

# UCSF

**MAGAZINE**

Winter 2016



## **White**Wash

Biomedical research doesn't reflect the diversity of the American population



# UCSF MAGAZINE

WINTER 2016



**POWERED UP!**  
Construction worker Francisco Mercado helps renovate the Clinical Sciences Building on Parnassus. The project is just one of the many ways UCSF fuels San Francisco's economy. Read about our economic impact in "Big Picture," page 22.





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COVER PHOTO ILLUSTRATION: DAVID ARKY; THIS SPREAD: NOAH BERGER



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**UCSF is deeply ingrained in the fabric of San Francisco – it is one of the most gratifying aspects of being a part of the University.**

Every day, I see evidence of our core commitment to improving the health and well-being of our community, whether in the lab, in the classroom, at the bedside, or in our neighborhoods.

This commitment is summed up in the feature *Big Picture*, where

we reveal the results of our first economic and fiscal impact report since 2010.

The cumulative value of all our activities in employment, job creation, operations, construction, and spending is \$8.9 billion – a 24-percent increase over six years.

I couldn't be more proud of our contributions to the health and vitality of the Bay Area. Following *Big Picture* is a photo essay that embodies the impact we are making. Please take a moment to glimpse our points of community contact – the people we have connected with along the way.

In the articles *White Wash* and *Through the Looking Glass*, we demonstrate the power of precision medicine, from its broadest capacity as a public health tool to its most personalized application as an instrument for devising cures for individuals with rare diseases. *White Wash* explores how UCSF is fostering a more equitable approach to biomedical research, which all too often does not reflect the diversity of our country's population. In *Through the Looking Glass*, parents, clinicians, and scientists speak about working collectively to discover new treatments for childhood epilepsy. Focusing on the condition with the telescopic power of precision medicine, scientists have identified therapies that are making a tremendous difference in young lives.

You've got a lot of fascinating reading in store – enjoy.

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

# UCSF MAGAZINE

FOR ALUMNI AND FRIENDS

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PHOTO: NOAH BERGER; ILLUSTRATION: CENTERS FOR DISEASE CONTROL AND PREVENTION

## 20 Years of *Transforming Women's Health*

Did you know that 42 percent of women having a heart attack don't experience the classic chest pain or pressure that men do? Women often have subtler symptoms – like shortness of breath, soreness in their throat and jaw, or nausea – which can easily be mistaken for indications of much more benign conditions like flu or indigestion. These are considered “atypical” symptoms in medical parlance because, until relatively recently, most clinical trials studied only men, missing key differences in health risks, symptoms, and treatments for women and girls.

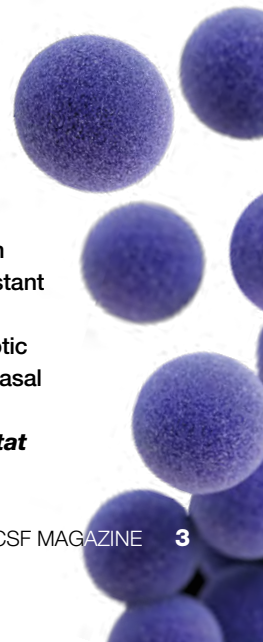
The UC San Francisco National Center of Excellence in Women's Health this year celebrates two decades of bringing attention to

and expanding awareness of such differences through research, clinical care, professional education, policy changes, community partnerships, and women's leadership. The center was designated one of six National Centers of Excellence in Women's Health by the U.S. Department of Health and Human Services in 1996, when women's health was associated primarily with reproductive medicine.

“My dream for the future,” says founding director Nancy Milliken, MD, “is that sex and gender approaches to research, clinical care, and education are in the DNA of UCSF and inform health care and policy across our nation and the world.”

“I wouldn't bet against a wily bacterium like *S. aureus*.”

Michael Fischbach, PhD, associate professor of bioengineering, on whether the bacterium that causes drug-resistant MRSA infections will adapt to a new antibiotic produced by human nasal bacteria, in the online medical publication *Stat*





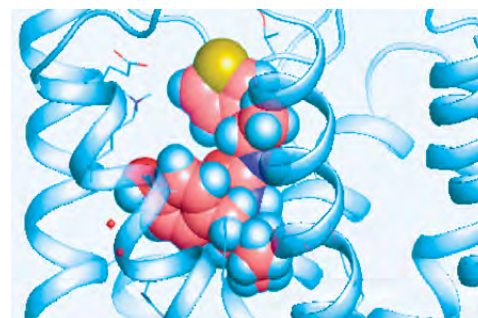
## Researchers Develop Safer Opioid Painkiller From Scratch

Imagine a painkiller as effective as morphine but without its sometimes deadly side effects.

That's the potential of a new drug co-created by Brian Shoichet, PhD '91, a professor of pharmaceutical chemistry at UC San Francisco; Bryan Roth, MD, PhD, at the University of North Carolina at Chapel Hill; Peter Gmeiner, PhD, at Friedrich-Alexander University in Germany; and 2012 Nobel Laureate Brian Kobilka, MD, at Stanford University. Notably, the new drug does not interfere with breathing – the main cause of overdose deaths from prescription painkillers, as well as from street narcotics like heroin; it also does not cause constipation, another common opioid side effect. In addition, the new drug appears to sidestep the brain's dopamine-driven addiction circuitry, as it does not cause drug-seeking behavior in mice.

Just as important as the drug itself is the radical new method the team used to create it. Drug discovery typically begins by tweaking the structure of a successful drug like morphine, to try to get rid of its side effects while maintaining its primary function. But Shoichet and his colleagues sought to create an entirely new chemical compound that would block pain without causing opioids' undesirable side effects.

To do this, they started from scratch – with computational techniques that let them explore more than four trillion different chemical interactions – and then used the newly deciphered atomic structure of the brain's "morphine receptor" to custom engineer a novel drug candidate. This computational approach, called molecular docking, was pioneered in the 1980s at UCSF's School



The new, safer opioid drug candidate, PZM21, is shown docked on the brain's morphine receptor, the mu-opioid receptor.

of Pharmacy by Shoichet's mentor, Professor Emeritus Tack Kuntz, PhD.

More work is needed to establish that the newly formulated compound is truly non-addictive and to confirm that it is safe and effective in humans. But if the initial findings are borne out, they could transform the fight against the rising epidemic of addiction to prescription painkillers.

## INSTANT Gratification?



How do our bodies let us know when we've satisfied those pesky thirst and hunger cravings?

Research by Zachary Knight, PhD '05, an assistant professor of physiology, is coming up with surprising answers in mouse studies that may have implications for the perpetual human quest to manage our weight.

Knight's study shows that specialized brain cells in mice "predict" a feeling of hydration, deactivating long before liquids the mice consumed changed the composition of their blood. The results stand in stark contrast to current views of thirst regulation, which

hold that the brain signals us to stop drinking only after it registers changes in blood concentration or volume.

Knight and colleagues, including several UC San Francisco neuroscience graduate students, previously identified a similar mechanism governing hunger. A 2015 study showed that hunger neurons in mice shut off in response to the sight and smell of food, well before any food was consumed or could signal *enough*.



“The older you are, the worse the hospital is for you.”

**Kenneth Covinsky, MD '88, Edmund G. Brown Sr. Distinguished Professor of Geriatrics, on the fact that patients over age 65 tend to fare less well during hospital stays than younger patients, on NPR's *All Things Considered***



## Ask the Expert: A Cavity Cleanse

John Featherstone, PhD, dean of the UCSF School of Dentistry, has upended his field with a new philosophy.

### **What causes tooth decay?**

The human mouth contains bacteria that feed on the fermentable carbohydrates we ingest. They produce acid, the acid dissolves our tooth enamel, and we end up with dental caries, which is the scientific name for cavities. Multiple species of bacteria – at least 10 and maybe more – contribute to dental caries.

### **How did you discover the bacterial connection?**

Forty-two years ago, I started trying to unravel the basic mechanism of how and why decay occurs in the mouth. There were several of us around the world who approached the question from different scientific points of view to come up with a better understanding. We wanted to develop a risk assessment protocol or a caries prediction protocol. The result was CAMBRA.

### **What is CAMBRA?**

CAMBRA – which stands for Caries Management by Risk Assessment – is a philosophy of preventive dentistry that precisely assesses the risk of decay and addresses it with treatments and therapies calibrated to the risk level. We determine the level of risk for an individual: low, moderate, high, or extreme. The next step is to deliver therapies tailored to that particular person that will help bring their risk level down. This is, essentially, precision health.

### **What causes higher risk?**

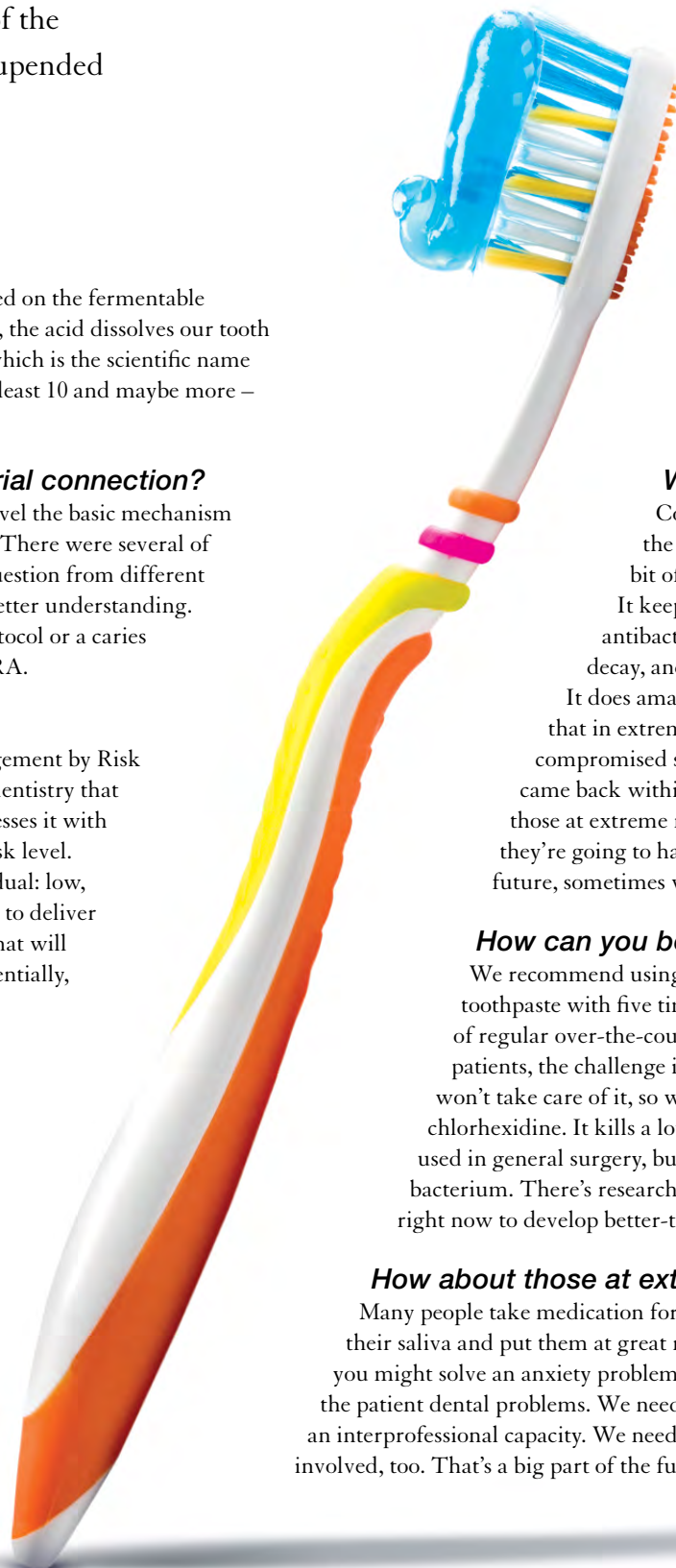
Compromised saliva flow. Saliva, the fluid in your mouth, can be a bit of a nuisance, but it's essential. It keeps your mouth moist, it has antibacterial properties, it repairs tooth decay, and it protects against gum disease. It does amazing things. Our data tell us that in extreme-risk patients – those with compromised saliva production – 88 percent came back within two years with new decay. In those at extreme risk, you can basically guarantee they're going to have new decay in the very near future, sometimes within six months.

### **How can you beat a high risk level?**

We recommend using a prescription-strength fluoride toothpaste with five times the fluoride concentration of regular over-the-counter toothpaste. Yet in high-risk patients, the challenge is so great that fluoride alone won't take care of it, so we also use an antibacterial called chlorhexidine. It kills a lot of bacteria and is sometimes used in general surgery, but it's not targeted to a specific bacterium. There's research going on around the world right now to develop better-targeted antibacterials.

### **How about those at extreme risk?**

Many people take medication for various health issues that dry up their saliva and put them at great risk for dental decay. For example, you might solve an anxiety problem with a drug but end up giving the patient dental problems. We need to interact with physicians in an interprofessional capacity. We need to get nurses and pharmacists involved, too. That's a big part of the future of this field.





## Sizing UP Cancer's Clues

Thanks to two studies co-led by UC San Francisco scientists, a new genetic test may help breast cancer patients avoid chemotherapy, while a genetic marker may offer clues to the mystery of why a daily aspirin seems to help prevent certain cancers.

### Steering Clear of Chemo

In the breast cancer work, researchers used a test measuring the activity of genes that control the growth and spread of breast tumors to identify women with a low risk of recurrence and therefore little to gain from chemotherapy. Called MammaPrint, the test was developed by Laura van 't Veer, PhD, director of Applied Genomics at the UCSF Helen Diller Family Comprehensive Cancer Center and co-lead author of the paper describing the discovery.

Using MammaPrint to profile a 70-gene signature in tumors surgically removed from nearly 6,700 patients, researchers found that nearly half of the participants with early-stage breast cancer – who would traditionally receive chemo – could avoid it, despite having clinical signs indicating a high risk of recurrence.

Five years after their surgery, almost 95 percent of the patients who had high clinical risk but low genetic risk and who had elected not to receive chemotherapy were still alive – a survival rate only 1.5 percent lower than for those who did choose to have chemotherapy.

### New Info on Daily Aspirin

In the study of aspirin's effect on cancer, Dvir Aran, PhD, a postdoctoral scholar at UCSF, and Audrey Lasry, a PhD student at the Hebrew University of Jerusalem, showed that a previously unidentifiable type of low-grade inflammation may explain the way many different forms of cancer begin.

