCLA Broad Stem Cell Research Center, Drs. Memarzadeh and Xing aim to engineer potent immune cells, the T cell, to target those antigens while sparing the surrounding non-cancerous tissue.

But one of the dirtiest of the many dirty tricks in ovarian cancer's arsenal is that it's not merely the tumor cells that fight back. Lili Yang, PhD, a professor of microbiology, immunology and molecular genetics and a member of the UCLA Jonsson Comprehensive Cancer Center, has studied many other cancers, and she says one thing that stands out to her about ovarian cancer is that its tumor cells are surrounded by a uniquely challenging microenvironment. This is in part because of its location at the base of the peritoneal cavity, which is an area of the body with a particularly high concentration of cells that inhibit an immune response. "It probably has the highest percentage of those inhibitory cells," Dr. Yang says.

She likens them to a brick wall into which a treatment slams head-on, stopping it from working. While treatments such as immune checkpoint therapy, which allow the body's own immune response to kick in by blocking the proteins that would otherwise inhibit it, have so far been effective in treating other cancers such as melanoma and lung cancer, not so for ovarian cancer. "Its success with ovarian cancer is minimal," Dr. Yang says. "There's something special about this cancer, and this could be one of the reasons."

To address this challenge, Dr. Yang and Dr. Memarzadeh have collaborated closely, starting with a study in which they took 10 tumor samples from patients whose cancer had recurred following chemotherapy and 16 tumor samples from patients who had not yet undergone chemotherapy. By profiling how the cell populations changed before and after treatment, they could identify specific molecular targets for immunotherapies.

Dr. Yang was already working on a special type of super-charged immune cell that can fight not just the cancer cells themselves, but also the inhibitory cells that surround them. With an additional tweak, she and Dr. Memarzadeh thought it could be particularly well-suited for tackling ovarian cancer.

They eventually created what is called a CAR-equipped iNKT cell. It is bioengineered to have the features of a natural killer (NK) cell, as well as those of a T cell, the two types of cells

that are the body's main soldiers when going to war against disease and foreign pathogens. When they analyzed patient tumors, Dr. Yang says, they found that iNKT cells can target tumor cells through potent NK features, such as NK receptors, and also modulate the tumor microenvironment via T-cell receptor recognition. The T-cell component helps clear out the microenvironment of the cells that support tumor growth or prevents the immune response from working. The scientists could also identify the correct proteins to enhance these killer cells with chimeric antigen receptors, or CARs. The resulting CAR-equipped iNKT cells, referred to as CAR-iNKT cells, are capable of targeting the most highly resistant tumor cells, the ones that revert back into an almost stem-cell like state to evade attack — "the worst cells," as Dr. Yang refers to them. This three-pronged approach has already shown promise in animal models, and Dr. Yang and Dr. Memarzadeh hope to meet with the U.S. Food and Drug Administration to explore a clinical trial by the summer of 2027, once the pre-clinical studies have concluded.

As she continues to move forward with her research, working hand-in-hand with collaborators at UCLA and across the country to develop new approaches and new therapies to tackle this deadly disease, Dr. Memarzadeh is committed to the fight for as long as is necessary. "I'm trying to solve ovarian cancer," she says emphatically. "I'm not going to quit until we do."

> "I feel hopeful. My focus is now on what's coming next – new clinical trials and surgeries and early detection tests and prevention."
>
> — Flower Miller

For Flower Miller, and Dr. Memarzadeh's other patients, those are powerful words. "I feel hopeful," Miller says, for herself and for other women who may face this terrible diagnosis in the future. "My focus now is on what's coming next — new clinical trials and surgeries and early detection tests and prevention. I saw Dr. Memarzadeh the other day at a fundraising luncheon, and she had a clear message for us. 'I'm not stopping,' she said. And I believe her. She's going to be the one who does it."

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

Dr. Memarzadeh had a clear message for attendees of a recent fundraiser: "I m not stopping." Says Miller, I believe her.

THE VAULT GUY

Dr. Leonard Rome's lab discovered an odd, abundant component of cells in the 1980s — and he's still trying to figure out what it does.

By John Travis

LEONARD ROME, PHD, SWITCHES OFF THE OVERHEAD LIGHT in the small room, leaving it illuminated only by a computer monitor and the fluorescent screen at the base of a towering electron microscope. Qing Lou, a PhD student who works with the David Geffen School of Medicine at UCLA biological chemist, points to some ovoid smudges within the circular green glow of the microscope display. With a twist of a dial and a click of a mouse, she brings the shadows into focus and snaps a picture. Dozens, maybe hundreds, of barrel-shaped particles suddenly fill the computer monitor.

"There they are," Dr. Rome says, like a proud father showing off his children.

These are vaults, enigmatic cellular structures that he and his then-postdoc, Nancy Kedersha, PhD, discovered back in 1986, when Dr. Rome was a new dad with bushy black hair and a Tom Selleck-style mustache, and Ronald Reagan was still the U.S. president.

Vaults, he and others would show, are the most massive particles made naturally by human cells, and among the most abundant. Most of our cells have roughly 10,000 of the structures, with the number rising to perhaps 100,000 in certain immune cells. Many other animals make them, too. Their abundance — and the resources cells must pour into making them — suggests vaults have some essential function. But despite decades of work by Dr. Rome and other "vaulters," their purpose is unknown. "It's a real puzzle," says Joana Vidigal, PhD, a biologist at the National Institutes of Health (NIH) who recently probed the role of RNA found inside vaults.

SPENCER LOWELL/TRUNK ARCHIVE

Dr. Leonard Rome surrounded by 3D models of vaults, the mysterious components of cells his lab discovered in the 1980s.

COURTESY OF DR. LEONARD ROME

Dr. Nancy Kedersha (bottom right) and others in the lab of Dr. Leonard Rome (top second from right) pondered their discovery of vaults.

Over the decades, various hypotheses have been proposed, including that vaults help ferry things around inside cells or clear toxins. And one by one, promising ideas were dismissed or lost momentum as supporting evidence failed to materialize. Initially enthusiastic about Dr. Rome's and Dr. Kedersha's discovery, NIH lost interest in funding basic research on vaults as the years wore on without answers. "There were periods in my career when I was depressed," Dr. Rome says.

Yet, Dr. Rome's fascination with vaults hasn't faded, even as other researchers — including Dr. Kedersha — moved on. And now, with help from other funders and labs, he has turned from basic research on vaults to studies of how they might be exploited in medicine and other fields, as nanoscale vessels for delivering therapies and more.

The ones in the microscope on this day were produced in genetically modified yeast and loaded with an immune signaling molecule called CCL21 that has shown tumor-fighting potential. Vault Pharma, a company co-founded by Dr. Rome that works out of an incubator space at UCLA, hopes to start a clinical trial in late-stage cancer patients next year. It would mark the first time synthetic vaults have been injected into humans, and perhaps the beginning of a new turn in the spotlight for these mysterious organelles.

Dr. Rome is now 77, with three grown sons. His hair has turned white, and his impressive mustache is long gone. He retired in 2020 but is now officially back at UCLA with one lab bench, a postdoc and some undergraduates under his wing. (Nobody noticed he left, he jokes, because the COVID-19 pandemic had everyone working at home.)

From a small office at UCLA's California NanoSystems Institute (CNSI), which he helped design and, for a period, directed, he spends his days consulting on vault research with other UCLA labs, as well as the small Vault Pharma team. He occasionally fields calls and emails from scientists learning about the structures for the first time.

And Dr. Rome is still forming new collaborations. In one audacious effort, he and a lab in St. Louis, Missouri, have stuffed viruses into vaults in a bid to solve a major problem in gene therapy. He's aided by his infectious enthusiasm. UCLA environmental engineer Shaily Mahendra, PhD, years ago became a vault convert, loading synthetic ones with enzymes designed to break down groundwater contaminants. She and Dr. Rome now have backing from foundations and federal agencies to see whether the encapsulation helps the enzymes work better and last longer when dispersed across land or in water. "No one says 'no' to Lenny," Dr. Mahendra laughs.

The lab held a competition to name the unidentified cellular objects, which were shaped like tiny U.S. footballs.

