



UCSF

MAGAZINE


Summer 2016

Free
to be
Oliver

MS Breakthrough • Science Goes 3-D • The End of AIDS?

UCSF MAGAZINE

SUMMER 2016



LIGHT BRIGHT: UCSF's longtime public health partner has a new hospital and new name: Zuckerberg San Francisco General Hospital and Trauma Center. Fourteen permanent works of public art grace the facility, including this terrazzo floor, designed by Rupert Garcia, which lights up the main lobby.



FEATURES

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Caring for kids struggling with their gender identity.

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Not long after I arrived at UCSF in the early 1980s,

young people in our city began dying in droves of a mysterious illness. Soon identified as AIDS, the disease cascaded into one of history's worst epidemics.

Many UCSF physicians and nurses stepped up to care for these patients, an experience so profound that some then devoted their careers to fighting HIV/AIDS. Now, after decades of perseverance, a few are

on the verge of finding a cure. Their story on page 30 embodies the compassion, collaborative spirit, and dedication that propel UCSF's scientific success.

Those same qualities also spurred another recent breakthrough. As you will read on page 18, neurologist Stephen Hauser spent years collaborating across institutions and industry in his quest to stop multiple sclerosis. His unwavering drive has led to a new drug that has shown amazing results in patients with the disease.

We are on the verge of even more success in improving lives, thanks to two extraordinary partners who share our belief in the power of collaboration and compassion. Sanford I. "Sandy" and Joan Weill have donated \$185 million to establish the UCSF Weill Institute for Neurosciences. They and other generous donors are fueling a trajectory of scientific inquiry into brain and nervous system diseases that will no doubt lead to further sweeping improvements in health and wellness. You can read more about the Weills' gift – the single largest in UCSF's history – on page 36.

I'm proud to serve at the helm of a university where no disease is too daunting to take on together.

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

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FOR ALUMNI AND FRIENDS

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ASK THE EXPERT: **Healthy Aging**

Upon becoming a centenarian, rheumatologist Ephraim Engleman, MD, addressed his senior status with good humor, often sharing his top-10 list of “commandments” for longevity. “Enjoy your work, whatever it is, or don’t do it,” was one. Since he died last year at 104 doing what he loved – working at UCSF – you could say he walked the talk. We recently asked several UCSF faculty members to offer one piece of advice to someone who wants to age healthily.



Preserve your hearing

Margaret Wallhagen, BS '70, MS '71, RN, PhD, gerontologist and professor and interim chair of physiological nursing

“Protect your hearing because it is so essential to staying actively engaged. Avoid loud arenas or listening to loud music through headphones. If you have a problem, arrange a hearing evaluation, because there are things that can be done. Also, the only thing you can control is your response to things. People’s attitudes to challenges and opportunities that come their way affect how they age.”



Get physical

Joel Kramer, PsyD, neuropsychologist and director of neuropsychology at the Memory and Aging Center
“Studies now show that regular exercise is one of the

best things you can do to keep your brain healthy. Exercise can also improve mood and sleep, which promote better brain health too.”



Brush and floss

Donald Curtis, DMD, professor of preventive and restorative dentistry (and a third-generation dentist)
“The average 70-year-old is

more susceptible to tooth decay and tooth loss than the average 7-year-old, and studies have shown that missing 10 or more teeth has a huge impact on quality of life. A lifelong maintenance approach to oral health is important.”



Nourish your soul

Kirby Lee, PharmD '02, MAS, associate professor of clinical pharmacy and an expert in medication management for older adults

“Participate in activities that feed your soul. Whether they are physical, mental, social, artistic, spiritual, indoor or outdoor, it doesn’t matter. Pursuits that feed the soul help give you a sense of purpose and accomplishment, which contribute to wellness across the life span as we ride the ups and downs on this roller coaster ride of life.”



Exercise right

Benjamin Ma, MD, orthopedic surgeon and chief of the UCSF Sports Medicine Center
“I would say exercise, but it

must be appropriate and regular. By appropriate I mean the exercise you do must suit your body type and be right for your condition, so as not to cause injury.”



Skip sugar (and follow these other pieces of advice)

Donald Abrams, MD, chief of the Hematology-Oncology Division, Zuckerberg San Francisco General, and integrative oncologist, UCSF Osher Center for Integrative Medicine

“Avoid sugar. Eat real food. Keep moving. Sleep well. Be flexible in body and mind. Embrace aging.”



Eat mindfully

Mary Ellen DiPaola, RD, a dietitian for more than 25 years and an educator at UCSF for many patients with kidney disease and diabetes

“Be thoughtful about choices: enjoy regular meals, mindfully chosen, consisting of whole, fresh, and local foods, with adequate fluids.”



Watch your numbers

Nelson Schiller, MD, cardiologist and founder of the UCSF Electrocardiography Laboratory

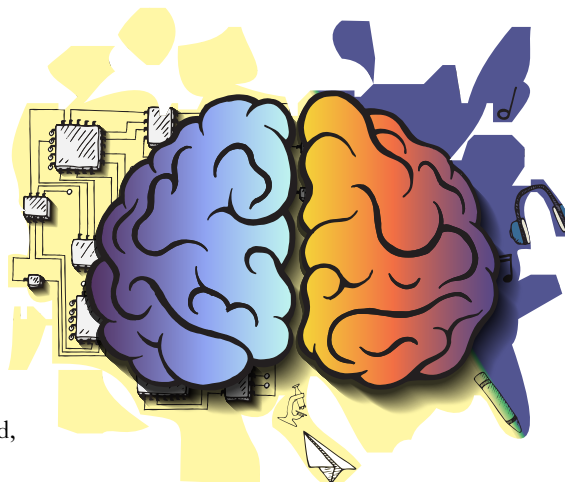
“Insist that your doctor keep your cholesterol and blood pressure under strict control and faithfully take all medications.”

Your Brain on *Jazz*

When Herbie Hancock improvises at the piano, the specific emotions he wants to convey determine which of his brain regions are activated and to what extent – according to the results of a study on which Charles Limb, MD, an avid jazz musician and the Francis A. Sooy Professor of Otolaryngology at UC San Francisco, was senior author.

The project, led by first author Malinda McPherson, a classical violist who previously worked with Limb, built on earlier research using functional magnetic resonance imaging (fMRI) to understand brain activity during musical improvisation, free-style rapping, or caricature-style drawing. When musicians improvise, researchers found,

their brains' dorsolateral prefrontal cortex (DLPFC), which helps in planning and



monitoring behavior, was deactivated, but when they play from memory it was not. The deactivation may be necessary for artists to give free rein to their creative impulses.

Musicians in the study played a small keyboard while in the fMRI scanner. McPherson, who at the time was an undergraduate at Johns Hopkins, where Limb conducted the research, found that deactivation of the DLPFC was greater when the musicians were asked to improvise based on the emotions of a smiling woman in a photograph than of the same woman in a mildly distressed state.

“The bottom line is that emotion matters,” says Limb.

“You can’t add bright lights or install a handrail for someone living under a bridge.”

Margot Kushel, MD, resident alumna and faculty member in UCSF’s Center for Vulnerable Populations, on the growing health needs of America’s elderly homeless, as quoted in *ThinkProgress*

Cannabis-Based Drug Reduces Seizures in Children

Uncontrolled seizures can seriously impact a child’s brain and neurocognitive development. Now, investigators from UCSF Benioff Children’s Hospital San Francisco may have discovered a new treatment for young patients with epilepsy that doesn’t respond to standard antiepileptic drugs.

In a multicenter study led by UCSF, researchers administered a purified cannabinoid to children with intractable epilepsy. Called Epidiolex, it comes in liquid form and contains no tetrahydrocannabinol (THC), the psychotropic component in cannabis. The drug reduced the frequency of seizures, reports Maria Roberta Cilio, MD, PhD, principal investigator of the study and director of research at the UCSF Pediatric Epilepsy Center.

“This trial is testing a pioneering new treatment for children with the most severe epilepsies,

for whom nothing else works,” she says, adding that it’s a first step in testing the drug’s safety and efficacy.



ILLUSTRATION: MUSHROOMSTORE; PHOTO: ESKMANS

Scientists Shed Light on Stem Cell Differentiation

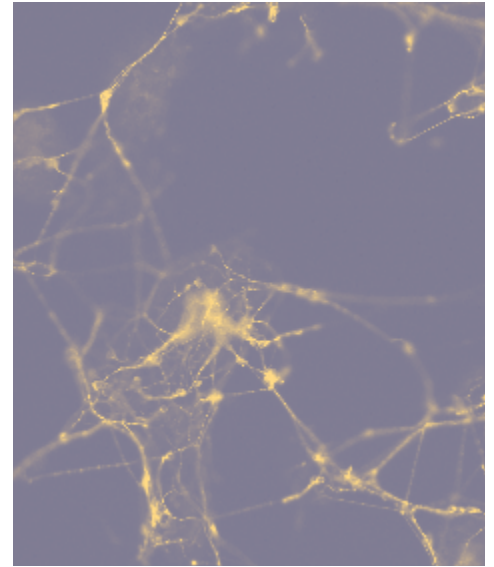
Imagine a day when scientists could use patterns of different-colored lights to signal stem cells to become blood or nerve cells, or even a liver or heart, ready to be transplanted into a patient.

We may be one step closer to that day, thanks to a team led by UC San Francisco's Matthew Thomson, PhD, a researcher at the Center for Systems and Synthetic Biology. Thomson and his team developed a method to precisely control embryonic stem cell differentiation with beams of light. They also discovered an internal timer within stem cells that can be activated with a consistent, appropriate molecular signal.

Getting stem cells to form particular tissues and organs en masse has proven far more difficult than scientists expected, partly because the genes encoding the signals can discriminate between authentic developmental cues and other signals. How they manage that had remained a mystery.

Thomson and colleagues cracked the mystery with pulses of blue light, which switched on a gene that signals the cells to differentiate. Signals that were strong enough and long enough quickly activated the cells' transformation process, while those that were too weak or too brief were ignored completely.

"The cell is not a puppet," says Thomson. "It's an agent that is constantly interpreting information, like a brain."



Children's Health Rapidly Improves with Sugar Reduction

Reducing consumption of added sugar, even without reducing calories or losing weight, has the power to reverse chronic metabolic diseases in children, including high cholesterol and blood pressure. That positive effect was evidenced in as little as 10 days in a study led by

Robert Lustig, MD, MSL, a resident alumnus and pediatric endocrinologist at UCSF Benioff Children's Hospital San Francisco, and Jean-Marc Schwarz, PhD, of Touro University California.

Metabolic syndrome is a cluster of condi-

tions – increased blood pressure, high blood glucose levels, excess body fat around the waist, and abnormal cholesterol levels – that occur together and increase the risk of heart disease, stroke, and diabetes as well as disorders previously unknown in the pediatric population, such as non-alcoholic fatty liver disease and type 2 diabetes. The syndrome disproportionately affects Latinos and African-Americans.