Scientists have long known that people who take a daily aspirin or other nonsteroidal anti-inflammatory drug (NSAID) are less likely to get colorectal, breast, or a number of other kinds of cancer. But they haven't known



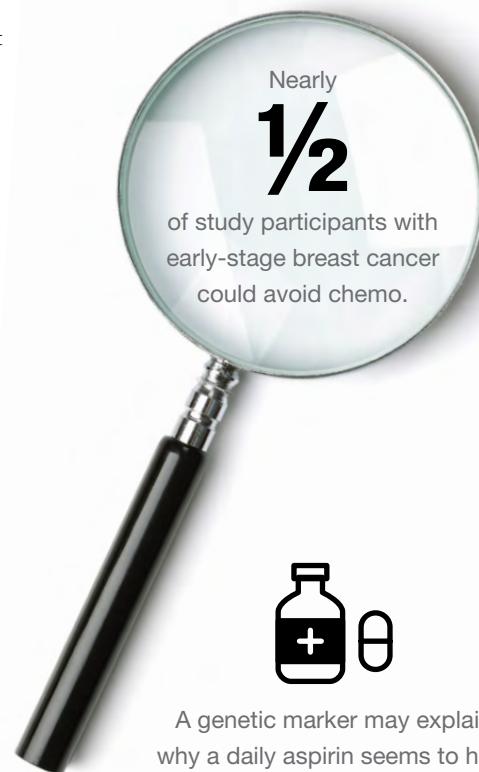
Molecular biologist Laura van 't Veer developed the genetic test called MammaPrint.

why, especially since inflammation does not appear to be a factor in most of the cancers that aspirin helps prevent.

The new study shows that the low-grade inflammation, known as para-inflammation, may be part of the reason. Parainflammation has been linked with cancer-promoting mutations and in several cancers is potentially associated with increased mortality.

Aran and Lasry's study found para-inflammation in a quarter of human cancers, which confirmed findings from mouse studies; furthermore, they discovered that cancer cells treated with NSAIDs showed reduced parainflammation.

Identifying parainflammatory cancers could lead to several important advances, including treatments designed to target parainflammation. The finding also opens the possibility of developing a genetic test that, as MammaPrint does in breast cancer, helps guide therapeutic decisions after initial treatment – in this case, taking NSAIDs.



Nearly  
**1/2**  
of study participants with  
early-stage breast cancer  
could avoid chemo.

A genetic marker may explain why a daily aspirin seems to help prevent certain cancers.



## Chan Zuckerberg Biohub to Spur Unprecedented New Collaboration

Funded by a \$600-million commitment from Facebook CEO and founder Mark Zuckerberg and his wife, pediatrician Priscilla Chan, MD '12 and resident alumna, UC San Francisco will join forces with Stanford University and UC Berkeley in a new biomedical science research center at Mission Bay. The Chan Zuckerberg Biohub is the first philanthropic science investment made by the Chan Zuckerberg Initiative, which has set a goal to cure, prevent, or manage all diseases by the end of the century.

Co-leading the Biohub are biochemist Joseph DeRisi, PhD, the Bowers Professor and Tomkins Professor at UCSF, and Stephen Quake, PhD, a professor of bioengineering and of applied physics at Stanford. DeRisi is renowned for his use of genomic technologies to study malaria and viruses and to diagnose unknown infections; Quake has invented many widely used biological measurement technologies and the first noninvasive prenatal genetic test to replace amniocentesis.

The Biohub's initial research projects will transform scientists' understanding of health and disease. Its Cell Atlas will be a map, available to all researchers, that reveals the different cell types that control the body's major organs.

# Can we cure all diseases in our children's lifetime?



Facebook CEO Mark Zuckerberg and his wife, pediatrician Priscilla Chan, announce the Chan Zuckerberg Biohub at an event at UCSF Mission Bay in September.

The Cell Atlas will also depict the internal machinery of cells in unprecedented detail, allowing scientists to examine the connections between disease and cellular breakdowns.

The Infectious Disease Initiative will explore new ways to create drugs, diagnostic tests, and vaccines against the many infectious diseases that still threaten much of the world, such as HIV, Ebola, and Zika. And a Rapid Response Team can immediately devote scientists and advanced research technology to

develop new ways to fight a sudden outbreak.

“The Biohub cements the Bay Area’s position as the premier environment for collaborative scientific partnerships that will create revolutionary health advances,” says UCSF Chancellor Sam Hawgood, MBBS. “The incredible vision of Priscilla Chan and Mark Zuckerberg will resonate with the international scientific community and re-energize scientists around the world.”

“This step back that we’ve taken is a little medieval, thinking that vaccines are going to hurt children, when really it’s one of the most healthy and scientific discoveries we’ve had in our lifetimes.”

Gena Lewis, MD, pediatrician at UCSF Benioff Children’s Hospital Oakland, who lobbied for California’s new law requiring schoolchildren to be vaccinated, regardless of their parents’ personal or religious beliefs, on **KCBS**



## NERDS and NURSES Unite to End Alarms that Cry Wolf

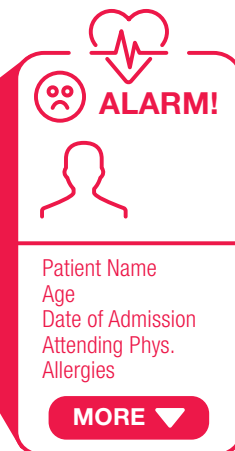
If the smoke alarms in our homes went off 100 times a day, seven days a week, in the absence of fire, most people would either disconnect them or replace them with more-accurate devices. But what if all alarms on the market were designed to go off with similar inaccurate frequency?

That's roughly the situation that clinicians in hospital intensive care units (ICUs) face every day, since monitors measuring patients' heart rates, ECG rhythms, blood pressures, oxygen levels, and other vital signs go off constantly – usually for reasons unrelated to a true change in patients' clinical status.

Not surprisingly, clinicians tend to ignore, turn down, or turn off these alarms, especially since their experience bears out what researchers measured in a recent UC San Francisco study: that in a day's time, each ICU bed averages 187 alarms. There's a false-positive rate of over 88 percent for arrhythmia alarms, for example. The frequency with which alarms go off exacerbates a related problem: that despite their remarkable sensitivity, ICU monitors still miss some critical clinical events, in part because they cannot adequately synthesize disparate data points to give clinicians appropriate early warnings.

This situation, termed “alarm fatigue,” explains why an interdisciplinary team of researchers – led by School of Nursing faculty Xiao Hu, PhD; Michele Pelter, RN, PhD '01; and Richard Fidler, PhD '14 – is working furiously to create a “super alarm.” This device would aggregate disparate data, capture trending patterns, and filter out false alarms, so alerts sound only in situations that truly demand clinical attention.

To achieve these aims, the team jokes, they've formed a powerful alliance “between nurses and nerds,” a phrase coined by Barbara Drew, RN, PhD '90, former director of the ECG Monitoring Research Lab and lead author of the alarm study. Hu is a biomedical engineer; Pelter is a critical care nurse, scientist, and current director of the ECG Monitoring Research Lab; and Fidler is a nurse anesthetist and director of a clinical simulation lab in the San Francisco VA Health



The super alarm might have a dashboard that displays a numeric score, which the super alarm algorithm generates and which represents the probability of risk for a patient. Users can then drill down into detailed patient information with one click.

Care System, where the usability of medical technology is tested. They head a group of like-minded clinicians, data scientists, software engineers, and IT experts working on the super alarm.

“Head nerd” Hu is an expert in signal processing and machine learning, which enables him to design tools that get thorough and accurate information from the body's “signals” and to generate or modify alarm algorithms based on changing data inputs. The super alarm will use these processes to recognize clinically important patterns more quickly and with more reach than is humanly possible, while filtering out irrelevancies – little bits of information that don't mean anything until they come together as part of a big pattern but that today set off all those false-positive alarms.

The super alarm has already helped the team identify patterns that until now have remained obscure: individualized patient signals that change over the two to three hours before a patient has a cardiac arrest



or loses the ability to breathe. With 90-percent accuracy, they have succeeded in predicting situations when an ICU patient is going to go into cardiac arrest and need resuscitation, at a manageable alarm frequency.

With this success as a foundation, the group is now running an NIH-funded study to complete more comprehensive testing of the super alarm in UCSF ICUs. The super alarm will run in the background, while clinicians simultaneously monitor patients using today's standard of care.

Pelter notes that the super alarm performs some of the same functions as ICU nurses: watching and recognizing trends.

“With all the data we have these days, we don't always have the human bandwidth to filter, synthesize, and recognize when a pattern indicates real clinical urgency,” she says. “However, engineers can grab a multitude of data points and bring them together, and clinical nurses can help determine which are truly important and need to be acted upon.”



## Radically Revised Education

Young doctors today face a slew of tough challenges: health disparities, devastating new infectious epidemics, opioid addiction, and chronic diseases like diabetes that affect entire communities. Solving these problems requires more than just medical knowledge – it demands a fresh way of working as a health care professional. Recognizing this need, the UC San Francisco School of Medicine launched a radically revised curriculum this fall. Called Bridges, it stresses teamwork and trains students to continuously ask questions and collaborate with other health professionals and scientists to find answers. Bridges students will be immersed in clinical training early and will pursue a research project spanning their medical school experience. UCSF's budding physicians should graduate well prepared to lead the way in a complex world of care.



The new Bridges curriculum is considered one of the country's most innovative medical training programs currently offered at a medical school.

## APPtitude?

We've all experienced the frustration of learning a new technology. But when it comes to the health apps that more than half of Americans carry on their smartphones, current designs make them practically unusable to those who stand to benefit the most.

That is the finding of new research led by Urmimala Sarkar, MD, MPH, an associate professor of medicine at the Center for Vulnerable Populations. The study involved 26 participants who self-identified as having diabetes or depression or who served as caregivers for elderly patients at Zuckerberg San Francisco General Hospital (ZSFG). A majority of ZSFG patients qualify for publicly funded insurance or do not have insurance. All the participants were English-speaking and most had routinely used the internet prior to the study, though not all were smartphone/tablet users.

However, with few exceptions, participants were unable to fully navigate the apps' functions, and most expressed frustration and disappointment with the experience. As a group, they completed only 51 percent of data-entry tasks across all apps and successfully retrieved data from the same apps less than half the time.

This finding demonstrates the need to involve target patient populations in designing future health-related apps.





## Best in CLASS

UC San Francisco biochemist Bruce Alberts, PhD, has instigated far-reaching changes in science and science education. His accomplishments have been so profound that he received the 2016 Lasker-Koshland Special Achievement Award in Medical Science, one of the highest honors in biomedicine. Alberts' contributions to understanding DNA replication have led to major advances in medicine, while his efforts as president of the National Academy of Sciences have led to reforms in national science education standards that favor active learning through inquiry-based instruction.

Locally, Alberts co-founded the UCSF Science & Health Education Partnership (SEP), a collaboration with San Francisco's public schools to teach students and enrich science curricula for children from backgrounds that are underrepresented in the sciences. The program is one of UCSF's longest-running community outreach programs and is recognized internationally

Watch a video honoring Alberts' work at [bit.ly/alberts-award](http://bit.ly/alberts-award)



as a model partnership. The opportunities it has provided have been transformative for children who might not have otherwise found their way into science.

"I am not deeply concerned about how many scientific facts the public knows,"

Alberts has said. "It is much more important that every educated person acquire 'scientific habits of mind,' always insisting on making decisions based on logic and evidence."

"This wasn't a very expensive intervention. It cost, over time, about 4 cents per student, per day."



Anisha Patel, MD, MSPH, MSHS, postdoctoral alumna, assistant professor of pediatrics, on a recent federal law requiring school cafeterias to offer free water to students, to **Public News Service**

## UCSF Medical Center Ranks Seventh in Nation

For the 15th consecutive year, UCSF Medical Center has been ranked among the nation's top 10 hospitals, earning the seventh spot in *U.S. News & World Report's* 2016-2017 "Best Hospitals" survey.

The UCSF Helen Diller Family Comprehensive Cancer Center joined the Medical Center this year in being the most highly rated health care provider in Northern California. In addition, top honors in Northern California went to the UCSF teams in diabetes and endocrinology, gynecology, nephrology, neurology and neurosurgery, orthopedics, rheumatology, and urology.



In a separate set of pediatric rankings, UCSF Benioff Children's Hospitals placed among the nation's premier children's hospitals in all 10 pediatric specialties and were rated best in the Bay Area in five disciplines: cancer, diabetes and endocrinology, neonatology, neurology and neurosurgery, and urology.



## FACULTY ACCOLADES

**Bruce Alberts**, PhD, Chancellor's Leadership Chair in Biochemistry and Biophysics for Science and Education, received the 2016 Lasker-Koshland Special Achievement Award in Medical Science, one of the nation's highest honors in biomedicine. (See story, "Best in Class," on the facing page.)

**Melinda Bender**, RN, PhD, assistant professor of family health care nursing at the Institute for Health and Aging, was named a Philippine Nurses Association of America Leadership Fellow.

**Andrew Bindman**, MD, professor of medicine and of epidemiology and biostatistics and a faculty member at the Philip R. Lee Institute for Health Policy Studies, was named director of the U.S. Agency for Healthcare Research and Quality (AHRQ), a major division of the Department of Health and Human Services (HHS). He reports directly to HHS Secretary Sylvia Matthews Burwell and will be on leave from UCSF while serving in the role.

**Michael Brainard**, PhD, professor of physiology and of psychiatry and a Howard Hughes Medical Institute Investigator, and **John Rubenstein**, MD, PhD, Nina Ireland Distinguished Professor of Child Psychiatry, were elected to the American Academy of Arts and Sciences, one of the country's oldest learned societies and independent policy research centers.

**Penny Brennan**, PhD, adjunct professor at the Institute for Health and Aging, was named a fellow of the Gerontological Society of America.

**Charles Craik**, PhD, postdoctoral alumnus and professor of pharmaceutical chemistry, received the Protein Society's Emil Thomas Kaiser Award, which recognizes "a recent, highly significant contribution in applying chemistry to the study of proteins." Craik studies proteases and other enzyme complexes associated with infectious diseases and cancer.

**Joseph DeRisi**, PhD, Albert Bowers Professor in Biochemistry and Gordon M. Tomkins Professor; **Elissa Epel**, PhD, professor of psychiatry; and **Bruce Miller**, MD, A.W. and Mary Margaret Clausen Distinguished Professor in Neurology, were elected to membership in the National Academy of Medicine, one of the highest honors in the fields of health and medicine. DeRisi was also elected to the National Academy of Sciences, one of the highest honors accorded to American scientists.

**DorAnne Donesky**, MS '90, RN, PhD '03, associate professor of physiological nursing, was named a Macy Faculty Scholar by the Josiah Macy Jr. Foundation and selected for the Sojourns Scholar

Leadership Program by the Cambria Health Foundation. The Macy program aims to accelerate reforms in health professions education, and the Sojourns program to advance palliative care.

