

# Dazed and Confused

Why is it so hard to study marijuana?

# **UCSF MAGAZINE**

Summer 2017

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# CAMP BRAINPOWER

High school students from across the Bay Area came to Camp UCSF in April to examine a human brain, help fill teeth, tour labs, study fruit flies, and more. Organized and led by UCSF students, the annual event allows budding scientists to explore careers in health care.

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In April, UCSF faculty, students, and trainees were among thousands of scientists and science advocates across the nation who participated in the March for Science.

Hundreds attended a Stand Up for Science teach-in at Genentech Hall and joined rallies on campus and throughout the Bay Area. The following day, 45 students, postdoctoral scholars, staff, and

faculty traveled to Washington, D.C., to bring our message directly to lawmakers.

Standing up for science is *not* about politics. There is no such thing as "liberal science" or "conservative science."

Standing up for science is about adequate health care. America's great legacy of publicly funded science has safeguarded the health of Americans and many others around the globe. In the years ahead, basic science and clinical research may end Alzheimer's, lead to revolutionary cancer treatments, and unlock solutions to other intractable diseases.

Standing up for science is also about funding. Federal funding for the health sciences benefits every American, but the National Institutes of Health is facing proposed cuts for 2018. UCSF has been a top recipient of NIH funds for many years, and it has been our privilege to fulfill our pact with taxpayers by consistently applying our scientific discoveries to real-world treatments.

In the months and years ahead, we at UCSF will do everything in our power to ensure that Congress maintains America's investment in science, and we will continue to advocate strongly for affordable health care.

I could not be more proud to be part of this incredible scientific community, and I am deeply thankful to know that we will always stand up for science, together.

am Hawgood

Sam Hawgood, MBBS Chancellor Arthur and Toni Rembe Rock Distinguished Professor

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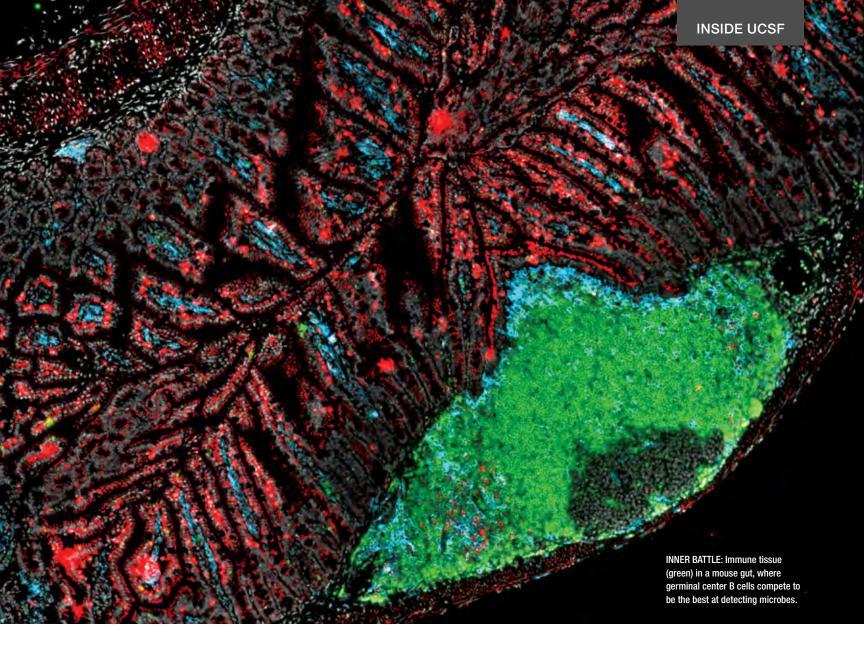
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# **GUTS** and **GLORY**

Everyone knows the story of Darwin's finches: The ones that adapted best to the environment of the Galapagos Islands reproduced and thrived, while those that did not died out.

What's less well known is that our immune system functions in much the same way. Humans' biggest enemies – bacteria and viruses – are constantly evolving, sometimes in as little as 20 minutes. Our immune cells must evolve just as rapidly, or the invading microbes will make us sick.

The gut biome is an especially rich environment in which to study the question of how our immune cells accomplish this rapid evolution. And, as it happens, it's also an especially rich environment visually. A microscopic image of immune tissue in a mouse intestine (above) was recently selected for UCSF's Science in Focus series; the program highlights both the beauty of science and the groundbreaking research behind the chosen images.

This particular image was the work of Lauren Rodda, a UCSF graduate student in biomedical sciences who studies how certain immune cells, called germinal center B cells, accomplish this evolution. In order to match the mutation rate of microbes, they undergo rapid cycles of mutation, proliferation, and selection, promoting the reproduction of those able to make antibodies against encroaching microbes.

This process "mimics the evolution of all organisms that has been going on for eons," says Rodda, who works in the lab of Jason Cyster, PhD, a professor of microbiology and immunology. "The germinal center B cells keep evolving to become better at detecting the microbes precariously poised on the other side of the gut barrier."



## Ask the Expert: The Science of Sleep

Ying-Hui Fu, PhD, a UCSF professor of neurology and a pioneer in the study of sleep and genetics, explains the science behind strange sleep patterns and shares why shut-eye is more important than you think.

# What ignited your interest in the genetics of sleep?

In 1996, I was introduced to an older woman who had spent her life going from doctor to doctor, trying to understand why her sleep schedule was so unusual. She always went to bed around dinnertime and got up in the middle of the night. To her, these strange hours – what's known as early-lark behavior – felt like a curse. Her granddaughters had similar sleep schedules, and she was afraid the unconventional pattern would ruin their lives.

#### What did you discover about her?

We identified a genetic mutation that was responsible for her family's odd sleep schedule. She was thrilled because for years she'd been told that it was all in her head. In reality, she had a mutation that required her to follow that shifted sleep schedule in order to function normally. Since then, we've identified hundreds of other families who exhibit this extreme early-lark behavior, as well as 50 families known as "natural short sleepers."

# How did you discover these natural short sleepers?

While we were studying extreme early larks, we found a mutation in two members of a small family of extreme early-risers. Interestingly, they didn't go to bed early to compensate for their early wake-up. After more in-depth study, we realized that they were in an entirely new category – a group we now call natural short sleepers.

# Can anyone become a natural short sleeper?

I don't believe there's any safe way to do so, and I wouldn't advise people to try it. Our brains are intricate machines with many intertwined neural pathways. These pathways dictate mood, sleep, and cognitive function, and if you try to manipulate one pathway, you'll likely affect another. One day, though, we may have enough knowledge to intelligently tweak the system and help people sleep more efficiently.

#### What's the most common misconception about sleep?

That it's not important. All the evidence shows that it's like food, water, and air – we can't live without it. Sleep influences everything, from how happy we are to how quickly we process information, and those who sleep poorly have an increased risk of virtually every known disease. Poor sleep is a slow killer.

# How are sleep and disease connected?

Alzheimer's disease is a great example. When we're awake toxins accumulate in the brain, and while we sleep our brain cleans out those toxins. Levels of amyloid beta, a protein linked to Alzheimer's disease, are highest when we go to bed and lowest when we wake up because of this natural scrubbing process. So if you get less sleep, amyloids may accumulate in your brain and put you at greater risk of Alzheimer's.

# How much does sleep influence cognitive function?

It's enormously important. People are not living to their full potential without highquality sleep. If you sleep just two hours less each night for two weeks, you'll function at about 70 percent of your capacity.

#### What do you do to sleep better?

I go to bed at the same time every night, I avoid scary movies and exciting books before bed, and I use earplugs. People need to figure out what they're most sensitive to – like sound, light, or temperature – and create the right environment.



# Can a Common Antibiotic Prevent Zika?

Each year, thousands of babies are born, mostly in Brazil and Latin America, with undersized heads and brain damage – a condition known as microcephaly – because their mothers were bitten by a mosquito carrying the Zika virus. Scientists do not understand how the infection leads to microcephaly, which occurs in up to 13 percent of babies born to pregnant women who are infected. There is no preventative treatment.

That may be changing, thanks to a team of UCSF researchers who found in lab studies that azithromycin, a common antibiotic regarded as safe for use during pregnancy, effectively prevented infection of fetal tissue with the Zika virus.

The research was led by UCSF's Joseph DeRisi, PhD, the Bowers Professor and Tomkins Professor and co-president of the new Chan Zuckerberg Biohub, and Arnold Kriegstein, MD, PhD, the Bowes Professor and director of the Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell



Graduate student Hanna Retallack helped make the breakthrough discovery about the Zika virus.

Research. Graduate student Hanna Retallack and postdoctoral scholar Elizabeth Di Lullo, PhD, conducted many of the experiments in the DeRisi and Kriegstein labs and were first authors of the article reporting the results.

The team's experiments revealed that Zika is more likely to infect brain cells with an abundance of a protein called AXL, which serves as a gateway for the invading virus. The researchers then screened 2,177 drugs, all known to be safe in pregnancy, for an ability to block Zika infection of brain cells; they identified several that did, including azithromycin.

DeRisi is now working with Brazilian colleagues in hopes of launching a clinical trial that tests whether azithromycin lowers the risk of fetal harm in pregnant women infected with Zika virus.

## Beginning the Conversation about the End

Discussing how and where you want to be cared for at the end of your life is not easy for anyone. But according to a study led by Krista Harrison, PhD, a geriatrics research fellow at UCSF, it seems especially hard for seniors who are African American or Latino or who have less education or income.

What kinds of measures should doctors take, and not take, to keep you alive? Who do you want to make those decisions if you are no longer able to do so? What's an advance directive, and how do you complete one?

These are the kinds of questions that many older adults – more than one in four, according to estimates – and their families tend to avoid, despite significant efforts to promote advance care planning and growing awareness of its benefits. And all too often, this failure lands families in the mire of the legal system.

Fortunately, a new patient-friendly online resource called PREPARE (prepareforyourcare.org), developed by UCSF and UCSF-affiliated researchers, along with colleagues from the Veterans Health Research Institute, makes it easier to think through and talk about end-of-life issues.

The site, tailored for typically underserved populations, takes people through exercises that help them identify what is most important to them as they age and provides real-life examples of situations they may encounter. It also provides guidance on how people can make informed medical decisions and communicate their wishes. PREPARE puts these decisions where they belong – in the hands of patients and their families, rather than doctors or courts.



# "Let the lake do its work.

Nooshin Razani, MD, a pediatrician at UCSF Benioff Children's Hospital Oakland, who leads patients on field trips to parks as part of a program emphasizing nature as medicine, in the **San Francisco Chronicle** 

# No. 1 for NIH Funding among Public Institutions

In 2016, UCSF was the top public recipient of biomedical research grants from the National Institutes of Health for the sixth consecutive year and the second-highest recipient among all public and private institutions nationwide. UCSF's four schools – dentistry, medicine, nursing, and pharmacy – all ranked first in their fields in federal funding for biomedical research and graduate-level training for the fourth consecutive year. A grand slam for UCSF's mission to advance health worldwide!

## Autism Researchers Discover Genetic 'Rosetta Stone'

Scientists have identified a number of genes that predispose children to both autism spectrum disorders (ASDs) and early-onset epilepsies. But why mutations in a single gene can lead to the two different disorders has remained unknown.

Now, a team affiliated with the UCSF Weill Institute for Neurosciences may be close to unraveling the mystery. The finding "could serve as a molecular 'Rosetta Stone' to illuminate autism pathology," says Matthew State, MD, PhD, an internationally recognized expert on the genetics of autism. He is the Oberndorf Family Professor and chair of psychiatry at UCSF, though he wasn't directly involved with the study.

The researchers – Stephan Sanders, MD, PhD, assistant professor of psychiatry; Kevin Bender, PhD, assistant professor of neurology; and Roy Ben-Shalom, PhD, a postdoctoral researcher in Bender's lab – for the first time identified how specific genetic defects in a single neuronal protein can lead to either early-onset epilepsy or ASD. The pivotal factor appears to be whether the mutations boost the protein's function or sabotage it. Based on earlier studies by Sanders, researchers had already identified 65 genes in which mutations presage a strong likelihood of autism. Among them was SCN2A, a gene that encodes a nerve-cell protein involved in electrical signaling. Dysfunction in this protein had previously been linked to epilepsy.

In the current study, the researchers examined how mutations associated with ASDs affected SCN2A function and then modeled these effects on neuronal activity in the brain. Using computational models of neurons, they found that SCN2A made the neurons more excitable in children with early-onset seizures, but interfered with the neurons' ability to send electrical signals in children with ASDs.

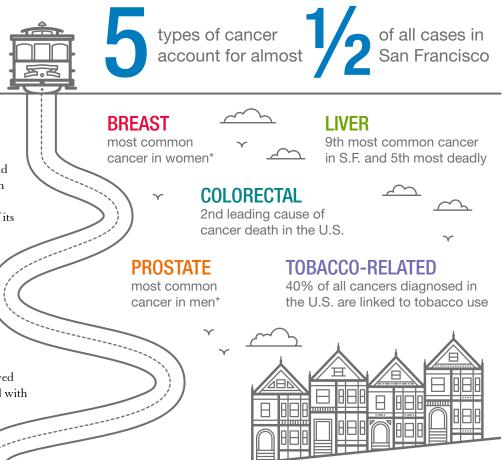
"These findings solidify SCN2A's status as one of the most important genes in autism," Bender says. "They give us a place to start exploring exactly how changes in early brain development lead to this condition."

# Taking On San Francisco's LEADING KILLER

Cancer kills more San Franciscans than any other cause of death. Each year, more than 4,000 residents are diagnosed with the disease, and more than 1,300 die from it. Yet cancer experts say that up to half of all cancers could be prevented if we eliminated the behaviors and social circumstances associated with increased risk of the disease.

That's why UCSF joined in November with the City and County of San Francisco, the San Francisco Department of Public Health (DPH), and health care and community organizations to launch the San Francisco Cancer Initiative (SF CAN) – a major public health effort thought to be the first of its kind in the U.S.