DR. ROME DEBATED MAJORING IN ART OR chemistry as an undergrad when his art teacher gently suggested the latter was a more practical option. He later switched to biochemistry, which at the time involved a lot of cell biology. His first lab, at UCLA, focused in part on a cellular structure: lipid spheres known as clathrin-coated vesicles. They transport enzymes to organelles called lysosomes to help break down other molecules.

When Dr. Kedersha joined Dr. Rome's group in 1983, she was fresh out of a doctoral program at Rutgers University, but had previously worked for years as a lab tech. The two were nearly the same age and quickly developed a rapport. Dr. Rome assigned her the task of comparing the vesicles entering lysosomes with the ones exiting. When she used a gel to separate different kinds of vesicles based on their electrical charge, she unexpectedly saw an additional band, indicating structures of another kind. Unable to identify them, she tried flooding her cell preparations with a heavy metal stain before looking at them with an electron microscope.

Like islands in an ocean, white ovoid outlines appeared amid the background puddle of stain — vaults. The stain was rolling off the structures, revealing their shape. Follow-up experiments revealed that more traditional stains for the lipid membranes common to many cell components did not bind to vaults' protein-only shells, one reason they had gone undiscovered for so long.

The lab held a competition to name the unidentified cellular objects, which were shaped like tiny U.S. footballs. Some suggested grenades or raspberries. Romesomes was a popular choice, which Dr. Rome quickly countered with Kedershacules. But when the postdoc remarked that she thought the objects' outline resembled the vaulted ceilings in cathedrals, the name stuck.

A heady time followed, lab members recall. Some of the women donned fake mustaches that mimicked Dr. Rome's as they all toyed with possible explanations for what they had found. Dr. Kedersha discussed vaults and other science with Dr. Rome on power walks he was doing to lose weight. "I loved working with Lenny," she says.

Whenever he met another biologist, he'd pull her vault micrographs out of his wallet, where they nestled with his kids' pictures, and ask what the scientist thought. One suggested a contaminating virus. A hasty experiment disproved that but revealed another surprise: Vaults contained snippets of RNA, albeit ones far too short to be a viral genome.

Confident the lab had something unprecedented, Dr. Rome mailed the work to one of the top basic research journals, *Cell*. Its famously opinionated editor, Benjamin Lewin, rejected the submission without sending the manuscript out for review. The journal would be happy to reconsider, he added, once the lab identified a function for vaults. Crushed, the team pivoted to a more specialized cell-biology journal, and the paper was quickly published.

OVER THE YEARS, DR. ROME'S LAB AND A few others have built up a more detailed picture of vaults. About 10 million times smaller than a football, a vault is still large for a cell — about three times the mass of the much-better-known ribosomes that translate RNA into proteins. Each is made up of 78 copies of the elongated major vault protein (MVP), aligned somewhat like staves in a barrel. Inside are clumps of two other proteins and the short vault RNA (vRNA).

The genes for these vault components are found in diverse eukaryotic organisms — those that pack their DNA in the nucleus and share other cellular features — with notable exceptions that include insects, plants and fungi. Bacteria also seem to lack them. A 2013 study constructed a family tree of all the organisms known to have vaults and concluded they date back to a hypothetical last common eukaryotic ancestor billions of years ago. Over evolutionary time, some lineages evidently lost them.

Based on their barrel shape, Dr. Rome initially wondered whether vaults pick up and released cargo within the cell, perhaps plying routes from the nucleus to other locations. Vaults seemed to gather around gateways known as nuclear pore complexes and might fit their opening. "It's a perfect match," he told *Science News* in 1996.

Dr. Kedersha had her own views. She was struck by her observation that macrophages, amoeba-like cells in the immune system, had the most vaults of any human cells. She also recalled another lab's discovery that slime molds — simple organisms that can form a blob and creep along the forest floor — have three copies of the gene for MVP, compared with one in humans, suggesting they need more vaults. She suspects vaults have a role in

cell locomotion, perhaps by regulating expression of other proteins that form extensions that help cells get around.

Dr. Kedersha's and Dr. Rome's paths diverged five years after that first vault paper. Dr. Kedersha joined a biotech firm, honing her talents at photographing and characterizing cancer cells with antibodies and stains. Later, she returned to academia to teach and work in Paul Anderson's lab at Brigham and Women's Hospital. There, she discovered another previously unknown component of cells called stress granules, cytoplasmic "vortexes" of messenger RNA (mRNA) and proteins created when cells face challenges like energy depletion or viral infection. The granules, which seem to sort mRNA so they can later be translated into proteins or degraded, were the main focus of Dr. Kedersha's research career.

In contrast, Dr. Rome went all in on vaults, shedding other lab projects. In 2014, his lab showed vaults are made in an unusual way, by an assembly line of ribosomes. As each new copy of MVP is synthesized, the strand immediately layers onto the ones made before, and the vault shell slowly emerges as if from a biological 3D printer.

The rapid assembly process means there's virtually no free MVP left in cells, making it difficult to investigate potential vault function by targeting and inactivating the proteins. The team also found that MVPs don't form fixed chemical bonds with their neighbors. Instead, weaker noncovalent interactions bind them into a shell. This lets vaults "breathe," exposing gaps that might allow relatively small molecules to get inside.

Meanwhile, other labs were racking up provocative and confounding findings of their own. In 1996, European cancer researchers investigating a protein that's unusually abundant in drug-resistant cancer cells cloned the gene and discovered that it resembled the gene for MVP in rats. Working with Valerie Kickhoefer, PhD, in Dr. Rome's lab, the group then found that the drug-resistant cancer cells generated many more vaults than nonresistant ones, suggesting the structures might sequester or expel chemotherapies. But to investigators' frustration, stopping the production of vaults, or MVP, didn't make the cells more susceptible to drugs.

Underscoring the mystery of vaults, in 2002 a Dutch team disabled the gene for MVP in a line of mice. The rodents lacked vaults yet developed normally, seemed to be healthy, reproduced and lived as long as regular mice. Subsequent knockouts of the two other vault-protein genes also left mice unscathed. And Dr. Vidigal's team at NIH recently disabled the mouse vRNA gene — only to find that those rodents, too, display no major changes, they reported in a preprint last year.

"The pathologists found no problems in any of the tissues analyzed," Dr. Vidigal says. "I have never seen a case where a set of genes is exceptionally conserved, highly expressed, produces a huge structure, and when you get rid of them, you see virtually nothing, even at the molecular level. It's crazy."

BACK IN 1987, DR. ROME'S LAB EASILY WON an NIH grant to study the newfound objects, with the highest grant score he would ever receive from the agency. A second NIH proposal took two resubmissions before getting approved. A third was finally granted in 1996, after three tries, but when it ended a few years later, the agency rejected Dr. Rome's subsequent vault applications. As NIH developed vault fatigue, Dr. Rome got creative, turning to the National Science Foundation, private foundations, companies and others for funding. He found success by focusing less on what vaults might naturally do and more on what could be done with artificial ones.

In 2001, his lab reported something unexpected: When they added the rat MVP gene to moth cells, they produced virtually normal, but empty, vaults. The three other components were not needed to form the structures. That got him wondering: Could these empty vessels be put to use?

At the time, Dr. Rome, who had become a dean of research in UCLA's school of medicine, was helping develop the university's part of a new $100 million statewide nanotechnology effort backed by California's governor — what would become CNSI. With an apparent easy way to make nanocontainers, Dr. Rome was soon talking to anyone looking to deliver enzymes, drugs or anything else into the body. Vaults are already in human cells, after all, so Dr. Rome argues they are unlikely to provoke an immune response, unlike vessels made from foreign substances.

UCLA cancer immunologist Steven Dubinett, MD (RES '84), now dean of the David Geffen School of Medicine at UCLA, joined the vault bandwagon soon after. He had been pioneering CCL21 therapy for cancers, based on evidence that the protein stimulates immune-cell proliferation and other responses. Dr. Dubinett's initial strategy was to inject CCL21 directly into tumors. That elicits a strong antitumor immune response, but it is short-lived. Hoping to avoid repeat injections, his lab was looking into more enduring approaches, such as engineering a patient's own cells to make CCL21. Dr. Rome suggested what might be a simpler solution: Stuff CCL21 inside vaults, where it might leak out slowly.