Forty-three Latino and African-American youths with metabolic syndrome ate from a menu that allowed fruit but replaced high-sugar foods with other carbohydrates – such as bagels, cereal, and pasta – as well as with “kid food” – including potato chips and pizza – so that the children still consumed the same number of calories from carbohydrates as before.

After just nine days on a sugar-restricted diet, virtually every aspect of the participants' metabolic health improved, without a change in weight. Their diastolic blood pressure, triglycerides, and LDL-cholesterol (known as the “bad” cholesterol) all decreased, and their glucose tolerance and insulin resistance were markedly improved.

Weighing the Costs of Care

Third-year UC San Francisco medical student Brian Shaw remembers watching his dying mother suffer from cancer and wondering about the futility of her treatment.

Bay Area physician Jessica Nutik Zitter, MD, MPH, recalls, as a new doctor, preparing a 55-year-old woman dying from advanced cancer and septic shock for a routine but painful procedure to monitor her decline. A nurse appeared in the doorway, held her hand to her ear like a telephone, and loudly said, “911. Get me the police. They’re torturing a patient in the ICU at St. Joseph’s Hospital.”

On that day, Nutik Zitter says, she learned a valuable lesson: “Even well-meaning doctors can perpetuate patient suffering by hiding behind interventions rather than communicating with their patients.”

These recollections illustrate the human side of a national movement to carefully weigh health care value – a treatment’s potential benefit measured against its potential costs, including physical and emotional suffering by the patient and family as well as economic costs, both personal and systemic.

For a health professional, answering the simple question “What is the value of what I’m proposing to do?” requires checking one’s instinctive desire, honed by years of training, to save life at any cost. It also requires listening carefully and making medical decisions based on the patient’s preferences.

The growing interest in health care value is part of an effort to change a “culture that’s overrun with overuse,” says Christopher Moriates, MD, a UCSF hospitalist and resident alumnus who teaches the concept to his internal medicine residents.

But, emphasizes Moriates, “This is not about taking things away from physicians or patients. It’s about stewardship. We want to increase the *appropriate* use of care.”

He and other experts at UCSF’s Center for Healthcare Value (CHV) are pursuing this goal by conducting practice-based research, sharing results with colleagues, and training the next generation of caregivers in value-based decision-making.



UCSF student Brian Shaw spearheaded a course on high-value care, led this year by fellow students (from right) Vicky Hwang, Tabitha Vase, Sherry Yamamoto, and Ilana Garcia-Grossman.

Thanks to Shaw, who aims to be a surgeon, that training for the past two years has included a 10-week elective, Introduction to High Value Care, offered by the School of Medicine but open to students from any of UCSF’s four professional schools.

With George Sawaya, MD, who holds the Robert B. Domush Chair in Obstetrics and Gynecology Education and directs CHV’s training initiatives, Shaw developed the curriculum that engages students, through lectures and discussions, in issues facing today’s providers. Taking over from Shaw for the second year’s offering are four medical and nursing students. The elective has enrolled approximately 30 students in each class.

Listening to Nutik Zitter and the other experts who share their experiences, it’s soon clear the training is less about saving money and more about honoring patients’ wishes and avoiding unnecessary suffering.

Shaw envisions a day when such discussions are standard. “What I would hope,” he says, “is that all individuals are actively participating in their care – that providers go beyond just discussing the risks and benefits and more fully incorporate patient values into clinical decisions.”

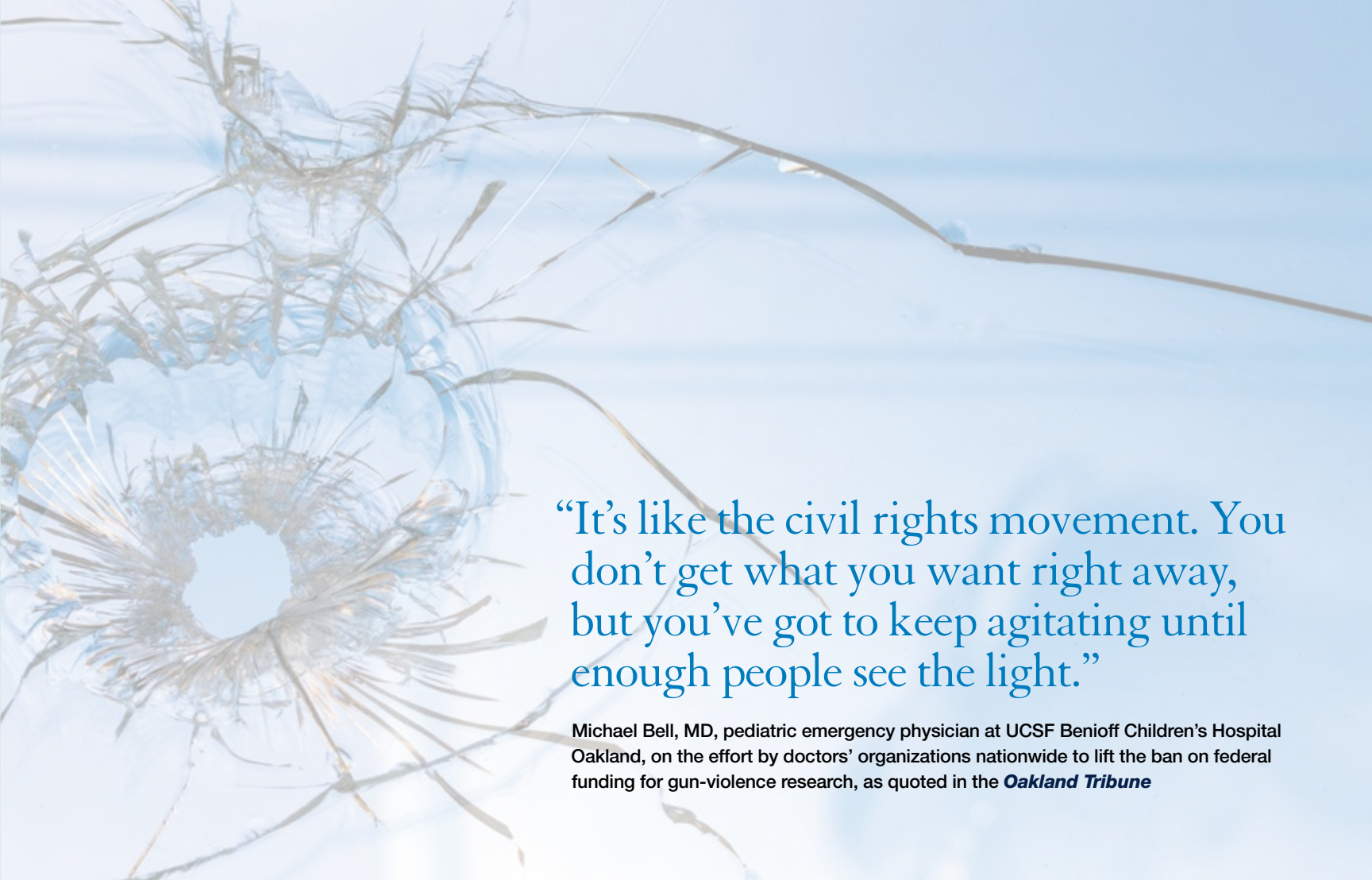
– Mark Hoyer

Smart Savings

1 Generic drugs can be more effective than brand-name counterparts. Why? Generics are cheaper, so patients are more likely to get refills on time and less likely to miss doses.

2 Annual Pap smears – previously the standard of care – resulted in many false positive results, sometimes leading to painful biopsies and treatments that potentially increased risk for pregnancy complications. Research by scientists at UCSF and elsewhere led to revised guidelines, which now suggest that most women get a Pap smear every three years.

3 As evidence began mounting that blood transfusions are overused in clinical settings, the CHV led UCSF hospitals in changing that practice. By tracking individual statistics on transfusions and showing that more did not equal better, transfusion rates were reduced by more than 25 percent.



“It’s like the civil rights movement. You don’t get what you want right away, but you’ve got to keep agitating until enough people see the light.”

Michael Bell, MD, pediatric emergency physician at UCSF Benioff Children’s Hospital Oakland, on the effort by doctors’ organizations nationwide to lift the ban on federal funding for gun-violence research, as quoted in the *Oakland Tribune*

Traveling Teeth

UC San Francisco scientists recently discovered that the cells which turn into teeth in mice are not born in place but migrate. Understanding this process may yield insights about organ development across all mammalian species and may even have implications for understanding – and preventing or interrupting – abnormal cell growth, such as occurs in cancer.

How the genetic code instructs organs to form in the right positions in the bodies of different animals has long puzzled scientists. The assumption was that organs grow in place from clusters of homogeneous precursor cells expressing a gene called *Fgf8*.

But a team led by Ophir Klein, MD, PhD, the Larry L. Hillblom Distinguished Professor in Craniofacial Anomalies and a postdoctoral

alumnus, discovered that tooth precursors first organized themselves into a rosette-like structure in the back of the mouth near the jaw’s hinge. They then broke up and flowed on cue toward the correct spot for teeth.

Further experiments showed that a distinct group of cells acts as a target for the migrating tooth precursors. With the help of a signaling protein, these target cells lead the traveling progenitor cells to the proper position in the jaw.

Because of similarities between migrating protomolars and certain invasive cancers, scientists hope that understanding the mechanisms that guide this organ migration might one day lead to the ability to block related processes in tumors.



Tackling San Francisco's Housing Crisis

In 2014, San Francisco earned the dubious distinction of being the most expensive rental market in the country, according to industry statistics, outpacing even New York City.

Over the past five years, prospective students' concern about the cost of living in the Bay Area, on top of their student loan debt, has been by far the number-one reason why accepted students elect not to attend UC San Francisco. And skyrocketing rental rates in San Francisco are the principal driver of the cost-of-living concern.

"For UCSF, the greatest current threat to our excellence is the high cost of living in our community.... We're losing talent at all levels, in all segments of our community," said Daniel Lowenstein, MD, executive vice chancellor and provost and a resident alumnus, in a recent speech to the Bay Area Council.

University-owned housing, which costs 36 percent less on average than other rentals, is currently available (by lottery) to only about one-third of the graduate and professional students who need housing – and demand is only growing.

That leaves two out of three students facing difficult housing choices. For those receiving need-based financial aid, the choices are even tougher. While the monthly amount budgeted for off-campus housing as part of financial aid packages has increased by almost 60 percent over the past 10 years, the \$1,465 allocation is well below the \$2,200 average cost for a single room in San Francisco, according to figures supplied by UCSF Housing Services.

University leaders, led by Lowenstein and Clare Hansen-Shinnerl, MBA, EdD, associate vice chancellor of campus life services, are urgently seeking creative solutions to grow the pool of affordable housing options. UCSF's Long Range Development Plan calls for more than doubling the housing at the Parnassus and Mission Bay campuses by 2035.

Recognizing the need for immediate action, too, the university recently took these actions:

- Completed the acquisition of three properties in the Dogpatch neighborhood



Source: Zillow Rent Index

that are being evaluated for new student/trainee housing, pending environmental review.