The coalition will initially seek to ramp up screening and intervention efforts focused on some of the most common cancers, including those of the prostate, breast, liver, and colon, as well as tobacco-related cancers – forms of the disease that disproportionately affect racial and ethnic minorities and individuals who are socioeconomically disadvantaged (see the adjacent graphic for details about these five cancers). Conceived and supported by UCSF, the initiative was launched with a \$3-million private donation. In addition to boosting screening and prevention efforts, SF CAN is seeking to increase access to care and improve the results of treatment.



\* other than skin cancer

"When you don't see people who look like you, it can cause you to say, 'This doesn't look like a field I can thrive in."

UCSF pediatrics resident Julie Boiko, MD, MS, on a study she led that found women doctors are underrepresented as grand rounds lecturers, in *Stat* 



## A Remarkable "New" American

It started with a spreadsheet drawn up by three undocumented students. They titled it "We Are Going to Med School." Today, the organization born from that page, Pre-Health Dreamers (PHD), has 700 members in 42 states.

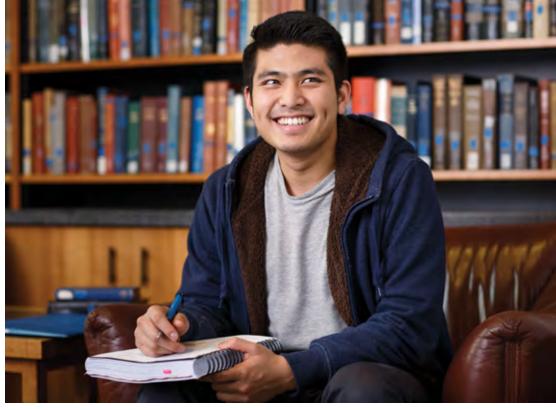
Jirayut "New" Latthivongskorn, who just completed his third year at UCSF's School of Medicine and is the first undocumented student in the school's history, is one of PHD's three co-founders. (The others are Angel Ku, a PhD student at UCSF, and Denisse Rojas Marquez, the first undocumented student at the Icahn School of Medicine at Mount Sinai.) Their goal was to create a community, serve as a resource, and advocate for other undocumented students hoping to pursue careers in health or science.

#### A National Spokesperson

When Latthivongskorn speaks, it's hard to imagine him as a 9-year-old immigrant from Thailand who was uncomfortable talking to his American classmates. Today, he is an eloquent and confident spokesperson for the rights of immigrants and the undocumented.

To be sure, he's had plenty of chance to develop skills and poise. Since his undergrad years at UC Berkeley, he's helped advance immigrant rights through ASPIRE (Asian Students Promoting Immigrant Rights through Education, the nation's first pan-Asian undocumented immigrant-led organization), Educators for Fair Consideration, and PHD. In California, he's lobbied for granting in-state tuition to undocumented students, for limiting local law enforcement collaboration with federal immigration actions via the TRUST Act, and for allowing undocumented immigrants to obtain professional licenses and to access loan forgiveness programs. He also partnered with the Association of American Medical Colleges (AAMC) to expand its fee assistance program to students in the Deferred Action for Childhood Arrivals (DACA) program.

Currently, as a member of University of California President Janet Napolitano's Advisory Council on Undocumented Students,



Forbes magazine selected New Latthivongskorn, an immigrant rights advocate and UCSF medical student, as one of its "30 Under 30" most influential people in the country.

Latthivongskorn has been working to improve support services, create financial aid programs that are not tied to federal funds, and pass UC-sponsored legislation to remove legal and financial barriers faced by undocumented students.

"I'm still the only undocumented student in medical school at UCSF," he says. "My hope is that medical schools will begin actively recruiting people like me – that they'll go beyond merely saying that they will consider your application and say instead, 'We want to make your education here a reality."

#### **Creating New Worlds**

Both the *Wall Street Journal* and the *Atlantic* have written about Latthivongskorn's journey, and *Forbes* magazine selected him as one of its "30 Under 30" most influential people in the country. In April, the U.S. Public Health Service awarded him its 2017 Excellence in Public Health Award, a national honor given to medical students who help "protect, promote, and advance the health and safety of our Nation."

Latthivongskorn is quick to point out that his accomplishments have been possible only because of the sacrifices of his family and the tireless work of many organizations and

#### Filling a Need for Physicians

The AAMC estimates that the projected **physician shortage** in the U.S. could be as high as **105,000** by **2030**.

A study published in *Academic Medicine* estimated that **DACA students** represent a **potential workforce** of between **5,400** and **31,860 future physicians**.

Statistics show that students from underrepresented populations, and **undocumented students** in particular, are **more likely to practice in underserved communities**.

individuals. It is *their* stories that he would like to help spread.

"We're at a point where a lot of undocumented students are getting into graduate and professional programs, which is an amazing, beautiful thing," he says. "We're no longer talking about five students across the country. We're talking about hundreds of students, at many different universities."

## **Cutting** through the Clamor

In noisy environments, such as subway cars or crowded restaurants, it can be hard to perceive critical speech fragments – distinguishing the "s" sound in "faster" from the "k" sound in "factor," for example. Nevertheless, we are often able to discern the complete word, a phenomenon known as "phoneme restoration."

Now, research led by two members of the UCSF Weill Institute for Neurosciences – Matthew Leonard, PhD, assistant professor of neurological surgery, and Edward Chang, MD '04, professor of neurological surgery – has revealed the mechanism by which the brain accomplishes this feat.

The researchers did so by monitoring neural activity in a group of epilepsy patients awaiting surgery. Devices placed directly on the patients' brains as they engaged in listening tasks recorded the real-time dynamics of the perceptual "filling in," which takes just a few tenths of a second. They found that a part of the brain that is deeply involved in speech perception responded to missing phonemes as if those sounds were actually present. Even



more intriguingly, the researchers discovered that another area in the brain's frontal lobe "predicts" which word a listener will hear well before the sound has begun to be processed by the brain's auditory areas. The study reveals a bit more about the human brain's remarkable ability to bring clarity to the clamor all around us.

"It's like working for NASA in the 1960s.... That sense of discovery, that sense that you're changing the world."

> Oncologist Alain Algazi, MD, a specialist in head, neck, and skin cancer, on the emergence of immunotherapy, on *PBS NewsHour's* "Leading Edge" series

**INSIDE UCSF** 

# "This is a transformative project for our city."

Malia Cohen, a member of the San Francisco Board of Supervisors, on a new research building approved by the board for **Zuckerberg San Francisco General Hospital (ZSFG)**. Each year, UCSF physicians at ZSFG treat more than 4,000 patients – including the city's most vulnerable – regardless of their ability to pay. In a unique, 150-year-old partnership, UCSF faculty provide all physician care at ZSFG, while also teaching and conducting research. The new facility, to be paid for by UCSF at no cost to city taxpayers, will provide much-needed research space for more than 800 physician-scientists, trainees, and staff.

## Surprise – Lungs Make Blood

UCSF scientists have discovered that lungs help produce blood. New technology allowed the researchers to look inside a live mouse lung, where they found large bone marrow cells known as megakaryocytes releasing blood platelets. Scientists previously believed platelets formed mainly in bone marrow, but now it appears that over half of blood platelets form in the lungs. The investigators also discovered that the lungs are full of blood stem cells. Their findings could provide new approaches to treating blood-related diseases, according to the study's senior author. Mark Looney, MD, a professor of medicine and of laboratory medicine and a resident alumnus.

## **Coffee Lovers, Take Heart!**

If you've ever struggled to follow a doctor's recommendation to reduce your caffeine consumption, take heart. According to a study by UCSF researchers, that recommendation, based on decades-old research, may be unwarranted.

The researchers examined chronic consumption of caffeinated products over a 12-month period to determine whether caffeine produces extra heartbeats. Such cardiac activity can, in rare cases, contribute to a heart attack or a stroke. The study, the largest to date to evaluate dietary patterns in relation to cardiac rhythms, found no association between regular caffeine consumption and extra heartbeats.

That is good news for lovers of coffee, tea, and chocolate, which increasingly have been touted as having numerous health benefits.

"We may unnecessarily be discouraging consumption of items...that might actually have cardiovascular benefits," says the study's senior author, Gregory Marcus, MD, MAS '08. "Given our recent work demonstrating that extra heartbeats can be dangerous, this finding is especially relevant," adds Marcus, a fellowship alumnus, Endowed Professor in Atrial Fibrillation, and director of clinical research in the UCSF Division of Cardiology.

# FACULTY ACCOLADES

Four UCSF researchers were among 84 Faculty Scholars in a new program for promising early-career scientists funded by the Howard Hughes Medical Institute (HHMI), the Simons Foundation, and the Bill and Melinda Gates Foundation. **Edward Chang**, MD '04, professor of neurological surgery; **Adam Frost**, MD, PhD, assistant professor of biochemistry and biophysics and Herbert Boyer Endowed Professor; and **Markus Müschen**, MD, PhD, professor of laboratory medicine, were named HHMI Faculty Scholars. Also, **Michael Fischbach**, PhD, associate professor of bioengineering, was named an HHMI-Simons Faculty Scholar. The first cohort of scholars will receive a total of \$83 million in five-year grants ranging from \$600,000 to \$1.8 million.

Leslie Dubbin, RN, PhD '14, assistant adjunct professor of social and behavioral sciences, was selected by the Robert Wood Johnson Foundation as one of its first Interdisciplinary Research Leaders. With Irene Yen, PhD, MPH, associate professor of medicine and of epidemiology and biostatistics, and Susan Neufeld of BRIDGE Housing, she will investigate the impact of public housing renovations on the health and social well-being of San Francisco public housing residents.

Kathy Giacomini, PhD, professor of bioengineering and therapeutic sciences and co-director of the UCSF-Stanford Center of Excellence in Regulatory Sciences and Innovation, received the Henry W. Elliott Distinguished Service Award from the American Society for Clinical Pharmacology and Therapeutics. The award recognizes outstanding efforts by a member in the organization's behalf.

Kathryn Johnson, RN, MSN, associate clinical professor of community health systems, received the American Psychiatric Nurses Association's Award for Excellence in Leadership. Johnson, a psychiatric nurse practitioner who treats adolescents and adults in her Santa Cruz practice, was recognized for her work as a mentor, teacher, and leader.

**Ophir Klein,** MD, PhD, resident alumnus, Charles Epstein Professor in Human Genetics and Hillblom Professor in Craniofacial Anomalies, received one of two new National Institute of Dental and Craniofacial Research Awards for Sustaining Outstanding Achievement in Research. The grants are intended for "ambitious longer-term projects of extraordinary potential." Klein will use his funding to study the regenerative properties of craniofacial and dental stem cells (see story, page 26). **Susan Lynch**, PhD, associate professor of medicine, and **Peter Stock**, MD, PhD, resident alumnus, and professor of surgery, were among *Foreign Policy* magazine's 100 Leading Global Thinkers of 2016. Lynch was tapped for her work showing that the gut microbes in some 1-month-old infants predict a threefold higher risk of developing allergic reactions by age 2 and asthma by age 4. Stock was recognized for his success in lobbying the California legislature to allow HIV-positive individuals to donate organs to HIV-positive recipients.

Walter Miller, MD, resident alumnus, and professor emeritus of pediatrics, received the 2017 Fred Conrad Koch Lifetime Achievement Award, the highest honor bestowed by the Endocrine Society, the world's oldest and largest organization of scientists and physicians devoted to hormone-related issues.

**Ricardo Muñoz**, PhD, professor emeritus of psychology, was elected a Fellow of the American Association for the Advancement of Science. He was recognized for his distinguished contributions to the prevention of major depression and the development of online interventions to improve mental health worldwide.

**Jennifer Perkins**, DDS, MD, resident alumna, and assistant professor of oral and maxillofacial surgery, was the 2017 recipient of the Junior Faculty Award presented by the American Dental Education Association (ADEA); the ADEA Council of Students, Residents and Fellows; and Colgate-Palmolive Co.

**Brian Shoichet**, PhD '91, professor of pharmaceutical chemistry, received the American Society for Biochemistry and Molecular Biology's DeLano Award for Computational Biosciences. The award recognizes "the most accessible and innovative development or application of computer technology to enhance research in the life sciences at the molecular level."

#### DAVID JULIUS RECEIVES "BABY NOBEL"

**David Julius**, PhD, chair of the Department of Physiology and Morris Herzstein Professor, received a prize widely known as the "Baby Nobel" – the Canada Gairdner International Award, given annually to five scientists who have made significant contributions to understanding human biology and disease. It is one of the most prestigious prizes in biomedicine because out of the 388 scientists granted Canada Gairdner Awards since 1957, 84 recipients have gone on to win a Nobel Prize. Julius received the prize for determining the molecular basis of somatosensation – how we sense heat, cold, and pain.

# **Dazed and Confused**

# Marijuana legalization and research:

what we don't know could heal - or harm

by Janet Wells



PHOTO: ELENA ZI

a Paul McCartney concert at San Francisco's AT&T Park in 2010, Matthew Springer, PhD, wasn't shocked to be surrounded by a haze of marijuana smoke. He was, however, amazed that the audience tolerated it without complaint.

"All of these people knew to avoid smoke from cigarettes, because the public health community has been saying that for decades," recalls Springer, a professor of medicine at UC San Francisco. But, he adds, "we haven't been given that message about marijuana smoke, so people thought that it was different – that it was somehow okay."

Was it? Springer wondered.

Now that recreational, in addition to medical, marijuana is legal in California – thanks to the resounding approval in November of Proposition 64's Adult Use of Marijuana Act – there is renewed urgency about seeking more information on the drug's health effects, both positive and negative.

UCSF scientists recognize marijuana's contradictory status: the drug has significant proven and potential therapeutic uses, but it can also lead to tremendous public health problems. Everyone agrees that a stronger evidence base is key.