**Yoshimi Fukuoka**, MS '99, RN, PhD '03, associate professor of physiological nursing, and **Martha Jessup**, MS '79, PhD '01, RN, professor emerita at the Institute for Health and Aging, were named fellows of the American Academy of Nursing.

**Deborah Greenspan**, BDS, DSc, postdoctoral alumna, professor of clinical oral medicine, chair of Orofacial Sciences, and Leland and Gladys Barber Distinguished Professor in Dentistry, received an honorary doctorate of medicine and surgery from the Faculty of Medicine of the University of Helsinki.

**Susan Hyde**, DDS '92, MPH, PhD, associate professor of preventive and restorative dental sciences, chair of the Division of Oral Epidemiology and Dental Public Health, and dentistry director of UCSF's Multidisciplinary Geriatrics Fellowship, and **Dick Gregory**, DDS, associate clinical professor of preventive and restorative dental sciences, received a Special Citation in Dental Journalism from the International College of Dentists for guest editing two issues of the *Journal of the California Dental Association* dedicated to the oral health of older adults.

**Michael Merzenich**, PhD, professor emeritus of otolaryngology and former Francis A. Sooy Professor of Otolaryngology, received the Kavli Prize in Neuroscience for his pioneering work on the brain's plasticity. He shared the \$1-million prize with Carla Shatz, PhD, of Stanford and Eve Marder, PhD, of Brandeis.

Academy Health's Interdisciplinary Research Group on Nursing Issues presented **Ulrike Muench**, RN, PhD, assistant professor of social and behavioral sciences, with its New Investigator Award, and **Joanne Spetz**, PhD, professor at the UCSF Institute for Health Policy Studies, the Department of Family and Community Medicine, and the School of Nursing's Department of Community Health Systems, with its Research Mentorship Award.

**Sophia Saeed**, DMD, associate professor of preventive and restorative dental sciences, received the Outstanding Faculty Member award from the American College of Dentists' Northern California Section.

**Francis Szoka**, PhD, professor of bioengineering, was named Mentor of the Year by the American Foundation for Pharmaceutical Education. He has mentored 28 graduate students and 49 fellows, who hail his enthusiasm, creativity, and leadership.





PHOTO: GABRIELA HASBUN

Tim Wood enjoys a quiet moment at home with his daughter, Piper.



# Through the Looking Glass

A window on the quest by  
parents and scientists to  
end pediatric epilepsy.

by Claire Conway

Piper Wood had her first seizure in a setting meant for sunscreen, snorkels, shovels, and pails. The island was remote – that was the point of this family vacation. Six months old and turning blue, Piper finally calmed down and drew breath again after the island’s well-trained doctor brought her hour-long seizure to a halt by administering a mix of morphine and water into one of her tiny veins. Tim and Ashley Wood needed to get their daughter to a better-equipped hospital immediately, but night had fallen and no medevac could land in the dark. Word spread quickly, and, one by one, villagers arrived in their cars and parked side by side with their headlights shining on the runway.

Eight years later, Piper’s path is still illuminated by the bold and remarkable acts of people surrounding her. Piper was diagnosed with Dravet syndrome, a catastrophic form of epilepsy that presents in the first year of life and is marked by fierce seizures, sometimes hundreds in the course of a day, that eventually lead to cognitive and social impairment. Dravet is epilepsy at its most extreme; some seizures can be lethal or so intractable that children end up being intubated to resume the flow of oxygen. Yet even milder forms of epilepsy – with less frequent or different types of seizures – can upend families.

“An epilepsy diagnosis is very difficult to deliver to a family because the sheer nature of seizures is just so unpredictable,” says Joseph Sullivan, MD, director of UC San Francisco’s Pediatric Epilepsy Center and Piper’s neurologist. “In our pediatric patients with epilepsy, about a third continue to have seizures, even with optimal treatment.”

Piper is among them. So are Lew Parker and Sam Vogelstein. At times, during the course of their treatment, all three could be doing just fine at school or on a lazy Sunday and then, suddenly, time stops and a seizure hits.

In families that know to expect one or two seizures a week, if their child has had only one by Thursday, for example, do they make that trip to the grocery store?

“It’s a chronic illness that rocks your very core stability,” says Jen Parker, Lew’s mother. “To me, the biggest difference from so many terrible medical diagnoses that can befall people is that you never rest again. It’s not like with other illnesses where finally at night you get a child to bed and you can recover. Nighttime is Lew’s most dangerous time.”

There are several types of seizures, and most are not as dramatic as the stiffening and jerking of grand mal seizures – or tonic-clonic, as they are more commonly called – yet they are just as intrusive. Sam

“To me, the biggest difference from so many terrible medical diagnoses that can befall people is that you never rest again.”

– Jen Parker

has had as many as 100 seizures a day, between 10 and 20 episodes an hour, during which his eyes glaze over, his head bobs, and his jaw slackens. After 15 seconds or so, he would regain consciousness and resume his sentence, pack his lunch, or block a joust in a fencing match. As he drifted in and out during the course of the day, Sam’s literal absence of mind made it difficult for him to be fully present for lessons at school and lessons in life.

These children have more than epilepsy in common. Their parents have partnered with physicians and scientists to relentlessly test and defy conventional medical wisdom, tear through red tape, and reimagine a whole new care delivery model. They’ve done it for love, fear, and change – not just for their kids, but for those in the waiting room next to them. And their physicians and scientists have jumped fences into territories foreign to them. The partnerships they’ve forged and the ground they’ve covered are an audacious tale of 21st-century medicine in a university medical center.

## A maelstrom of the mind

Epilepsy is as common as breast cancer and more common than multiple sclerosis, cerebral palsy, and Parkinson’s disease combined. It affects 1 in 26 people in the U.S. – including more than 300,000 children under the age of 14 – with a wide spectrum of biological, cognitive, and psychological consequences. Yet some 70 percent of the time, doctors can’t identify the cause of a child’s epilepsy.

Seizures happen when the electrical currents that regulate interactions among neurons surge and create a firestorm of activity. “Our brains are governed by a balance between excitation and inhi-

biton,” explains Maria Roberta Cilio, MD, PhD, director of research at UCSF’s Pediatric Epilepsy Center. “When that balance is right, our thoughts and movements flow nicely. If a group of neurons is not working properly – they might start firing all together – our bodies move against our will and produce a seizure.”

Nearly 80 percent of the human brain is developed by age three, and intractable seizures can wreak havoc with that critical process. When they’re less than two minutes long, seizures themselves don’t induce brain injury. However, if they are frequent, they can impact cognition. And when seizures last longer than 15 minutes, studies have shown that they can potentially induce brain damage. “The big question is whether the seizures are doing damage,” says Cilio. “It is very likely that in children with genetic diseases, it’s the underlying genetic defect that may cause cognitive impairment, more than the seizure itself.”

For instance, the gene defect that causes Dravet syndrome, an SCN1A mutation, interferes with the brain’s sodium channels, which regulate the firing of neurons. All told, there are more than 70 such genetically caused epilepsies that involve similar problems in potassium and calcium channels essential to brain function. Physicians try to bring seizures under control while they search for therapies targeting these underlying causes.

Born in Italy, Cilio left Europe to direct the Neonatal Epilepsy Program in UCSF’s Neuro-Intensive Care Nursery (NICN). The first of its kind in the world, the NICN is exactly where she needed to be to save kids and move the field forward. “The NICN is a place where babies are diagnosed as early as possible so you can try treatments that address the cause,” says Cilio. “If you diagnose later, you are only addressing the symptoms,” she adds. Her recent studies have shown that a drug called carbamazepine – an older antiepileptic used very rarely, if at all, in the NICN – promptly and safely controls seizures in neonates with benign and severe forms of neonatal epilepsy. Spared millions of seizures over the course of a lifetime that would likely have been cut short, these children and their brains are thriving.

## Just how many is too many?

The idea came to them on the John Muir Trail. Piper’s doctor, Joseph Sullivan, and dad, Tim Wood, were on an annual backpacking trip organized by friends they had in common. Conversation that foggy morning inevitably turned to Piper, who was struggling. The only treatment that had shown any efficacy – a high-fat, low-carb, low-protein ketogenic diet – was faltering, and she was having two- to three-day cycles of 20 to 30 seizures a day.

Wood had a gut instinct that Dravet was far more prevalent than 1 in 30,000 – an estimate derived a half-century ago, well before the gene for Dravet, SCN1A, was discovered in 2001. There’s much at stake in getting the diagnosis and prevalence of Dravet right. Early on, the disorder can look like benign febrile seizures, a much milder form of epilepsy that may be treated with drugs that can exacerbate Dravet. And with an





Parents like Tim Wood (shown with two of his kids, Owen and Piper) work tirelessly to loosen epilepsy's grip on their children by questioning the boundaries of science and care.

assumed small universe of patients, the pharmaceutical industry had little incentive to invest in finding new, more effective therapies.

"This is me shouting, a dad with a daughter who's got Dravet," exclaims Tim. "I had to do something. I am a salesperson with a certain skill set. I wanted to brand Dravet, make it a household name."

Against the backdrop of the High Sierra, Sullivan had an idea. He would approach a colleague at UCSF – Yvonne Wu, MD, MPH, who is both a pediatric neurologist and an epidemiologist – and ask her to use electronic health records from Kaiser to see if they could prove that Dravet was more prevalent. Two years and over 125,000 electronic health records later, Wu found that the incidence of Dravet is actually double the old estimate. "We were able to show that Dravet is not so rare," says Wu. "It is something all pediatricians need to consider when they see kids who are presenting with febrile seizures."

Wu is confident that the study will have an impact and save lives. She credits Sullivan and Wood for the impetus. "It is very grounding to partner with patients and families," she says. "Sometimes, as researchers and physicians, we get caught up in trying to understand the answers to questions that are burning in our minds but may not be the most important questions to families who are actually affected by the disorder."

Patient families bring about change and, just as important, community. "People out there with a voice, like Tim [Wood], get momentum going, and it hits a tipping point," says Sullivan. "In the

course of my five years of child neurology and epilepsy training, we identified only one or two children with Dravet. Now I have 40 kids with Dravet in my practice. And I can direct them to a foundation and a Facebook page. This gives families identity and support. It really impacts their kids' treatments."

## When risks match rewards

Evelyn Nussenbaum, Sam's mom, was sitting in a room with the CEO of a company that manufactures a purified strain of cannabinoid that has been stripped of tetrahydrocannabinol (THC), the psychotropic component of marijuana that gets people high. The CEO had flown in from London to UCSF to talk to Nussenbaum and her son's doctor, Cilio, about administering their drug, Epidiolex, to Sam. The drug had never before been tried in a person with epilepsy, nor in a child, and Sam would be taking it at a dose that was double, by percentage of body weight, what anyone else had ever taken.

The two were hashing out the rules of what would be Sam's own clinical trial – which would be conducted in London, given the complexities of laws in the U.S. governing cannabinoids. Sam had 68 seizures on Thursday, his first day in London. At the end of that day, they picked up the Epidiolex at the hospital pharmacy and started the medication that night. Sam had 10 seizures on Friday, five on Saturday, 10 on Sunday, and six on Monday. A vast improvement.





Left: Scott Baraban and Joseph Sullivan in the UCSF Epilepsy Research Laboratory, where Baraban is using zebrafish to aid drug discovery. Right: Zebrafish offer many advantages in finding new cures rapidly.



“In three days, Sam was taking a zip line above Hyde Park, with a helmet and harness,” says Nussenbaum. But they couldn’t bring Epidiolex home – it would literally have been a criminal act.

Cilio spent countless hours defining a treatment protocol – including establishing rules for dosing, laboratory testing, and clinical and EEG evaluations before and during treatment. She filled out reams of paperwork, talked to government officials, won approval from UCSF’s Institutional Review Board, and lobbied the U.S. Food and Drug Administration (FDA) to allow a compassionate-use trial of Epidiolex, which the FDA classifies as a drug at high risk for abuse. Three months later, she got the permit and a visit from a Drug Enforcement Administration agent, who insisted she store the drug in a half-ton steel safe in her office. UCSF Benioff Children’s Hospital San Francisco would become the first U.S. facility ever to administer Epidiolex to children with epilepsy. Along with Sam, Piper and Lew were among the very first patients to receive the drug.

Now, three years later, Sam has been seizure-free for 10 months on a drug cocktail that includes Epidiolex. He is thinking about getting his driver’s license. Piper’s initial response was encouraging, but she is still struggling with weekly seizures. Lew had a negative response to the drug. Cilio has wrapped up a trial of Epidiolex in 162 patients, with results showing a 36-percent reduction on average in monthly motor seizures. Cilio believes that, though it’s not a magic bullet, the cannabinoid in Epidiolex can be a useful tool, in either plant-derived or synthetic form and especially in combination with other antiepileptic drugs.

Though the process was arduous, Cilio believes Epidiolex was a

goal well worth seeking for her patients. “A long chain of people were brave in this story,” says Cilio. “When I present on this topic, I am clear that this study was possible because I was at *this* institution.”

## From fish tank to bedside

Sullivan met Scott Baraban, PhD, in a hallway soon after starting at UCSF, years ago. They both were working on Dravet, though Sullivan’s focus was on patients and Baraban’s on research. As director of the Epilepsy Research Laboratory in the Department of Neurological Surgery, Baraban was busy honing a zebrafish-based approach to Dravet – one he has since perfected. Dravet may be the first of many forms of epilepsy aided by the humble zebrafish. There are more than 70 known types of epilepsy of genetic origin, and the Baraban lab is creating a zebrafish model for every one of them. He uses a new technology called CRISPR to impose the exact genetic glitch in the fish that children like Piper have. Then, following discussions with Sullivan, he models the clinical symptoms in zebrafish.

“Joe tells me exactly what symptoms patients have and the specifics of what medications he uses and in what sequence,” says Baraban, who now holds the William K. Bowes, Jr., Endowed Chair in Neuroscience Research. “These conversations directly contributed to how we decided we would validate our models. Do our Dravet fish have seizures? Do our Dravet fish react the same way to the same treatments? The answer to both questions is yes.”

Zebrafish offer many advantages in finding new cures rapidly. Unlike mice, which may produce only one or two pups per litter with





# Care Built on Community

the mutation, adult zebrafish can give birth within a week to over 100 larvae with the same mutation. The larvae have no scales, so they absorb drugs from the water surrounding them, enabling the researchers to test multiple drugs on up to 100 larvae at a time. Baraban and his colleagues recently developed a microfluidic chip that records the EEG activity of the fish to measure a given drug's effectiveness against electrical seizures. And, because the fish are translucent, scientists can also use sophisticated neuroimaging to watch the activity of their entire brains while they are having seizures. All of these approaches were pioneered in the Baraban laboratory.