- Signed a letter of intent with UC Hastings School of Law to develop three properties on the law school campus in the Tenderloin area that might add as many as 1,120 housing units.

The dearth of affordable housing impacts recruitment not just of graduate and professional students, of course, but of medical residents, postdoctoral fellows, and faculty and staff as well. It also threatens to undermine the university's ongoing commitment to diversifying the talent pool.

Keeping the cost of living affordable for recruits is crucial, Lowenstein emphasizes, in order to sustain and advance the diversity of both the UCSF community and the city. And developing new housing will benefit all San Franciscans by contributing to the city's overall housing supply.



Average Rents in the Inner Sunset (the area surrounding the Parnassus campus)

Studio	\$2,122
One-bedroom	\$2,800
Two-bedroom	\$3,355
Three-bedroom	\$3,900

UCSF Health: New Name, Expanded Care

Delivering innovative, high-quality, high-value care to people throughout the Bay Area and beyond has always been at the heart of UC San Francisco's health care system. That system now has a new name, UCSF Health, which reflects the expanding opportunities to improve care and provide greater access to services for a

larger number of people in the region.

For decades, many of the entities that make up UCSF Health operated independently. Integrating them will make it possible to develop consistent performance metrics system-wide, creating greater transparency regarding prices, costs, and clinical outcomes.

The system comprises UCSF Medical Center, UCSF Benioff Children's Hospital San Francisco, the UCSF Faculty Group Practice, the separately licensed UCSF Benioff Children's Hospital Oakland, Langley Porter Psychiatric Hospital and Clinics, Benioff Children's Physicians Medical Foundation, and joint ventures with John Muir Health and Hospice by the Bay.

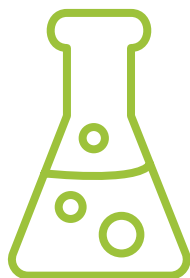
The transformation of these separate entities into an integrated health care network is at the heart of an effort to provide more patient-centered, effective, and affordable care; to improve access; to capitalize on partnerships; and to fulfill "UCSF Vision 2020," a strategic roadmap to maximize quality in clinical services and to enhance patients' experience.

Over time, the integrated system will allow more streamlined and secure sharing of patients' electronic medical records and clinical research data – giving providers who partner with the system better access to information that will allow them to improve the health of patients and populations.

"UCSF is responding to a revolution now under way in health care," says UCSF Chancellor Sam Hawgood, MBBS, "delivering care that is more patient-centered, effective, and affordable."



UCSF Health launched an ad campaign last fall featuring patients. One of them, Miguel C., is learning to walk again after an accident, thanks to support from UCSF's Orthotics and Prosthetics Center.



“One myth about chemicals is that the U.S. government makes sure they’re safe before they go on the marketplace.”

Tracey Woodruff, PhD '91, MPH, director of UCSF's Program on Reproductive Health and the Environment, on toxic chemicals' effects on our health, as quoted in the *New York Times*

Game-changer for Type 1 Diabetes?

A new cell-based therapy that aims to re-educate the body's immune system is showing great promise in protecting insulin-producing beta cells, according to a phase I trial led by scientists at UC San Francisco. That's welcome news for

those with recent-onset type 1 diabetes (T1D) who have lost the majority of their beta cells by the time they are diagnosed – and as a result require insulin injections.

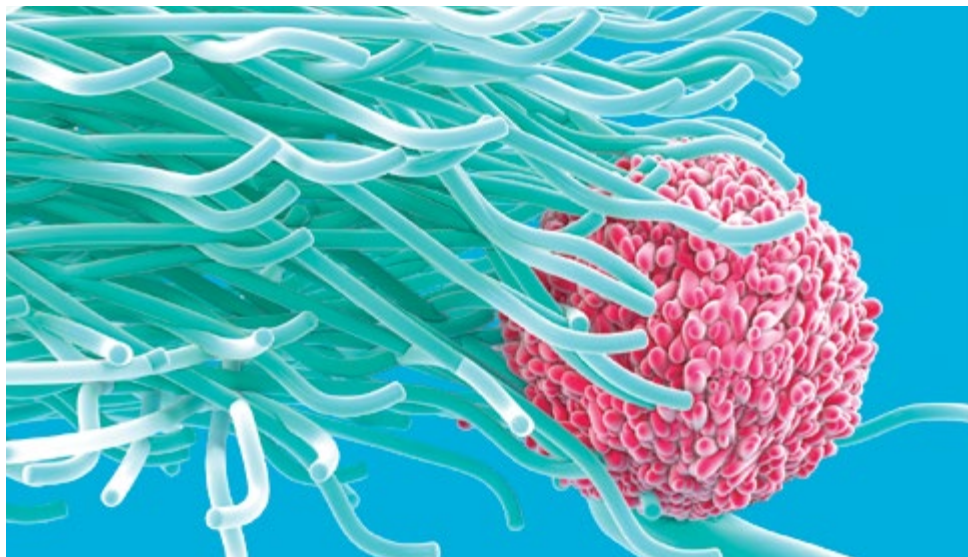
In T1D, the immune system, instead of

protecting against infection, goes awry and kills insulin-producing beta cells in the pancreas. Most immunotherapeutic approaches seek to suppress this misguided immune response, but that brings with it an increased susceptibility to infection or cancer.

The trial team, led by Jeffrey Bluestone, PhD, the A.W. and Mary Margaret Clausen Distinguished Professor in Metabolism and Endocrinology at UCSF, used specially treated T cells called Tregs to dampen the immune system's assault on beta cells, while leaving its infection-fighting capabilities intact. The Tregs were derived from trial participants' own cells, using a technique developed by Bluestone and colleagues.

Tregs hold great promise for treating other autoimmune diseases, such as rheumatoid arthritis and lupus, as well as for combating the effects of organ transplantation, cardiovascular disease, neurological diseases, and obesity.

A phase II trial to test the efficacy of the Treg therapy is planned.



“It is particularly interesting to note that those who believe alcohol to be heart healthy actually drink more alcohol. Whether their belief causes this behavior, or merely justifies it, remains an interesting unknown.”

Cardiologist Gregory Marcus, MD, MAS '08, and fellowship alumnus, on a study suggesting that people who believe in the health benefits of alcohol tend to consume more of it, as quoted in the *Chicago Tribune*



PHOTOS: FLYFLOOR, LUISMOLINA

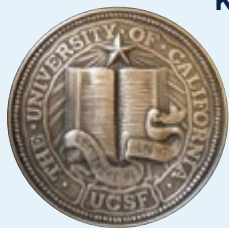
FACULTY ACCOLADES

Leslie Benet, PhD '65, professor of bioengineering in the School of Pharmacy, is the 2016 recipient of the Remington Honor Medal, the American Pharmacists Association's highest honor. He was cited for his half-century career as a scientist, educator, and leader and his impact on pharmaceutical research and practice.

Kirsten Bibbins-Domingo, MD '99, PhD, the Lee Goldman, MD, Endowed Professor of Medicine; **Andrew Bindman**, MD, professor of medicine, health policy, epidemiology, and biostatistics; **Atul Butte**, MD, PhD, professor of pediatrics; **Tejal Desai**, PhD '98, professor of bioengineering; and **Shinya Yamanaka**, MD, PhD, professor of anatomy and a Nobel Laureate, were elected to membership in the National Academy of Medicine (formerly the Institute of Medicine).

Two of the nine national awards presented annually by the Association of American Medical Colleges went to members of the UCSF faculty. **Gurpreet Dhaliwal**, MD, professor of medicine, won the Alpha Omega Alpha Robert J. Glaser Distinguished Teacher Award, honoring "gifted teachers," and **Elisabeth Wilson**, MD, MPH, resident alumna and the Permanente Medical Group Professor of Primary Care, won the Arnold P. Gold Foundation Humanism in Medicine Award, honoring "a caring and compassionate mentor in the teaching and advising of medical students."

Marylin Dodd, PhD, RN, professor emerita of physiological nursing, was designated a "Living Legend" by the American Academy of Nursing. The academy's highest honor, the designation recognizes Dodd's contributions to patient self-care and the science of symptom management.



Kathleen Dracup, RN, PhD '82, professor and dean emerita of nursing, received the 2015 UCSF Medal, the University's highest honor, for outstanding contributions in patient care, research, and teaching. She was recognized for her leadership, compassionate care, and scholarship, as well as her pioneering transformation of the nursing profession.

Sophie Dumont, PhD, assistant professor of cell and tissue biology in the School of Dentistry, received the National Institutes of Health's New Innovator Award, which supports unusually innovative research by early-career investigators.

The School of Dentistry's Center to Address Disparities in Children's Oral Health – led by **Stuart Gansky**, DrPH, the John C. Greene Professor of Primary Care Dentistry and vice chair for research in the Department of Preventive and Restorative Dental Sciences – received three grants from the National Institutes of Health totaling nearly \$21 million. The funding will permit the center to continue its work to prevent oral disease and promote oral health in children, especially in low-income and minority populations.

Lisa Kroon, PharmD, resident alumna, the chair and Thomas A. Oliver Endowed Professor of Clinical Pharmacy, was named a fellow of the American Pharmacists Association Academy of Pharmacy Practice and Management (APhA-APPM). The designation honors academy members for exemplary professional achievements and service to the profession through activities with the APhA and other organizations.

Monica McLemore, PhD '10, MPH, BSN, assistant professor of family health care nursing, was named one of 10 "Culture of Health: Breakthrough Leaders in Nursing" by the Future of Nursing: Campaign for Action.

Louis Ptáček, MD, the John C. Coleman Distinguished Professor in Neurodegenerative Diseases, and **William Seeley**, MD '99, associate professor of neurology, were named fellows of the American Association for the Advancement of Science, the world's largest general scientific society.

Michal Staninec, DDS '80, PhD, health sciences clinical professor emeritus of biomaterials and bioengineering in the School of Dentistry, and **Sophia Saeed**, DMD, associate professor of preventive and restorative dental sciences, received awards from the Northern California Section of the Pierre Fauchard Academy, an international dental honor organization. Staninec received the Faculty Recognition Award, which salutes a senior faculty member for excellence in dental education, and Saeed received the Faculty Development Grant, which provides funding for a project.

James Wells, PhD, the Harry Wm. and Diana V. Hind Distinguished Professor in Pharmaceutical Sciences and chair of pharmaceutical chemistry, was elected a fellow of the National Academy of Inventors. Wells' pioneering innovations in protein engineering and in identifying small molecules to aid in drug discovery have yielded more than 60 patents, launched three companies, and led to the creation of two UCSF technology centers.



**FREE TO BE
HE, SHE, THEY**

UCSF's pioneering Child and Adolescent Gender Center is helping a growing number of families seeking advice – and, increasingly, medical intervention – to help a son or daughter's physiology match their gender identity.

By Janet Wells



PHOTO: GABRIELA HASBUN

Transgender teen Oliver Bishop at his high school in the Sierra foothills, where he leads the marching band.