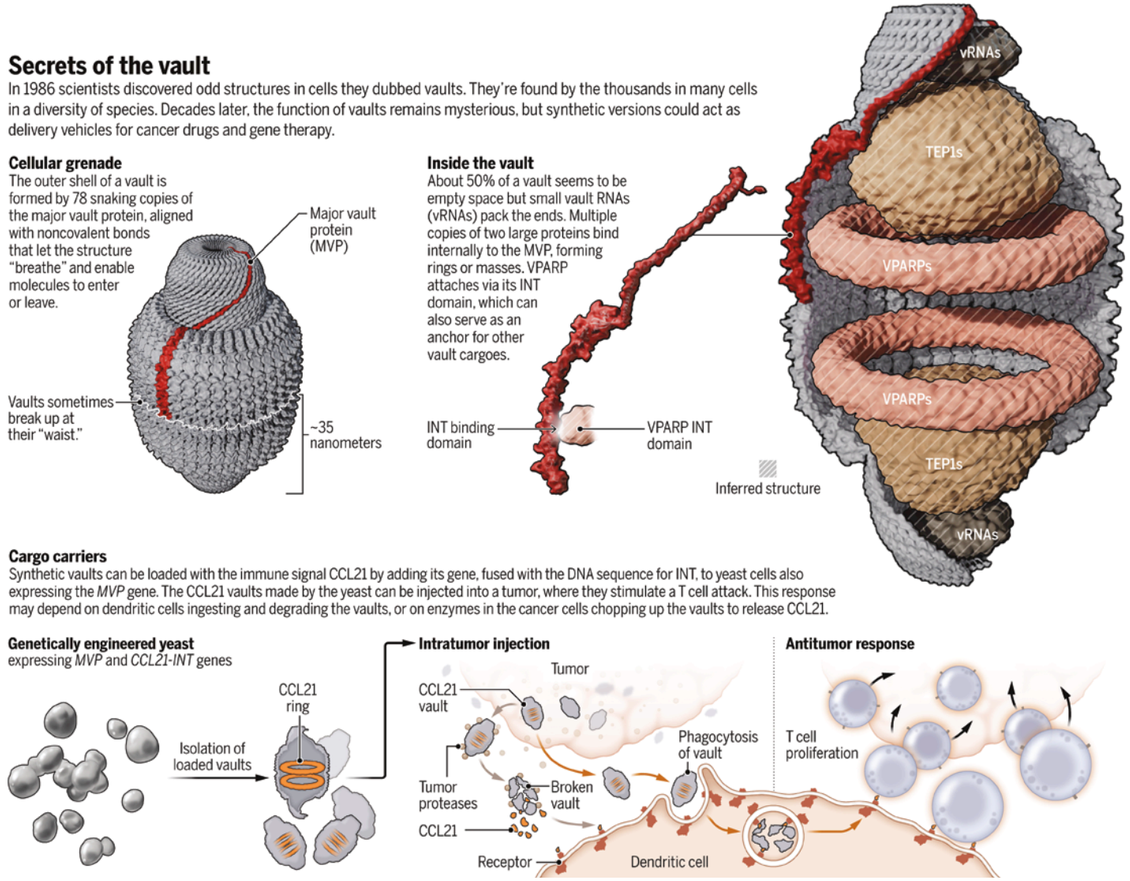
There are now a few ways to add molecules inside synthetic vaults, but Dr. Kickhoefer, a molecular biologist and biochemist, developed what has become the favored method. One of the proteins inside vaults, VPARP, has a domain called INT that binds to an interior-facing bit of MVP. When Dr. Kickhoefer grafted INT onto other proteins, by adding the DNA for it to their genes, the modified molecules slid into the empty vaults.

More than a decade ago, a biotech company licensed Dr. Rome's work from UCLA, hoping to use vaults to deliver cancer drugs. But it abandoned the

Dr. Rome went all in on vaults, shedding other lab projects. In 2014, his lab showed vaults are made in an unusual way, by an assembly line of ribosomes.

SPENCER LOWELL/TRUNK ARCHIVE

Dr. Rome prepares a grid that will hold a sample of vaults under an electron microscope.



A. FISHER/SCIENCE; (DATA) H. ZOU ET AL., STRUCTURE 26:4 (2018)

effort, and in 2013 UCLA reclaimed the intellectual property and Dr. Rome launched Vault Pharma to pursue this strategy himself with CCL21 and other potential drugs. Then a corporate takeover in 2018 dealt a devastating blow. Vault Pharma had partnered with a firm called Protein Sciences to develop a commercial process to make loaded vaults in insect cells. But weeks before production of CCL21 vaults was scheduled to start, a company that had little interest in the project bought Protein Sciences and the vaulters were suddenly cut off.

It's taken years to recover, says Oliver Foellmer, Vault Pharma's CEO. With help again from Dr. Kickhoefer, now semiretired herself, Vault Pharma crafted an arguably simpler, better way to mass produce vaults to clinical trial standards. They add the human MVP gene and the gene for the desired cargo, tweaked to include INT, into yeast cells so that loaded vaults are made in one fell swoop. "We can make vaults now by the gram, perhaps kilograms," Dr. Rome says.

Yet Vault Pharma still needs to raise $10 million or so to conduct its CCL21 cancer trial.

Amid a broad cooldown in biotech investing, venture funds and larger drug and vaccine companies have been reluctant to pick up the trial's tab.

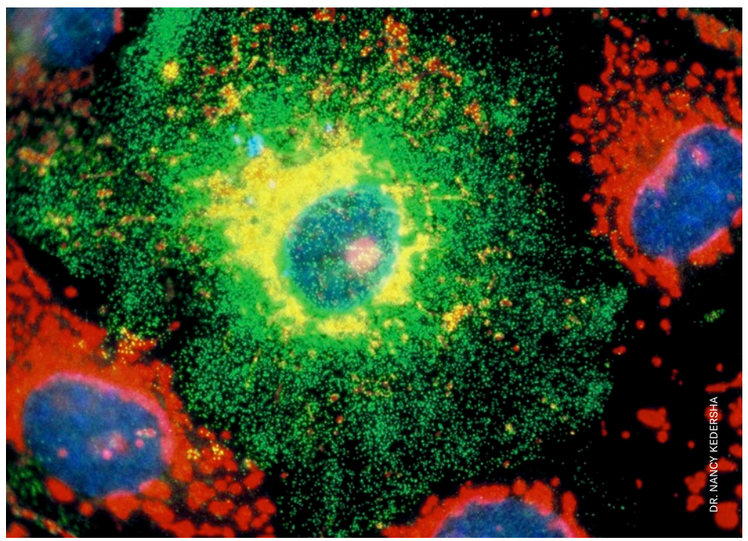
UNDAUNTED, DR. ROME HAS OTHER POSSIbilities in mind for vaults. One is helping gene therapy address a major hurdle. The strategy often relies on typically harmless viruses known as adeno-associated viruses (AAVs) to deliver therapeutic genes. But it's tough to target AAVs to individual tissues. Worse, AAVs often don't work because many people — 40% by one estimate — have already been exposed to the viruses naturally and make antibodies targeting them. "The preformed immunity seems a real showstopper," says David Curiel, MD, PhD, a gene therapy researcher at Washington University in St. Louis. And even patients who don't have detectable levels of AAV antibodies can have dangerous, even deadly, immune reactions if physicians use high doses of the virus to ensure enough of a gene is delivered.

Several years ago, Dr. Curiel and his PhD student, Logan Collins, were brainstorming ways to "stealth" the delivery of an AAV into a patient's cells when Collins recalled reading about vaults. "It might have been middle school or high school, maybe on Wikipedia," he says. "I was so fascinated by their ability as a capsule to hold things." Attaching targeting molecules such as antibodies to the exterior of vaults might also allow them to be directed to specific tissues.

Dr. Curiel had heard of vaults, too, and Collins proposed they try to jam AAVs into one. The idea sat unexplored, however, until Dr. Curiel reached out to Dr. Rome about two years later. Dr. Rome, too, had long thought vaults could be a gene-therapy vector or carry mRNA for vaccines — substituting for the lipid nanoparticles in COVID-19 shots, for example. But he and others have had trouble getting synthetic vaults to hold gene-length DNA or RNA.

Over a Zoom chat, Dr. Rome updated Collins and Dr. Curiel on vaults, and they in turn described a potential way to get a virus to stick inside the structure: a "molecular glue" Dr. Curiel's lab had previously developed. Collins used it to stick INT to the surfaces of AAVs so they latch onto MVP inside vaults. Then he mixed the viruses into a solution of synthetic vaults Dr. Rome had shipped from UCLA.