Is second-hand marijuana smoke as dangerous as tobacco smoke? What are the possibilities for its clinical use, and why is it so hard to study them? As new laws create a new industry, are we forgetting the hard-won public health lessons from battling Big Tobacco?

"We are left with so many questions," says Reto Auer, MD, MAS '13, who launched a study on marijuana and cognitive function while he was enrolled in UCSF's Training in Clinical Research program. Published in *JAMA Internal Medicine* in 2016, the findings showed that study participants who reported long-term marijuana use experienced some memory problems by midlife.

"Academically it's interesting to be in a field where so little is known," Auer adds, "but it's a shame we can't better inform the public."

## The Feds:

## just say 'no' to research

Marijuana, now legal by a doctor's order in 29 states and recreationally in eight states (plus the District of Columbia), remains in the same class federally as heroin and LSD – a Schedule I drug, designated as having "a high potential for abuse" and "no currently accepted medical use." Federally, marijuana is considered more dangerous than prescription opioids like OxyContin and Vicodin, which were linked to more than 15,000 deaths in 2015 and are responsible for epidemic levels of addiction and abuse, according to the U.S. Centers for Disease Control and Prevention.

"Every day, I see patients who benefit from using cannabis as medicine," says Donald Abrams, MD. "It's a benign and safe agent that's been used for thousands of years." Abrams, who studies the safety and pain relief properties of marijuana, is the Osher Foundation Professor of Integrative Medicine, chief of the Hematology-Oncology Division at Zuckerberg San Francisco General Hospital, and a resident alumnus.

Studying marijuana means navigating complex regulatory hoops, including reviews by the Food and Drug Administration (FDA), the Drug Enforcement Administration (DEA), the National Institute on Drug Abuse (NIDA), and at UCSF, the Research Advisory Panel of California.

Included in the DEA's stringent regulations for purchasing, storing, documenting, and disposing of marijuana is the requirement that each lab must have an alarm-controlled, locked container that is physically attached to the floor or wall and to which access is limited.

"The DEA visited and determined that we had to do more to bolt down the locked freezer," says Judith Hellman, MD, a professor and vice chair for research in the Department of Anesthesia and Perioperative Care. It took close to a year to get the approvals, says Hellman, who studies the immune modulating effects of cannabinoids (see profile on page 15).

"It was kind of comical, with all of these medical marijuana dispensaries scattered around town, sitting in my office and talking about everything we had to do to get a small amount of THC, cannabidiol, and cannabinol – 400 milligrams – to use over [the course of] a year," recalls Hellman.

#### What's in a name: a marijuana / cannabis primer

A complex botanical compound, "cannabis" is recognized as the general scientific name of the plant and its products. "Marijuana," originally spelled "marihuana," has a politically tangled and unverified linguistic history. According to the Oxford English Dictionary, the term may have been derived from the Mexican-Spanish word for "prisoner," an etymology favored by campaigns against the drug in the 1930s. An American Heritage reference work further suggests that the word was promoted by opponents of marijuana who wanted to "demonize the drug with a foreign-sounding name."

## **Restricted supply:**

#### restricted research

The humor would likely be lost on the DEA, which long designated NIDA – part of the National Institutes of Health (NIH) – as the sole source of cannabis for scientists. Until recently, NIDA, under an exclusive government contract in place since 1968, paid the University of Mississippi \$69 million in 2015 to grow all the country's research-grade marijuana. While the DEA opened production to other growers last year, none have yet been able or willing to comply with the agency's regulatory requirements.

The roadblocks to studying marijuana go beyond regulatory obstacles, says Abrams, who co-authored a chapter on barriers to such research in a 2017 report titled *The Health Effects of Cannabis and Cannabinoids*. This landmark report was published by a committee of the National Academies of Science, Engineering, and Medicine (NASEM) of which Abrams was a member.

One obstacle, he explains, is the limit NIDA puts on varieties of the drug that can be used in research. Different strains of marijuana have varying chemical components, so they ameliorate clinical symptoms differently. Cancer-related nausea and poor appetite, for example, are better relieved by cannabis high in THC, the psychotropic component of marijuana (see sidebar). However, there is evidence that chronic pain, inflammation, and insomnia are better relieved by cannabis high in cannabidiol (CBD).

"In the past, NIDA pretty much only had low-THC, zero-CBD strains," says Abrams, who has battled with federal agencies to procure cannabis with higher levels of THC and CBD for his current research on easing symptoms for patients with sickle cell anemia. It's even more difficult for researchers who want to look at newer delivery systems. "Right now, cannabis oil is popular," Abrams continues. But "because the NIDA supply has not yet been trialed in humans, if I write a proposal to try to study it, the FDA will say it's a 'novel molecular entity' and make it difficult to do."

NIDA's focus on substance abuse can be another challenge. "A lot of the studies that NIDA has supported look at the downsides. Studies about the benefits are rarer," says Abrams, who is also an integrative oncologist at the UCSF Osher Center for Integrative Medicine. "You have to use NIDA's cannabis but need to get funding from somewhere else."

These barriers to conducting comprehensive research – which mean patients and providers may lack treatment options and policymakers may lack a full evidence base – constitute "a public health problem," concludes Abrams.

But there may soon be a small break in the funding dam, at least in California. Proposition 64 once again commits state support to the Center for Medicinal Cannabis Research, housed at UC San Diego. The state legislature established the center, thanks to a budget surplus in 1999, with \$9 million in funding. That money is long gone, but the new law earmarks \$2 million annually – out of an expected \$1 billion to be raised from the taxes levied on recreational marijuana retailers and growers – for the center's research.

## Marijuana:

## the new Big Tobacco

Stanton Glantz, PhD, the American Legacy Foundation Professor of Tobacco Control and director of the UCSF Center for Tobacco Control Research and Education, has a less rosy view of California's new law.

First, he argues, the legislation won't help fill the state's coffers because of the substantial costs associated with regulation, enforcement, and the increased health care burden. Second, "we're creating a major market which is going to be eventually taken over by large corporations, with very sophisticated product engineering and marketing capacity," says Glantz, who has published widely on the effects of secondhand smoke, as well as the public health and policy impacts of recreational marijuana legislation.

"Today's marijuana products are very low tech – groundup leaves in a piece of paper, like a cigarette in about 1880. Today's cigarettes and junk food are highly engineered products. Cigarette companies use technology like varying the porosity of the paper or using burn enhancers or adding sugar to make [the product] more addictive. It's designed to maximize consumption," says Glantz.

#### Cannabis: a breakdown

THC (delta-9-tetrahydrocannabinol): the main psychoactive component of cannabis; induces feelings of euphoria. Therapeutic uses: reduces nausea and chronic pain; stimulates appetite. **CBD (cannabidiol):** the main nonpsychoactive component of cannabis; relaxes the mind and body. Therapeutic uses: reduces inflammation, insomnia, sleep apnea, spasticity, and pain.

**CBN (cannabinol):** the secondary psychoactive component of cannabis, formed as THC ages. CBN has no painkilling effects and is associated with headache and lethargy rather than euphoria.



#### Cannabinoids: powerful promise in fighting infection

Five years ago, a news article about the use of cannabis for medical conditions – including chronic inflammation – piqued the interest of Judith Hellman, MD, a professor and vice chair for research in the Department of Anesthesia and Perioperative Care.

Could the drug, she wondered, also ease acute inflammation? The focus of Hellman's research is postoperative sepsis – a total-body immune response to bacterial, viral, fungal, or parasitic infection that causes dysregulated inflammation, severely damaging organs and tissues.

Currently, there are no approved sepsis-specific therapies. After decades of research, the mainstays for treatment remain antibiotics and the support of dysfunctional organs and systems. But these measures do not have a stellar success rate; sepsis still has a mortality rate of over 30 percent.

"We're looking for new ways to reduce inflammation during that initial onslaught, the first couple of days," says Samira Khakpour Lawton, a 2017 PhD candidate and a member of Hellman's lab. "We thought that targeting the body's cannabinoid receptors could be a logical therapeutic." in the lengthy process of applying for federal and state approvals, she turned her attention to endocannabinoids. These chemical compounds are naturally synthesized in the human body and activate the same cannabinoid receptors, which are involved in a variety of physiological processes, including immune responses.

There are a half-dozen acknowledged endocannabinoids, and it's unclear, says Lawton, what they all do or what triggers their production. In the Journal of Biological Chemistry in 2014, Hellman's group reported the discovery of an endocannabinoid that potently modulates cellular inflammation. They speculate that the endocannabinoid system represents what may be a "novel immune regulatory system" to ameliorate inflammatory disorders, including sepsis. Hellman now has the regulatory approvals to add phytocannabinoids to her research and is starting with the plant's three major components – THC, CBD, and CBN.

"There's a good chance they will have similar immunemodulating effects," Hellman says, "and perhaps more powerful."

"It was kind of comical...talking about everything we had to do to get a small amount of THC." — Judith Hellman

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#### Marijuana and tobacco: both go up in toxic smoke

"I want to err on the side of safety." — Matthew Springer

8

Matthew Springer, PhD, a professor of medicine, isn't antidrug or anti-marijuana. After a decade of research on tobacco and more recent work on cannabis, he is simply anti-smoke.

Just one minute of exposure to secondhand smoke from marijuana diminishes blood-vessel function in rats to the same extent as exposure to secondhand tobacco smoke. Furthermore, the harmful cardiovascular effects last considerably longer – more than 90 minutes, compared to less than 30, says Springer, the senior author of a 2016 study on the subject in the *Journal of the American Heart Association*.

"Whether it was marijuana with THC or placebo marijuana with no cannabinoids, it was the same," Springer says. "This is a result of exposure to smoke from burning plant material." Springer, who has published widely on the effects of secondhand smoke, acknowledges that his study didn't "prove" that marijuana smoke is harmful for humans. "There's the distinction between proving something is harmful and [knowing it is] harmless," he says. "I want to err on the side of safety."

Springer's current research measures cardiovascular sensitivity to new delivery systems for tobacco and marijuana – such as e-cigarettes, which aerosolize liquid solutions of nicotine or THC, and so-called volcano vaporizers, which heat rather than burn the plant material.

"If smoke itself is the problem, it's logical to expect that leaf vaporizing might prevent that," he says, cautioning that the results are not yet in. "If you want people to make better lifestyle decisions, it's important to show if something really is better." While the new law initially gives preference to smaller growers, delaying for five years the issuance of licenses to cultivate large tracts (22,000 square feet or more), the state's licensing program doesn't go into effect until January 1, 2018. During the current legal limbo, licenses are being issued by local jurisdictions for industrial-sized operations. Marijuana will eventually be dominated by big business, and those corporations, says Glantz, "will exercise tremendous political power to protect their profits."

A policy analysis led by Glantz and published in *PLoS Medicine* in 2016 encouraged the establishment of a state monopoly on production, distribution, and sales to prevent the legalized marijuana industry from becoming, as he puts it, the "next big tobacco or alcohol."

Instead, the new law advances marijuana as a business opportunity, largely regulated by the Department of Consumer Affairs. The Department of Public Health has "no meaningful role in terms of the kind of big demand-reduction program that we think is needed," Glantz says.

While applauding the new law for decriminalizing marijuana use, Glantz wishes it could have been done "without creating a big new public health mess. We've had 50 to 60 years of trench warfare with the tobacco industry to get where we are today. Getting sensible tobacco regulation has been a gigantic battle. That's the way it's going to be with marijuana."

Matthew Springer, too, is concerned that California's legalization of recreational marijuana will fail to protect public health. After that night at AT&T Park, he immediately set out to add exposure to marijuana smoke to his studies on secondhand tobacco smoke (see profile on page 16). "That was a crystallizing moment," Springer says. "There are toxins from burning any plant material."

While the state's new law prohibits smoking marijuana in public "there will be more opportunity," Springer points out, "for people to be exposed involuntarily.

"Three times I've gone up to people in underground subway stations and asked them not to smoke marijuana there," he says. "They were so stoned I couldn't get through to them. People who smoke tobacco are lucid. People who are drunk may not be lucid, but they're not exhaling smoke in your face."

## Next up:

## a political backlash?

Reto Auer, who is now an assistant professor at the University of Bern in Switzerland, continues to research the health effects of marijuana in collaboration with U.S. colleagues. He co-authored his latest findings with his UCSF mentor Mark Pletcher, MD '98, MPH, resident alumnus, and a professor of epidemiology and biostatistics; published in the online edition of the *American Journal of Public Health* in February, their analysis found no link between marijuana use and cardiovascular disease in middle age.

Auer and Pletcher conducted their analysis using data from the Coronary Artery Risk Development in Young Adults (CARDIA) study, which followed more than 5,000 Americans aged 18 to 30 for over 25 years, beginning in 1985. By analyzing existing data, they didn't have to deal with the regulatory scrutiny faced by researchers who work directly with the drug.

Switzerland, where possession of small amounts of marijuana has been decriminalized but not legalized, has its own byzantine rules and political wrangles about marijuana research, particularly regarding recreational use. But the situation there is not nearly as challenging as in the U.S., where "the laws are so hard," Auer says.

The NASEM report that Abrams contributed to – the first review since 1999 of research on the human health impacts of cannabis use – sought to ease those onerous regulatory barriers. In late January, two weeks after the report's release, a bill was introduced in the House of Representatives in accord with one of the report's recommendations to advance research efforts: a federal rescheduling of marijuana.

However, that bill may languish. In a reversal of the previous administration's policy, White House officials announced in February that they expect "greater enforcement" of current federal marijuana laws when they conflict with laws in states where recreational use is permitted. Whether that will have a further chilling effect on research remains to be seen.

"It would be a real shame if medicinal marijuana research was put in jeopardy because it's a drug used recreationally," Hellman says. "It's really time for us to understand how it works, what doesn't work, and how it's beneficial. We should be studying it like any other drug."