Oliver Bishop has sandy blond hair styled like a 1940s screen idol's and a scruffy beard and sideburns that frame his wide smile. A senior in high school, he is busy – singing with his school's award-winning jazz choir, leading the marching band, teaching music lessons. Outgoing and popular, he was elected homecoming king in the fall.

Bishop, 18, was assigned female at birth and had spent years trying – and failing – to make peace with that status.

The disconnect he felt with his body didn't matter so much when he was young, a tomboy in his hometown in California's Sierra foothills. He refused to wear dresses, played on a coed baseball team, and ran around in swim trunks with no top.

Things changed abruptly in fourth grade, when he started puberty. He tried to fit in, growing his hair long and wearing more feminine clothes. He was increasingly miserable and unable to name what was wrong. His grades plummeted. He chopped off his hair.

"A buzz cut, that took a lot off me emotionally," he says. But he still felt trapped in a body growing more feminine by the day. By the time he reached high school, his distress was at a crisis level. He thought about suicide.

"I didn't know how to fix it," he says. "I didn't have anything to strive for."

A few months before his 15th birthday, Bishop stumbled across the word "transgender" online. He read about people who had had medical treatment to align their bodies with their gender identity – their inner sense of who they are.

"*Bam*, my life changed," he says. "It lifted a major weight to find out I could do something about all this pressure I had been feeling."

Coming out to his parents, however, "was an ordeal." He wrote a letter but never gave it to them. Finally, he blurted it out when his mother dropped him off at a friend's house for the night. "Mom, I'm trans," he said, jumping out of the car. His father stopped speaking to him for months.

"We live in a small, conservative place," Bishop says. "The community I was raised in didn't have any idea of what transgender was."

His parents didn't understand, says Bishop. But they loved him and knew he – and they – needed help. Their family doctor mentioned UCSF's Child and Adolescent Gender Center. At their first appointment, both of his parents cried.

"I thought they were upset," says Bishop. "But it was because they were so happy to see people who understood me."

That visit, he adds, "changed everything."

A shifting landscape

The conversation on gender identity has surged into the mainstream in recent years, with the emergence of celebrities like Caitlyn Jenner, the

"In the rawest
form, the
center saved
my life."
– Oliver
Bishop

Bishop was the first in his small town to come out as a transgender person. UCSF's Gender Center, where he sought care, has seen its patient load more than triple in the past three years.



bestselling book *Becoming Nicole*, and the award-winning Amazon series *Transparent*.

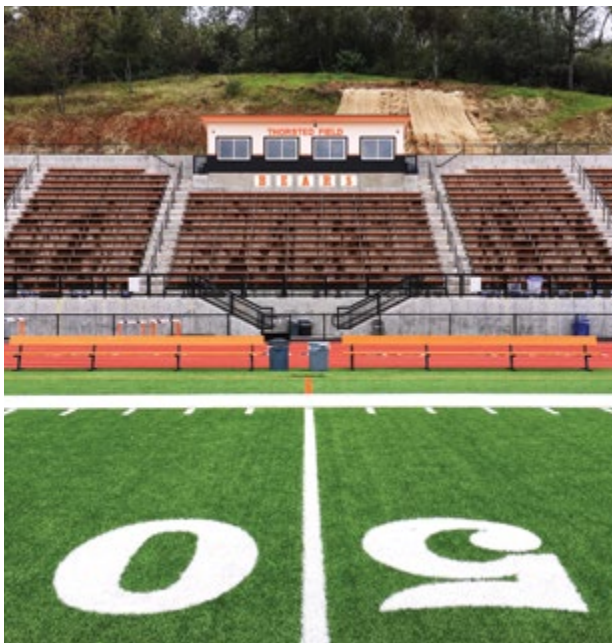
Half of adults aged 18 to 34 now see gender as a spectrum from male to female, not as a binary assignment, according to a survey conducted last year by the website Fusion.net. The American Dialect Society's 2015 Word of the Year was the singular pronoun "they" as an alternative to "he" or "she."

The rapid shift in attitude is more than cultural. California recently mandated that public school students have access to bathrooms, locker rooms, and sports teams based on their gender identity, regardless of the gender on their records.

Significantly, in 2013, the *Diagnostic and Statistical Manual of Mental Disorders* – American psychiatry's clinical bible – replaced "gender identity disorder" with "gender dysphoria."

As a result, cross-gender identity in itself is no longer considered a mental illness, much as homosexuality was reclassified in the 1970s. The focus instead is on distress stemming from incongruence between the gender that individuals are assigned at birth, based on their physical characteristics, and their internal gender identity.

That distress can reach alarming levels: Transgender youth have a two- to threefold increase in risk of depression, anxiety disorder,



PHOTOS, FROM LEFT: GABRIELA HASBUN, STEFAN HUNDHAMMER, AUDREY FEELY

suicidal ideation, and attempted suicide, according to a 2015 study in the *Journal of Adolescent Health*.

“Not treating is not a neutral option”

In 2009, UCSF’s Division of Pediatric Endocrinology got a phone call from the father of a 12-year-old who was assigned female at birth but identified as male.

“He asked if we provided puberty blockers,” says Stephen Rosenthal, MD, then clinic director for the division. “We had never provided services for transgender people. I was aware they were on the planet, but I thought they just emerged in adulthood and went through transition with hormones and surgery.”

Rosenthal, a postdoctoral alumnus, started digging but encountered a paucity of academic literature on transgender youth. Finally, he came across a European journal article outlining the “Dutch protocol” – now the foundation of the Endocrine Society’s clinical guidelines for the treatment of transgender youth.

“I began to learn the history and risks faced by transgender individuals and the life-saving benefits of puberty blockers,” Rosenthal says. “Not treating is not a neutral option.”

Such blockers – gonadotropin-releasing hormone (GnRH) agonists – are not new. In the 1980s, GnRH agonists became the gold standard treatment for precocious puberty, to selectively turn off production of sex hormones in very young children exhibiting mature sexual traits. “It’s completely reversible,” Rosenthal says. “You take them off it, and they resume puberty.”

For people with gender dysphoria, the secondary sex characteristics that emerge in puberty – breast development, menstruation, and redistribution of body fat in females; growth of facial and body hair, deepening voice, and enlargement of the genitalia in males – can feel like deformities.

“You can take those kids who are really suffering, put puberty on pause, and give them time to figure out what their gender identity really is,” Rosenthal says. “The beauty of the blockers is that a girl doesn’t have to worry about having an Adam’s apple or a deepened voice. The quality of life for someone blending in according to their gender identity is much better.”

A multidisciplinary approach

The health challenges faced by transgender youth – and the dearth of treatment options – inspired Rosenthal to pursue a unique model of one-stop care.

Launched in 2010, with Rosenthal as medical director, UCSF’s Child and Adolescent Gender Center is the only program in the country with an interdisciplinary team of directors who offer medical, mental health, educational/advocacy, and legal expertise to support gender nonconforming youth and their families.

Clinic patients – who range from as young as three years old through their mid-20s – receive mental and physical evaluation and care. Legal and advocacy staff members are available to advise them on issues ranging from insurance reimbursement and coming out at school, to changing names and genders on documents.

Rosenthal and his team watch patients for cues – “persistent, insistent, consistent” declarations of who they are, often from a young age, he says – and signs of clinical distress associated with gender dysphoria.

Easing transitions for kids and parents

If it appears warranted, patients are prescribed puberty blockers and, for older teens, cross-sex hormones – testosterone or estrogen – to kick-start the puberty that matches their gender identity. Some individuals choose, once they reach age 18, to have genital revision surgery, in which case appropriate referrals are made.

“We’re working with families to support young people in more fully becoming themselves,” says Molly Koren, MSW, a clinical social worker at UCSF Benioff Children’s Hospital San Francisco.

The family-focused approach is key: Parents often need guidance as much as their children.

“When a child says, ‘I’m not the gender you think I am,’ that can be a showstopper,” says Diane Ehrensaft, PhD, the Gender Center’s director of mental health as well as a private-practice psychologist in Oakland. “Some parents say, ‘Not on my watch. No way am I signing off on a medical intervention. When they’re 18 they can do what they want.’ I say, ‘You’re absolutely right, you’re the ones minding the shop, but let me share with you the risk factors of holding back.’”

“This is our kid”

Those risks weighed heavily on “Emily” (not her real name) and her husband. Photos in their sun-filled Silicon Valley home show their 10-year-old son and his older sister, “Kelly,” who has the same pre-Raphaelite honey blond hair and bright hazel eyes as her mom.

Five years ago, they were a family with two sons.

“When she was four years old, she asked me why did I make her a boy? And could she go back inside my tummy and come out as a girl? And if she died could she come back as a girl? That just broke my heart,” says Emily (who requested pseudonyms to protect the family’s privacy).

A therapist advised them not to confuse Kelly by allowing her to wear dresses, but to compromise with boy’s clothes in flowing, ethnic fabrics and colorful Hawaiian prints. It didn’t help. She was increasingly shy and anxious and wanted everything girly.

One day Emily got a call from her husband, who was in his car listening on the radio to Joel Baum, MS, the Gender Center’s director of advocacy as well as the director of education and training for the Oakland-based

Asking his parents if he could turn into a boy for his fifth birthday wasn’t the first – or last – time Shay pushed back at the gender he was assigned at birth. He refused to wear dresses, cut his hair short, and roughhoused with his friends – all boys.

“You think, ‘Oh, he’s just probably a tomboy,’” says his father, Wayne.

Now in eighth grade, Shay, 14, plays flag football and is a soccer goalie on South Bay club teams. He wears athletic shorts, sweats, and shirts, loves video games, banters with his dad, and teases his 11-year-old sister. The only evidence of “difference” from other boys his age is a small circular scar on his arm where a puberty blocker is implanted under the skin.

Five years ago, Shay identified as “gender fluid” on the UCSF Child and Adolescent Gender Center’s spectrum of female (1) to male (10).

Puberty blockers, says Wayne, “bought us time.” Now a firm “10” on the spectrum, Shay transitioned from “she” to “he” in fourth grade and legally shortened his birth name from “Shayna” a year ago. He plans to start taking “T” – testosterone – this year to initiate male puberty.

Wayne credits the Gender Center and Medical Director Stephen Rosenthal, MD, for easing Shay’s – and his family’s – transition: “He gets it. He takes the time to get to know you and makes sure you have the knowledge and the resources.”



Gender Center director Stephen Rosenthal (left) visits with Shay and his father, Wayne.

nonprofit Gender Spectrum. “You’ve got to turn on the radio,” he told her. “I think this is our kid.”

Emily was horrified to learn about the high rates of harassment, school failure, and suicide among transgender youth. “I couldn’t talk about it without weeping. I kept going to all these images in our culture for transgender people, that they’re on the edge, disenfranchised,” she says. “I was thinking, ‘I can’t lose my kid. I don’t care what her gender is. I’ve got to get on the other side of those statistics.’”

Her path forward, she says, was “unconditional acceptance of my child’s truth.”

The family started regular visits to Gender Center clinics and let Kelly be their guide. She grew her hair long. In third grade, she switched her masculine birth name to a gender-neutral nickname. At age nine, she transitioned socially, becoming “she” to relatives, friends, and classmates.