"In less than three years, we have tested more than 2,000 FDA-approved drugs using this Dravet fish. We have found five promising drugs," says Baraban, "and they are going straight from zebrafish to patients, in some cases." That's a process that typically takes 15 years and costs \$800 million. Baraban and his team went from concept to patient in less than five years and for less than \$5 million.

Sullivan is testing one of those promising drugs, fenfluramine, right now. Another, lorcaserin, is being tested in Colorado, and Baraban just published his latest results in the journal *Brain*. All five children being treated with lorcaserin are having fewer seizures, and one child has experienced an extraordinary 90-percent reduction. The primary side effect is relatively harmless – appetite reduction.

As promising as lorcaserin or fenfluramine may be as treatments for epilepsy, they never would have surfaced if Baraban hadn't used a study design that eliminates investigator bias. He and his colleagues buy libraries of drugs and do the testing blind. Then, once they identify drugs that show signs of efficacy, they work backward to figure out the common mechanism. Their first unexpected discovery of an effective drug was clemizole – an antihistamine, a class of drugs known to worsen seizures. That discovery was published in the journal *Nature Communications* in 2013. They have since determined that clemizole, as well as three subsequently identified drugs (lorcaserin, fenfluramine, and trazodone), act on serotonin receptors to create an inhibitory response that counteracts the abnormal excitatory impulses that characterize seizures.

To greatly expand this zebrafish-based precision medicine approach, Baraban has created fish for 20 of the genetically based forms of human epilepsy. He has about 50 more to go. "Once we have all these fish in-house, we plan to put them in an open resource center that maintains zebrafish colonies," says Baraban. "Then any lab can just order a fish and start their research."

That way, scientists anywhere can search for treatments for Piper and Lew and Sam all at once and as fast as they can.

"A lot of what we do in clinic is listen," says Joseph Sullivan, MD, director of the UCSF Pediatric Epilepsy Center. "We give families that sense that they are not alone. I tell them, 'I have many other patients who are in your same scenario.'"

Sullivan has acted on all that listening to create a new model of care delivery that addresses the whole child and the whole family. Called the Pediatric Epilepsy Center of Excellence (PECE), the center will provide new services to surround families with a compassionate, facilitative care community. With input from parents like Jen Parker, he is working hard to build out the program – which he says is near and dear to his heart – one specialist at a time.

Parker, whose six-year-old son, Lew, has a drug-resistant form of epilepsy, has spent more than her fair share of time in doctors' offices and actively participates in focus groups of families with kids who need constant care. Parker not only identifies with the stories of other families, she logs those anecdotes into the fount of knowledge she shares with Sullivan.

"The marital and employment issues are quite real. Some parents divorce or have to stop working," says Parker. "PECE exists to show that you can change outcomes if you provide better support for the whole family. It's where fear and hope exist together."

In its nascent stages, Sullivan's program is being built out to include the following experts:

- **Educational liaison** to assist families searching for appropriate educational placements, given the high incidence of learning differences associated with epilepsy.
- **Clinical trial coordinator** to provide patients with improved access to new therapies and trials.
- **Pediatric psychiatrist** to monitor and follow families' personal journeys, while providing individualized treatment and support.
- **Marriage and family therapist** to help families deal with the impact of epilepsy.
- **Family wellness specialist** to offer a range of complementary therapies, including yoga, mindfulness, meditation, and stress management.





# Search Engine

How artificial intelligence techniques are bringing order and efficiency to the hunt for new drugs.

by *Jacoba Charles*

A better cure for cancer – and other illnesses – could already be in existence, hidden right under our noses.

The problem is that possible new lifesaving drugs are created much faster than scientists can study them. Millions of untested compounds wait, jumbled together in no particular order in vast repositories called compound libraries.

“These libraries are basically like black boxes right now,” says Steven Altschuler, PhD, a professor of pharmaceutical chemistry at the UC San Francisco School of Pharmacy. “You imagine that somewhere in there is some chemical that might be the key to unlocking any question that you have – but how are you going to find it?”

A new search method that blends cellular biology and computational analytics may be the answer. A husband-and-wife research team at UCSF – Altschuler and his longtime spouse and collaborator, Lani Wu, PhD, also a professor of pharmaceutical chemistry – have developed a way to do the job much faster and at a fraction of the cost of the traditional method. The work involved designing a new kind of cell, writing some new software, and then parsing the resulting landslide of data.

“We were very lucky to be there at the right time and see the connections,” says Altschuler. “Going in, we didn’t even realize that there was a need for this.”

The couple was uniquely poised to develop this method, as their work is informed not only by their current collaboration but also by their earlier shared careers in other fields. They have worked together since they met as students almost 30 years ago. “We met in the mailroom,” Altschuler says. “It was the first day of grad school for her; I was a second-year.”

The pair started out their parallel careers in mathematics and went on to work for Microsoft, then for a biotech firm, before moving into academia.

“Most of us wouldn’t even think of an analogy between drug discovery and what they were working on at Microsoft with image recognition and things like that,” says Matthew Jacobson, PhD, chair of the

Department of Pharmaceutical Chemistry, who recruited Altschuler and Wu to UCSF. “To me, this just shows the power of bringing people with different types of backgrounds into biology and drug discovery.”

## Too much of a good thing

Screening compounds for potential medical uses has to date been both time-consuming and expensive. For example, a lab looking to develop better chemotherapeutic agents would likely be interested in DNA-damaging drugs that have yet to be tested. Usually, researchers are looking for drugs that affect the chain of cellular events by which a given disease advances or can be treated – a biochemical process known as a pathway. An unknown number of such compounds are likely available in libraries housed at universities and pharmaceutical companies around the country. But how to find them?

“Over the last few decades, drug discovery has tended to be fairly pragmatic,” says Jacobson. “We tend to make various simplifying assumptions about how things work inside cells.”

Often, scientists search for new drugs using carefully engineered “reporter cells” to screen for sought-after compounds. These cells are designed in a lab to change in a unique way when a compound achieves a desired effect, indicating to researchers that they have a match. However, this method tests for just one purpose at a time – and it costs hundreds of dollars to test each “mystery” compound. This means researchers generally can afford to screen only a small, random subset of the available compounds.

Envision a compound library as a massive box containing thousands of unorganized,

unlabeled photographs. The current method is akin to each researcher pulling out a handful of photos and looking through each handful to find pictures of one particular person. They may be able to identify a few, but every future project has to start from scratch.

“Whenever anyone goes in there with a specific question, they might find 12 chemicals that are interesting to them, and the rest just go right back into the bin,” Altschuler says.

## A new way forward

By contrast, imagine a method that digitizes the photos and then screens them with a program akin to facial recognition software. This is the first step in Altschuler and Wu’s new method, which categorizes reporter cells in much the same way that Facebook tags photos of your friends: by digitally identifying their features.

Now, when a compound library with unknown properties is screened with reporter cells, the software can identify which of those compounds is generating a desired response. The cost for each test drops from hundreds of dollars to a dollar or less, Altschuler says.

That was phase one of the work. More recently, the couple has found a way to test drugs for multiple purposes at a time using this same principle. An experiment that their team described in *Nature Biotechnology* this past January used only one type of reporter cell to screen nearly 11,000 drugs from multiple compound libraries for six disease pathways. That’s like using facial recognition software to digitally sort through hundreds of thousands of photos – think of multiple boxes stored in Grandma’s attic – and tag photos of six different people at once. Up until now, researchers would have had to do one experiment just to find photos of Steve, a separate one to find photos of Lani, and so on.

“The ability to do very sophisticated mathematical analyses basically allows them to identify the effects of drugs much more sensitively than other approaches have been able to do,” Jacobson says.

This may sound straightforward enough, but consider the fact that researchers had previously found it difficult to coax a single reporter cell into partitioning multiple unidentified drugs into categories of usefulness. Yet Altschuler and Wu not only did that but also yielded results that can be processed digitally – making it clear that this is a quiet but revolutionary breakthrough.

“The grand challenge here is really trying to understand how administering a drug to a cell affects not just one individual protein but the entire network of proteins and, ultimately, the cell’s behavior,” Jacobson says.

## Seeking an ORACL

Standard reporter cells essentially work like matching cards in the children’s game known as Memory: when a new compound generates a response that resembles that of a known drug, it tells researchers that the two operate on a similar pathway and are likely to affect the target disease in a similar way. Over the last decade, such geneti-

cally encoded reporter cells have become increasingly popular in biotech research.

But Altschuler and Wu wanted to design a single, versatile type of engineered cell that would report when a compound matched multiple different pathways – something that had never been done before. Instead of trying to reason their way to a solution, the team decided to seek a boost from chance: Using the fluorescent tags that are used to build reporter cells, they put roughly 600 cells through the DNA tagging process – but did not attempt to control where the tags landed.

They hit the jackpot. In their initial pool of potential reporter cells, they found one



“It’s actually not that different from maybe a music recommender. Music gets classified, and you say what genre you like, and it tries to bring back some more like that.”

– Steven Altschuler

that was 94-percent accurate in discriminating among six diverse cancer-relevant drug classes. They named it ORACL, which stands for Optimal Reporter cell lines for Annotating Compound Libraries.

“They just randomly tried stuff and found that there is a tremendous amount of information in a very small number of proteins – you don’t even have to really think too hard about what they are,” Jacobson says.

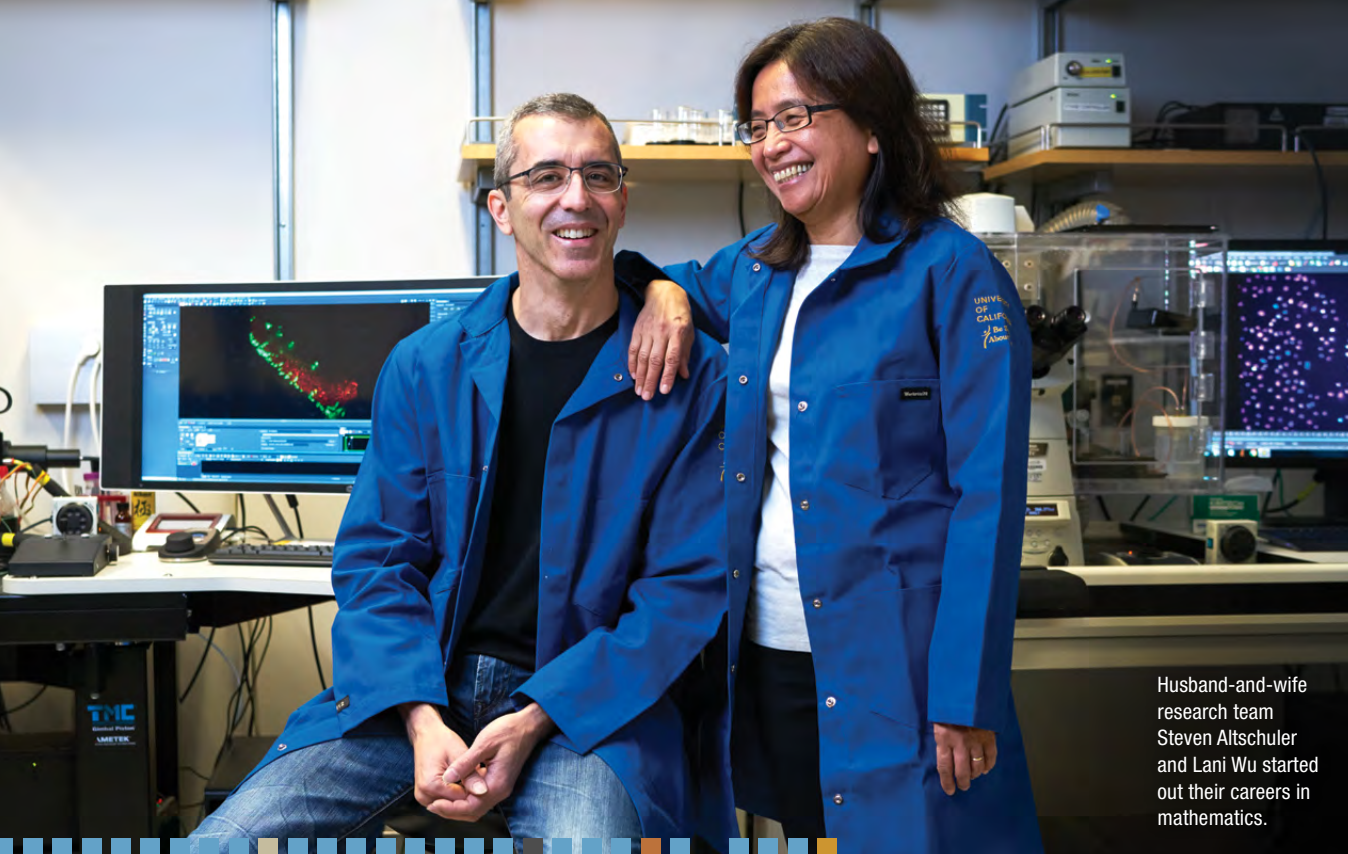
The challenge with such a versatile reporter is to know what it’s saying. The human eye can distinguish only some of a reporter cell’s responses – for example, the way DNA-damaging drugs make the reporter swell up or the way certain cellular inhibitors make it grow long, spiky arms. But other changes can be identified only by computer – which is also the only way to parse the sheer volume of data.

This is a trend that has been on the rise throughout the field. “Data science is a big part of biology right now,” Wu says.

“No human being could look at this,” Altschuler says. “The changes are too subtle, the numbers of conditions are too large, for any human to assess. This really required innovations in identifying cells, extracting properties of the cells, and comparing how the cells had changed in different conditions.”







Husband-and-wife research team Steven Altschuler and Lani Wu started out their careers in mathematics.



A senior researcher in the lab tested the process before the machines took over. Jungseog Kang, PhD, dripped nearly 11,000 compounds and 38 reference drugs into the waiting mouths of tiny wells full of ORACL cells. Once the cells had reacted to the compounds, they were photographed through a microscope. Then, photos were analyzed by software developed by a graduate student, Charles Hsu, producing digital profiles that were matched to those of reference drugs. The results were cross-checked by a literature review and experimentation. In the end, the method proved 94-percent accurate.

“A lot of the magic is in the software, [in] being able to extract maximal information out of a minimal number of experiments,” Jacobson says. “Basically, they are asking, ‘Might it do something interesting and useful? And if so, does it look like anything we’ve seen before? Or is it something totally new?’ And both categories are interesting.”