The surprisingly simple plan worked, the team reported in a preprint first posted in November 2023. Under the right conditions, an AAV or two would slip into a vault and stay there. And when those vaults were added to cells, the viruses released their genetic cargo, allowing it to be expressed. As important, when the cells were surrounded with AAV-targeting antibodies, the vaults slipped by them like a stealth aircraft. Dr. Curiel thinks the tactic has a real chance to solve the AAV immunity problem.



Vaults (green dots) populate most animal cells by the thousands, including these monkey kidney cells.

> "The optimist in me is that before I die someone will figure out what vaults do."

THE CLASSIC CELL BIOLOGY TEXTBOOK, *Molecular Biology of the Cell*, hasn't mentioned vaults in any of its seven editions, which span 40 years, says UC San Francisco cell biologist Bruce Alberts, PhD, an original and current author. Dr. Alberts doesn't doubt that vaults could be vital in some way, perhaps serving some very specific function that's hard to replicate in the lab. "For example, vaults may be part of the massive war with viruses, enabling cells and organisms to survive a type of virus that we don't even yet know anything about," he says. But Dr. Alberts says he and his textbook co-authors don't like to flood students with unknowns, so vaults haven't made the cut.

Dr. Kedersha finds that omission "sad." Even a few paragraphs on the vault mystery in the renowned tome might have inspired a reader to come up with a solution. "Science isn't a compendium of facts; it's a process," she says. But she's not losing sleep over it. The stress granules she discovered are in textbooks. "That's a win," she laughs.

As for Dr. Rome, he doesn't regret devoting a career to chasing what some might see as a white whale. He still has a list of about a half-dozen potential vault functions that intrigue him. And he acknowledges one more possibility: Perhaps they don't do anything. Instead, they may simply be "rocks" that a cell can mine for amino acids in times of need.

Hoping to inspire a new generation of vaulters — and shake loose a few more ideas — he launched a series of online videos in 2024. On "The Vault Guy," his YouTube channel, Dr. Rome mixes jokes and cartoonish animations with serious discussions of scientific methods, funding and publishing. With a little more than 1,000 subscribers to date, the series isn't exactly going viral. But some viewer just might be the person who finally solves the great mystery.

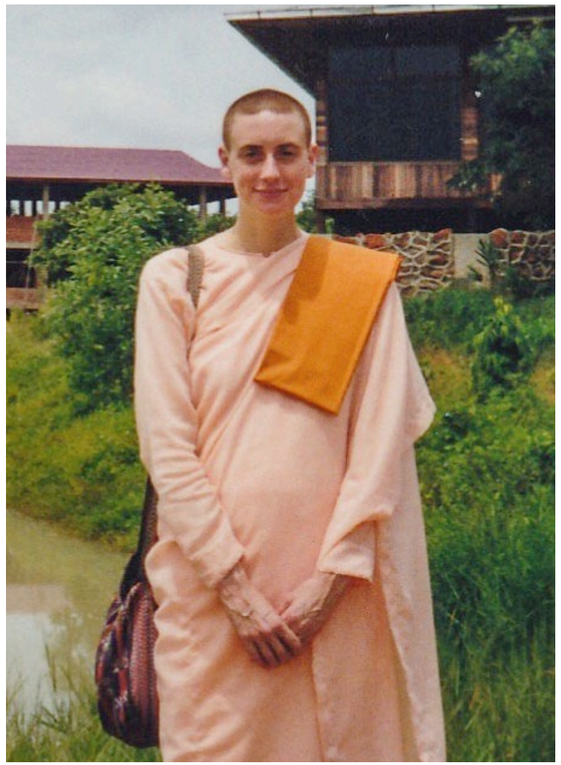
"The optimist in me is that before I die someone will figure out what vaults do," Dr. Rome says.

John Travis *is managing news editor for* Science, *in which this article originally was published (Volume 384, Issue 6700). It has been updated and is reprinted with permission from the American Association for the Advancement of Science.*

A Mindful Visionary

By Sandy Cohen

MILO MITCHELL



COURTESY OF DIANA WINSTON

As educational director of the UCLA Mindful Awareness Center and director of UCLA Mindful, Diana Winston has brought meditation practice to thousands. As a Buddhist nun in Myanmar (right), she sought her own enlightenment.

LONG BEFORE DIANA WINSTON brought meditation practice to thousands as director of UCLA Mindful, she was ordained as a "bhikkhuni" — a Buddhist nun. And before that, two pivotal experiences shaped her interest in meditation and her future path.

The first was while traveling through Asia after graduating from Brown University. Winston joined friends at a meditation retreat in Dharamsala, India, where she heard a teaching that spoke to her deeply. It was a discussion about common preoccupations that trap human beings in suffering — praise and blame, pleasure and pain, gain and loss, fame and disrepute — and how meditation was a way out. "I heard it, and I was, like, 'This explains my life,'" recalls Winston, who had up to that point been doggedly pursuing success and perfection. "From there, I started diving deeply into meditation practice."

That led to her next illuminating experience, which came during a meditation retreat. Winston was part of a contingent that met the Dalai Lama. He directly addressed her interest in the intersection of meditation and social justice, characterizing mindfulness practice as an act of service and a way of cultivating a more peaceful world. "That experience is one of the most guiding moments of my life," she says.

That insight from the Dalai Lama would inform the trajectory of Winston's life and fuel her passion for sharing secular mindfulness, which she's done at UCLA since 2006. From her earliest days of learning mindfulness — the practice of intentionally paying attention to present-moment experiences with curiosity and kindness as a way of becoming familiar with the nature of the mind — Winston wanted to share it. Initially, she focused on mindfulness practices to support political activism.

Winston was working with the Buddhist Peace Fellowship in Northern California when her meditation teacher suggested she go to Myanmar (formerly known as Burma) to continue her studies, and even become ordained as a Buddhist nun. Winston secured a meditation visa and found herself in an ancient monastery in the Burmese jungle. Deeply committed to the practice, she meditated 16-to-18 hours a day, breaking only for sleep and two meals before noon each day. She was ordained, shaved her head and wore salmon-colored robes. "I want to get enlightened," she remembers thinking. "And if I practice the way it's been done for thousands of years, particularly as a Buddhist nun, I should be getting enlightened by January."

The pressure she put on herself to achieve enlightenment wasn't unlike the perfectionism that drew her to seek relief in meditation in the first place. Yet, she found that the harder she tried, the more difficult everything became. She was about to give up monastic life when she stumbled upon a Tibetan Buddhist text that introduced her to a different approach to meditation, far less rigid than the style she'd been practicing. Where she was struggling to reach enlightenment, this book said the mind was already free. All she had to do was tap into her inherent awareness. "It was like the balm to my crazy, competitive soul," she says.

Those teachings would go on to guide her future work, including writing *The Little Book of Being: Practices and Guidance for Uncovering Your Natural Awareness*, published in 2019. Winston eventually left the monastery, taught meditation at an elementary school in India and traveled to Sri Lanka. After returning to the U.S., she was invited to train with Jack Kornfield, PhD, a former Buddhist monk who helped pioneer mindfulness teachings in the West in the 1970s. Winston has, Kornfield says, "a visionary spirit."

"From the beginning, she has cheerfully worked to pass on the practices that changed her life, starting with teens and moving on to all who could benefit," he says. "UCLA is lucky to have her."

UCLA behavioral genetics researcher Sue Smalley, PhD, saw something special in Winston, whom she met while studying the effects of mindfulness training on adolescents with ADHD. When Dr. Smalley later created the Mindful Awareness Research Center (MARC) at UCLA, she invited Winston to serve as its educational director.

Winston helped build the MARC program, developing public courses in mindful awareness practices that have reached thousands of people worldwide and been studied by academic researchers at UCLA and other institutions. She also helped create the UCLA Mindful app, which offers free meditations in 19 languages. Since 2023, Winston has been director of UCLA Mindful, which promotes mindfulness education within the UCLA Health System and beyond. She continues to lead free weekly meditation sessions and classes for the public, along with paid programs for those seeking more in-depth study.