#### Drug of choice: a comparison

**Cannabis:** 22.2 million Americans aged 12 and older report having used cannabis in the past month, making it the most popular illicit drug in the U.S. Appeal: euphoria and relaxation. **Tobacco:** 36.5 million Americans smoke cigarettes, the leading cause of preventable death and disease in the U.S. Appeal: adrenal stimulant. **Alcohol:** 136 million Americans – 56 percent of adults – report drinking in the past month. Appeal: euphoria and sedation.

# EXPESSION

# THEY'RE IN OUR WATER, FOOD, AIR, FURNITURE. ARE THE CHEMICALS WE ENCOUNTER EVERY DAY MAKING US SICK?

by Molly Miller

When her kids were young, Tracey Woodruff, PhD, MPH, knew more than most people about environmental toxics. After all, she was a senior scientist at the Environmental Protection Agency (EPA). But even she never dreamed, as she rocked her children to sleep at night, that the plastic baby bottles she used to feed them contained toxic chemicals that could leach into the warm milk.



Back then, in the late 1990s, it wasn't widely known that the chemicals used in plastic sippy cups and baby bottles can potentially disrupt child development by interfering with the hormone system. That, in turn, could alter the functionality of their reproductive systems or increase their risk of disease later in their lives.

"When I had babies, I did many of the things we now tell people not to do," says Woodruff, who for the past decade has been the director of UC San Francisco's Program on Reproductive Health and the Environment (PRHE). Also a professor in the University's Philip R. Lee Institute for Health Policy Studies, she earned her doctorate in 1991 from a joint UCSF-Berkeley program in bioengineering and then completed a postgraduate fellowship at UCSF.

Woodruff's children have since grown into physically healthy teenagers, but many children are not as lucky. Unregulated chemicals are increasing in use and are prevalent in products Americans use every day. Woodruff is concerned by the concurrent rise in many health conditions, like certain cancers or childhood diseases, and the fact that the environment is likely to play a role in those conditions. What motivates her is the belief that we need to know more about these toxics so we can reduce our exposure to the worst of them and protect ourselves and our children from their harmful effects. (Woodruff points out that the word "toxics" as a noun means any poisonous substances, from either chemical or biological sources, whereas "toxins" are poisons only from biological sources, either plant or animal.)

The PRHE is dedicated to identifying, measuring, and preventing exposure to environmental contaminants that affect human reproduction and development. Its work weaves together science, medicine, policy, and advocacy.

For example, research over the past 10 years by UCSF scientists and others has showed that bisphenol A (BPA) – an industrial chemical used since the 1950s to harden plastics in baby bottles, toys, and other products – is found in the blood of those exposed to items made with BPA and that it can harm the endocrine systems of fetuses and infants. As a result, the Food and Drug Administration (FDA) outlawed BPA in baby products in 2012, and some manufacturers developed BPA-

free products. But now scientists believe the chemicals that replaced BPA may be just as harmful.

Furthermore, BPA is only one in a long, long list of chemicals we encounter every day in our homes, schools, workplaces, and communities. And scientists have barely scratched the surface of understanding them. Of the thousands and thousands of chemicals registered with the EPA for use by industry, the agency has regulated only a few.

"In the last 50 years, we have seen a dramatic increase in chemical production in the United States," Woodruff explains. Concurrently, there's been an increase in the incidence of conditions like attention deficit hyperactivity disorder (ADHD), autism, childhood cancers, diabetes, and obesity. "It's not just genetic drift," Woodruff maintains.

And we're *all* at risk from increasing chemical exposure. The water we run from our taps, the lotion we smear on our skin, the shampoo we rub in our hair, even the dust in our houses is full of synthetic chemicals

#### Preventing exposure in babies

PRHE experts do more than just measure such trends. They also collaborate with clinical scientists and obstetricians at Zuckerberg San Francisco General Hospital (ZSFG), so their findings directly benefit pregnant patients. "We partner with the clinical scientists," explains Woodruff, "because they look at treatments for disease, and environment might be a missing factor in the cause and prevention of disease."

Though environmental toxics affect us all, there's a reason PRHE focuses on pregnant women and children, Woodruff adds. Exposure to even tiny amounts of toxic substances during critical developmental stages can have outsize effects. So exposure to toxics is especially detrimental to fetuses, infants, and young children, as well as preteens and teenagers.

"If you prevent the problem at the beginning, you get a lifetime of benefits," says Woodruff.

The U.S. Centers for Disease Control and Prevention (CDC) began measuring human exposure to chemicals in 1976. These so-called "biomonitoring" studies found a range of toxics in subjects' blood and urine – substances like DDT, BPA, air pollutants, pesticides, dioxins, and phthalates. Phthalates, for example, are a class of chemicals known to be endocrine disruptors but widely used as softeners in plastics and as lubricants in personal-care

The water we run from our taps, the lotion we smear on our skin, the shampoo we rub in our hair, even the dust in our houses is full of synthetic chemicals.

products. Biomonitoring has determined that women of reproductive age evidence higher levels of phthalates than the population at large. One reason, says Woodruff, is that young women use more products like perfume, deodorant, shampoo, and conditioner.

Woodruff herself recently led a study in which UCSF researchers collected blood samples from pregnant women at ZSFG. After the women delivered their babies, the researchers collected umbilical cord blood samples – and discovered that almost 80 percent of the chemicals detected in the maternal blood samples had passed through the placenta to the cord blood. It was the most extensive look yet at how the chemicals that pregnant women are exposed to also appear in their babies' cord blood (and followed an earlier study by Woodruff that marked the first time anyone had counted the number of chemicals in the blood of pregnant women). Published in the Nov. 1, 2016, print edition of *Environmental Science and Technology*, the study also found that many chemicals were absorbed at greater levels by the fetuses than by the pregnant women.

Now, Woodruff is hard at work on a new grant from the federal Environmental Influences on Child Health Outcomes (ECHO) Program. It aims to correlate children's exposure to toxics with their developmental outcomes from birth to age four.

The good news is that the work done by Woodruff and her team shows a clear impact. Following bans (some permanent and some temporary) on certain phthalates, for example, UCSF researchers measured declines in the urinary concentrations of the permanently banned types in a representative sample of the U.S. population.



#### Crusader for a healthy environment

Woodruff's degree is in engineering, and she notes that in the 1980s, when she was in school, a lot of engineers went into the defense industry. "People talk about joining the military to serve their country," Woodruff says. "I also wanted to do something positive for society, and I felt joining the EPA was the best way to serve my country."

She spent 13 years at the federal agency, as a scientist and policy advisor, studying the effects of air pollution on children's health. The topic interested her, she says, "because children are vulnerable and can't speak for themselves." Her analysis of data collected under the Clean Air Act, for example, found that air pollution is linked to infant mortality. She also determined that pregnant African American women had higher exposure to air pollution and more adverse pregnancy outcomes than the population at large.

Nearly 25 years later, her work at UCSF is motivated by the same sense of advocacy and zeal. She joined the PRHE in 2007, shortly after its founding by Linda Giudice, MD, PhD. "What we do," she says, "is bring the best scientific tools from the varied fields at UCSF to bear on uncovering and better understanding the links between the environment and health and translate that science into prevention by improving public policy."

While Woodruff has many influential scientific publications to her name, she's also a sought-after guest for radio interviews and talk shows. She even appeared in a popular 2013 documentary, *The Human Experiment*, narrated by Sean Penn. In response to questions from the public, she tries to strike a practical note. "You don't want to freak people out," she says. "At the same time, people assume if they can buy it, it's safe. That is just not the case."

In her own home in Oakland, Woodruff has made slow changes over time. "I got rid of carpet...the padding can contain toxic chemi-

cals. I waited to

buy a couch...too

long according to

laughs. (Couches

retardants didn't

become available

in California until

changed its flam-

mability standard

in 2014, making

it possible to sell

couches that are

flammability-safe

but are made

after the state

my family," she

without flame-

"<u>We do not</u> <u>always consider</u> <u>EPA a public</u> <u>health agency,</u> <u>but it is.</u>"

#### - Tracey Woodruff

without flame-retardant chemicals.) "I still have a couch that probably has flame-retardants, but I am just ignoring it. We eat mostly organic to reduce pesticide exposure. Less is more in personal-care products," she adds.

Does she make her own shampoo?

"Oh, my God, no," she answers. "Who has the time? This should not be a burden to people. Systems should be in place so that we can be free of the burden. This is why we need the EPA, and this is where policy comes in.

#### Policies for the people

"It's important for people to realize there are things you can do to lower your exposure to toxic chemicals, but some things you can't do." (See the sidebar for ways to lower your exposure.)

For example, Woodruff explains, Americans would have had a hard time limiting their exposure to lead before leaded gasoline became illegal in 1996 (though the phaseout started in the mid-1970s). Until then, no amount of personal awareness could protect someone from lead – it was in the air that everyone breathed.

She offers another example specific to the PRHE's efforts. "When California outlawed flame retardants," she says, "we saw levels decrease by about two-thirds in the blood of pregnant patients at ZSFG. Through these studies, we can evaluate the effectiveness of public policy. It's clear that when the government acts to reduce exposures to toxic chemicals...we see a positive change. We do not always consider EPA a public health agency, but it is."

Woodruff and her colleagues also have been working over the last several years to help strengthen the federal Toxic Substances Control Act (TSCA) of 1976. It was well recognized that the law was flawed and allowed thousands of chemicals to be used in the marketplace without testing for safety, she explains. When bipartisan calls to strengthen the law led Congress to amend it in 2016, PRHE experts partnered with obstetricians and gynecologists to provide scientific evidence about the need for improved standards, deadlines, and transparency. As rules for the amended TSCA are rolled out over the next two years, "we'll be right in there to promote the use of science for the public's health," says Woodruff.

She's also bringing environmental toxics to the attention of her UCSF colleagues in other disciplines. "One of the reasons we love being at UCSF is we can learn from people who are doing completely different things," she says. For example, she is working with researchers who study the placenta, since her 2016 study showed that environmental toxics permeate the placenta. And with developmental biologist Diana Laird, PhD, an associate professor in the Center for Reproductive Sciences, Woodruff is co-leading the Environmental Health Initiative (EHI). The EHI's goal is to involve researchers from throughout UCSF – from the biological, population, and translation sciences – in solving and preventing the environmental burden of disease, starting with ensuring healthy pregnancies.

"The EHI will link faculty across the campus, to add an environmental component to their work," Woodruff says. "We have already hosted several networking events and symposia with the Research Development Office toward our goal of 'norming' the environment within the research community. We want people to be saying, 'We need to address the environmental consequences to fully solve health issues.'"

"This is about prevention," she concludes. "People talk about nutrition and social competencies of health. There's another thing, which is the physical environment. The missing ingredient is toxics in the environment."

# **Protecting Your Family From Toxics**

Here are some recommendations from the PRHE. More advice is at tiny.ucsf.edu/personalcare.

# Use nontoxic personal care products.

Many such products contain ingredients that can harm reproductive health, but safer options are available.

#### Choose safer home improvement products.

Many paints, glues, and flooring materials release toxic chemicals and volatile organic compounds (VOCs) long after you complete a project. Ask for VOC-free and water-based products.

#### Mop and dust often.

Toxic substances like lead, pesticides, and flame retardants are present in household dust. Use a wet mop or wet cloth to regularly clean floors and flat surfaces.

#### Remove your shoes inside.

Outdoor shoes can carry toxic chemicals into your home.



# Clean with nontoxic products.

It is easy and cheap to make effective, nontoxic cleaners with common ingredients like vinegar and baking soda.

# Don't dry-clean your clothes.

Many dry cleaners use toxic chemicals. Hand-wash delicate clothes or ask your dry cleaner to use water instead of chemicals.

# Avoid pesticides and herbicides.

Toxic chemicals used to kill insects, rodents, weeds, bacteria, mold, and other noxious animals and plants can also harm your health.

# Select flame-retardant-free foam products.

Crib mattresses, nap mats, and other upholstered products can contain flame-retardants, which can harm health and affect a child's brain. Instead, select foam products labeled as "flameretardant-free" or tagged as compliant with TB-117-2013.

# Avoid toxics in your food and water.

Whenever possible, eat organic food to reduce your exposure to pesticides. If you can't buy organic produce, choose the fruits and vegetables with the

least pesticide residue and avoid the most contaminated ones.

# Keep mercury out of your diet, home, and garbage.

Eat fish with lower levels of mercury. Replace your mercury thermometer with a digital one. Don't throw items containing mercury (such as old thermometers or compact fluorescent bulbs) in the trash.

# Avoid canned foods and beverages.

Eat fresh or frozen fruits and vegetables. This limits your exposure to BPA, a toxic substance used in the lining of most cans.

# Limit foods high in animal fat.

Many toxic substances build up in animal fat.

#### Avoid lead exposure.

Any home built before 1978 may have lead paint. There may also be lead in household dust and garden soil.

#### Use less plastic.

Choose glass, stainless steel, or ceramic containers for food. Don't use plastic containers for hot foods or drinks and use glass

instead of plastic in the microwave, because heat makes plastic release chemicals.





Mei-Ling Wong, RN, MS '13, remembers the nights when her mother would vanish. It was the first clue in Wong's 5-year-old mind that her mother was a nurse. Wong would climb into her parents' bed, searching and crying. "I wanted to use more tissues than I needed so that I could pile them up on the bedside table for my mom to see after her shift," recalls Wong.

Peggy Cadbury, RN, BS '79, smiles, listening to her daughter's remembrance.

Wong is a little groggy as she retells the tale, having just come off a 12-hour night shift of her own in the pediatric intensive care unit at UCSF Benioff Children's Hospital San Francisco. As cranky as she was as a kid about such a schedule, Wong decided to follow in her mother's footsteps.