The ORACL found 100 new compounds that fit one of six drug classes. And it had still more to reveal. To the team’s surprise, additional clusters of potentially useful compounds were identified, despite not being in the experiment design – including glucocorticoids and ATPase inhibitors, which can treat autoimmune conditions and cancer, respectively.

“That was really cool,” Altschuler says. “That means it’s a way to go fishing even beyond what we thought we were going to catch.”

## Tip of the iceberg

Seated at a sterile stainless steel hood, postdoctoral scholar Louise Evans, PhD, has taken over from Kang. Sliding a bristling phalanx of

nearly 100 pipettes back and forth on a mechanical arm, she is helping move the ORACL on to its next step. Compared to the number of compounds that remain uncategorized, this experiment’s 10,000-compound sample is the tip of the iceberg.

“Once you get into the hundred-thousand- to a million-compound range, that would be considered pretty interesting for a phenotypic screen in academics,” Altschuler says. “But I’m not sure that the size of the library you screen is the most important thing.”

The vision is that in the future, the ORACL method will lead to compound libraries that are indexed and searchable according to each compound’s effect – instead of being the black boxes that they are today.

“In principle, we hope a researcher can come to us with a type of compound they are interested in, and we can go into our database and say, ‘We’re going to recommend a few different ones that are just like it for you,’” Altschuler says. “It’s actually not that different from maybe a music recommender. Music gets classified, and you say what genre you like, and it tries to bring back some more like that.”

The next step is likely a partnership with the private sector, where there are the resources to test the method on a larger scale.

“There is a hunger in the pharma companies for new approaches, a willingness to try things,” says Jacobson. “Drug discovery is a long and exceedingly painful process. In the short run, the impacts will come through just scaling up this new approach. I think in the next few years, it will come clear whether this is going to be widely adopted or not.”

# Invested in Community

1,763  
UCSF  
inventions in  
active use

## Economic Powerhouse

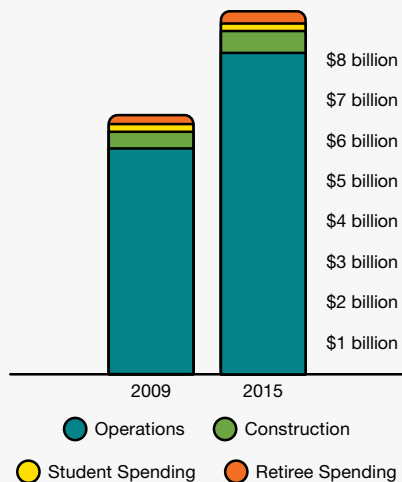
The numbers are in, and UC San Francisco's economic engine is revving up. In our first economic and fiscal impact report since 2010, UCSF has once again proven itself to be a fierce force in San Francisco – fueling the city with an economic output of \$6.5 billion a year. The overall impact jumps to \$8.9 billion annually for the broader Bay Area.

View the full report online: [ucsf.edu/economic-impact](http://ucsf.edu/economic-impact)

## Economic Output

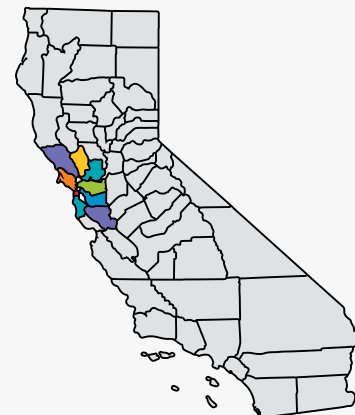
Since 2009, UCSF's annual economic output has increased 28 percent in San Francisco and 24 percent in the overall Bay Area.

UCSF's Total Economic Output in the Bay Area



\$6.5 billion a year  
estimated economic  
output in San Francisco

\$8.9 billion a year  
estimated economic  
output in the Bay Area



9,133  
citations  
annually in  
peer-reviewed  
journals



## Top Employer

UCSF is the second-largest employer in San Francisco, next to the City and County of San Francisco. It is the fourth-largest employer in the Bay Area.

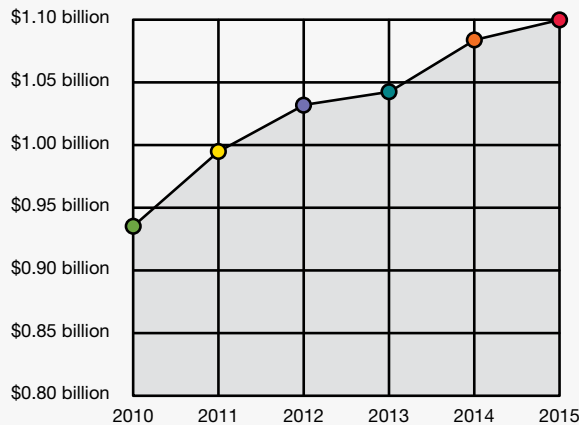
24,143  
Employees at UCSF

42,700  
Bay Area jobs  
generated by UCSF

185+  
startups  
attributed  
to UCSF

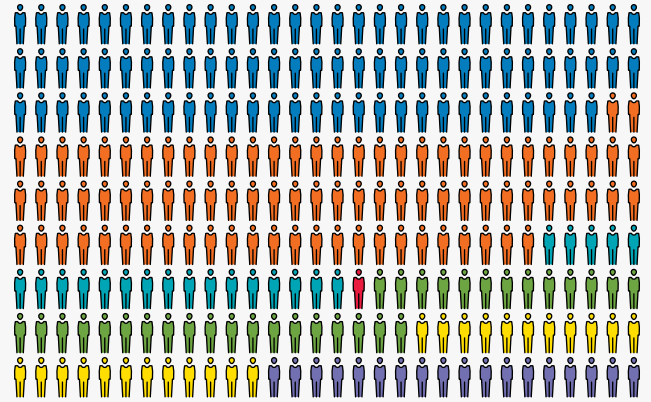
## Research and Development Spending

In 2015, UCSF accounted for \$1.1 billion (19 percent) of the total research and development money spent in San Francisco.



## Types of Jobs Created

UCSF's impact on the local economy is broad and varied, creating jobs in San Francisco and beyond, in health care, biotechnology, education, and other industries.



- Administrative & Support Staff
- Health Care
- Managers/Senior Professionals
- Academic Administrators
- Faculty & Lecturers
- Student Assistants
- Researchers

\$560 million  
in annual NIH  
funding to UCSF

1,490  
UCSF  
patents in  
active use

## Community Champion

UCSF's impact on the city and region is expansive and diverse, improving countless lives – whether through a steady job, an ingenious discovery, a top-tier health sciences education, or a life-saving treatment.

\$127.8 million  
annually in uncompensated  
and charity care

# Community Connection

Impact can be expressed in numbers, dollar signs, or bar graphs. But when it comes right down to it, people are at the center of UC San Francisco's work in the community. We meet them every day – from kids who visit our mobile clinics to high school students who discover their calling in our labs to older adults who find camaraderie and song through a study on aging. Our community members are the soul of UCSF – and their wellness is what we are all about.





## Warriors

In a group effort, the Department of Orthopaedic Surgery, its Amputee Comprehensive Training (ACT) program, the AMP1 team, and the Golden State Warriors' camp coaches created a basketball clinic for patients with amputations and their families. Here, Deborah Bevilacqua, at left, shows Alex Moorehead how to set up for a three-point shot. Bevilacqua is a member of the ACT program, a community of amputee athletes who encourage participation in sport and help give others the courage and skills to get back to the activities they love.





## Fresh Start

There were days when climbing the hills of Parnassus to deliver the morning's first batch of bread to campus weren't so easy for Bernardo Newson. His kidneys were failing and, even though his sister was willing to give up a kidney for him, his doctors at a neighboring institution left him on dialysis for 11 months instead. Once Newson made it to UCSF, our transplant team leapt into action. Nine years, one daughter, and a promotion later, Newson is ever thankful. Last time he was spotted on campus, he insisted on buying donuts for a nurse who had left her cash at home. "Any little way I can give back, I do," says Newson. "I owe my life to this place."




PHOTO: NOAH BERGNER





## Second Chances

Abigail Miller, who received a kidney transplant in 2008, and her big sister Bizzy joined 300 people gathered for UCSF's 19th Annual Chris Mudge Pediatric Transplant Picnic to celebrate a second chance at life.



### Say "Aah"

Dental student Jessica Lam coaxes 3-year-old Lucas Morales into a tentative "Aah" so she can check his teeth for cavities. This mobile clinic in the Outer Mission District is one of many run by UCSF students to help meet the health needs of at-risk populations within their own neighborhoods.





## Street Smarts

Mishal Durran, a San Francisco high school sophomore, worked in an immunology lab last summer as part of UCSF's Science & Health Education Partnership (SEP). For nearly 30 years, UCSF scientists have partnered with local educators to improve K-12 science education through SEP. The summer internship program touches the lives of students who show promise but may never have considered science or even higher education. A survey of former interns who graduated from high school between 2000 and 2003 found that nearly 90 percent were pursuing graduate/professional education in the sciences.



PHOTO: NOAH BERGER





## Seniors Sing

Community of Voices is not your ordinary choir. It is a network of 12 choruses at senior centers throughout the city that is part of a study investigating the potential health benefits of being a member. After a round of songs, Study and Choir Coordinator Dana Pounds tests choir member Ruth Aviles' balance and lower body strength. Funded in part by the National Institutes of Health, UCSF neuroscientist Julene Johnson, PhD, is also looking at whether participation affects mood, loneliness, and memory.

PHOTO: NOAH BERGER





WHITE



WASH

**STEVEN MENDOZA WAS FIVE WEEKS OLD WHEN HE FIRST LANDED IN THE EMERGENCY ROOM.** His skin was dusky gray, his eyes were rolling back in his head. The doctors and nurses at Zuckerberg San Francisco General Hospital (ZSFG) swarmed around him, peppering his distraught parents with questions: Did he have epilepsy? Had he suffered some trauma? “No, no,” his mother, Fabiola Gudiel, responded. “No puede respirar!” *He can’t breathe.*

*by Janet Wells*



Fabiola Gudiel snuggles with her son, Steven Mendoza.





A flexible tube inserted into Steven's trachea kept his airway open while he was rushed by ambulance to the pediatric intensive care unit at UC San Francisco Medical Center. He stayed there for seven days, recovering from a respiratory infection.

At age six months, after continued breathing problems, Steven was diagnosed with asthma. Treatment? That was trickier. Steven didn't respond as well as hoped to a shifting array of medications, leaving him either exhausted and drowsy or hyperactive. He was also plagued by croup. The family's one-room apartment in San Francisco's Excelsior District was spotless, thanks to Gudiel's housekeeping. But she couldn't do much about the damp, dank carpeting or the cracked and strangely bulging walls.

"Before he even reached preschool, Steven had 11 episodes requiring oral corticosteroids in the hospital or urgent care. That's unheard of," says Kimberlee Honda, RN, MS, director of the ZSFG Pediatric Asthma and Allergy Clinic.

Steven is now four and a half years old. His survival is more than an example of lifesaving patient care. His case is also an illustration of UCSF's compelling imperative to advance cutting-edge biomedicine and health equity for an increasingly diverse population.

## PRECISION PUBLIC HEALTH

"You can match a blood transfusion to a blood type," President Obama said in announcing his Precision Medicine Initiative last year. "What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature?"

"Precision medicine" is the starring attraction of today's health care, with \$215 million in federal funding and heady promises of transforming disease prevention and treatment by leveraging advances in genomics and data analysis.

With 15 publications on the subject and more than two dozen related research and development projects in the pipeline, UCSF is at the forefront of the precision medicine endeavor. In fact, the term was coined in a 2011 National Academy of Sciences report co-authored by several UCSF faculty, including Susan Desmond-Hellmann, MD, MPH, and resident alumna, while she was chancellor of the University. Her successor as chancellor, Sam Hawgood, MBBS, has identified precision medicine as a priority to strengthen the University's impact on local and global health, economics, and innovation.

But even ardent fans of the approach caution that precision medicine could too easily become *privileged* medicine, undercutting another of the University's foundational mandates: serving vulnerable populations.

"Precision medicine has the potential to be extremely expensive to develop and manage – and fraught with opportunities for voltage drops, losing patients along every step of the way," says Dean Schillinger, MD, resident alumnus, chief of the UCSF Division of General Internal Medicine, and director of the Health

Under the care of ZSFG's multidisciplinary team, Steven Mendoza has made many fewer trips to urgent care for treatment of his asthma.



Communication and Health Literacy Program at ZSFG's Center for Vulnerable Populations (CVP).

To help navigate the tension between a low-cost, one-size-fits-all approach and individually tailored medicine, UCSF hosted a Precision Public Health Summit in June, convened by the White House Office of Science and Technology Policy and the Bill & Melinda Gates Foundation. A key takeaway: "Telescoping out" is as important as "telescoping down" to the genetic level.

"After taking into account our individual genetics, we have different behaviors; different social backgrounds; different places where we live, eat, pray, sleep," says Sam Oh, PhD, MPH, an associate researcher at the UCSF School of Medicine and an epidemiologist at the UCSF Center for Genes, Environment, and Health.

Neighborhood is one key proxy for health disparities, indicating significant variations in air quality, housing, and social environment: "Depending on where you live, there are different stresses on you and your psyche and different risk factors for disease and response to treatment," Oh adds. "It's also about your interactions with law enforcement or how easy it is to access health care."

Consider Oakland, where the number of African American men killed on its streets in the past decade nearly matched the number who graduated from its high schools ready to attend a state university, the *San Francisco Chronicle* reported.

## IN PURSUIT OF HEALTH EQUITY

UCSF's "tremendous depth" in epidemiological, genotype, and molecular research – together with the strong expertise in vulnerable patient populations of UCSF Benioff Children's Hospitals and partners San Francisco Veterans Affairs Medical Center and ZSFG – uniquely positions the institution to foster a more holistic and equitable approach to both patient care and research, says Schillinger.





Postdoctoral scholar Marquitta White (left) and Esteban Burchard (right), director of UCSF's Asthma Collaboratory lab, are studying genetic and environmental influences on asthma in minority children.

## Diversity matters

Treating an elderly, non-smoking Chinese woman with metastatic lung cancer:

“That’s a death sentence, but she’s been alive for over 10 years. Why? A drug called Tarceva. Early research didn’t show much effect on lung cancer outcome except in one small group – Asian female non-smokers. It’s good they had some Asian women in the study, or they wouldn’t have discovered the drug’s significance.”

— Tung Nguyen, MD, the Stephen J. McPhee, MD, Endowed Professor of General Internal Medicine and co-director of the UCSF Multiethnic Health Equity Research Center

Studying genetic risk factors for asthma in African American children:

“Asthma hits African American and Latino populations the hardest, and by 2020 minorities will be a majority of the child population for the first time in U.S. history. This is a very serious public health issue and one that really touched home with me. I have four nephews, and three have asthma.”