Intensely private, Kelly wanted no emails to parents, no classroom announcement. Just a quiet switch in pronouns. Her elementary school administrators and teachers – faced with their first transitioning student – were “incredibly supportive,” says Emily, who sought out staff training and put Kelly in a classroom with only one student who knew her from “before”: her best friend.

Now 13, Kelly has a matchstick-sized implant under the skin near her left bicep to suppress the male hormones her body produces. She’s blossomed into a “beautiful, smart, artistic, empathetic, fun kid,” Emily says. “I’m like, ‘Whoa! I hit the jackpot.’ But it was a definitely a process and a journey for our family, and our daughter, to come to understand who she was.”

Building the evidence base

The Gender Center’s patient load – now more than 300, with about 10 new referrals a month – reflects the explosion in the number of transgender youth seeking specialized services across the country, says Rosenthal.

Families come from as far as Alaska, Florida, and Egypt for weekly clinics offered in San Francisco and a new location in San Mateo. A clinic at UCSF Benioff Children’s Hospital Oakland is in the works.

The Gender Center’s approach may be in demand – and the standard of care for persistent gender dysphoria – but it’s not without controversy.

In the May 2015 issue of *Pediatrics*, one group of critics lambasted the gender-affirming model for reinforcing “the delusions of gender identity-confused children.” Citing the lack of long-term data on medical transitions, the critics called the approach an “ideology-driven social experiment.”

UCSF, along with three other academic institutions with dedicated transgender youth centers, are addressing that lack of evidence with a \$5.7-million grant from the National Institutes of Health (NIH).

The five-year study – the first of U.S. transgender youth funded by the NIH – will evaluate the physiological and psychosocial impact of puberty blockers and cross-sex hormones.

“We’re really excited to pool our resources,” says Rosenthal. “This study will help to effectively and safely guide the clinical care of these youth.”

Righting the “wrong” puberty

By age 15, Oliver Bishop was on a dual regimen of testosterone, plus puberty blockers to keep his endogenous estrogen from competing with the male hormones.

He came out to his classmates by creating a second Facebook account with his new name, chosen after he asked his mom what it would have been if he had been born male: Oliver, after his great-grandfather.

While he had to endure a second puberty, and he’ll need to take testosterone for the rest of his life, he’s had no second thoughts about transitioning.

The summer after his sophomore year, he had “top” surgery – a double mastectomy and male chest contouring – in San Francisco. To pay for the procedure, which was not covered by insurance, he used earnings from years of showing and selling pigs at the Tuolumne County fair.

“It’s a lot of money for a 15-year-old,” he says of the \$8,000 price tag. “But I appreciate it every day.”

His family’s insurance also wouldn’t cover a puberty blocker implant, so Bishop at first chose cheaper but “gnarly” monthly shots. Later, concerned about unknown long-term effects of the blockers, and hating the painful shots, he opted for a hysterectomy at age 16 – performed by the same family doctor who had delivered him.

While Bishop can almost seem blithe at times about his transition, it hasn’t all been smooth. There are still derogatory remarks. His extended family has had a mixed response.

But he doesn’t waste time worrying about the stings. The first in his small town to come out as a transgender person and to medically transition, he’s been a role model for peers who share nontraditional gender expressions. He’s on a glide path to graduation, his grades are high, and he plans to pursue a degree in music education. In June, he’ll undergo the first in a series of “bottom” surgeries to create male genitalia.

His only regret, he says, is not finding UCSF’s Gender Center sooner. “To not go through the wrong puberty, those kids are lucky,” he says. “That’s a team effort. You have to show [gender dysphoria], and parents have to catch it.”

He doesn’t take his parents’ evolution, or their support, for granted. “I couldn’t have done this without them. And I would not have been able to make it without the Gender Center helping me and my parents understand, and medically transition,” Bishop says. “In the rawest form, the center saved my life.”



With one drug to shut down its progression and another to undo its damage, plus a worldwide effort stalking the origins of multiple sclerosis, the disease doesn't stand a chance.

By Claire Conway

Alexandra Solal's 47th year was remarkable by any measure: she climbed Mount Kilimanjaro, ran two half-marathons, completed a half-Ironman, and started a CrossFit gym habit before work with a friend. It was also the year she woke up half paralyzed. Determined not to alarm her son, she commando-crawled to her closet, dressed on the floor, and called her gym buddy to take him to school. "When my friend pulled in, she saw me propping myself up between our two cars and started to cry," recalls Solal. "That's when I knew it was bad."

Solal's story is more dramatic than most. Multiple sclerosis (MS) usually sets in with neurological symptoms that evolve over a few hours or days – eye pain, vision loss, double vision; numbness or tingling in the hands or feet; leg weakness; loss of balance. But the gradual onset belies the ferocity of the immune system's attack on the myelin protecting our nerves. Just as the insulation on a power cord ensures electricity's safe passage, myelin safeguards the passage of signals from our brain to the rest of our body. If myelin degrades, so does the messaging, until it breaks down entirely.

Stopping MS in its tracks

Yet, like her disease's onset in 2013, Solal's trajectory with MS will be dramatically different than that of patients diagnosed a generation ago. Her neurologist, Stephen Hauser, MD, just announced a new MS

drug that's far more effective than high-dose interferon beta – a standard treatment – at reducing brain inflammation and lesions. Hauser, chair of neurology and Robert A. Fishman Distinguished Professor in Neurology, led the trial, which was sponsored by Hoffman-La Roche and conducted at over 200 centers worldwide in patients with the disease's most common form, relapsing-remitting MS. The drug, ocrelizumab, targets a type of white blood cell called B-lymphocytes. Compared to interferon, ocrelizumab reduced clinical MS attacks, blocked the development of new myelin inflammation by over 95 percent, and delayed disability progression by 40 percent.

"The results were beyond spectacular," says Hauser, who has been named inaugural director of the new UCSF Weill Institute for Neurosciences (see story, page 36). "This therapy essentially stops the inflammatory relapsing form of MS in its tracks and appears to do so safely." Hauser spent decades collaborating across institutions and industry and bucking convention to lay the groundwork for ocrelizumab.

More good news followed. There's been no therapy for the primary progressive form of the disease (PPMS), which affects 10 to 15 percent of the 400,000 Americans with MS. But a related trial showed that ocrelizumab is 24 percent more effective than a placebo in slowing PPMS's progression and staving off brain lesions and degeneration.

The next steps will be to develop evidence-based rules for using this well-tolerated and highly effective drug. Currently, physicians delay prescribing the most effective therapies, due to their toxicity.

“We are optimistic that with aggressive therapy that can be given safely at the beginning of the disease, the long-term outcomes, which are measured in decades, will be far superior to what they are today,” says Hauser. “These results should allow us to ask if shutting down brain inflammation at a very early stage in the disease might prevent late progressive MS altogether.”

This is good news for both newly diagnosed patients like Solal and for those further into their journey with MS. UCSF scientists are shutting down MS from every angle: by killing, with ocrelizumab, the immune-system agents responsible for attacking myelin; by repairing damage already done; and by isolating ways to prevent MS’s onset.

Reversing the damage

Ari Green, MD, MCR, has the acute sense of time that MS clinicians and scientists develop. He points to slides showing a patient’s brain atrophying over seven years. Meter-long nerve fibers are exposed and broken. Green, the Debbie and Andy Rachleff Distinguished Professor in Neurology and director of UCSF’s Multiple Sclerosis Center and Neurodiagnostics Center, likens these fibers to bridges with missing sections, so signals can’t span them.

“Here’s how that damage impacts the patient,” explains Green, a resident alumnus. “At 10 or 15 years, people leave work; at 20 years, an overwhelming majority need help walking; and by 30 years, many are in wheelchairs. We’ve made progress with our new anti-inflammatory therapies, but it’s still not enough. Every patient already has damage even before we see them for the first time.”

Green and neuroscientist Jonah Chan, PhD, who also holds a Rachleff Distinguished Professorship in Neurology, hope to reverse nerve damage with a drug that induces cells to rewrap exposed axons with protective myelin – a process called remyelination. “We know that some axons in our MS patients’ brains lack myelin,

“In fact, this is the only drug in history that helps with brain repair, and it can be bought at Walgreens.”

– Jonah Chan

and if we can get the myelin around them, we can salvage them and improve our patients’ quality of life and hopefully prevent progression,” says Green.

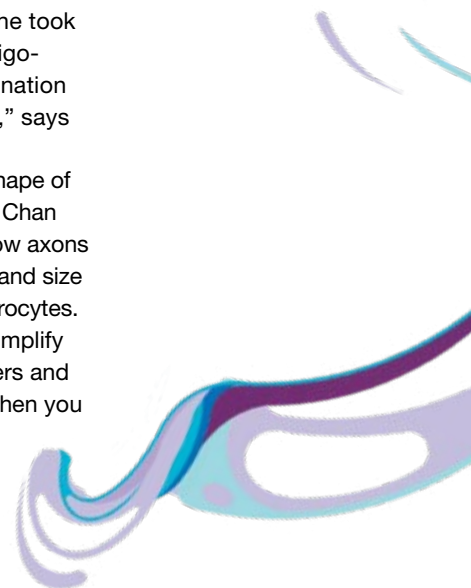
Their target is oligodendrocyte precursor cells, which mature into the oligodendrocytes that insulate the axons with myelin. These precursor cells are found throughout MS patients’ brains. “In some areas in MS brains, remyelination is actually occurring, but right next to it might be lesions where no repair is happening,” says Chan. “Something is halting these cells from remyelinating.”

Ever mindful of time, they decided to screen FDA-approved, readily available drugs to see if any had the potential to induce remyelination. Yet such a process is long and problematic. “First you have to isolate and grow neurons, then you have to coculture them with oligodendrocytes and stimulate myelin to form – all the while making sure the neurons remain healthy,” says Chan. “To screen a thousand drugs would literally take a lifetime, and you still wouldn’t know if the effects were cell autonomous to oligodendrocytes or an indirect effect on the neurons.”

Instead, Chan followed a hunch that changed the metrics and the rules entirely. Experts had long assumed that axons signaled oligodendrocytes that they needed wrapping. Chan suspected that if he took dead axons and put them in a petri dish with oligodendrocytes, they might actually start the myelination process anyway. “People thought he was crazy,” says Green, “but he was correct.”

Next, he spun out plastic nanofibers in the shape of axons. “The cells started to wrap the fibers, too,” Chan recounts. “So we no longer had to isolate and grow axons for modeling myelination.” Replicating the shape and size of the axon was enough to engage the oligodendrocytes.