When MARC began, few universities offered mindfulness instruction, and even fewer offered courses for the public, says Marvin G. Belzer, PhD, who leads sessions for UCLA Mindful and taught a semester-long undergraduate course on mindfulness practice and theory at UCLA before retiring in 2023. "Diana was the visionary" behind MARC's public-facing classes, Dr. Belzer says. "Radical accessibility of these mindfulness practices was part of the mission from the beginning."

Winston also created a yearlong mindfulness teacher-training program at UCLA, which has more than 550 graduates since 2011, and is a founder of the International Mindfulness Teachers Association, which upholds credentialing and training standards for mindfulness educators worldwide.

After devoting her life and career to mindfulness, Winston delights in the growing popularity of the practice. "Twenty years ago, I'm knocking on the door at UCLA saying, 'Hey, there's this thing called mindfulness. It's good. Let me tell you why,'" she says. "Now, so many people know and love mindfulness."

She remains passionate about sharing the practice with anyone who's interested, driven by the idea the Dalai Lama expressed decades earlier: Mindfulness helps people experience greater joy, clarity and wisdom, which ultimately contributes to a more just, compassionate world. "The best part of my job is watching people transform, seeing people's lives get better and better," Winston says. "And it's seeding compassion, seeding wisdom, seeding self-awareness on a larger cultural level."

Sandy Cohen *is a senior writer for UCLA Health Marketing Communications and a former national reporter for* The Associated Press.

For more information about UCLA Mindful, scan the QR code or go to: uclahealth.org/uclamindful

AWARDS & HONORS

Dr. Carol Bennett, professor of urology, received the Jean Fourcroy Leadership Award from the Society for Women in Urology.

Dr. Ronald Busuttil (RES '77), Distinguished Professor of Surgery Emeritus, received the Medawar Prize from The Transplantation Society.

Dr. Robert A. Cherry, UCLA Health chief medical and quality officer, was awarded Physician of the Year by Press Ganey.

Dr. Anne Churchland, professor of neurobiology, received the Pradel Research Award from the National Academy of Sciences.

Dr. Utibe Essien, assistant professor of medicine-in-residence, was named one of 10 Emerging Leaders in Health and Medicine by the National Academy of Medicine.

Dr. Tiki Hayes, assistant professor of molecular and medical pharmacology, received the Lung Cancer Research Foundation Minority Career Development Award in Lung Cancer and the Cynthia M. Page Merit Award for Innovation in Lung Cancer Research.

Dr. Catherine Juillard (MD '05, RES '12), professor-in-residence of surgery, received the American College of Surgeons/Pfizer Academic Global Surgeon Award.

Dr. Fred Kass, UCLA Health oncologist, was named Physician of the Year for Santa Barbara County by the Central Coast Medical Association and received the Breast Cancer Resource Center of Santa Barbara's Healing Through Compassion Award.

Dr. Lisa A. Nicholas, associate professor of obstetrics and gynecology, received the Women in Medicine Award from the National Association Council on Concerns of Women Physicians.

Dr. Antoni Ribas (FEL '98, '01), director of the tumor immunology program at the UCLA Health Jonsson Comprehensive Cancer Center, was inducted in the Class of Fellows of the Academy of Immuno-Oncology by the Society for Immunotherapy of Cancer.

Dr. Mina Sedrak, director of the Cancer and Aging Program at the UCLA Health Jonsson Comprehensive Cancer Center, received the Susan G. Komen Rising Star Research Award.

Dr. Amy Vandiver (RES '22), assistant professor of dermatology, received the Sagol Network GerOmic Award for Junior Faculty.

$20 million gift establishes UCLA Saul and Joyce Brandman Foundation Center for Lung Health

By Christi Carras

TODD CHENEY/UCLA PHOTOGRAPHY

Joyce Brandman (left) and Dr. John Belperio.

UCLA Health has received a $20 million donation from the Saul and Joyce Brandman Foundation to create a lung health center for pulmonary disease research, prevention and treatment. The UCLA Saul and Joyce Brandman Foundation Center for Lung Health, named after the longtime philanthropists and supporters of the university, will also function as a training destination for scientists and physicians studying lung disease.

"There's nothing more important than our research," said Joyce Brandman, who established the center in honor of her late husband, Saul Brandman. "Because if we don't have the research, then what do we have?"

The formation of the center comes at a crucial moment for Los Angeles, which this past winter was devastated by wildfires that have spurred widespread concerns about air quality and long-term wellness. General awareness and interest surrounding respiratory illness has also increased significantly in the wake of the COVID-19 pandemic.

Dr. Steven M. Dubinett (RES '84), dean of the David Geffen School of Medicine at UCLA and associate vice chancellor of UCLA, deemed the foundation's gift "both transformational and timely, given the effects of the California wildfires on air quality and lung health."

One of the center's priorities is to evaluate risk among individuals who have an elevated exposure to environmental hazards, such as air pollution, in pursuit of novel interventions. "I always think of these issues with lungs for older people, but that's not necessarily so," Brandman said. "Why couldn't it happen to a child, with all of this in our air? I do know that if they are patients at UCLA, their doctor will do everything they possibly can."

In addition to funding research, training, fellowships, equipment, symposia, therapeutic development and other activities, the gift from the Brandman Foundation will also be used to endow an administrative chair reserved for the director of the center, as well as a pair of term-appointment chairs supporting faculty in the UCLA Division of Pulmonary, Critical Care, Sleep Medicine, Clinical Immunology and Allergy. One term-appointment chair will focus on lung health acceleration while the other will explore lung health innovation.

The center is also expected to expand patient access to clinical trials and harness emerging technologies to help determine risk of lung cancer, interstitial lung disease, chronic obstructive pulmonary disease (COPD) and other conditions.

Dr. John Belperio, chief of the Division of Pulmonary, Critical Care, Sleep Medicine, Clinical Immunology and Allergy and Guitiara Pierpoint Endowed Chair in Interstitial Pulmonary Fibrosis, will serve as the center's inaugural director. "The extraordinary effect of this gift on our research and community cannot be overstated," Dr. Belperio said. "This vital support will empower our team to make significant advancements in a stunning array of areas, from risk prediction and early disease detection to drug efficacy and lung transplantation. The City of Los Angeles and the field of pulmonary medicine owe the Saul and Joyce Brandman Foundation a debt of gratitude."

Brandman dedicated the lung health center to her husband, who had COPD and other respiratory issues. She recalled paying for extra seats on flights to accommodate her husband's oxygen tank so that they could travel and make the most of their final years together. What motivates Brandman to invest in pulmonary disease research is a desire to prevent others from experiencing what her husband went through.

"He knew when his quality of life was over," Brandman said. "What are you going to do but accept it? He had to accept it. I had to accept it. And life does go on. But I know he would be so happy to see the research that John is going to be doing with the money we're giving."

Physician-scientists at the center will investigate various causes of lung diseases in order to develop new prevention strategies, diagnostic tests and treatments. They plan to take an equitable approach to their research, working to address health disparities that make pulmonary illness more prevalent among veterans and under-resourced communities.

The foundation's investment will also enable UCLA to open a fund supporting the creation of the center and research initiatives overseen by its director, as well as a fund advancing the work of the Saul Brandman Endowed Chair in Pulmonary Arterial Hypertension, currently Dr. Richard Channick. "As someone whose work has directly benefited from the Brandmans' generosity and passion for pulmonary care, I can personally attest to the life-changing impact of their contributions," Dr. Channick said. "This visionary project, which will cultivate generations of leaders in the field, is in good hands."

An active and philanthropic member of the Jewish community, Brandman has served on the boards of American Friends of the Hebrew University, Beit T'Shuvah, Brandman University, Eisenhower Health and Los Angeles Jewish Health, as well as the McCallum Theatre, the UC Riverside Foundation and the Brandman Centers for Senior Care.

This marks the single largest donation from the Saul and Joyce Brandman Foundation to UCLA over three decades of giving to various health initiatives and beyond. The family's legacy also encompasses the Saul and Joyce Brandman Breast Center at Cedars-Sinai Medical Center and the Brandman Centers for Senior Care at Los Angeles Jewish Health. "I probably hope to accomplish much more than can be done," Brandman said. "All we can do is continue with our research. Because the research will tell us where we're going to go and where we're going to end up."