— Marquitta White, PhD, postdoctoral scholar, UCSF Asthma Collaboratory

Discovering a genetic variant that protects Latinas from breast cancer:

“We know of about 90 markers that affect breast cancer, mostly from the Caucasian population. Our study was relatively small, with 3,000 Latinas, yet we found something with a very strong protective effect. No matter how much you amped up the sample size in Caucasians, you wouldn’t have found it.”

— Elad Ziv, MD '96, resident alumnus, and professor of medicine, UCSF School of Medicine





Physician Tung Nguyen (left) has conducted research on health disparities among African American, Asian American, and Latino patients.

“It’s not just basic bench science,” he says, likening the effort to UCSF’s response during the AIDS epidemic in the 1980s, when he was chief medical resident at ZSFG. “When we tackled a problem like AIDS, it was understanding the virus, understanding the bathhouses, understanding mother-child transmissions.”

Indeed, what helped Steven Mendoza, the young asthma patient, as much as therapeutics was UCSF’s focus on social and environmental determinants around health.

Gudiel, now 39, moved to San Francisco from Central America 12 years ago and had never heard of asthma before her son’s diagnosis. ZSFG’s pediatric asthma clinic – a multidisciplinary collaboration that includes community health workers, behavioral health specialists, a nutritionist, and a lawyer – helped Gudiel become an expert in telling the difference between asthma symptoms and the barking cough of croup.

She also learned about deadly environmental triggers for her son’s breathing problems: mold, dust, vermin, humidity, second-hand smoke. Gudiel asked the landlord to fix the walls and carpet in the family’s apartment, to no avail.

“It was disgusting,” Gudiel says in Spanish, with Silvia Raymundo, one of the clinic’s community health workers, translating. “The landlord would come and paint over the

## Bridging the research diversity divide

Luis (not his real name), a Salvadoran immigrant, was invited to participate in a UCSF clinical trial. He wasn’t interested. His cancer – initially misdiagnosed by a small-town clinic – continued to progress. His co-workers had to cover his shifts when he came to UCSF for treatment. He couldn’t afford to take more time off work and by that point was wondering if any doctor could help him.

Broader obstacles to recruiting participants for clinical trials – particularly minorities – include historical exploitation in medical research and cultural and language barriers. Even if the trial advances science, it rarely offers participants a cure.

But after two years, Luis changed his mind. “His energy was going, and he had lost a lot of weight,” says Daniel Dohan, PhD, a professor of health policy and social medicine and co-lead of the EngageUC initiative. “He had developed a strong relationship with his oncologist, and she again suggested a research study – for treatments that might help him feel better and help other people. That clearly appealed to him.”

With more than 1,400 clinical trials ongoing and more federal funding for biomedicine research last year than any other public university in the country, UCSF is one of the busiest health research institutes in the world. Increasing diversity in research is a top priority because it elevates both science and health equity. Here are three examples of the University’s multifaceted approach.

**EngageUC:** The University of California’s five medical centers serve a

diverse patient population of about 13 million – one-third of the state’s population. To effectively investigate health needs and treatments at the genomic level, a long-term UC goal is to create a web-based repository of patient blood samples collected during clinical care. Step one is building transparency and community ownership for the project. Led by UCSF, EngageUC held in-depth focus groups this year to understand the cultural and trust issues around participation in a biobank.

**Special Populations Initiative:** A portion of an \$85-million National Institutes of Health grant awarded to UCSF’s Clinical and Translational Science Institute will support a renewed focus on all aspects of patient-oriented research within and across low-income and minority populations, children, and the elderly. The initiative will leverage clinical and research expertise at UCSF Medical Center at Parnassus and Mt. Zion, Zuckerberg San Francisco General Hospital, UCSF Benioff Children’s Hospitals in Oakland and San Francisco, the Veterans Administration Hospital in San Francisco, and community partners.

**Clinical Trials Finder:** In the fall of 2016, UCSF launched a revamped user-friendly website for patients, their families, and referring physicians, with concise information about open clinical trials and, for those interested in participating, clickable links to contact investigators for further details. A grant application has also been submitted to extend the system UC-wide and translate it into languages other than English.



mold, but the wall would get inflated and crack, and you could see the mold again.”

In 2013, Raymundo visited the apartment, noting chipping paint, damaged window frames, and a severe mold infestation. The clinic wrote a letter to the landlord, requesting immediate remediation. Rather than make repairs, the landlord offered Gudiel and her family a different unit. They could barely afford the 20-percent rent increase – \$300 a month – that came with it, but the move, along with fine-tuning Steven’s medication regimen, has paid off. This past year, the family’s frantic trips to urgent care were down by half.

## REFLECTING AMERICA

Given UCSF’s goal of improving quality of life through research into health and disease, it’s an “absolute necessity” that research accurately reflects demographics, says Executive Vice Chancellor and Provost Daniel Lowenstein, MD, resident alumnus, and the Aird Professor of Neurology.

Science, Lowenstein says, has failed to meet that challenge for “a very, very long time.”

For decades, the vast majority of U.S. epidemiological studies reported on cohorts with very few women or even none altogether. The number of non-white participants? Even fewer.

Despite Congressional mandates aimed at diversifying clinical research and improvements in gender parity, little else has changed in the last 30 years: Since 1993, less than 2 percent of 10,000-plus National Cancer Institute-funded clinical trials and less than 5 percent of National Institutes of Health-funded respiratory studies have included enough minorities to be relevant. Those figures were published in *PLoS Medicine* in December 2015 by Oh and Esteban Burchard, MD, MPH, resident alumnus, and the Harry Wm. and Diana V. Hind Distinguished Professor in Pharmaceutical Sciences II.

With these diseases hitting minority populations at a disproportionate rate, and with drugs affecting people differently based on their genetic backgrounds, the lack of diversity in research is already having serious impacts on care for the nearly 40 percent of the U.S. population with non-European heritage. Additionally, health disparities cost the U.S. an estimated \$300 billion a year in medical care, lost wages and productivity, family leave, and premature death.

“Generalizing results from research performed in one racial/ethnic group to another can work reasonably well, or it can have fatal consequences,” Burchard, Oh, and a co-author from Stanford wrote in a February editorial in the *American Journal of Respiratory and Critical Care Medicine*.

One striking example is asthma – the most common chronic disease among children worldwide. In the U.S., minority kids like Steven – his Nicaraguan and Salvadoran parents likely have a mix of Native American, Caucasian, and African ancestry – are at far higher risk of having asthma than their white peers.

Puerto Ricans and African Americans also tend to have more

severe asthma that is harder to control with common drugs, and African American children die of asthma-related episodes at four times the rate of white children. Why? There haven’t been definitive answers, because almost all of the genetic studies of asthma have included only white patients.

## GENETIC VS. RACE-BASED RESEARCH

Burchard, as director of the UCSF Asthma Collaboratory, has spent 18 years collecting DNA samples of African American and Latino kids to study genetic and environmental influences on asthma. He now has more than 10,000 samples – the country’s largest such collection from minority children with asthma.

This treasure trove of data has led to several significant studies. One, led by Marquitta White, PhD, a postdoctoral scholar in the Asthma Collaboratory, recently identified both new genetic risk factors and the fact that only a tiny fraction of known factors for asthma apply to African American children – a crucial step toward improving diagnosis and treatment.

By recruiting people into genetic studies by race, however, Burchard and his colleagues have come under fire from critics pointing to a scientific legacy – like the infamous “Tuskegee Study of Untreated Syphilis in the Negro Male” – that has persecuted people of color rather than advancing their interests.

“We look at genetic ancestry, at things we can measure. Racial and ethnic groups don’t have a basis in biology,” explains White, who identifies as African American and has African, European, and “a little block of Southeast Asian ancestry” in her genome.

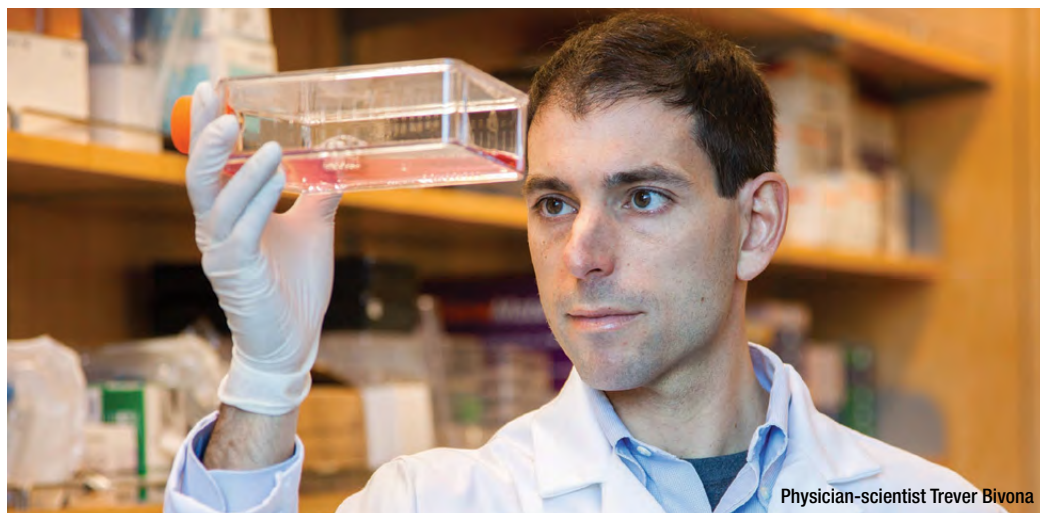
“So many of us are from admixed populations,” she says, using the term for new genetic lineages introduced from the interbreeding of two or more previously isolated populations. “The percentages of those parent populations can affect susceptibility to disease or response to medication.”

Diversity in science is not just “science done well,” as Oh says. It’s also vital to health equity.

“This country is plagued by racial and ethnic disparities in some of the most deadly diseases,” Burchard says. “The only way we will make progress in decreasing that burden of disease is by understanding why it occurs. We can’t understand that without including diverse communities in our research.”



## Bold Innovation Program Fast-Tracks Precision Medicine Research



Physician-scientist Trevor Bivona

Imagine a world in which a single human cell could be separated from a tumor and dissected to reveal each distinct cancer-causing genetic mutation. Imagine a physician-scientist then using that information to precisely individualize the most effective treatment for that specific cancer. These exciting advances are being studied today in projects recently funded by UC San Francisco's George and Judy Marcus Program in Precision Medicine Innovation.

One of the projects – developed by Trevor Bivona, MD, PhD, and James Fraser, PhD, both associate professors at UCSF – looks at explicitly treating disease-driving genetic mutations; it may eventually produce a method of activating or inhibiting specific mutations in proteins. If their project is successful, a whole new class of drug therapies could be developed to activate or inhibit proteins that cause cancerous mutations.

The program fast-tracks precision medicine research and was established through a \$4-million gift from longtime UCSF supporters George and Judy Marcus. “We are really honored to be a part of this program,” says Bivona. “Creative funding like this is transforming innovation in medicine.”

The program selected 12 projects encompassing 24 departments and 36 scientists across UCSF. The winning proposals cover the breadth of precision medicine and include projects analyzing genome-wide structural variations, developing a novel approach to rheumatoid arthritis treatment, personalizing lung cancer oncology, and more.

“The George and Judy Marcus Program is a pivotal institutional investment in precision medicine at UCSF,” says Chancellor Sam Hawgood, MBBS. “Precision medicine is a field that is poised to transform health. The Marcuses’ generosity is spurring daring ideas and speeding their translation from the lab to patient care. Their visionary partnership is creating excitement across the university and accelerating our contributions to this important field.”

Precision medicine is an emerging approach to disease treatment and prevention, using biological and biomedical data to develop

personalized treatments and guide more precise, predictive, and preventive care.

“Funding brave ideas and collaborative innovation in science and medicine is a priority for us,” says George Marcus. “UCSF is full of scientists thinking outside the usual framework. We are proud to be associated with pushing research to the next level.”

The George and Judy Marcus Program fosters high-risk, high-impact team science. However, in contrast to most other research funds, the Marcus Program is on an accelerated timeline. Not only is the period from application to funding fast-tracked, but all projects must be able to yield a discovery within the one-year funding period.

“A very important and exciting aspect of this program is speed,” Bivona says. “Speed matters in scientific research when you have bold ideas and are forming compelling collaborations. You want the momentum, you want it early, and you want to sustain it.”

To spark even more novel ideas and connections, the program hosted a mixer in October where basic scientists networked with researchers experienced in clinical, social, behavioral, and population studies.

George Marcus is a member of the UCSF Foundation Board of Overseers and a former UC regent. He and his wife, Judy, developed the concept for the Marcus Program based on insights gathered during George's years of service to the University and his partnership with the chancellor. The couple also recently donated \$1 million to support basic science PhD students through the George and Judy Marcus Discovery Fellowship Fund and \$1 million to the Chancellor's Annual Fund.

“Like the chancellor, we see personalized medicine as the future of health,” says George Marcus. “Encouraging team science at UCSF is an investment in that future.”

– Carol Pott

# Alumni Hub

## Celebrating a Half-Century of Impact

By the mid-1960s, UC San Francisco achieved full administrative independence, becoming the ninth UC campus and the only one devoted exclusively to the health sciences. Each of its four schools was renamed “School of,” the Graduate Division was established, and UCSF was on its way to becoming the top-ranked academic research university it is today.

At Alumni Weekend 2016, we honored those who graduated in 1966 with 50-year medallions, which were placed around their necks by current students. In the following pages, learn a little more about some of the honorees pictured below and 12 other distinguished UCSF alumni who attended the reunion festivities. We celebrate them and all our alumni for serving their diverse fields, advancing health in their communities, and ensuring UCSF’s continued ability to educate the next generation of health care leaders.



Whether you graduated in 1967 or 2007, book your room now for Alumni Weekend 2017, April 7-8, at San Francisco’s Fairmont Hotel. Call 800/441-1414 or visit [ucsfalumni.org/aw](http://ucsfalumni.org/aw) for more details.



# SCHOOL OF DENTISTRY



## DENISE ALEXANDER, DDS '86

**Hometown:** Los Angeles, Calif.

**Now:** Panama City, Fla.

**Position:** Senior dentist,  
Northwest Florida Reception  
Center, Main Unit

**Hobbies:** Painting, calligraphy,  
interior decorating, bicycling

Denise Alexander practices dentistry in one of the most challenging settings imaginable: a state prison. She credits her upbringing in a dangerous South Central Los Angeles neighborhood with giving her the grit, resilience, and commanding presence to care for toughened prisoners. And she credits UCSF with giving her the foundational skills and exceptional professional judgment to do her best work, no matter what the circumstances.