This enabled them to radically hasten and simplify the process. “We found that if we take those fibers and fabricate them straight up like pillars in a dish, when you





Stephen Hauser

B is for Believer

Hauser's hard-fought path to ocrelizumab – from bedside to bench and back again – started during his residency in the 1970s. He recalls the event vividly. It was the wedding of one of his first patients with multiple sclerosis, held in her hospital room. A Harvard-educated lawyer with a job in the White House, she was just 27 when MS struck. He met her soon after her parents committed her to a psychiatric facility for sudden onset of altered behaviors and judgment lapses – signs of MS taking hold of her frontal lobe. Within weeks of her diagnosis, she lost the capacity to speak, swallow, breathe, and use her right side. “She was in her wedding gown, in a wheelchair, connected to a breathing tube and a feeding tube,” recalls Hauser. “Her fiancé and parents were there; the room was drab but decorated beautifully for the occasion. It was a memorable day.”

Soon after, he told his mentor that beating MS would be his life's work. Like all his contemporaries, Hauser had been taught that MS is an autoimmune disease and that the immune system's T cells were the culprit. This conventional wisdom was built on a mouse model of MS called experimental allergic encephalomyelitis (EAE), a disease that can be transmitted in mice using just T cells. “The fact that it didn't even look like MS was ignored,” says Hauser. In MS, only brain and spinal cord myelin is affected, whereas EAE models involved the peripheral nerves and showed a different pattern of tissue damage.

Haunted by this dichotomy, he spent the next decade trying to develop a better laboratory model for MS. He and his colleagues finally succeeded in the '90s. But he couldn't induce the new model by transferring just T cells. “So we began transferring antibodies, which are the chemical products of B cells, and they did nothing,” recalls Hauser. “We then transferred T cells and the antibodies together, and it worked – it was a eureka moment.” Next, they examined brain tissue samples from people with MS and found the same antibody and B-cell deposits as in the model. This was strong evidence that MS was not driven solely by T cells, making B cells and their antibodies potential new targets.

In 1997, the Food and Drug Administration (FDA) approved the first B-cell therapy, rituximab, for treatment of B-cell lymphoma. With colleagues, Hauser applied for National Institutes of Health funding to try rituximab in MS patients, but the agency rejected the application, still convinced MS was a T-cell disease. He then spent 18 months persuading Genentech to host an early-phase clinical trial. “They told me, ‘This is not plausible; we grade the likelihood of success as less than 15 percent.’” However, Genentech also recognized a huge unmet need for patients and, defying expectations, they chose to do the trial anyway. Hauser says their hopes weren't high “because the FDA permitted us to only give patients a single dose of the drug. But instead we saw something dramatic,” he recalls. “By reducing B cells, the effect on MS was immediate and profound. From that moment, the field of MS shifted to focus on B-cell immunology.”

Rituximab, however, is a chimeric monoclonal antibody, meaning it's composed of part human and part mouse protein. Immune reactions against the mouse protein can be troublesome for some patients, especially with repeated doses. “But ocrelizumab is derived primarily from human protein, so we are hopeful that with long-term use, it will be better tolerated and also more effective than rituximab,” says Hauser.

“With these wonderful results against relapsing MS and finally a treatment that works at least partially for PPMS, my hope is that there will be new octane in academia and industry to make even more meaningful advances,” says Hauser. “MS is no longer a black box. There is so much more that can be accomplished, and we need to build upon this important success.”



WRAP ARTISTS: At left, Ari Green and Jonah Chan hope to reverse nerve damage with a drug that induces cells to rewrap exposed axons with myelin, while Sergio Baranzini, right, is studying the microbiome of MS patients to pinpoint the disease's origin.

put the oligodendrocyte precursor cells with the pillars, they mature and wrap them,” says Chan. “If I make the base of the pillar large and taper it to a small tip, we could determine the extent of growth.” They could then easily compare the relative effectiveness of the drugs by examining how much of the pillars were wrapped.

Chan handed plates populated with pillars, plus 1,500 drug candidates, to a postdoc to test. “What we thought would take a lifetime took my postdoc two weeks,” recalls Chan. He identified multiple clusters of promising compounds – including an antipsychotic, a bronchodilator, and an antihistamine that shared a common trait. These compounds blocked acetylcholine receptors that inhibited precursor cells from differentiating and making myelin. After checking its safety profile, Green chose the antihistamine for further testing – and purchased 100 tablets on Amazon for \$8.

“It was a first-generation antihistamine approved in 1972 and is now a generic drug,” Green says. “There have been second- and third-generation editions because it causes drowsiness. The drug passes through the blood-brain barrier to histamine receptors in

the brain, rather than simply affecting histamine receptors in the skin or nose.”

After impressive lab results, they ran a clinical trial, measuring patients’ reaction times before and after taking the drug for a few months. The transmission speed of electrical signals in their brains improved – clear evidence the axons sending signals to their visual cortex were being remyelinated and their messaging capacity was being restored, though the effect was modest.

“In fact, this is the only drug in history that helps with brain repair,” says Green, “and it can be bought at Walgreens.” And from discovery to completed trial took just 2½ years, rather than 10 to 20 years, which could translate to preventing patients from needing a wheelchair. Yet making the compound truly effective would require boosting the dose tenfold. “It has too many other side effects to take the dose up that high,” says Chan. “We’re confident there’s a better drug out there with a bigger payoff and fewer side effects.”

Green and Chan have accelerated the search by licensing their drug-testing technique to a company with libraries of millions of drugs and the capacity to look at every molecule ever designed to be given to people. “The most important thing about our trial might not even be this drug,” says Chan. “It might be that we’ve shown and can measure an effect for a drug in this space – brain repair.”



“That means the MS microflora has something that helps initiate or perpetuate the disease.”

– Sergio Baranzini

Nipping MS in the bud

In 2004, UCSF launched EPIC, a longitudinal study of 500 people with MS using the most advanced imaging, molecular, cellular, and bioinformatics techniques. Two years ago, a spin-off study called ORIGINS started examining incipient MS.

“With ORIGINS, we focus on the newly diagnosed patient, who had his or her first symptom yesterday,” says Sergio Baranzini, who has spent his career identifying genes associated with MS. Participating physicians throughout California and Nevada, upon hearing of telltale symptoms like tingling in hands, weakness in legs, or vision loss in one eye, contact, via a hot line, a team of UCSF neurologists who can immediately perform a detailed work-up – including a blood draw, an MRI, a visual assessment, B lymphocyte studies of spinal fluid and blood, and a stool sample. Results are delivered to the referring doctors fast.

Baranzini’s interest is in the stool sample. Here’s why: If one identical twin has multiple sclerosis, the other twin has only a 30-percent chance of having the disease. If the genome confers just a 30-percent risk, where’s the other 70 percent from? “What’s not genetic has to be the environment,” says Baranzini, who holds the Heidrich Family and Friends Endowed Chair in Neurology. “But how do you measure the environment?” Patients are notoriously bad at recalling exposures, especially from their early years.

About three years ago, he started collecting stool samples to see if MS patients had a different composition of gut bacteria than their spouses, despite similar environmental exposure. “Some bacterial species are more prevalent in MS patients, some less, but they are different,” says Baranzini. In collaboration with Mount Sinai, Caltech,

and UC San Diego, he and colleagues introduced MS microflora into mice born in completely sterile environments. “When we induced the disease, they got very sick, much more so than mice receiving the spouse’s microflora,” says Baranzini. “That means the MS microflora has something that helps initiate or perpetuate the disease.”

Last year, Baranzini and his collaborators started the International Multiple Sclerosis Microbiome Study, involving specialists from all over, including Boston, Edinburgh, Buenos Aires, and Munich. They hope to establish the characteristic MS microbiome by collecting samples from 2,000 patients and controls over three years. “If we know exactly what imbalance creates an environment for MS,” he says, “we can search for noninvasive, safe ways to restore it through probiotics, antibiotics, a combination, or a change of diet.”

Nowhere to hide

So a targeted diet and supplements may keep MS from gaining traction, avoiding damage altogether. Or, if the disease does get a toehold, ocrelizumab may shut it down. And, soon, Chan and Green may perfect a remyelination agent to actually repair damage.

Multiple sclerosis is finally out of time. Solal, who just completed a competitive bike race benefiting MS research, will no doubt make good use it.

Looking for a better way to die

By Patricia Meagher

On June 9, California will become the fifth state in the nation to legally allow terminally ill individuals to end their own lives. Gov. Jerry Brown signed the End of Life Option Act into law in October 2015, after the state legislature passed the bill during a special session on health care. We spoke with several UCSF experts in end-of-life and palliative care (see box) about the law and about what it might mean for California providers and patients.

Robert Brody, MD, resident alumnus
Professor of medicine and family and community medicine; chief,
Pain Consultation Clinic, Zuckerberg San Francisco General

Brody has been advocating for aid in dying for 20 years, ever since a 40-year-old hospice patient with ovarian cancer asked him for help ending her life. “We had many conversations, and she made me read the book *Final Exit*, about self-deliverance,” he says. “We were able to find a way, legally, to meet her goals.”

Under the new law, Brody says, these scenarios will take place primarily in home settings by patients under the care of hospice and primary care physicians, as well as oncologists, cardiologists, neurologists, and other specialists who treat patients with terminal illnesses. But the law will do much more than help those patients, he says; it will also lead to advances in end-of-life care in every health care setting.

“We can predict what will happen in California by looking at other states that have enacted these laws,” Brody says. “The number of hospitals that had palliative care units went way up. The percentage of people who enrolled in hospice went way up. **We will have more open discussion about death**, and end-of-life care will improve.”

Barbara Koenig, RN, PhD '88
Professor of medical anthropology and bioethics; director, UCSF
Bioethics Program

“**The ethics issues raised by the law are profound**,” Koenig says. “Who should control the moment of death? Should individuals ask their clinicians for help? These questions take you to the heart of the doctor-patient relationship and the caregiver’s role as healer.”

Considering the law’s impending implementation a “bioethics emergency,” she quickly mobilized a UCSF-hosted conference of thought leaders last December, to help practitioners navigate the law’s ethical and practical challenges.

As an anthropologist studying end-of-life care, Koenig has been thinking about aid in dying since Californians first voted on its legalization in the 1990s. Initially opposed to legalizing it because of social justice concerns, she is now rethinking her position, given the advent of health care reform. “In Oregon,” she adds, “**the fight over the law led to improvements in care for everyone**, so it has had some unintended positive outcomes.”

Steven Pantilat, MD '89, resident alumnus
Kates-Burnard and Hellman Distinguished Professor in Palliative
Care; founding director, UCSF Palliative Care Program

“The end-of-life option is driven by concern that people have of being trapped in an intolerable situation,” Pantilat says. The law, he notes, will help a few individuals who meet its strict criteria: terminally ill patients who have the mental competence to request lethal drugs and to take those drugs themselves, without assistance from another person. But palliative care can alleviate most suffering, he adds, and that’s where medical care should be focused.

“What the law doesn’t address is that **most people with serious and even terminal illnesses want to live as long and as well as they can**, which is what palliative care offers,” Pantilat says. “We have a thousand ways to manage symptoms like pain, nausea, and shortness of breath and to provide psychosocial and spiritual support. That’s not a reason to end your life.”