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

Christi Carras *is a senior writer for UCLA Health Sciences Development.*

TODD CHENEY/UCLA PHOTOGRAPHY

(From left) Hilton Chodorow, Dr. Dale Abel, Dr. Richard Channick, Dr. John Belperio, Joyce Brandman, Dr. Steven M. Dubinett, Jeff Raich, Michelle Rubin and Dr. Eric Esrailian.

UCLA Rape Treatment Center Celebrates 50th Anniversary

By Allie McFarland

GETTY IMAGES

(From left) Johnese Spisso; UCLA Chancellor Julio Frenk and his wife, Dr. Felicia Knaul; and Dr. Jane Halladay Goldman.

Friends of the Rape Treatment Center (RTC) at UCLA Santa Monica Medical Center gathered to celebrate its 50th anniversary on October 27, 2024, at the Skirball Cultural Center. The event also raised crucial funds for the RTC and Stuart House, the latter of which provides care for sexually abused children and their families.

Chair of the Rape Treatment Center Advisory Board Paige Adams-Geller opened the program by welcoming attendees and introducing special guest Connie Britton, an Emmy- and Golden Globe-nominated actress. Britton focused her remarks on the RTC's role in changing the cultural narrative around rape and sexual assault. She noted Rape Treatment Center founder Gail Abarbanel's work with legendary television producer Norman Lear to bring awareness of sexual violence to millions of Americans.

Britton concluded with an inspiring call to action: "As we enter into our next 50 years of transformative work, let's join together to get the word out so everyone knows that this incredible place exists and is available, and so that no one ever has to be marginalized, isolated and alone in the horror of sexual assault again."

Johnese Spisso, MPA, president of UCLA Health, CEO of the UCLA Hospital System and associate vice chancellor of UCLA Health Sciences, followed Britton, thanking attendees and acknowledging Abarbanel's long-time service to survivors of sexual violence. She also reaffirmed UCLA Health's commitment to the RTC and Stuart House. Said Spisso, "We will continue to uphold the transformative legacies of these programs, ensuring that everyone in our community has access to preeminent care for sexual assault."

Spisso introduced Dr. Jane Halladay Goldman, director of the Rape Treatment Center and Stuart House. Dr. Halladay Goldman, who began her career as a receptionist at Stuart House, reflected on the progress the RTC has made over the past five decades. She detailed the program's close partnerships with law enforcement to help victims achieve justice and government agencies to shape policy related to sexual violence. Leaders in both of these spheres were in attendance, including Los Angeles Police Chief Jim McDonnell and Los Angeles County Supervisor Lindsay Horvath.

Other speakers included special guests Saffron Burrows and Melina Kanakarades; Mimi Morningstar, senior director of development of the Rape Treatment Center; and Eula Smith, vice chair of the Rape Treatment Center Advisory Board. They described how the RTC and Stuart House have changed the trajectories of victims' lives, from individual care to legal advocacy.

Adams-Geller again took the stage toward the end of the program to tell her own story of sexual assault and how the RTC supported and empowered her during a difficult time. She described her relationship with Jane Willens, a tennis star turned social worker, who devoted her entire counseling career to survivors of rape and sexual assault.

Willens passed away unexpectedly in December 2023. To honor her memory, the RTC established the Jane Willens Award to recognize extraordinary acts of service in the community. Beth Cranston, legal counsel for the Rape Treatment Center, presented the inaugural award to Darrell Preston. Preston, a restaurant owner, provided key evidence in a high-profile rape and murder case that happened along the Venice canals in 2024. Mary Klein, the surviving victim of the crime, joined Preston on stage in an emotional moment.

To end the day on an upbeat note, attendees pledged their support in a live fundraiser. The event was a success, bringing in more than $1 million for RTC and Stuart House programs.

For more information, contact Mimi Morningstar at: 310-770-2888

Allie McFarland *is a senior writer for UCLA Health Sciences Development.*

UCLA Health Center for East-West Medicine Raises $3 Million for Integrative Care

By Christi Carras

TODD CHENEY/UCLA PHOTOGRAPHY

(From left) Roland Tellis, Johnese Spisso, Beth Friedman, Dr. Katie Hu, Dr. Ka-Kit Hui and Gerard Bush.

The UCLA Health Center for East-West Medicine (CEWM) raised over $3 million for integrative care during its yearlong 30th anniversary campaign, which culminated in December in a special event at Chelsea Restaurant in Santa Monica. The event, marking three decades since the inception of CEWM, was hosted by UCLA Santa Monica Medical Center Board Member Roland Tellis and co-chaired by UCLA Health System Board Co-Chair Beth Friedman.

"This place holds a very special place in my heart. Yes, as a donor and supporter, but more importantly as a patient whose life has been profoundly touched by the care I receive here," Friedman said of the Center for East-West Medicine. "Many of you know that I've been a longtime believer in the power of integrative medicine. But it wasn't until I came to the center that I truly understood its transformative potential."

The event opened with a performance by UCLA's Jade Lotus Dance team — a student-led troupe that celebrates Chinese and Vietnamese culture through movement — followed by remarks from CEWM leaders and a reception with food, drinks, sugar painting, calligraphy, herbal tea and more.

Other distinguished participants included Dr. Ka-Kit Hui (MD '75, RES '78), founder and director of CEWM and Wallis Annenberg Endowed Chair in Integrative East-West Medicine; Dr. Edward Hui (MD '01, RES '04, FEL '06), clinical chief of CEWM; Gerard Bush, integrative medicine ambassador for UCLA Health; and Johnese Spisso, MPA, president of UCLA Health, CEO of the UCLA Hospital System and associate vice chancellor of UCLA Health Sciences. East-West medicine faculty — including Dr. Sara Ptasnik (FEL '23), Dr. Ricky Chang (FEL '21) and Dr. Andrew Shubov (FEL '15) — and board members from UCLA Health and the UC Board of Regents were also in attendance.

"As we celebrate 30 years of integrative East-West medicine at UCLA under the vision and leadership of Dr. Ka-Kit Hui, we are excited to continue his legacy of transforming lives through the continued expansion of clinical services, the growth of our research portfolio [and] the diversification of our educational offerings," said Dr. Katie Hu (RES '15, FEL '17), associate director of CEWM.

Dr. Hu added that proceeds from the fundraising campaign will allow the center to bring integrative care to new populations, including adolescents and under-resourced communities. CEWM recently launched the East-West Pediatric Program, which will collaborate with national and global pain and mental health experts to create specialized education materials for children and their families and/or caregivers. The program will also expand access to integrative health services for children and community health partners.

CEWM comprises four stand-alone clinics across Los Angeles County and an inpatient consult service at UCLA Santa Monica Medical Center. It is home to 20 physicians and 10 acupuncturists. Trained in both conventional biomedicine and traditional Chinese medicine, CEWM physicians collaborate with primary care providers and UCLA Health colleagues of various disciplines to improve patients' health and optimize wellness.

In anticipation of the center's 30-year milestone, UCLA Health recently created the Ka-Kit Hui Legacy Fund for Excellence in East-West Medicine. The center plans to use the funds to train a wider range of health care professionals and enhance collaboration across the university's academic medical network. Donations to the fund will also support the development of targeted health and education programs serving local communities.

For more information, contact Noah Green at: 424-325-8184

Christi Carras *is a senior writer for UCLA Health Sciences Development.*

DONATIONS & GIFTS

PROUD SIBLINGS HONOR THEIR FATHER'S WORK

TODD CHENEY/UCLA PHOTOGRAPHY

(From left) Dr. Kamal A. Batniji; Dr. Steven M. Dubinett, dean of the David Geffen School of Medicine at UCLA; and Dr. Dinesh Chhetri.

The UCLA Department of Head and Neck Surgery celebrated the installation of Dinesh K. Chhetri, MD, as the inaugural holder of the Kamal A. Batniji, M.D., Endowed Chair for Humanitarian Care and Innovation in Laryngology and Head and Neck Surgery. The chair was established thanks to the generous philanthropy of siblings Rami Batniji and Rola Batniji Gordon to honor and recognize their father, his career and his lifelong commitment to professional service. "Our father has always been a pioneer in shaping the field of head and neck surgery in Los Angeles and was an integral pillar of the UCLA Head and Neck Surgery program in its formative years," Batniji and Batniji Gordon said. "We always envisioned the chair holder as someone who would serve the local community while also advancing global otolaryngology care." Dr. Chhetri, professor and department vice chair, is known internationally as an academic laryngologist and head and neck surgeon and is passionate about training surgeons throughout the world.