"I am well equipped to handle daily surgical extractions, lip and facial lacerations, and evaluations of facial dislocations and fractures," she says. "I also understand how oral health relates to overall health, so counseling in this area is a big part of my job. My UCSF education is what gave me that judgment ability."

**DENTIST MAKES AN IMPRESSION:** Her dream to become a dentist began at about age 15, when she needed to have

her wisdom teeth extracted. "I could see that the dentist was the boss," she says. "He had people working for him who did what he told them to do. I thought, *This is what I'm going to do.*"

Reaching her dream was no easy task. She had a low GPA and frequently missed school to help her mother with a home day care business. Her high school counselor encouraged her to choose a less ambitious vocation, but Alexander was determined.

**MOVING UP:** With the help of a recruiting team from the Educational Opportunity Program in Los Angeles, she became the first person in her family to attend college. She followed a winding route from Nairobi College in East Palo Alto (where she earned a scholarship), to San Francisco State, then UC Berkeley, and finally UCSF.

She recalls her early months at UCSF as exciting but also difficult. "I'd call my mom, who had encouraged me to go to college," she says. That was all

the reassurance she needed to forge ahead.

**ONLY DENTISTRY:** After graduation, Alexander began a private dental practice in Berkeley that ultimately lasted 25 years. She decided to retire to Florida but found herself drawn back to her profession when she learned

of the state's dentist shortage. As she was about to return to work, she wondered whether she still had a passion for dentistry. "I realized that it was running a business that had made me want to retire," she says. "I love dentistry itself."



## GARY ARMITAGE, DDS '66, MS '73

"In 1966, Perry Ratcliff, one of my mentors at UCSF, encouraged me to apply for an internship with the Public Health Service, which kept me from being drafted during the Vietnam War and started my wonderful 46-year career at UCSF. It shows you the impact a mentor can have on one's career; it is real, it's tangible, and it is lifelong."

“My patients are like family. It’s the most rewarding part of my work.”



**YURI KANEDA, DDS '88**

**Hometown:** Kyoto, Japan

**Now:** Chula Vista, Calif.

**Position:** Dentist in private practice

**Hobbies:** Bikram yoga, traveling

Yuri Kaneda moved around a lot as a child – from Japan to Ohio to Nebraska to Illinois. But then her family arrived in San Diego when she was in her teens, and California has been home ever since. Other than her eight years in the Bay Area – four at UC Berkeley and four at UCSF – she has stayed in the San Diego area, running a successful private dental practice there for 21 years.

Her keen interest in dentistry was inspired by her paternal grandmother, who was a dentist in Japan. Kaneda recalls seeing a photo of her grandmother with her dental school cohort,

one of only two women in the graduating class.

“She was a trailblazer,” Kaneda says. “I kept that in the back of my mind as I thought about my own future career.” For the daughter of a social worker and a minister, service to others was also a priority.

**BAND OF DENTISTS:** She headed north for college, earning a bachelor’s degree in microbiology and immunology, then back south to UC San Diego, where she worked in a lab focused on growth plate research. When she learned that two friends were entering dental school, she

thought of her grandmother and decided to go for it. At UCSF, she made lifelong friends within her tightly knit class.

“Our class really banded together,” she says. “We worked hard and helped each other out.”

**FINDING FAMILY:** Just as she built long relationships with her UCSF classmates, Kaneda treasures the lasting bonds she has with her patients. Many of them have followed her to three different office locations and grown up under her care. “It’s the most rewarding part of my work,” she says. “My patients are like family.”

She remains active in the UCSF Dental Alumni Association and attends Alumni Weekend every year. She continues to take classes to improve her technical and clinical skills; is a board member of the Japanese American Historical Society of San Diego; and has begun traveling extensively with her husband, David, a high school biology teacher whom she married after finishing her first year of dental school. So the travels that began in her childhood continue today.

“We hope to travel all over the United States and around the world,” she says.



# SCHOOL OF MEDICINE

## VIVIEN D'ANDREA, MD '86

**Hometown:** Palo Alto, Calif.

**Now:** Los Altos, Calif.

**Position:** Internist, Palo Alto Medical Foundation; assistant clinical professor, Stanford University School of Medicine

**Hobbies:** Playing music, skiing, traveling, volunteer work

## GEORGIA PUNG, MD '86

**Hometown:** Richmond, Calif.

**Now:** Mill Valley, Calif.

**Position:** Pediatrician, Golden Gate Pediatrics; clinical associate, UCSF

**Hobbies:** Gardening, exercise, travel, health advocacy education



Georgia Pung, left, and Vivien D'Andrea, right

**As Vivien D'Andrea and Georgia Pung were pursuing their medical education at UCSF, AIDS was ravaging the city, and promising therapeutics were years away. They both rotated on the AIDS ward at San Francisco General Hospital (now Zuckerberg San Francisco General) and quickly learned the weight of their new roles.**

"We were young doctors in training and bonded with these people, but we knew they were going to die," Pung says. "It was an incredible educational experience and a big shock to the system."

**YOUNG AMBITIONS:** Early on, Pung dreamed of being a

NASCAR driver or a CIA agent, but she became a teen hospital volunteer and turned toward health care. With a B.S. in kinesiology from UCLA, she followed her high school friend Janice Low, MD '84, to UCSF.

"I loved physiology, public health, and working with kids," Pung says. For 10 years, she taught students and residents as a clinical instructor at Harbor-UCLA Medical Center. Then, as a mother of three, she took a break from her practice to volunteer in their schools – tutoring, teaching, and running health programs – before returning to practice nine years ago alongside her kids' longtime pediatrician, Eileen Aicardi, MD '74.

### COMPASSIONATE MEDICINE:

D'Andrea spent three summers as a nursing assistant at Stanford Hospital to pay for college. She was deeply affected by physicians who hurriedly delivered bad news to their patients with little sensitivity.

"I wanted to be a doctor who takes time and really gets to know patients," she says. This led to her customized major at UC San Diego in medical sociology and the doctor-patient relationship.

D'Andrea has been practicing internal medicine for 25 years, seeing her long-term patients through the ups and downs of their lives and loving the

continuity of care she is able to provide. She is active in medical education and, as a dedicated violinist, subspecializes in music medicine, treating tendinitis, performance anxiety, overuse syndrome, and other ailments that affect musicians.

### 34 YEARS AND COUNTING:

D'Andrea and Pung have kept in touch over the years and quickly rekindled their friendship at their class's 30th reunion. Now that Pung's youngest son is a freshman at Stanford, near where D'Andrea lives, their paths are intersecting once again, and they're planning to expand their relationship beyond their annual holiday letters to more in-person get-togethers.



**JEFFREY KANG,  
MD '81, MPH**

**Hometown:** Princeton, N.J.

**Now:** Fort Lauderdale, Fla.

**Position:** President, ChenMed, LLC

**Hobbies:** Building computers; remodeling homes with his wife, Brenda

**During his junior year at Harvard, Jeffrey Kang traveled to China to visit relatives. When they asked what he was going to do for a living, and Kang told them he planned to pursue law, his extended family was not as impressed as he expected.**

“They asked, ‘Why not be a doctor?’” Kang says. “They told me that the human body is the same all around the world, and I could always come home and serve the motherland. It was a compelling case.”

Although he has remained in the U.S., Kang took the advice to heart. He spent a year working as a paralegal for the United Farmworkers Union in Southern California, then returned to Harvard and promptly switched his major to biochemistry.

**FOCUSED ON SERVICE:** After graduating, he came to California to pursue an MD at UCSF and a master’s in public health at UC Berkeley. He also helped create the Bay Area Asian Health

Alliance and the Tenderloin Senior Outreach Project, among other health-advocacy projects.

“I was less focused on grades and more focused on service, and I really enjoyed it,” Kang says. After an internal medicine residency, he worked for the Boston nonprofit Urban Medical Group, a primary care practice for the elderly and disabled that ran like a “medical home” before the term was even coined. Within six months he was running the group, a position he held for 10 years.

“Because of my public health training, I thought on a larger scale about society,” he says. “I saw that medicine is a service fueled by altruism and passion, but it also has to operate as a business.”

**MEDICAL HOME:** Next came a White House Fellowship, followed by seven years as chief medical officer at the Centers for Medicare and Medicaid Services. Among other responsibilities, he set out to improve Medicare’s coverage of medical homes, which provide patient-centered primary

care, and established the National Quality Forum, Hospital Compare, and other widely used quality measurements.

“I wanted to figure out how best to measure performance and how to pay for value,” he says. Kang moved to the private sector in 2002 and for the past year has

served as president of ChenMed, which provides innovative primary care for low-income seniors in six states.

“I’m back to caring for underserved seniors in a medical home model – work that began for me in San Francisco,” Kang says. “My work has taken me full circle.”



**A. BRENT EASTMAN, MD '66,  
School of Medicine  
Alumnus of the Year**

“Obviously, San Francisco in the 1960s was an interesting place to be. I thought, ‘If I’m going to go to medical school in a large city, this is one of the best cities to be in and one of the best medical schools in the country.’”



# SCHOOL OF NURSING

## CASEY JONES, MS '16

**Hometown:** Colorado Springs, Colo.

**Now:** Arua, Uganda

**Position:** Clinical nursing instructor, Muni University; nurse, Arua Regional Referral Hospital

**Hobbies:** Scuba diving, hiking, cooking, writing



**Casey Jones has seen the world. He's circumnavigated the planet, spent three years as a scuba instructor in Mexico, and served in the Peace Corps and AmeriCorps. Now he's pursuing a long-held dream of working as a nurse in Africa, lecturing in a new bachelor of nursing science program and providing care in a rural hospital that lacks critical infrastructure.**

Jones started out in the liberal arts, earning a degree in Spanish from Knox College, which included a year studying abroad in Barcelona. Then the Peace Corps sent him to Guatemala, where he worked on an agroforestry project.

"Language was a way for me to see the world," he says.

Returning to the U.S., he spent 20 years in a variety of jobs: bread baker, composting specialist, and free clinic coordinator in Oregon.

**NURSING CALLS:** "The work in the free clinic really captured my heart," he says. "I started to think seriously about nursing school." Jones did his diving stint in Mexico before making that big commitment, then attended Linfield College in Oregon to complete his BS in nursing. For the next 10 years, he thrived on working as a cardiac ICU nurse at a Level I trauma center, where he found himself increasingly attracted to palliative care.

"I assisted many patients and families who needed help accepting that death was coming," he says. UCSF's palliative care nursing minor prompted him to complete a master of science degree as an adult gerontology clinical nurse specialist in critical care and trauma.

**INTO AFRICA:** This past summer, he arrived in Arua, Uganda, as one of four UCSF alumni working in Africa through

the Global Health Service Partnership, a capacity-building collaboration of the Peace Corps, the U.S. President's Emergency Plan for AIDS Relief, and Seed Global Health.

In Arua, he's learning the local dialect, cooking local cuisine, and planning to explore more of the world, from its heights (climbing Mount Kilimanjaro) to its depths (scuba diving in Lake Malawi).



## GLENDA CAMPOS, BS '66

"My first job after graduation was as a summer camp nurse in Aptos, near Santa Cruz. I had been a camper there, too, so I took comfort in knowing the setting and the people. Even though it was a rather gentle entry into my professional life, I kept asking myself, 'Am I old enough to be doing this?'"

“I was shaped and transformed by my UCSF experience.”



**MARY NYQUIST KOONS,  
MS '81**

**Hometown:** Minneapolis, Minn.

**Now:** Eugene, Ore., and Truckee, Calif.

**Position:** Numerous board memberships; author, *Slogans for Serenity: 52 Quilted Meditations*

**Hobbies:** Quilting, sewing, knitting, travel

**For Mary Nyquist Koons, the practice of nursing extends far beyond the clinic, and its tools include more than the stethoscope and syringe. From Oregon to Uganda, Koons has provided nursing to a wide variety of people in unique and inventive ways.**

By sewing handbags out of colorfully wrapped condoms, she raised awareness of sexual health among adolescents. By teaching mothers in Jinja, Uganda, how to sew, she provided a new source of income so that local children could go to school and eat healthier food. By quilting an enchanting map of the Truckee River Watershed, she educated

residents about the relationship between a healthy earth and healthy bodies.

**ENTER NURSING:** Sewing and fashion were her passions as Koons was growing up in Minneapolis. The idea of pursuing nursing came along when she was attending the University of Minnesota and working as a pediatric ward clerk at the university hospital.

“I saw what nurses did and was so excited by the chance to really make a difference in the lives of children and families,” she says.

**LEADERS IN TRAINING:** After graduating, she worked in

mental health nursing and began to think about teaching nursing, for which she would need further training.

“I asked one of my professors the best place in the country to get a graduate nursing degree, and UCSF was the immediate answer,” she says. “I was shaped and transformed by my experience at UCSF. I was trained to be a leader and prepared to take on any number of roles in nursing.”

Sandra Weiss, RN, PhD, now interim dean of the School of Nursing, was an influential mentor. “She was and is my hero,” Koons says. “What most interested me about health care was

the emotional aspect of illness. Dr. Weiss was interested in the language of touch and the link between emotional and physical health. She took me under her wing.”

**ALL ABOUT HEALTH:** In the more than 30 years since she left UCSF, Koons has integrated her many skills to help people, young and old, locally and globally.

“I’ve found that people can relate to art and beauty in a way that accesses different parts of the brain than other forms of education,” she says. “But for me, it’s all about health promotion. I look at the world through the lens of nursing.”



## SCHOOL OF PHARMACY

**KENNETH HOROWITZ,  
PHARM D '66****Hometown:** Newark, N.J.**Now:** Hermosa Beach, Calif.**Position:** Special projects pharmacist, Torrance Memorial Medical Center**Hobbies:** Swing dancing, exercising, hiking, traveling

**As a kid, Kenn Horowitz was shy and withdrawn, especially compared with his gregarious twin brother. But UCSF brought him out of his shell. He was living in a new city; getting involved in student leadership, including two years as president of UCSF's student chapter of the California Society of Health-System Pharmacists (CSHP); and making lifelong friends.**

"Pharmacy school exceeded my expectations," he says. "I received an excellent, forward-looking education. I excelled scholastically and socially."

**PHARMACIST IN THE MAKING:**

Interested in math and science as far back as he can remember, Horowitz planned to become a research chemist so he wouldn't

have to interact with people. But when he was an undergrad at UCLA, a teaching assistant suggested he consider pharmacy instead, and Horowitz soon got a job at the medical center pharmacy, making deliveries and soaking up knowledge. He matriculated at UCSF after two undergraduate years.