They both attended UCSF School of Nursing, 34 years apart. Cadbury matriculated at the age of 30, a decade older than most of her classmates. She had spent three years in Southeast Asia during the Vietnam War, working for a Quaker rehabilitation center. Among her duties was assisting amputees with job training, since they couldn't be farmers anymore. By the time she left there in 1975, Cadbury was conversant in Vietnamese, on a mission to become a nurse, and in love. She had met the man who would be Mei-Ling's father, Ching Wong. He said goodbye to her in a poem. "He wrote, 'The world is still round, you and I will meet again,'" says Cadbury. They reunited in America when he was finally able to get out of Vietnam.

The family lives near UCSF Medical Center on Parnassus, the perfect commute for Cadbury during the years she worked with patients on the 14th floor of Moffitt-Long Hospital. "I was on the general surgery postsurgical unit," says Cadbury. "I loved the bedside – helping people get well."

Yet sometimes they don't – but even then the work has its rewards, notes Wong. "Knowing that we have done all that we could – standing all through the night, laserfocused on perfect strangers – and having people acknowledge that is pretty wonderful," she explains.

Though a generation apart, mother and daughter say the same thing got them both through nursing's most challenging moments. "Nursing is about 'team," says Cadbury. She found team not only at the bedside, but also when she moved on to research, working on clinical trials until her retirement six years ago.

Wong nods. "When the walls come down after someone dies, you look to the people who you have struggled through it with," she says. "These are the most traumatic moments of parents' lives, and we experience this trauma on a daily basis. It's the team that gets you through."

Wong also looks to "place" for grounding and renewal. On the hardest mornings, she and all the nurses naturally gravitate to the windows. Sometimes, she says, she'll stand outside on the lower patio, glance up, and see nurses at the windows on every floor – searching the horizon for first light at the end of their shift.

She recently had a patient who had been fighting for his life all night. The nurses knew the little boy wasn't going to make it. "He died at 6 a.m.," recalls Wong. "He had a room with a view of the bay. At 6:15, we all looked to the window and saw the most epic sunrise. It was as if his soul was lifting. It was an end and a beginning."

– Claire Conway

Mei-Ling Wong and her mother, Peggy Cadbury, photographed on the pediatric ICU roof garden of UCSF Benioff Children's Hospital San Francisco at sunrise, April 14, 2017.





# Ophir Klein is growing teeth,

which is just slightly less odd than what Jeffrey Bush is growing – tissues that make up the face. Jason Pomerantz is growing muscle; Sarah Knox is growing salivary glands; and Edward Hsiao is printing 3-D bone using a machine that looks about as complex as a clock radio. Together, these members of the UC San Francisco faculty are cultivating organs of the craniofacial complex – the skull and face – which too often go terribly wrong during fetal development. Deformities of these bones or soft tissues, the most common of birth defects, can cut life short by blocking the airway or circulation. Or they can disfigure a face so profoundly that a child struggles to see, hear, or talk. Perhaps most painful of all, such deformities render children physically *other*, potentially leading to a lifetime of corrective surgeries and social isolation.

As director of the UCSF Program in Craniofacial Biology, Klein orchestrates a multisite research endeavor to translate basic science findings in tissue regeneration into improved treatments for these kids. Using stem cells from patients with craniofacial deformities, Klein, Bush, Pomerantz, Knox, Hsiao, and their colleagues are growing tiny functioning segments of organs, called organoids, to figure out exactly when and how in fetal development such design flaws occur.

They are among scientists across UCSF who are cultivating cellular systems such as miniature brains and breasts from patient cells. They serve as dioramas of disease – models derived from human cells – either displacing or complementing the mouse models that have served science well, though inexactly, for many years. The effort is one of the most obvious and viable payoffs to date from stem cell science. With these organoids, physicians and scientists can not only trace the pathways of normal and abnormal development, but also test drugs and other treatments for their effectiveness in humans. Organoids are also one tiny step toward the ultimate goal of generating complete organs, as a way to circumvent rejection issues and save the lives of those who now die waiting for transplants.

As the reservoirs of human development, stem cells take it upon themselves to tirelessly renew and differentiate into the myriad cell types required to build out a body from an embryo. In creating an organoid, typical construction metaphors do not apply. There are no building blocks to nail, stack, or solder and no job-site supervisor barking orders. "That's not how biology works," says Zev Gartner, PhD, an associate professor of pharmaceutical chemistry. "It is a self-organizing process," he explains, a process that starts in the womb with embryonic stem cells (ESCs) or, in the case of organoids, induced pluripotent stem cells (iPSCs). iPSCs are mature cells that are stripped back to their earliest stage of development using a process devised by UCSF Professor of Anatomy Shinya Yamanaka, MD, PhD, who won a Nobel Prize for discovering the process. To make organoids, iPSCs are put through a series of solutions, then added to a gel that mimics the squishy 3-D cellular matrix of the embryo. The gel provides the right conditions for them to get to work.

"Take an organ like the lung. Its basic functional units are a tube and a sac, and outside that sac are capillaries that allow gas exchange. Hundreds of millions of tubes and sacs make a lung," explains Gartner. "You can make the little sacs and the tubes in a dish as an organoid model. But we don't know how to drive the self-organization of those units into much more complex, elaborate, highly ramified structures." The fundamental limitation of organoids is that they lack the vasculature that brings nutrient-laden blood to fuel the evolution of the larger structure.

Gartner notes that people who work with stem cells tend to focus on either regenerative medicine or disease modeling. Those interested in disease make models of tissues so that they can understand how diseases work, while those interested in regenerative medicine try to make models of healthy tissue that could be transplanted. Gartner straddles both camps. He grows breast organoids. "The mammary gland is great because we can simultaneously think about these two phenomena as two sides of the same coin," he says. "One is regenerative medicine through self-organization, and the other is understanding the progression of breast cancer through a breakdown in self-organization."

So there's potentially a triple payoff in stem cell science: By deducing how a breast forms itself, Gartner might figure out how to grow the entire organ. By tracing how cancer throws a wrench in the works, he may be able to target ways to stop that process. And by growing a human organ in a dish, he avoids making crossStem cells take it upon themselves to tirelessly renew and differentiate into the myriad cell types required to build out a body from an embryo.

species assumptions or putting animals or humans at risk in testing potential drugs to cure breast cancer, greatly accelerating the push toward a cure.

## Regenerate

On Klein's team, Jeffrey Bush, PhD, an assistant professor of cell and tissue biology, looks at organoids through the lens of disease. The organoids he grows model craniofrontonasal syndrome – a birth defect that is caused by a mutation in a single gene and that dramatically impacts the shape of the face and head. He knows from studies reproducing craniofrontonasal syndrome in mice that the first place something goes wrong is in a cell type called the neuroectoderm. To create an organoid to study this, he obtained skin cells from Pomerantz, an associate professor of surgery, who has patients with the syndrome who were willing to donate tissue samples. Such col-

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# **The Bone Printer**

Bone grows like a runaway train in Edward Hsiao's patients with fibrodysplasia ossificans progressiva (FOP). The slightest bump or injury can set off a spurt of bone growth that can fuse their vertebrae, lock their joints, or even freeze up their rib cages, leaving them unable to breathe.

No one, to date, has successfully engineered bone. Hsiao, MD, PhD, is hoping to spark the process with the help of a 3-D printer from Organovo, a firm that specializes in bioprinting technology. From iPSCs, he can make many of the essential ingredients of bone, including mesenchymal stem cells, endothelial cells, and macrophages. "We are putting cells into the equivalent of an ink. Then we will print the structures with the ink, let the ink dissolve, and leave the cells," explains Hsiao. "The hope is that the cells can then recapitulate the normal developmental process."

If the approach is successful, Hsiao hopes to use the resulting models to test drugs and other treatments to halt or prevent bone deformities. Down the line, his progress also stands to transform bone and joint replacements. Through his work with FOP, he's uncovered one mechanism that drives rapid bone growth. "In these patients, we know that mature bone formation can happen in as quickly as two weeks, so it is possible to grow bone in an adult. We need to understand how to modulate that," says Hsiao. "Someday, my dream would be to be able to identify the cells we need, give someone a drug that induces the right genes and recruits the right cells to the correct site, and have the cells rebuild the joint from scratch." 2 6 6 3

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Zev Gartner is growing breast organoids with precise ratios of normal and tumor cells (shown at left) to understand how cell-cell interactions contribute to tumor growth.

laborations between basic scientists and clinicians are key to bringing research out of the lab and into patient care.

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"We studied this simple system to see how this mutation affected the organization of these cells," says Bush. His group has filmed cells as they rush about to self-organize when they're mixed together. In those films, he explains, "you can see that the mutated cells, which are dyed red, segregate from the normal cells, which are green - they are like oil and water." In other words, the mutated cells completely disrupt the behavior of all the cells. By contrast, in the films of cells without the mutation, all the cells circulate easily among one another, like fish in an aquarium. This understanding has allowed Bush to begin to think about a drug that blocks this separation. He has several promising candidates that his team will test in pregnant mice. "Right now," he says, "there isn't a single drug that we can use for any kind of structural birth defects. If we could show that a medication blocks the effects of this mutation, it would serve as proof of principle that something besides surgery can be done. But we would have to know that it was safe for mother and child and that we could catch it early enough."

## Reconstruct

Jason Pomerantz, MD, a plastic surgeon, falls into the regeneration camp. His clinical work is typified by a recent eight-hour operation on a 17-year-old boy with Crouzon syndrome, a severely disfiguring condition affecting every organ in the craniofacial structure – muscle, bone, and skin. "My patient is excited for the outcome, but not about the process," says Pomerantz, surgical director of the UCSF Craniofacial Center. For three months, the patient will wear a large metal frame on his head with wires that will pull the bones in his face forward. Prior to the surgery, the boy's face was nearly concave, collapsed inward at the nose.

Yet bone is not all Pomerantz needs to work with to restructure a face. The subtle bends, creases, and curves of expression that make a face one's own are the work of tiny muscles. "Right now we can move a big muscle – say, from the thigh to the face – so that people can smile," he says. "But we can't reconstruct the fine ones that enable people to move their eyebrows up or move the eyeballs around. That requires little muscles. This is where we can make headway with stem cell biology.

"We have actually made a humanized organ in an animal," he continues, pointing to a picture of a mouse on his wall. Pomerantz is now considering incubating small human muscles in animals for use in his patients' faces. In a recent project, he inserted stem cells from human muscles into a mouse whose own muscle stem cells had been incapacitated. He then perturbed the muscle to stimulate regeneration. As the muscle healed, the cells created new muscle tissue, which the mouse's nerves innervated to make a functioning muscle. It's exactly the size of the muscles Pomerantz needs for full articulation of expression and function in a human face or hand.



## Create

Muscles are part of a vast and intricate system strewn throughout the body. Teeth, on the other hand, are islands unto themselves. "Teeth intrigue me from a regeneration perspective," says Ophir Klein, MD, PhD, chair of the Division of Craniofacial Anomalies, the Hillblom Professor of Craniofacial Anomalies, the Epstein Professor of Human Genetics, and a resident alumnus. "They are discrete organs – all the parts are there." More intriguing still is the fact that many rodents have the ability to grow their front teeth continuously. Elephants and walruses also have ever-growing tusks, and even some primates – lemurs – can regrow their teeth.

A tooth can be regenerated in parts. Stem cells can be used to grow the root, and then a crown can be added to complete the tooth. To generate a whole organ at once, Klein's colleagues are planning to partner with bioengineers who can produce a biocompatible material that could serve as a framing device to jump-start the creation of dentin, one of the hard components of a tooth. If they start with the right cells, then the scaffolding will give the cells the shape information they need to create the right design. But even that isn't Klein's endgame. "In my lab, we're interested in figuring out why humans can't regrow teeth," he says. "In studying species that can, we hope to unlock the regenerative potential in our own cells that might be turned off."

Klein's work to generate teeth is inspired by his patients with ectodermal dysplasia, a congenital disorder characterized by lack of sweat glands, hair, or teeth. Being able to generate the roots of teeth would be remarkable for these patients, since the rest can be done with a crown. Right now, they must be fitted with dentures.

Klein is also taking another tack to help these patients. "We completed a clinical trial of a drug that basically goosed up the development of the organs when they weren't forming properly," he says. The drug – a protein developed by Swiss collaborators of Klein's, based on studies of embryonic mice, who develop these

organs in early- to mid-gestation – was given to infants with the disorder right after birth. The trial was unsuccessful. Now, scientists in Germany are running a trial of the same drug, giving it instead to mothers carrying babies with this genetic disorder. The scientists will try to gauge what the best timing is for delivering the drug.

"What's great about this drug is that it doesn't seem to have any effects on any other organs besides teeth, hair, and sweat glands," says Klein. "Drugs for other conditions are far riskier, because they affect pathways that are important in the development of many organs."

Maintain

Sarah Knox, PhD, an assistant professor of cell and tissue biology, is using stem cells to figure out how to regenerate salivary glands compromised by radiation treatments for head and neck cancers or by craniofacial deformities. Her focus is on how the environment contributes to the activation and maintenance of the gland. The salivary gland, like all organs, is continuously replenishing the supply of cells and tissues it needs to function. Knox's research shows that the gland takes directional cues from nearby nerve cells not only to remain functional, but also to continuously

replace itself. Her organoids are made of cells from a patient and nerve cells (ganglia) from a fetal mouse. "We are trying to explore the relationship between the stem cells and the nerves," she says. "How do the nerves know the tissue is there? How do the nerves provide instruction and feedback? Individual cells die off and new cells have to replace them. Organoids are giving us insight as to where those new cells are coming from and how we keep repopulating [them] all our lives."