Laura Petrillo, MD '11

Clinical fellow, geriatrics, San Francisco Veterans Affairs Medical Center; co-organizer, UCSF End of Life Option Act Task Force

A study in contrasts inspired Petrillo's passion for end-of-life care. She observed that timely conversations with patients about their preferences could make the difference between someone spending his or her final days in the ICU or having a more peaceful death at home. "Medical care often proceeds in a prescribed way that's not necessarily what our patients want," Petrillo says. "It's important to have conversations to figure out what people really care about."

When patients are asking for something as drastic as ending their lives, she says, it's clear that end-of-life care needs improvement.

"The public interest in aid in dying represents dissatisfaction with the status quo around end-of-life care," Petrillo says, "and we should take that as a call to action." She has testified against aid in dying, concerned about the risk for abuse in disabled and vulnerable populations. But since the law passed, she has shifted her focus to provider education and palliative care advocacy to reduce the risk of harm.

Michael Rabow, MD '93, resident alumnus

Helen Diller Family Professor in Palliative Care; director, Symptom Management Service, UCSF Helen Diller Family Comprehensive Cancer Center

"Since the law passed, I've had lots of conversations with patients about it," Rabow says. "Often this is an expression of need to talk about death. But the good thing is that now, basic clinical skills absolutely must include being able to talk to patients about the end of life."

A recent study by Rabow on cancer outcomes confirmed previous findings that when palliative care is initiated early, patients require less intensive medical care, resulting in lower cost and bet-

ter quality of life. "The data are clear," he says, referring to a 2010 Massachusetts General Hospital study, which found that palliative care patients also lived 2.7 months longer and were less depressed.

Only a very few patients will pursue aid in dying, Rabow adds. In Oregon, for example, 2012 deaths under the law accounted for just 0.2 percent of all deaths, and about one third of those who fill prescriptions never use the lethal drugs. "I feel conflicted because the law will be costly to implement. It distracts us from the more than 99 percent of people who don't need help ending their lives, but they do need better medical care, pain management, and support."

Christine Ritchie, MD, MSPH

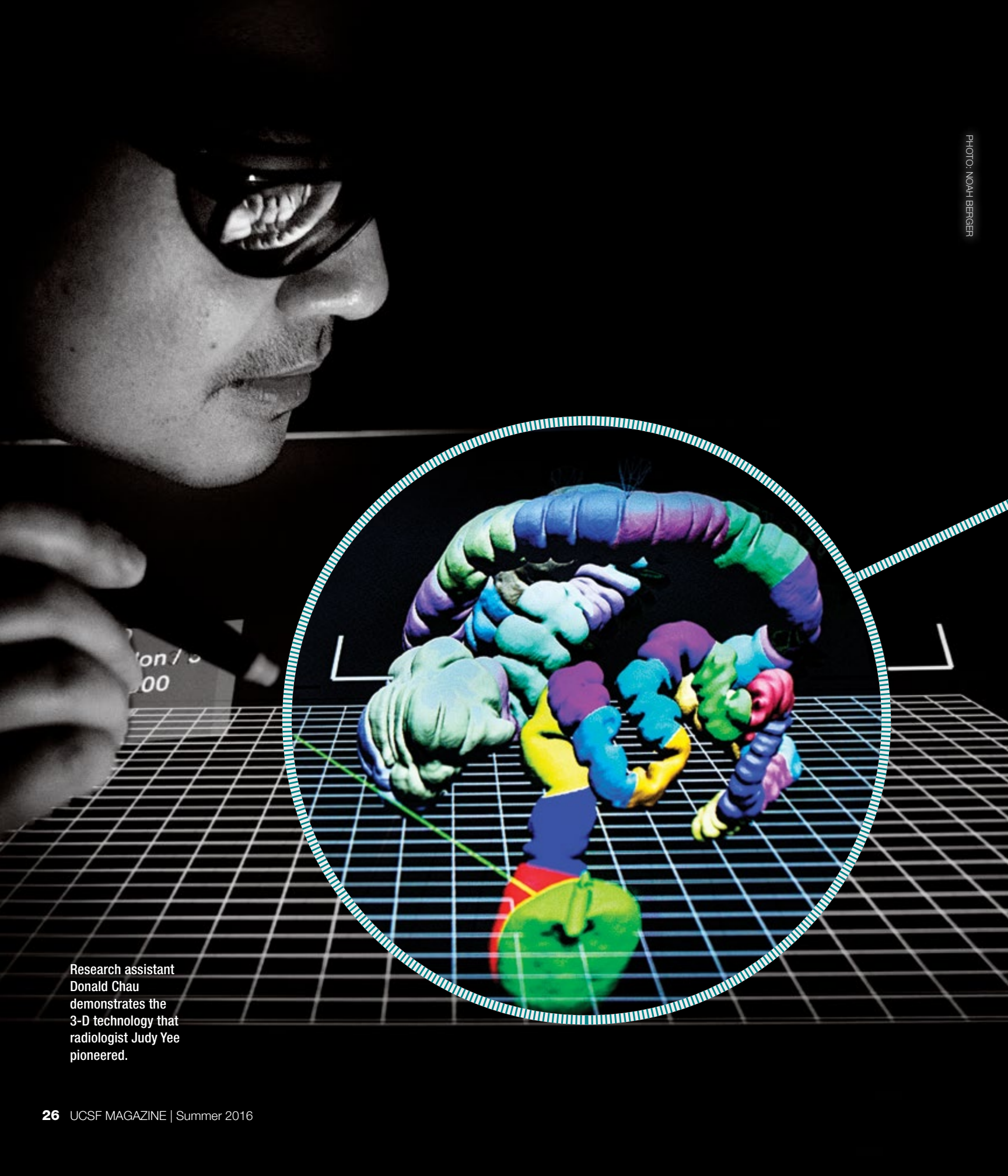
Harris Fishbon Distinguished Professor in Clinical Translational Research in Aging; immediate past president, American Academy of Hospice and Palliative Medicine (AAHPM)

"Making end-of-life options available throughout the state means that **we have to fill gaps in access to palliative care,**" Ritchie says. "The AAHPM is developing resources to help providers understand requests and conduct comfortable conversations with their patients," she adds. The California Medical Association, which dropped its opposition to aid in dying last year, and the American Academy of Family Physicians are also offering help for doctors on the front lines.

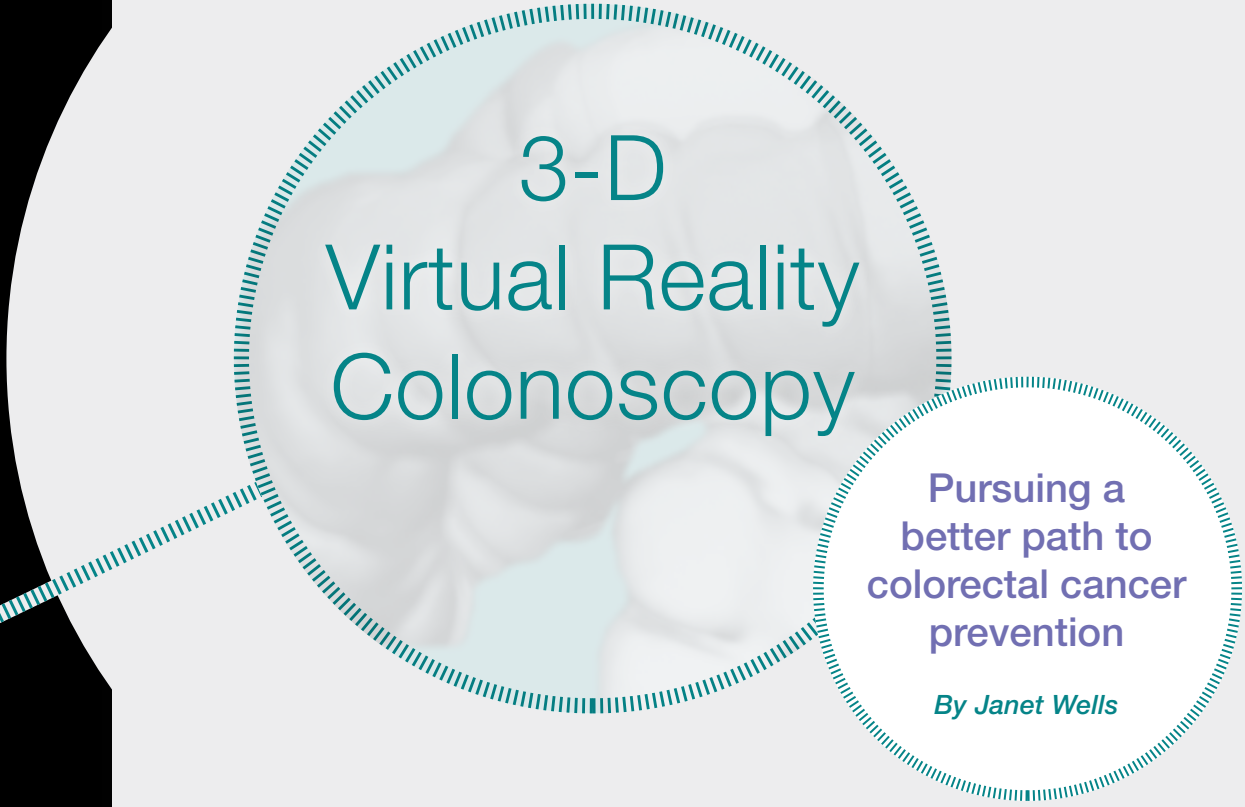
"There is concern that the law poses greater risk in California because of our larger and more diverse population," Ritchie says. "The fear is that older, sicker, and more vulnerable patients might feel compelled to seek aid in dying when they could have been better served by good end-of-life care they could not access," she adds. "California will be the biggest test yet of whether this law actually results in better access to palliative care."

What's in a name?

The term palliative care is often confused with hospice, but they are not the same. Both provide care for patients with serious and life-threatening illnesses, but hospice focuses on end-of-life care, while palliative care focuses on improving patients' quality of life throughout the course of a serious illness. Hospice care and aid in dying are reserved for individuals with a terminal diagnosis, defined by Medicare as a life expectancy of six months or less. Palliative care, in contrast, combines expert symptom management and psychosocial support with ongoing curative treatment. A relatively new medical field, palliative care was designated a board-certified specialty in 2007 and has been offered at UCSF since 1999, but its availability in U.S. hospitals varies widely.



Research assistant Donald Chau demonstrates the 3-D technology that radiologist Judy Yee pioneered.



3-D Virtual Reality Colonoscopy

Pursuing a
better path to
colorectal cancer
prevention

By Janet Wells

At UCSF's 3-D Imaging Lab, radiologist Judy Yee, MD, pulls up an image that looks more like a birthday party balloon animal than a patient's colon: a vibrant, color-segmented tube, torqued and twisted in on itself.

Created from thin slices of a computed tomography (CT) scan, the image appears three-dimensional on the flat screen. It can even morph into video "fly-through" views, enhancing polyps, lesions, and other precancerous anomalies. Yee refined this revolutionary blend of advanced graphical software and scanning technology – known as CT colonography (CTC) or virtual colonoscopy – as a far less invasive and easier-to-interpret alternative to conventional colonoscopies.