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

UCLA WOMEN'S CARDIOVASCULAR CENTER INSPIRES CONTINUING PHILANTHROPY

Dr. Marcy Gringlas, Joel Greenberg and their Seed the Dream Foundation continue to bolster the UCLA Women's Cardiovascular Center (WCC) with a three-year pledge to support its cardiac psychology program. Dr. Gringlas, a grateful patient and survivor of heart disease, and Greenberg helped launch the program in 2020 out of a strong belief in the WCC's mission to prevent heart disease. "The foundation's support has been instrumental to the center's success," said Dr. Karol E. Watson (RES '92, FEL '97, PhD '98), director of the WCC. "Now, at our 10th anniversary, this gift will ensure continued excellence in women's cardiovascular care for years to come." The latest commitment supports cardiac psychologist Dr. Anne Saltzman, who consults with patients to assess and treat health factors including emotional stability, level of support and quality of sleep. This holistic approach has been shown to decrease depression, anxiety and stress and improve overall health, all of which are paramount to long-term prevention, and treatment after a cardiovascular incident. "I am deeply grateful to Marcy and Joel for their generosity and belief in the power of holistic care," Dr. Saltzman said. "When we discuss the fears and challenges related to a major health issue, patients are better able to focus on improving their well-being and healing with happiness and humor."

For more information, contact Lindsey Walton at: 424-946-6102

ADVANCING BRAIN CANCER RESEARCH

Heart of the Brain raised $1.5 million for the UCLA Brain Tumor Center as part of the Los Angeles foundation's annual walk, Solefully Committed to Finding a Cure. The funds will support efforts to improve treatment for oligodendrogliomas, an uncommon type of brain tumor. Becky and Michael Neidorf founded Heart of the Brain in honor of their daughter, Isabel Neidorf, a cancer survivor who was diagnosed with an inoperable oligodendroglioma when she was 4 years old. The organization hosted the 2024 Solefully Committed walk in November on the UCLA campus, bringing survivors, families, advocates, health care professionals and community members together to raise awareness and money for brain cancer research. Proceeds from last year's event will benefit investigations overseen by Dr. Linda Liau (RES '97, FEL '98, PhD '99), chair of the UCLA Department of Neurosurgery, and Dr. Timothy Cloughesy (RES '91, FEL '92), director of the UCLA Neuro-Oncology Program.

GABRIEL MORA

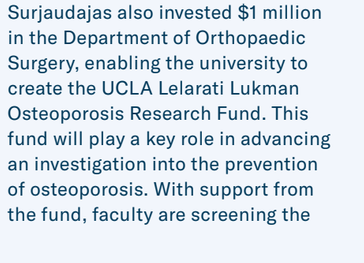
(From left) Dr. Timothy Cloughesy, Isabel Neidorf and Dr. Linda Liau.

For more information, contact Chantelle Eastman at: 310-562-9566

ELEVATING GERIATRIC CARE

The Schuman Family Foundation has gifted $2.6 million to the UCLA Innovation in Geriatric Medicine Fund benefiting the David Geffen School of Medicine at UCLA. Laura Schuman, president of the foundation, said that the family wished to recognize her father's legacy by supporting what she deemed an exemplary program that excels in caring for the aging community. Schuman also endorsed the vision of Dr. Brandon Koretz (RES '99, FEL '00), clinical professor of medicine in the Division of Geriatrics, holder of the Carol and James Collins Endowed Chair in Geriatric Medicine and director of the fund. "The great irony in geriatric medicine is that in order to provide the best possible care for the generation that came before us, we need to invest in the generation that's coming after us," Dr. Koretz said. "Ultimately, our goal is to drive groundbreaking discoveries that will significantly improve the lives of older adults and their loved ones."

For more information, contact Linda Gonzalez at: 626-558-8472



BROOKS TAYLOR

(From left) Margaret Preissman, Ronald Preissman, Irv Zuckerman, Christine Zuckerman, Dr. Brandon Koretz, Tracey Gluck, Henry Gluck and Laura Schuman.

ACCELERATING DISCOVERY IN DEMENTIA AND OSTEOPOROSIS

UCLA research in dementia and osteoporosis will be bolstered by a gift totaling $2 million from the Surjaudaja family. The family, who founded Indonesia-based laboratory clinic Biotest and Bank OCBC Indonesia, contributed $1 million to the Department of Neurology to help establish the UCLA Karmaka Surjaudaja Dementia Research Fund. Resources from the fund will support innovative research, including a study to determine genetic risk factors for Alzheimer's disease. The Surjaudajas also invested $1 million in the Department of Orthopaedic Surgery, enabling the university to create the UCLA Lelarati Lukman Osteoporosis Research Fund. This fund will play a key role in advancing an investigation into the prevention of osteoporosis. With support from the fund, faculty are screening the

COURTESY OF THE SURJAUDAJA FAMILY

Lelarati Lukman (right) and her late husband, Karmaka Surjaudaja.

levels of estrogen and vitamin D in female UCLA student-athletes to identify potential avenues to prevent and treat osteoporosis earlier in life.

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

GRATEFUL FAMILY SUPPORTS EARLY CAREER PULMONOLOGIST, RESEARCHER

The UCLA Division of Pulmonary, Critical Care, Sleep Medicine, Clinical Immunology and Allergy has received a $50,000 gift from the Salkin family, facilitated by Judge Valerie Salkin, to establish the Dorothy Salkin Memorial Fund. The Salkins were deeply touched and impressed by the care Dr. Lawrence N. Benjamin (FEL '22, PhD '24) provided Dorothy in her final days. Dr. Benjamin, a junior faculty member and researcher, will oversee the fund, which allocates crucial resources for his pulmonary investigations currently focused on increasing equitable access to lung cancer screenings. The new fund honors Dorothy's memory and is a testament to Dr. Benjamin's exceptional skills. The family looks forward to staying connected to Dr. Benjamin and continuing the meaningful association that began with Dorothy's care.

For more information, contact Larissa Harrison at: 310-592-5613

PRIYANKA KUMAR

Judge Valerie Salkin (left) and Dr. Lawrence N. Benjamin.

SUPPORTING WOMEN'S HEALTH RESEARCH

Nancy and Howard Marks have invested $5 million to endow a faculty chair in the UCLA Department of Obstetrics and Gynecology. The Nancy Marks Endowed Chair in Women's Health Research will enable the department to make significant advancements in reproductive care and

TODD CHENEY/UCLA PHOTOGRAPHY

(From left) Dr. John C. Mazziotta, Johnese Spisso, Dr. Beth Karlan, Nancy Marks and Howard Marks.

recruit physician-scientists leading the field. Dr. Beth Karlan (FEL '89), vice chair and professor of obstetrics and gynecology at the David Geffen School of Medicine at UCLA, has been appointed the inaugural chair holder. She is known for her work improving the detection, treatment and prevention of ovarian cancer and other gynecologic malignancies. During a recent event celebrating the establishment of the Marks Chair, Nancy Marks lauded Dr. Karlan's comprehensive body of work and noted that she has been her physician for more than 20 years. "Beth has something that sets her apart," Marks said. "She's developed a secret sauce that she shares with her patients. Dr. Beth Karlan is the dispenser of hope. In addition to all of her skills and talents, Beth infuses her patients with the belief that they can and will conquer their disease, and that's what separates her from the pack." The Markses have requested that the endowed chair be renamed in Dr. Karlan's honor when she retires.

For more information, contact Molly Moursi at: 424-273-9118

When a Cough is More than Just a Cough

By Constance Meyer

I SPENT MANY YEARS WORRYING ABOUT CANCER since my mother died from ovarian cancer when she was 45 years old, and her mother died from breast cancer when she was just 35. But I never gave much thought to heart disease. That, I believed, was a man's disease. I am 72 years old, physically fit, with blood pressure and cholesterol that always have been super low, and I walk three-to-five miles daily.

Then, in the spring of 2023, for no apparent reason, I started coughing non-stop. It was a dry, unproductive cough that at times left me doubled over and had me apologizing to anyone within earshot for the racket I was making.