## Consider

As head of the UCSF Program in Craniofacial Biology – which is based in the School of Dentistry and the Division of Genetics in the School of Medicine – Klein stands at one of science's most compelling crossroads: regenerative medicine and genetics. Far in the future, both fields have potential that seem like science fiction today. We live in a world where people die waiting for organ transplants. What if we could pull these organoids from their petri dish and supply them with the fuel they need to become full-blown organs? Such a feat would necessitate either a host embryo – perhaps from a pig, because pigs have organs the size of human organs – or some other biological foundation. Some scientists are hoping to jump"In studying species that can [regrow teeth], we hope to unlock the regenerative potential in our own cells"

- Ophir Klein

start organ development with "scaffolding," or cells engineered to speed the developmental process. Others are zeroing in on the genome, particularly in kids with craniofacial anomalies caused by just one mutation, like craniofrontonasal syndrome; for example, a tool called CRISPR could allow scientists to splice that gene out and replace it with a normal gene. But the tool has yet to be used in humans, let alone a human fetus.

Ethical questions pepper either route. At their best, stem cells regenerate tissues; at their worst, they go rogue and grow into a tumor. "Yet with gene editing tools like CRISPR, you literally have the potential to change the species," says Klein. And in both scenarios, the cells can act with unforeseen off-target effects. Klein and his colleagues are in continual discussion about the repercussions of their work with the director of UCSF Bioethics, Barbara Koenig, RN, PhD '88. "Gene therapy is an example of an exciting new treatment that cured one serious pediatric illness - severe combined immunodeficiency syndrome (SCID) - but the genes unwittingly led to the development of leukemia," explains Koenig. "Genetic and stem cell interventions must be painstakingly studied before application. And, once they are ready, who will regulate them? There are many questions yet to be answered. The challenges are most extreme when we talk about modifying an egg or sperm cell, where the changes are passed on to the next generation."

So Klein and his colleagues proceed with caution, curiosity, and awe. "The next decade will be an incredibly exciting time," says Klein. "With continual advances in human genetics and developmental and cell biology, we hope to be able to make drugs and use genetic tools to appreciably change the lives of our patients."

# Largest-Ever Gift to UCSF Honors Philanthropist Helen Diller

by Jane Feledy Goodman and Claire Conway

To honor and build on a lifetime of giving and charitable service by the late Helen Diller, the Helen Diller Foundation has granted \$500 million to UC San Francisco, a university to which Helen was both generous and devoted. The gift will be the largest single donation in UCSF's history and one of the largest ever to a U.S. university.

Helen's renowned compassion and lifelong commitment to improving the world for future generations as a philanthropist, advocate, and mentor has had a singular impact on UCSF and other higher education and charitable institutions.

The new gift is especially noteworthy for the unprecedented level of ongoing funding it will provide for the University's world-class faculty and talented students. This investment in public education underscores Helen's formative student experience, as she attended UC Berkeley and generously supported her alma mater and UCSF, along with Jewish communal needs, throughout her life.

## Longtime supporter of UCSF

This is the second time a grant in honor of Helen has made UCSF history. In 2003, the Helen Diller Foundation made a generous \$35-million donation, a foundational investment in the University's



burgeoning presence at Mission Bay, to support prostate cancer research and what is now the Helen Diller Family Cancer Research Building. Though the gift resulted in a building bearing her name, the recognition was less important to Helen than the possibility that it might inspire others to give.

Upon the gift's announcement, Helen said, "Our family is extremely enthused about cancer research at UCSF. By supporting the new Mission Bay campus, we are not only aiding the scientists researching a cure for this

devastating disease but we also have been presented with the joy of participating in the development of an entirely new section of this very beautiful city." Since 2003, the Helen Diller Foundation has made significant annual gifts and provided for a permanent endowment for the UCSF Cancer Center in Helen's honor. Those gifts have totaled more than \$150 million.

"My mother was dedicated to UCSF and to many other programs aimed at improving the lives and well-being of others through education, science, and the arts. I know this latest gift would be enormously gratifying to her," said Helen's daughter, Jackie Safier, president of the Helen Diller Foundation and a member of the UCSF Foundation Board of Overseers.

## 'Vision and trust' in innovation

Helen enthusiastically supported the research of Urology Chair Peter Carroll, MD, MPH, the Ken and Donna Derr-Chevron Distinguished Professor in Prostate Cancer, who through the years became a close family friend.

"Helen would have been astounded by the progress in cancer research and care that we have made in her name," says Carroll, a member of the UCSF Helen Diller Family Comprehensive Cancer Center. "She was an inspiring partner and, as a faculty member, I am deeply grateful to the Foundation for this magnificent new gift that will allow our faculty and students to spend their time pursuing groundbreaking discovery to transform the care of our patients at UCSF and around the world."

"The forward-thinking commitment of the Diller Foundation to support great science and brilliant people is exactly what drew me to UCSF from London," says Alan Ashworth, PhD, president of the UCSF Helen Diller Family Comprehensive Cancer Center and the E. Dixon Heise Distinguished Professor in Oncology.

"Gifts like this come from a place of vision and trust. Vision that we can and will change the state of things through research and trust that we will gather the right people to do it," Ashworth says. "We are thankful for the Foundation's generosity and are committed to exceeding all it imagined we could achieve." "This gift, in her name, will promote all that Helen stood for – education, hope, healing – for generations to come."

- Chancellor Sam Hawgood



## **Investing in brilliance**

The majority of the new commitment, \$400 million, will establish endowments in Helen Diller's name to support UCSF faculty and students, a critical University goal. This new commitment will increase UCSF's endowment, which currently stands at \$2.25 billion, by nearly 18 percent.

"The Helen Diller Foundation recognizes the extraordinary importance of endowment as we seek to attract the brightest talent," says Sam Hawgood, MBBS, UCSF's chancellor and the Arthur and Toni Rembe Rock Distinguished Professor, noting that UCSF and most other public universities lack the deep endowments of private peer institutions.

The endowed funds will be used in the following ways:

#### Faculty support

A \$200-million endowment will create a significant stream of faculty support in perpetuity.

Of this sum, \$100 million will be used to retain outstanding current professors and recruit preeminent faculty to UCSF by funding Helen Diller Distinguished Professorships. They may be awarded either to established UCSF faculty rising into leadership positions or to stellar senior faculty recruited from other institutions. These top clinicians and researchers will mold the next generation of health professionals and shape the culture of care in clinics and hospitals, while accelerating discoveries in laboratories. The commitment will significantly change the landscape of UCSF faculty funding. In the UCSF School of Medicine, for example, approximately 25 percent of faculty currently receive funding from the state or through professorships. The remaining 75 percent must raise nearly every dollar of their salaries, through either clinical practice or research grants. With the knowledge of dependable funding, Helen Diller Professors will have the opportunity to pursue research, initiate new lines of inquiry, teach and mentor students and younger colleagues, spend more quality time with patients, and take on the most difficult cases.

The additional \$100 million of faculty endowment will provide crucial start-up money for the Helen Diller Faculty Scholars program for early- and mid-career scientists. More and more, philanthropy plays a crucial role in helping young faculty launch their academic careers. Helen Diller Faculty Scholars will receive at least \$150,000 annually to establish laboratories, buy equipment, hire graduate students and postdocs, and generate the research results that lead to long-term funding from agencies such as the National Institutes of Health.

#### Student support

An additional \$200 million of endowment will support students at UCSF's four professional schools – the schools of dentistry, medicine, nursing, and pharmacy, all of which are ranked among the top in the

nation. This commitment increases the amount of funding available for scholarships by more than 150 percent.

The financial support from the Helen Diller Scholarship Program will allow many students, including first-generation college students, to graduate with a minimal amount of debt, giving them the freedom to pursue life-changing work in their communities.

"I am deeply grateful for the Helen Diller Foundation's forethought in investing in our remarkable faculty and students and those who will follow in their footsteps," says Hawgood. "It is a privilege to be surrounded each day by people who are so incredibly driven, focused, and collaborative, and Helen Diller truly understood this. She knew that the excellence of our people is what makes UCSF such a remarkable place, and I am honored to help steward this gift in support of Helen's vision."

#### Innovation Fund

The final \$100 million will create an Innovation Fund which can be drawn on, over time, at the discretion of UCSF's current and future chancellors.

Universities covet discretionary funds because most philanthropic gifts to academia are earmarked for specific purposes. In 2015-16, for example, UCSF raised nearly \$747 million, but less than 0.5 percent of those funds were discretionary.

"Unrestricted funds give me the flexibility and agility to respond to the rapid changes in the health sciences," says Hawgood. "These funds will seed areas that will redefine the future of health care and



could support priorities ranging from genomic surgery to cell engineering, from immunotherapy to microbiome research, and from neurotechnology to next-generation diagnostics for infectious and inflammatory diseases."

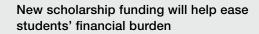
Discretionary funds also enable the chancellor to direct support toward other urgent areas of high-risk, high-reward research with potential global consequences, such as identifying the cause and preventing the spread of the Zika virus. These efforts are integral to future discoveries and embody UCSF's culture of interdisciplinary collaboration.

## Cultivating a legacy of care

Helen was born at Mount Zion Hospital – which is now part of UCSF – and raised on Pierce Street in San Francisco. Once her children had grown, she embarked upon an impactful career of philanthropy, with an emphasis on Judaism, education, science, and the arts. She described her style as a "hands-on approach," one where she didn't just give funds but created inspiring new programs. In her first major role in philanthropy, Helen served as the northwestern president of the American Friends of Hebrew University.

Helen valued and supported education at every level, from preschools to day schools to high schools to colleges – including UC Berkeley and UC Santa Cruz – to postgraduate education. In 2002, Helen made a \$5-million gift to UC Berkeley to support a multidisciplinary visiting Israeli scholars program and to fund fellowships and research grants in Jewish studies. At the time, it was the largest single gift supporting Jewish studies on that campus.

Helen was perhaps most proud of her Diller Teen Initiatives. Through the Diller Teen Fellows program, she created an international teen leadership program that is now operating in North America, Argentina, Australia, Israel, South Africa, and the United Kingdom. Diller Fellows explore their collective Jewish identity as well as how they want to make their mark in the world.





The average educational loan debt borne by 2016 graduates of UCSF's four professional schools



The Diller Teen Tikkun Olam Awards program has recognized hundreds of teens for their outstanding volunteer service in the community, for doing good work near and far – spreading religious pluralism, constructing water wells in Africa, building soccer fields, and donating books and supplies to at-risk youth in their schools from California to New Jersey, to mention just a few examples.

As a San Francisco native, Helen took a keen interest in the children of the city. She revitalized children's parks by supporting the reimagined designs of playgrounds in Dolores Park and the Civic Center. She also valued the role of the arts and culture in enriching human lives and was an avid collector of contemporary art. Helen proudly funded the de Young Museum entrance courtyard, new galleries in the expanding San Francisco Museum of Modern Art, and an annual Israel Antiquities Lecture Series at the Legion of Honor in San Francisco.

"Helen had unusual humility and an ability to remember the past but to live very much in the present," says Phyllis Cook, executive officer of the Helen Diller Foundation. "She figured out early on that life is more meaningful if we care for one another. I remember her saying, 'My parents did things in a small way because that is what they could do. Now we are doing what we are able to do.""

For her tireless and visionary work, Helen received the Lifetime Achievement in Philanthropy Award from the Association of Fundraising Professionals' Golden Gate Chapter in 2012. She also posthumously received the UCSF Medal, several months after she died in 2015, for her outstanding contributions to health.

"This gift, in her name, will promote all that Helen stood for – education, hope, healing – for generations to come," says Hawgood. "On behalf of all of us in the UCSF family, we are humbled to help fulfill her legacy."

## Creating Opportunities to Pursue UCSF's Public Mission

Now more than ever, when students graduate as health care professionals, the majority walk away with more than a diploma – they are also saddled with up to hundreds of thousands of dollars in debt. The financial pressure can be especially troubling for students like Amanda Voigt (at left), who hopes to work in primary care, and Nathan Kim (on page 33), who wants to care for underserved populations, career paths that tend to offer more modest incomes. The scholarships funded by the new \$200-million Diller endowment could, in the future, help such students choose UCSF.

"UCSF was my top pick because of its great reputation, especially for primary care education," says Voigt, a first-year medical student. "But the cost of living in San Francisco wasn't very favorable. At some other schools, I could live for a year on what it costs me to live here for three months." Only when Voigt was notified of her scholarships, which cover about 20 percent of her total costs, did she know she could attend her dream school. "I have to say that was one of the most exciting days of my life," she says.

Kim knew that the UCSF School of Medicine offered the mentors and commitment to social justice he was looking for, but coming from a low-income background, he nearly turned down the opportunity after receiving a generous scholarship from another medical school. Fortunately, a matching financial aid offer from UCSF allowed Kim to enroll at his first choice.

"Since high school, I've wanted to be an HIV doctor working in underserved communities," Kim says. "I was overjoyed to get in here, but it was like a God-given miracle when I got that financial aid email."

– Nina Bai



Tackling Childbirth-Related Mortality in the World's Poorest Place

A new UCSF School of Nursing program in Malawi will launch this fall in the hope of turning the tide on childbirthrelated mortality and addressing the nation's critical need for nurse and midwife training.

In Malawi, a small, landlocked nation in southeastern Africa, hardly anyone congratulates a woman who is pregnant. They will do so only after she gives birth, and then only if both mother and child survive.

That's because Malawi, the poorest country on the planet, has the world's highest rate of preterm births. Women there have a one-in-29 lifetime risk of dying from childbirth-related causes. And their babies also face dire odds: The neonatal mortality rate in Malawi is 22 per 1,000 live births, or one in 45.

Such statistics are almost unimaginable to those living in the U.S., where the maternal mortality rate is just one in 3,800 and the neonatal mortality rate is just four per 1,000 live births (or one in 250). But that discrepancy is all too real to Melanie Perera, MS '12, who spent three years training nurses in Malawi.

"In one year there," says Perera, "I saw more babies and children die than I'd seen in five years as a nurse at Stanford."