Horowitz earned his PharmD during the Vietnam War and went into the U.S. Public Health Service, where he helped people of the Cree and Chippewa nations on a Montana reservation. The work, combined with the area's natural beauty, was a life-changing experience.

"I was the first pharmacist at that location, and my clinical experience really kicked in," Horowitz says. "I was doing

X-rays and EKGs, putting on casts, whatever was needed."

**GREAT GIGS:** Since then, in a career centered in Southern California, Horowitz has worked in a wide range of contexts – from government relations to nursing homes to hemophilia clinics, from assistant pharmacy director at UC Irvine Medical Center to quality assurance director at a contract pharmacy management company.

Currently, he oversees special projects on a part-time basis for the pharmacy at Torrance Memorial Medical Center, bringing his extensive experience to bear on training young pharmacists, writing policies and procedures, participating on committees, and more.

"It's the greatest gig in the world for someone quasi-retired," he says.

He also stays involved with UCSF alumni activities, including helping organize his class's 50th reunion, and with CSHP, serving on its board, earning the Distinguished Service award in 2015, and being named Pharmacist of the Year in 2010 by its Southern California branch.

Along with his wife, Selma, Horowitz is enjoying a little more free time now, traveling, visiting with his grandchildren, and swing dancing.

"When I was growing up in New Jersey, I did the jitterbug," he says. "Now most swing dancing is the Lindy hop, so I've learned how to do that. We go out and dance every chance we get."



**IRIS TAM,  
PHARMD '91**

**Hometown:** San Francisco, Calif.

**Now:** Daly City, Calif.

**Position:** Vice president, patient access and quality, Otonomy, Inc.

**Hobbies:** Cooking, attending the symphony, travel, music

PHOTOS: DREW ALTZER, STEVE BABULJAK

Iris Tam says that UCSF gave her more than a pharmacy education. She also learned to network, collaborate, and take on leadership roles, including student body president. She applied those lessons to become a successful biopharmaceutical industry professional – and a reserve police officer, for seven years,

with the San Francisco Police Department. “I was very proud to serve,” she says. “It could be scary, but I fulfilled one of my lifelong passions.”

Tam, who first became interested in pharmacy in sixth grade, earned a bachelor’s degree in microbiology and immunology from UC Berkeley and was

determined to get her PharmD at UCSF. “UCSF was the only school I applied to,” she says.

**CHANGING COURSE:** She completed clinical and pharmacy administration residencies that prepared her for a position at Seton Medical Center and then was recruited to join PacifiCare, a managed care organization.

pies for patients.” Her current role includes conducting health economics and outcomes research and communicating with payers and managed care entities.

“The recent move has reinvigorated me professionally,” she says. “I love to work hard and create, and Otonomy is giving me those opportunities.”

“That was a turning point for me,” Tam says. “The opportunity to go in a different direction and learn something new opened my eyes to an aspect of health care I wasn’t aware of.” Next, she landed unexpected roles in medical affairs, first at Genentech and now at Otonomy, Inc., a startup that specializes in ear medications.

“If you had asked me as a student, I wouldn’t have dreamed of working for a drug company,” she says. “But now I appreciate the value of researching and developing new thera-

**COURAGE TO LEAP:** In addition to a busy professional life, she is raising two sons, ages 18 and 16; has taught pharmacy students from UCSF; is an aspiring life coach through her business, Create My Journey Consulting; and is a volunteer pharmacist with a federal disaster medical assistance team, a role that took her to New Orleans after Hurricane Katrina, among other missions.

Some of her undertakings have required great courage, but Tam is humble about her accomplishments. “Everyone has something inside them, a sense of wanting to help, an ability to make a leap,” she says. “That’s what I’ve listened to.”



**CYNTHIA EKBERG,  
PHARMD '66**

“It was an exciting time to be in pharmacy school, as our group was among the pioneers in studying drug dynamics, drug interaction studies, and direct patient counseling. My own career was short-lived, but my training came in handy when medical issues arose. After my husband’s passing, my mother lived with me for 11 years, to the age of 105!”



## GRADUATE DIVISION

**MARK DRESSER,  
PHD '00****UCSF Graduate Program:**  
Pharmaceutical Chemistry**Hometown:** Charlotte, N.C.**Now:** San Francisco, Calif.**Position:** Head of development  
sciences, Denali Therapeutics**Hobbies:** Cycling, hiking, travel

At 5:30 a.m. each weekday, Mark Dresser climbs onto his bike for the one-hour ride to work and, at around 7 p.m., starts the head-clearing ride home. He began this daily routine after he turned 40 and decided to take better care of himself. While committed to his own health, he is also working to improve the health of countless others by developing new therapeutics for cancer and Alzheimer's disease.

With no family members in technical professions, Dresser didn't have science on his radar until he got to high school. "I had great teachers who opened my eyes to the wonderful worlds of math and science," he says.

While earning his bachelor's degree in chemistry at Rensselaer

Polytechnic Institute, he had one of the best experiences of his life: a year working in a lab at the Swiss Federal Institute of Technology in Zurich. That sojourn also introduced Dresser to UCSF, since a colleague there was heading to UCSF for a postdoc.

**WORKING RELATIONSHIPS:** "UCSF seemed like the perfect match for me because I wanted to focus more on medical research," he says, motivated by his mother's diagnosis with an autoimmune disease and a cousin's early-onset Alzheimer's.

He remains closely connected to UCSF and to his mentor, Kathleen Giacomini, PhD, co-director of the UCSF-Stanford Center of Excellence in Regulatory Science and Innovation. "She taught me

science," he says, "but also perseverance, leadership, optimism, and how to establish working collaborations." During his UCSF years, Dresser also met his husband, John-Christopher Thomas.

**CAREER LEAP:** A year ago, after a long stint as director of oncology clinical pharmacology at Genentech, Dresser joined

Denali Therapeutics, a biotechnology company focused on neurodegenerative diseases like Alzheimer's. His role is to find effective, efficient solutions to technical challenges in the company's approaches to treating these formidable diseases. Dresser says that the next five to 10 years could be transformative.

"My passion for science has never diminished," he says. "I absolutely love what I do, and I learn something new every day – sometimes 10 things."

**ON A ROLE:** Dresser also serves as a mentor, especially to young LGBT scientists. "I knew no openly gay people in science as role models," he says. "Now that I'm in a leadership position, I feel it's important to show younger people that they can be openly gay *and* successful in science."



**ELIZABETH WATKINS, PHD,**  
Dean, Graduate Division;  
Vice Chancellor, Student  
Academic Affairs

"By the mid-1960s, the concept of the 'organized research unit' took root here, bringing together multi-disciplinary researchers to look at crucial scientific problems. That approach fostered the careers of Michael Bishop, Herbert Boyer, Stanley Prusiner, and Harold Varmus, who transformed UCSF into a major biomedical research powerhouse."



Jordan Mar, left, and Kevin Ebata, right

**Kevin Ebata and Jordan Mar were each drawn to science by an early spark. When they met up at this year's Alumni Weekend, they hadn't seen each other in several years – but, like many UCSF PhD and postdoc alumni, they both landed in the relatively small world of Bay Area biotech.**

“When you're part of UCSF, you end up building a strong community,” Mar says. “You inevitably run into people in biotech who have a UCSF connection.”

**IMMORTAL CELLS:** When Ebata learned about the links between cells, DNA, and disease in high school biology, he immediately wanted to know more. He earned an undergraduate degree in anatomy and cell biology and a PhD in experimental medicine at

McGill University. As a graduate student, he chose to work with stem cells.

“I was fascinated with how stem cells work, how they can self-renew, and how, in some ways, they are immortal,” Ebata says.

**IN THE ZONE:** Mar's interest in science began in sixth grade, when he read *The Hot Zone*, which details the origins of the Ebola virus. In those early days of the internet, it wasn't as easy as it is now to learn more. “I read anything I could that was science related,” he says.

During his undergrad years at UC Davis, Mar was deciding whether to pursue medicine or environmental sciences. He opted for microbiology, which could cover both fields, then surprised himself when he

pivoted from biofuels to the microbiome.

“I wanted to have an impact,” he says, “and I wanted to try something new, something I hadn't planned on.”

**PURSUIING PRECISION:** At UCSF, Ebata and Mar worked with inspiring mentors. Ebata was a postdoc with Miguel Ramalho-Santos, PhD, an associate professor in the Center for Reproductive Sciences. Mar recently completed his PhD with Susan Lynch, PhD, an associate professor of medicine and director of the Colitis and Crohn's Disease Microbiome Research Core.

For both, their early scientific sparks caught fire at UCSF and continue to burn brightly in their current positions.

## KEVIN EBATA, PHD, POSTDOCTORAL ALUMNUS

**Hometown:** Montreal, Québec, Canada

**Now:** San Francisco, Calif.

**Position:** Scientist, translational research, Loxo Oncology

**Hobbies:** Hiking; playing the guitar; trying new restaurants with his wife, Cassandre

## JORDAN MAR, PHD '16, BIOMEDICAL SCIENCES

**Hometown:** Castro Valley, Calif.

**Now:** San Mateo, Calif.

**Position:** Senior scientific researcher, biomarker discovery, Genentech

**Hobbies:** Skiing; snowboarding; fly-fishing; attending Oakland Raiders games with his wife, Florie

“I'm exploring biomarkers that have the potential to move precision medicine forward,” Mar says. “Biomarkers will make it easier to develop more precise therapeutic pathways and plans for patients.”

The same is true for Ebata. “My work is focused on developing highly specific medicines that target driver mutations in cancer,” he says. “I really enjoy working with a team focused on improving the lives of cancer patients.”





### While visions of sugarplums danced in their heads...

Eeeeeek, there's a mouse in the house! As evidenced by this 1974 photo, mice have a longstanding tradition of ringing in the season by dancing in the hallways of UCSF Benioff Children's Hospital San Francisco. The mice, sugarplums, and other fanciful creatures are really

dancers from the San Francisco Ballet. Despite their rigorous performance schedule, they find time to visit the hospital every year to stage a mini-*Nutcracker*, much to the delight of young patients who otherwise would be unable to enjoy Tchaikovsky's holiday favorite.



Quincy Petersen's mom snaps a photo of Quincy and pediatric nurse Katie Maniatis, RN, MSN, on Quincy's last day of intravenous chemotherapy.

## You Make Days Like This Possible

When leukemia patient Quincy Petersen first came to UCSF in the summer of 2013, her red blood cell count was so low that she couldn't walk. But her family found hope, compassion, and unmatched expertise in the form of resident alumna and renowned hematologist-oncologist Mignon Loh, MD.

Quincy's last day of intravenous chemotherapy was late in 2015. Today, she is cancer-free and enjoying life as a 7-year-old.

With every gift you make to UCSF, you make days like this possible. Thank you for helping us educate and train clinicians and scientists like Mignon Loh – and for supporting their extraordinary and life-saving work.

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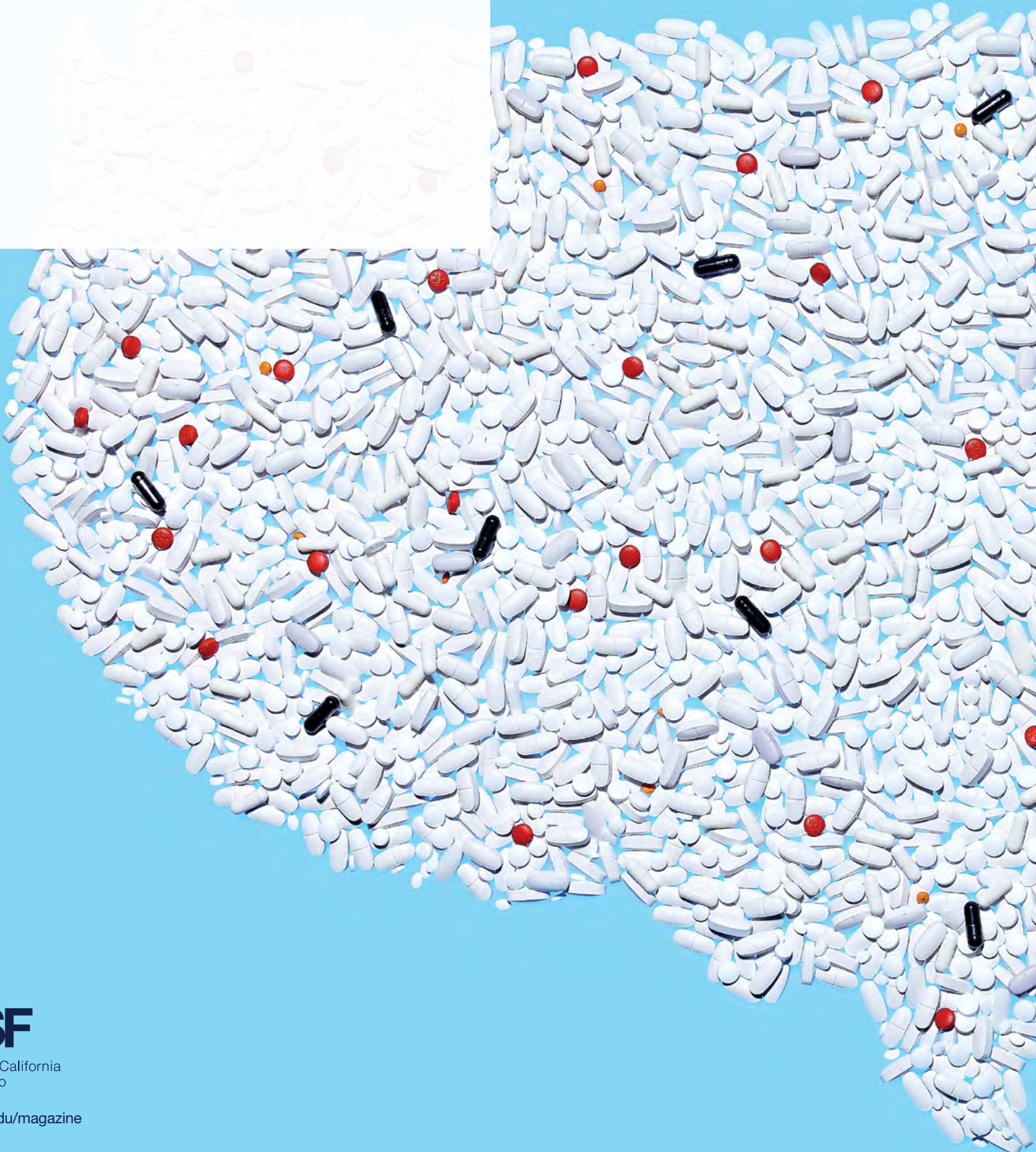


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