I ignored it for a few weeks, thinking it would go away, and then went to see my doctor, who chalked it up to asthmatic bronchitis. With oral prednisone and an inhaler, the cough simmered down — briefly, before coming back with a vengeance.

I went back to ignoring it.

A year went by, and I saw a different doctor, who put me on Flonase, an anti-allergy nasal spray. "Sometimes older people get a cough," she said.

Still, the cough persisted, and more doctors' visits followed. The pulmonologist I saw promised to throw everything, "including the kitchen sink," at it. Suspecting it was asthma, he put me back on albuterol and Flonase.

I am a violin teacher, and many of the parents of my students were concerned about my persistent cough. One of the parents, a doctor, said to me, "You're going to give me a heart attack hearing that cough."

My visits to doctors continued to see-saw back and forth. A CT scan of my lungs did show some abnormalities, a cloudy area at the bottom of my right lung referred to as "ground glass." An ENT also thought I had asthma, but also acid reflux, and she put me on a restricted diet to guard against gastroesophageal reflux disease — an unwelcome change since, as a pescatarian, I already adhere to a limited diet.

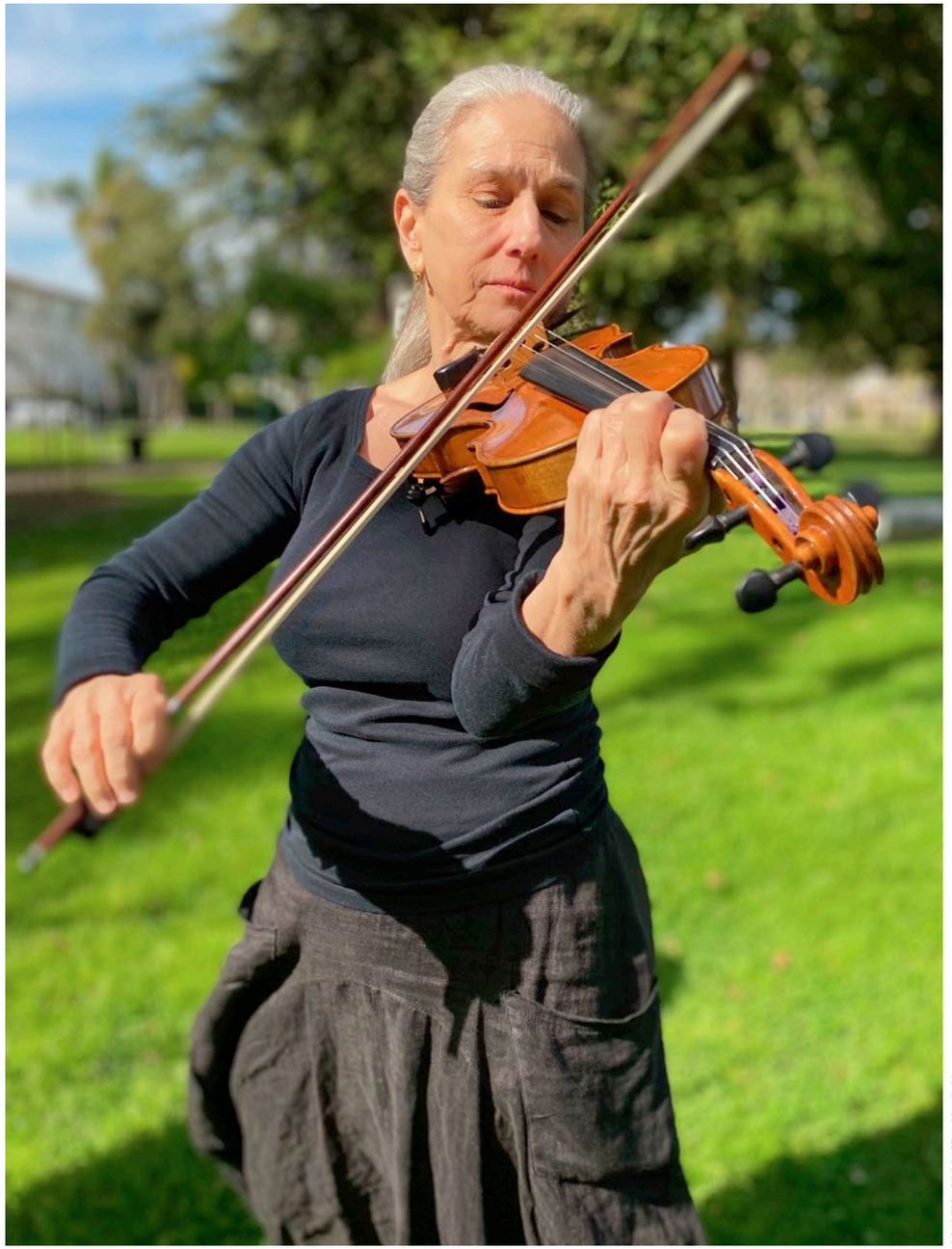
More medications were added to my growing list.

After a summer vacation with our extended family, during which my cough continued to make itself alarmingly evident, I went back to the doctor. During the visit, I remarked somewhat offhandedly that there was a history of heart disease on both sides of my family. "Let's get you checked out by a cardiologist," she said. I made an appointment at UCLA for the next available date, which was a few weeks later.

In the meantime, I mentioned to a new student's mother, Megan Kamath (MD '11, FEL '18), who is a cardiologist at UCLA and assistant clinical professor of medicine in the David Geffen School of Medicine at UCLA, that I would be seeing someone in her department in a couple of weeks. "Would you mind if I got you in sooner?" asked Dr. Kamath, who is an advanced heart failure specialist. "Why the rush?" I responded. "I've been wondering if your cough is connected to a heart issue," she said.

Things evolved quickly from there. A CT scan of my heart revealed an abnormality, and the doctor put me on a statin medication. I then had a stress test, which I was told would last about an hour. "Do you have any chest pain?" I was asked a few times. "None," I replied. Suddenly, the test was stopped, which I took as a bad sign.

A couple of hours later, while I was teaching, I got a call to say that the test was abnormal, and that I should immediately start taking baby aspirin and double my dose of statins. I was in shock. I didn't think I'd have a heart condition; I was always waiting for the shoe to drop with cancer. An angiogram to view the coronary arteries was scheduled, which revealed a severe blockage, 90-to-99%, in one of the major arteries.



COURTESY OF CONSTANCE MEYER

Constance Meyer spent years worrying about cancer after her mother's death at an early age. She never imagined her persistent cough might signal heart disease.

Even though I was still coughing my head off, I now had greater concerns occupying my thoughts.

On September 17, I underwent an angioplasty, during which a slim catheter was threaded through a blood vessel and a stent placed to open the blockage in my heart. As my husband and I drove home from the hospital that same evening, I suddenly realized that my cough was — gone! Not diminished, but completely GONE.

Here's what I've learned: Women can experience symptoms of coronary artery disease very differently than men. A persistent dry cough, for example, can be a symptom that may be more prevalent in women. When none of the medications or special diet prescribed for my cough had any appreciable effect, no one until Dr. Kamath considered that it might be associated with heart disease.

I am fortunate that I didn't have a heart attack, and I'm spectacularly lucky to have a student clientele that includes some doctors among the parents. And I am especially fortunate to have one parent in particular, a cardiologist who once before had a patient with a terrible dry cough that turned out to be the warning sign of a heart problem.

But not every woman with heart symptoms is so lucky. More needs to be done to educate both medical professionals and the public at large about the ways that heart disease can present differently in men and women. Even though I have a history of heart disease in my family — both of my grandfathers died from heart disease, and my father suffered his first coronary when he was 58 and then had two more — I never thought it might affect me. It was, after all, a man's disease, or so I thought. Since my own experience, I've discovered that my maternal aunt also had serious heart disease.

I hope that one day there will be a test for women who are at high risk for heart disease. But it can be a slow evolution: The pap smear, a test for cervical cancer, was invented in 1928, but it didn't become widely used until 1960.

Today, I am very grateful to be alive, and I am indebted to everyone who helped me — particularly to Dr. Kamath. I just hope that other women have an easier time than I did getting heart healthy.

***Constance Meyer** is a veteran session musician who has played on numerous film soundtracks and on recordings with such musicians as Jennifer Lopez and The Jacksons and live orchestral performances with Tony Bennett, the Kirov Ballet, ABT and Joni Mitchell.*

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