Perera didn't hesitate when she was asked by School of Nursing faculty members Kimberly Baltzell, RN, PhD '05, and Sally Rankin, RN, PhD '88, to direct a new program called Global Action to Improve Nursing and Midwifery (GAIN). Baltzell and Rankin, founding directors of the nursing school's Center for Global Health, created the program to train Malawian nurses in leadership and clinical skills and to offer on-site coaching for a year afterward. They hope the program will not only turn the tide on childbirth-related mortality in Malawi, but also help address the nation's critical need for nurse training.

GAIN will launch in September with a cohort of 20 Malawian nurses. The trainees will learn clinical practices based on World Health Organization standards, which range from identifying dangerous postpartum bleeding in mothers to implementing lifesaving skin-to-skin contact between mothers and preterm or low birth weight newborns. In creating the curriculum, program leaders are working closely with Malawian colleagues and international organizations such as Partners in Health.

The leadership training and ongoing mentoring are crucial. After the classroom training is completed, a nurse expert in midwifery or labor and delivery will coach the learners where they work, helping them improve clinical quality.

Train-the-trainer programs such as GAIN have shown dramatic results in other locales. After only one year of a pilot program at Gobabis District Hospital in Namibia, for example, maternal mortality dropped from 153 of every 100,000 live births to zero, while stillbirths were reduced by nearly half and early neonatal mortality by one third. Such training has also been shown to give a significant boost to the participating nurses' self-confidence.

Reflecting on her time in Malawi, Perera says, "I saw nurses grow in self-respect, in the knowledge that they each have a unique gift to bring to their practice. As they grow more confident, they become advocates for their patients."

Baltzell points to the even wider ripple effect of such improvements.

"When you lose a mother in childbirth, you lose a stabilizing force in the community," she says. "Orphaned children have long-term educational and economic deficits. The consequences are profound. Saving a mother's life saves the entire community from a whole constellation of effects."

- Mark Hoyer

## Alumni Hub

## Join your alumni network at UCSFCONNECT.COM



**Connect with UCSF Connect:** Joseph Lin, PhD '03 (left), was one of seven alumni from UCSF's Biomedical Sciences Graduate Program who answered questions from PhD students at Mission Bay one evening last spring. About 40 students attended the event, rotating from table to table to discuss various career options. Lin, an associate professor of biology at Sonoma State University, spoke about academia, while other alumni gave their perspectives on careers in industry, biotech, government, policy, and clinical settings.

Now it's easier than ever to join the alumni and student community through UCSF Connect, your new career and professional networking platform. You can register in less than two minutes using your LinkedIn or Facebook profile to connect with your alumni colleagues. Or you can volunteer for programs like the ones described in the following pages, to keep you engaged and offer current students a chance to learn from UCSF grads who have launched successful careers. Learn more at UCSFCONNECT.COM.

## SCHOOL OF DENTISTRY

## JEREMY HORST, DDS, PHD, RESIDENT ALUMNUS

Hometown: San Francisco

Now: San Francisco

**Position:** Pediatric dentist and postdoctoral fellow

Hobbies: Bicycling, hiking, spending time with family



Not long after Jeremy Horst arrived at UC San Diego for college, he began to feel bored by school and was more interested in being a DJ and going to parties.

Then, one summer break, he spent time with his grandfather, a physician who had made a key discovery about the diphtheria virus. Horst returned to school and, inspired by the possibilities of science, went from failing organic chemistry to receiving the highest grade in his class.

### CARING FOR COMMUNITY:

Horst earned bachelor's degrees in psychology and chemistry and stayed on at UCSD to get a master's degree in chemistry. While in San Diego, he also worked in – and eventually managed – a free dental clinic run by volunteer predental students and community dentists. The clinic cared for underserved populations, including uninsured children and homeless individuals.

"I saw a real need there," Horst says. "Putting science and dentistry together made sense for me, and it was a chance to make a difference." He soon began a DDS-PhD program at the University of Washington in Seattle, where he worked in the lab, using large databases to sequence the DNA of proteins that contribute to tooth development and craniofacial anomalies. In addition, he continued to volunteer in rural dental clinics.

## CAVITY KILLER: A native San

Franciscan, Horst was happy to return to the Bay Area for a postdoctoral research fellowship at UCSF with Joe DeRisi, PhD, professor and chair of biochemistry and biophysics and co-president of the Chan Zuckerberg Biohub. Now, Horst practices as a pediatric dentist one day a week and spends the rest of his time in DeRisi's lab, studying silver diamine fluoride (SDF), a promising, low-cost treatment for dental cavities that doesn't involve drilling or filling. "We have an abundance of evidence from clinical trials that SDF stops a lot of cavities and is safe," he says, noting that UCSF is setting guidelines for the use of SDF nationwide. "I've become a nexus for communication about SDF and have met some of my heroes in the field by traveling to conferences."

Horst is also trying to achieve some work-life balance so he can spend more time with his wife, Risa, and their daughter, Cadence.

"It feels like I've been in school forever," he says. "But UCSF is preparing me really well. It's truly fun to be in a lab led by a world leader in basic science."



## MICHELLE LACUES, DDS '06

Hometown: Redwood City, Calif.

Now: Redwood City, Calif.

**Title:** Dentist and owner of Lacues Dentistry

Hobbies: Travel, hiking, scuba diving, spending time with family, learning Italian

At the tender age of 15, Michelle Lacues was already demonstrating a talent for what would become her life's work. Helping out in her uncle's dental office, she transitioned over time from providing administrative support to serving as a dental assistant and found that she had an affinity for the profession.

"The idea of a private practice appealed to me – the flexibility, the opportunity to build a community, and to care for kids while watching them grow up," she says. Thus began her journey into dentistry and her path to UCSF.

ALL IN THE FAMILY: She attended the University of San Francisco, where she fell in love with science and received her bachelor's degree in biology, with a minor in chemistry. Following in the footsteps of her uncle, Michael Sala, DDS '89, she was inspired to attend UCSF School of Dentistry for her professional training. "My uncle spoke so highly of UCSF and got such a good education there," Lacues says. "I thought of it as the gold standard in dental schools." She had excellent instructors who liked to work closely with small groups of students to help them excel, she says. One mentor in particular – Joel White, DDS, chair of the UCSF Division of Preclinical Simulation – helped shape her approach.

"In fourth-year clinic, he taught me a lot about patient management but was hands off, letting me experience what it would be like when I was on my own."

**DEEP DIVE:** Now she has that private practice, in her hometown of Redwood City, just across the hall from her uncle's office. There, she sees patients from her closeknit community, many of them old high school friends and others she knew as a child, who now bring children of their own to her for dental care. "They all come to me by word of mouth," Lacues says. "I learned from my uncle that if you do right by your patients, these things take care of themselves."

When she can get away, she enjoys scuba diving, leaving the

cold California waters behind to head to Hawaii or the Caribbean. "I'm always a little nervous until the moment I get under the water," she says. "Unless you explore what's beneath the surface, you can't imagine the other world that's down there."

## CONNECT: TO SPREAD THE WORD ABOUT SCIENCE

The Dental Alumni Association (DAA) holds its annual Scientific Session in conjunction with Alumni Weekend, giving dentistry students an opportunity to present their research to a professional audience. As a student in 2012, Jeremy Horst received first place for his poster, "Computational drug discovery for dental caries." Michelle Lacues, as the 2016-17 DAA secretary and communications committee chair, now curates the competition.

## SCHOOL OF MEDICINE



### RHONDA LEVITT, MD '79

Hometown: Los Angeles

Now: Seattle

**Position:** Pediatrician (retired), Polyclinic Northwest Pediatrics

**Hobbies:** International travel, hiking, bicycling, camping

Recently retired after 35 years of pediatric practice, Rhonda Levitt continues to help young people get the best start in life. She and her husband, Chuck Cowan, MD, who is also retired, host UCSF medical students who are in Seattle for residency interviews. They welcome students into their home and introduce them to Seattle's vast medical and public health resources.

"We have been impressed with every one of them," Levitt says. "It's exciting to see UCSF students who are so bright and excited, so diverse in their backgrounds and interests."

#### SCIENCE AND CONSCIENCE:

Levitt grew up in Southern California with a politically active mother and an aeronautical engineer father. She landed at the ideal place to pursue her interests in science and community organizing – UC Berkeley, where she earned her bachelor's degree in biochemistry. Before starting medical school, she completed two years of graduate biochemistry studies and worked for Zero Population Growth and the San Francisco Interagency Pregnancy Council.

"I found that I liked clinical work more than abstract research," she says. "I felt I could make a greater contribution by working directly with patients."

**MEDICINE AND MORE:** Levitt's medical school class at UCSF was about 30 percent women, a significant increase over previous years. "It was an incredible class," she says. "We were interested in collegial, cooperative, group learning."

Once she got to Seattle – for a pediatric residency at Seattle Children's Hospital – she knew she'd found her permanent home. That meant more than just a place to practice medicine. There, Levitt raised two children, volunteered at the Country Doctor Youth Clinic's health service for homeless teens, and served on the board of the Northwest Women's Law Center; now, in retirement, she plans to volunteer both locally and overseas.

"I always felt strongly that I needed to do more than provide medical care," she says. It's a message she passed on to the medical students she taught over the years and that she now shares with students from UCSF who visit her home.

"I tell them that medicine is important, but life is more than medicine," she says. "To be a good doctor, you have to be part of your community."

## CONNECT: TO HELP STUDENTS FEEL AT HOME

In two short years, the Medical Alumni Association's HOST (Host Our Students as they Travel) program has won praise from hosts and travelers alike. Rhonda Levitt hosted Samantha Rawlins-Pilgrim in 2015, helping her offset residency interview expenses. "The program allows alumni to be reminded of what a special place [UCSF] is," wrote one host. "It's so inspiring to see that the future of medicine is in such superbly trained hands!"

"At UCSF, I formed lasting, supportive friendships and found some incredible mentors."





## SAMANTHA RAWLINS-PILGRIM. MD '16

Hometown: Boston

Now: Boston

**Position:** Internal medicine resident. Boston Medical Center

Hobbies: Re-exploring Boston, spending time with friends and family

Samantha Rawlins-Pilgrim has an overarching goal for her career: to help people, especially the underserved. She her father a neurologist - so days as a child in her parents' clinical offices and discussing interesting cases around the dinner table.

was raised by two physicians her mother is a psychiatrist and medicine has always been part of her life. She recalls spending She considered other careers,

including teaching and social work. But before she started college, she spent a summer working in a lab at Tufts University. Then she knew that medicine would be her path.

"I kept coming back to medicine, especially public health, because it fulfilled what I really wanted to do," she says.

#### **BUSY BEGINNING: Rawlins-**

Pilgrim wasted no time getting started with her education. While earning her bachelor's degree in Spanish and fulfilling her premed requirements at Yale University, she worked at an HIV/AIDS residential treatment facility, was a volunteer and interpreter at the student-run HAVEN Free Clinic, and served as director of AIDS Walk New Haven. She also joined an exchange program that took her to Santiago, Chile, for a semester and another exchange with the

HIV/AIDS branch of the Hong Kong Department of Health. After this ambitious beginning, she needed a very special place to earn her medical degree. She applied to numerous medical schools across the country but appreciated UCSF's focus on caring for the underserved.

#### PRIMED FOR SUCCESS: The

highlight of her experience at UCSF, she says, was participating in the Program in Medical Education for the Urban Underserved (PRIME-US), a five-year program that prepares medical students from diverse backgrounds to provide health care for vulnerable urban populations.

"PRIME was filled with likeminded people," she says. "I formed lasting, supportive friendships and found some incredible mentors." She still turns for guidance to PRIME-US Mentorship Director Elisabeth Wilson, MD, MPH, and HIV specialist Peter Hunt, MD, both resident alumni.

Now back in her hometown for an internal medicine residency at Boston Medical Center, she also plans to enroll in a master of public health program.

"I'm still at the beginning of a long road," she says. "It's exciting, but I'm humbled by all the things I don't know."

### ALUMNI HUB

## SCHOOL OF NURSING



### HARDEEP AULAKH, MS '16

Hometown: San Francisco and Orinda, Calif.

Now: San Francisco

**Position:** Nurse practitioner resident in adult-gerontology primary care, San Francisco VA Medical Center

**Hobbies:** Singing, playing the harmonium, painting

After Hardeep Aulakh earned her bachelor's degree in classics from UC Berkeley, she worked for a brief time in the banking profession but did not feel at home in that milieu.

She kept coming back to what her mother, also a nurse, called her "nurse-like tendencies," which had surfaced early in her childhood and were reflected in so many of her chosen activities. Aulakh had always enjoyed taking care of loved ones, volunteering at her local Sikh temple, and serving as a counselor in a camp infirmary. Such service felt natural, like a labor of love, so she decided to follow her heart and change careers. "I was already doing many of the things nurses do," she says. "I finally found my home."

**AMONG THE BEST:** Aulakh pursued training and worked as a certified nurse assistant and licensed vocational nurse, then earned a bachelor of science degree in nursing, with honors, from New York University.

Advancing her education at UCSF seemed like a natural next step, the wisdom of which was confirmed by her first visit.

"There was a strong energy to the campus," she says. "Everyone wanted to make the best of themselves and provide the best care for others. I knew I belonged there." She is full of praise for her many dedicated instructors, especially Clinical Professor JoAnne Saxe, MS '82, for making a genuine investment in her students' learning and careers.

## FOREVER LEARNING: Aulakh

earned her master's degree in nursing with a minor in diabetes, plus certification as an adultgerontology primary care nurse practitioner. Now she's halfway through a year-long residency at the San Francisco Veterans Affairs (SFVA) Medical Center, at Fort Miley, where she works on multidisciplinary teams delivering hands-on patient care, mentoring nursing students, and striving every day to refine her nursing and caregiving skills.

"Nursing is a profession that requires lifelong practice," Aulakh says. "UCSF and SFVA have given me the tools to be the best nurse practitioner I can be." Her residency has been so inspiring that she hopes to continue working at the VA long after she completes her residency program.

"It is an honor to care for veterans," she says. "I love listening to their stories, their experiences. It's humbling to know that I'm making a positive difference in their daily lives."



PHOTOS: SONYA YRUEL

When Candace Carter Miller arrived in Vietnam in 1971, during the height of the conflict there, she was a young nurse and a newly minted captain. "Everyone I knew had been there, including my father," she says. "There was no such thing as orientation; we were thrown into the deep end." She vividly remembers that time and believes it prepared her well for her future nursing career. "It was exciting, maturing, challenging, life changing."

**ARMY NURSE:** Born in the Panama Canal Zone, where her father was an Army colonel, Miller grew up on military bases around the world. She earned a bachelor's degree in nursing through the Walter Reed Army Institute of Nursing and, after a year with the 95th Evacuation Hospital in Danang, Vietnam, arrived at Letterman Army Medical Center, then an active facility on the Presidio of San Francisco.

Her initial focus there was on caring for kids with cancer, which made nearby UCSF the best place to continue her studies. "All pediatric Army cancer patients west of Colorado came to Letterman," she says. "Working with those patients could be so difficult, yet so rewarding."

> While earning a master's degree with help from the GI Bill, Miller transitioned from active duty to the reserves of the California Army National Guard.

**CARING FOR VETS:** After completing an oncology residency in Washington, D.C., she worked with adult cancer patients at

## CANDACE CARTER MILLER, MS '77

Hometown: Alexandria, Va.

Now: El Dorado Hills, Calif.

**Position:** Clinical nurse specialist (retired) in oncology and wound, ostomy, and continence care, Veterans Affairs

Hobbies: Learning Spanish, exercising, gardening, skiing, traveling, scuba diving

Hospice by the Bay in Marin County, Calif. Then, in 1980, she began a 32-year career in Veterans Affairs (VA) medical centers – first in San Francisco, then in Sacramento. She was the San Francisco VA's first oncology clinical nurse specialist (CNS) and set up its first formal chemotherapy infusion center. Later, she developed its wound clinic.

"I loved working for the VA and as a CNS, since I could develop roles for myself and have an impact on many areas of the hospital," she says. "I'm grateful for my time at UCSF because it taught me to be a leader."

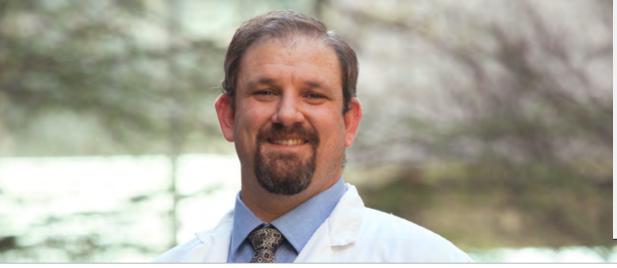
Like her father before her, she retired as a full colonel. Now she is enjoying spending time with her grown children and her husband, Doss Miller, who also worked at the VA for many years. She volunteers at her church and ushers at the Harris Center for the Performing Arts.

"I'm enjoying the arts now, after spending all my life in the sciences," she says.

## CONNECT: TO BUILD HANDS-ON SKILLS

The San Francisco Veterans Affairs Medical Center assigns second-year nurse practitioner trainees like Hardeep Aulakh to interprofessional teams, giving them a chance to work alongside medical residents and long-term professionals like Candace Miller to develop their hands-on patient care skills in a medical home model. "It's an incredible experience you're not going to get anywhere else," Aulakh says.

## SCHOOL OF PHARMACY



### DANIEL ZLOTT, PHARMD '07

**Hometown:** Poway and Yreka, Calif.

Now: Lovettsville, Va.

**Position:** Clinical pharmacy specialist, surgery and immunotherapy, National Cancer Institute

Hobbies: Gardening; photography; cooking; playing guitar, piano, and saxophone

Oncology pharmacist Dan Zlott and his wife, Jennifer, own a house on 30 wooded acres in rural Virginia. It's a peaceful refuge away from the bustling National Cancer Institute in Bethesda, Maryland, where Zlott has worked since leaving UCSF and his home state of California in 2007.

Although conducting oncology clinical trials can be frustrating, Zlott finds his work deeply fulfilling. "One of the most exciting things about my work is that every day is different," he says. "I'm part of a clinical research team that is constantly covering new territory and searching for solutions. It's bench to bedside and back again."

**SUPPORT STRUCTURES:** After his undergraduate studies at University of the Pacific, Zlott came to UCSF to earn his PharmD degree. He was following in the footsteps of his father, Les Zlott, PharmD '71, but he also believed that UCSF was the right place for him. "I knew early on that I was interested in research," Zlott says. "And when it comes to pharmacy and research, there's no better place than UCSF." Part of a tight-knit class, he quickly had a support structure to help him get through the intense program.

"What you learn is vital, but the classmates and professors are what make it memorable," he says. UCSF Professor of Bioengineering Leslie Benet, PhD '65, was an especially valuable mentor. In Benet's lab. Zlott helped synthesize a new antibody with the potential to combat leukemia. That inspiring experience gave him new insight into what would be, for him, the most rewarding application of his molecular biology knowledge: researching novel and effective cancer therapies.

"Cancer research requires an incredible amount of basic science understanding and cumulative learning," Zlott says. "It also requires pharmacists, because all cancer drugs have toxicities that have to be managed, and pharmacists are well trained in pharmacology and side effects."

#### FROM STUDENT TO MENTOR:

While at UCSF, Zlott had an opportunity to take a national leadership role as a student representative on the American Pharmacists Association board of trustees. Last year, he began a new three-year term and now gets to mentor students. "I provide guidance to give students a voice and direct their passion and energy to advance the profession," he says. "That's really important to me."

# CONNECT: TO MENTOR THE NEXT GENERATION

Each spring, the the Pharmacy Alumni Association and the California Society of Health-Systems Pharmacists' UCSF chapter co-host Mentor Night, offering current students an audience with UCSF alumni. Volunteers share stories from their professional lives and answer questions from students. After receiving great mentoring at UCSF, Dan Zlott and Marjorie Robinson are now giving back to students in their field.

"I knew that pharmacists could play a key role in fighting infectious diseases, including HIV."



### MARJORIE ROBINSON. PHARMD, RESIDENT ALUMNA

Hometown: Kingston, Jamaica

Now: Pembroke Pines, Fla.

Title: Associate director and HIV/HCV medical scientist, **Gilead Sciences** 

Hobbies: Watching professional tennis, reading, traveling, political advocacy

naturally to Marjorie Robinson; it was modeled by her family brother, Vernon."

Service to others comes

from her earliest days. Growing up in Jamaica, she watched as her pharmacist father provided care to the underserved and her mother volunteered in local orphanages. "My parents had a passion for serving the community," she says, "and they passed that on to me and my Today, Vernon runs the fam-

ily's retail pharmacy, which has served the same community in Kingston for 75 years. And Robinson visits Jamaica frequently to help at health fairs in impoverished areas and to consult with the government on HIV education. Her reach, however, has extended far outside her hometown – to New York, San Francisco, Florida, South Africa, and beyond.

### **KEEPING UP WITH**

**THOROUGHBREDS:** After doing pharmacy training in Jamaica, Robinson earned a bachelor's degree in pharmacy at St. John's University in New York City and then a doctorate in pharmacy at Nova Southeastern University in Fort Lauderdale, Florida. Long interested in helping HIV patients, she next set her sights on "the epicenter" of work on HIV/AIDS - San Francisco General Hospital, now Zuckerberg San Francisco General.

"I knew that pharmacists could play a key role in infectious diseases, including the HIV

epidemic," Robinson says. She was selected for an infectious diseases (ID) residency at UCSF. Joseph Guglielmo, PharmD, resident alumnus, now dean of the School of Pharmacy, was among her influential mentors and became a lifelong friend.

"I knew I was running with thoroughbreds at UCSF," she says. "As the only ID resident more than 20 years ago, I was just a pony. But you learn very quickly to be scientifically accurate and develop your strides and do the kind of thinking that gets you to innovative answers."

#### **BEYOND BOUNDARIES:**

Robinson wanted to help improve pharmacy training, using UCSF's program as an example. She became a professor at Nova, where she worked to advance the curriculum, a role she also took on at her alma mater in Jamaica.

- "It was important to me to help standardize the curriculum across borders," she says. "My UCSF education helped me improve pharmacy training in South Florida and throughout the Caribbean." After several years in academia, she moved into the pharmaceutical industry to work on clinical trials for HIV and hepatitis C therapies and to facilitate physician education.
- "At UCSF, I learned that my thoughts and ideas had value, that I did not need to conform to the usual boundaries," she says. "That strength has influenced how I approach everything."

## GRADUATE DIVISION



## CLAUDIO VILLANUEVA, PHD '07

Hometown: Ontario, Calif.

Now: Salt Lake City, Utah

**Position:** Assistant professor of biochemistry, University of Utah School of Medicine

Hobbies: Snowboarding, spending time with family

As a child, Claudio Villanueva didn't just play with his toys. He dismantled them to see how they worked, even though he wasn't always able to put them back together again. It's no wonder he became a scientist.

"In science, we're creating new knowledge, exploring, going into the unknown," he says. He now heads a biochemistry lab, where every day he gets to dive deep into the mechanics of metabolism and fat-cell development and investigate how they relate to physiology and disease.

**LEAP INTO SCIENCE:** Born in Nicaragua, Villanueva moved with his family to Southern California at age 9. He thought he would become a dentist, like his dad, and worked in the family practice as a dental assistant. But at California State University, San Bernardino, a tiny frog changed the course of his career. In a biology lab there, he became fascinated by the northern leopard frog's intriguing ability to regulate sodium uptake through its skin.

"I had to understand the molecular mechanism behind this process," he says. "In dentistry, you can identify problems, intervene, and have a positive outcome. But I pushed toward a PhD program because I wanted to be constantly learning."

### HELPING THE NEXT

**GENERATION:** Villanueva chose UCSF because of its revolutionary work in molecular biology. He wanted to study metabolism and its connection with diabetes – particularly type 2 diabetes, which is prevalent in Latino communities – and joined the lab of Robert Farese Jr., MD, resident alumnus, and a UCSF professor of medicine and of biochemistry and biophysics.

"I learned a ton in Farese's lab," Villanueva says. "I also learned how to talk about science, how to develop graphics, how to present at seminars. I can now do the science and also explain why it's important and interesting." After a postdoctoral fellowship at UCLA, Villanueva joined the faculty at the University of Utah, where he also serves as faculty adviser for the Society for Advancement of Chicanos/ Hispanics and Native Americans in Science. The chapter he oversees holds seminars where faculty from diverse backgrounds mentor young scientists and talk with them about career trajectories.

"It's a chance for college students to see someone who looks and sounds like them and has been successful," he says. "I also get to pass on the lessons I learned at USCF about the importance of communicating science."



## MARY KEIR, PHD '01

Hometown: Hood River. Ore.

Now: San Francisco

Position: Senior scientist.

Hobbies: Traveling, hiking, cross-country skiing, cooking

Mary Keir has hiked all over the Bay Area, on the Pacific Crest Trail, and in Patagonia. She says such treks give her a chance to think about where she's going in life as she's putting one foot in front of the other.

"Out there, the only other people you see are yak herders," she says of her time hiking high on the Mongolian Plateau, a rugged region in Central Asia. "You're far off any kind of grid. The only way to get anywhere is with your feet, so it takes time." Getting to her current position in biotech,

as a senior scientist at Genentech, has also required a long and thoughtful journey.

#### FROM CURIOSITY TO CURES:

Keir's grandfather and greatgrandfather were pharmacists in the small Oregon town where she grew up. She first became

> interested in science herself while reading about the growing HIV epidemic, and she was intrigued by the rigor of the scientific method.

After earning a bachelor's degree in biochemistry from Lewis & Clark College in Portland, Oregon, she had a chance to work directly on HIV therapies as a graduate student in the lab of Mike McCune, MD, PhD, chief of the UCSF Division of Experimental Medicine, who was and remains a significant influence on Keir's life and work.

"Working in Mike's lab was a satisfying way to play out my initial curiosity about

HIV cures," she says. "The work we were doing on highly active retroviral therapy changed a lot about the disease. I got to learn more and more about basic science and apply it in the lab."

She also enjoyed the collegial atmosphere of UCSF. "The way people approach problems stood out to me from the beginning," she says. "The goal was not to be the hotshot but to solve problems together."

#### CONTINUING DISCOVERY:

Following a postdoc at Harvard, she returned to the Bay Area and joined Genentech, where she was one of the first members of its biomarker discovery group. She now works on therapies for inflammatory bowel disease, following clinical trials through each of their phases.

"I get to watch the progression of these therapies, learn more about the biology of what's happening, test hypotheses, and then implement those findings," she says. "For me, it's a perfect job."

## **CONNECT: TO STEER FUTURE SCIENCE CAREERS**

The Biomedical Sciences (BMS) Graduate Program provides interdisciplinary training in tissue and organ function in development, physiology, and disease, giving students a multitude of career choices. Both BMS graduates, Mary Keir and Claudio Villaneuva are deeply involved in mentoring to help students find the best application for their interests and experiences.



## **Cat Scan**

Duke Ellington Morris is one cool cat. Rescued from a local shelter, Duke is now part of the San Francisco SPCA's Animal Assisted Therapy program. Pet therapy can reduce blood pressure, pain, depression, and stress, and Duke's mellowness earned him a spot in the ICU

at UCSF Medical Center. Perched in his catbird's seat atop a rolling cart, Duke goes room to room comforting patients. A recent TV news story catapulted Duke into the public eye, but he categorically ignores all the attention.

## UCSF

School of Dentistry students study in a Parnassus classroom.

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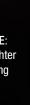
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SAVORING SUNRISE: A mother and daughter reflect on the nursing life. See page 24.