Yee, professor and vice chair of the Department of Radiology and Biomedical Imaging at UCSF and chief of radiology at San Francisco Veterans Affairs Health Care System, is now pushing radiology even further with holograms. Virtual holography CTC is the latest phase in her two decades of research committed to earlier, safer, life-saving detection of colorectal cancer. Though the disease is often preventable, it is the second most common cause of cancer deaths in the United States.

"When screening for breast cancer, lung cancer,

prostate cancer, and other malignancies, we're typically looking for the cancer itself. By then it's too late," Yee says. "Here we have a specific pathology that allows us to find a lesion (known as a polyp) before it turns into cancer. If we could just get more patients to come in for screening, we could certainly have a huge impact on preventing colorectal cancer."

Holography: radiology's future?

Yee slips on a pair of 3-D black metal-rimmed glasses and points a laser stylus at the monitor still displaying her patient's colon.

By flicking the stylus and turning her head while keeping her eyes on the monitor, Yee is suddenly "inside" the colon, moving through it, pulling it toward her, spinning it around.

As she moves, a computer monitor with stereoscopic optical technology tracks her glasses, which have different polarization in each lens, prompting her brain to construct a virtual holographic object that recreates the size and shape of the human anatomy. The stylus, working in tandem with advanced graphical processing of the CTC



The “aha” moment

A graduate of the Bronx High School of Science, Yee fell for the field of radiology in medical school, where she discovered how imaging blended her rich background in science and mathematics and had a wide variety of applications in medicine.

“We use images to work out the pieces of a puzzle,” she says. “It’s so gratifying to use those pieces to make a patient’s diagnosis and see how the patient responds to treatment. It allows you to participate in a continuum of care.”

Yee got her first look at CTC in 1997, at the annual meeting of the Society of Gastrointestinal Radiology. Inspired, she raced home and wrote a research proposal to further develop the technology, which she realized – even in its earliest stages – held the promise of a better experience for patients and a more effective screening tool for practitioners.

“Conventional testing for colon cancer was not reducing morbidity and mortality, and cancer rates in some areas were increasing,” Yee says. “Many individuals were not coming in to get screened for a malignancy that essentially could be prevented. There’s a fear of the invasive procedure.”

Her research has fostered numerous improvements, including lowering the radiation dose per scan by two-thirds, while maintaining high-quality detection of polyps and cancers; decreasing the amount of preprocedure laxative required; and increasing the sensitivity of computer-aided detection.

Yee’s current CTC research includes providing data on the protective effect of negative test results. She hopes to persuade the American Cancer Society to endorse CTC screenings every 10 years – the same schedule as conventional colonoscopy – instead of every five years.

She and her colleagues also are working to remove a financial stumbling block to CTC access: Medicare’s refusal to reimburse for the procedure, even though numerous private insurers cover it. Although a CTC test costs significantly less than conventional colonoscopy, many Medicare patients may not be able pay for the procedure out of pocket.

Judy Yee (left) says that if more patients would get screened, it could have a big impact on preventing colorectal cancer. She helped refine the virtual colonoscopy, which doesn’t require sedation, and the low-radiation-dose CT scan takes just 20 seconds.

image, allows her to “grab” the portion of the scan she wants to examine in more detail and interact with it in three-dimensional space.

“I don’t know of anyone else who is doing this,” Yee says, about UCSF’s blending of radiology with virtual holography. “You can cut away the parts of what you don’t want to see and manipulate it so that you improve what you do want to see. It’s a more engaging way to read large data sets. With the added dimension, you can see flat, more dangerous lesions better.”

The technology also has far-reaching promise for neurological, cardiac, and musculoskeletal applications, she adds.

“As the equipment evolves, it allows us to view the same disease processes in a completely different way so we can improve detection and diagnostic ability and streamline workflow,” Yee says. “This could go a long way toward helping show what radiology can bring to patient diagnosis and management for all different parts of the body.”

“CTC should be the frontline colorectal cancer screening tool, with only those patients who have a lesion sent on to the more invasive colonoscopy,” Yee says.

Building the evidence base

Now president of the Society of Abdominal Radiology and the author of more than 100 articles and 22 book chapters, Yee is an ardent promoter of CTC and its high-tech holographic cousin.

Her first study of the holographic imaging platform is in phase I, with CTC scans from 300 patients loaded and training of participating radiologists underway. Other UCSF explorations of holographic technology include a partnership with the Swedish company Phase Holographic Imaging to accelerate skin cancer research.

UCSF’s 3-D Imaging Lab, which Yee directs and where she developed the virtual holographic CTC process, melds the

“Conventional testing for colon cancer was not reducing morbidity and mortality, and cancer rates in some areas were increasing.”

– Judy Yee

application of advanced imaging with research and the education of trainees from UCSF and around the world.

More reminiscent of a high-tech company’s conference room than a medical facility, the lab is located at the San Francisco VA and is home to multiple computer workstations loaded with state-of-the-art imaging software, some of which is not yet on the market. The lab’s specialized holographic medical imaging workstation, the True 3D Viewer, was developed by the Mountain View, Calif.-based company EchoPixel, which credits Yee for advancing the field with her insights. Yee now uses holographic technology with about 20 percent of her cases.

The marriage of three-dimensional virtual reality technology with medicine has elicited comparisons to the ever-more-sophisticated world of video gaming. Is that, perhaps, where Yee got some of her ideas? “I’ve never played,” she says with a laugh. “The goal was to have an impact on a common malignancy. For so many patients who develop colorectal cancer, if they had just come in for screening, we could have prevented it.”

A LESS INVASIVE PROCEDURE

“Time for your colonoscopy!” Patients receive this dreaded directive to get screened, usually for the first time, around age 50. Even knowing the grim statistics – an estimated 132,700 new cases of colorectal cancer and 49,700 deaths in the United States in 2015, according to the American Cancer Society – doesn’t make colonoscopy any less of an ordeal.

The night before the test, there’s the “preparation,” which many patients find both challenging and unpleasant: No eating, except for Jell-O and clear liquids. Drinking a gallon of polyethylene glycol, a salty-tasting laxative. Spending hours near a toilet.

Then there’s the test itself: A six-foot-long flexible tube with a scope at one end is inserted the length of the colon, and a gastroenterologist “reads” the test as it’s happening.

“The procedure takes 20 to 30 minutes, and there’s a chance of perforation, bleeding, or infection,” Yee explains. “You have to receive sedation, or it’s painful. There’s a recovery period, so you have to take a full day off from work, and because of the anesthesia, you can’t drive home by yourself, so someone else has to take time off, too.”

The procedure does have its advantages. It’s covered by Medicare, and if lesions or polyps are detected, they often can be removed during screening because the patient is already sedated. Still, it’s not surprising that the avoidance rate is high: despite a 90-percent survival rate when colorectal cancer is detected early, fewer than half of those who should get screening for colorectal cancer do so.

CTC still requires a prescan laxative, but only 10 ounces instead of 128 ounces. The test involves inserting a small tube a few inches into the colon to inflate it with carbon dioxide. No sedation is necessary, and the total scan time is 20 seconds: 10 seconds lying on your back, 10 seconds on your belly.

“There’s a lower frequency of complications, and you can come in first thing in the morning and then go about your daily activities afterward,” says Yee, who enthusiastically points out that when President Barack Obama underwent his first screening (in 2010, at age 45, because African-Americans have a higher incidence of colon cancer), he chose CTC.

President Obama’s choice allowed him to keep his presidential powers during the screening. His predecessor, former President George W. Bush, transferred presidential authority to Vice President Dick Cheney twice for about two hours while under general anesthesia and in recovery for conventional colonoscopies.



Countdown to a Cure

Spurred by three decades of momentum and fresh funding, scientists mount a major effort to finally defeat AIDS.

By Carol Pott



PHOTO: STEVE BABULJAK

The sun, barely penetrating the summer fog, dully illuminated the hallways of San Francisco General Hospital (SFGH) on July 1, 1981, as Paul Volberding, MD, started his first day of rounds and met his first patient as a UCSF faculty member. For Volberding, that day and that patient are unforgettable.

“He was a 22-year-old man with a strong Southern accent,” recalls Volberding. “He was estranged from his family and completely alone.” The patient was covered with the reddish-brown lesions common to Kaposi’s sarcoma, a then-rare, slowly progressing cancer that usually afflicted elderly patients. “To see this young man with disseminated Kaposi’s, it was just striking – a very unusual situation,” he says.

Despite extensive interventions, the man died quickly from multiple infections. “Medically, he was amazing and challenging – but socially, too. Even our most disconnected and marginalized patients often have someone present to help.”

Soon after, Volberding’s rounds were filled with dying young people. “That first case told us where we were going to be for the next 30 years,” he says.

At the epicenter of an epidemic

That first patient inspired Volberding to begin the search for a cure to what soon became known as acquired immune deficiency syndrome (AIDS). AIDS is caused by the human immunodeficiency virus (HIV), a retrovirus that attacks the immune system. Volberding, director of the AIDS Research Institute and director of research for Global Health Sciences, came to UCSF in 1978 as a medical oncology fellow and researcher in the virology laboratory of Jay Levy, MD, who co-discovered HIV in 1984. Volberding left Levy’s lab to take the clinical job at SFGH (now Zuckerberg San Francisco General), not realizing that he was leaving a retrovirus laboratory to work in the middle of a retroviral epidemic.

With the outbreak rapidly expanding, Volberding and his colleagues were spread thin as the number of sick and dying patients increased daily, and haunting photos of skeletal young men filled the media. “It was a death watch,” says Jay Kerzner, a longtime patient of Volberding’s who was diagnosed with HIV in 1986. “People were just wasting away.”

In a time when gay men experienced open discrimination, hospitals also turned away patients out of fear and incomplete knowledge. Instead, Volberding stepped into the center of the maelstrom. His wife, Molly Cooke, MD, also worked in the middle of the epidemic as the hospital’s then-chief resident in medicine. Despite waking in a sweat from recurring nightmares about passing the virus to their young children, Volberding and two of his SFGH colleagues – Donald Abrams, MD, and the late Constance Wofsy, MD – founded one of the nation’s first AIDS-designated clinics in Ward 86 at SFGH. They also developed the San Francisco Model, a comprehensive treatment model emphasizing compassion and respect and encompassing



TEAM LEAD: CHARTING

Mike McCune, MD, PhD, resident alumnus; professor of medicine; chief of the Division of Experimental Medicine, UCSF

McCune started his career at UCSF in 1982 as an internal medicine resident and infectious disease fellow at the height of the AIDS crisis, when many infected patients were men his own age. “We were listening to the same music, eating out at the same restaurants, and experiencing the same cultural shifts – and yet, so many died,” recalls McCune. “At that time, there were some physicians who simply didn’t want to deal with what was going on; [but] I was moved to devote my scientific career to working on the epidemic.”

Being unable to provide anything but palliative care and symptom support inspired McCune to begin research to discover ways to reverse the disease. Considered a radical, McCune started with animal testing, infecting “humanized” mice with HIV using a hypodermic syringe. His award-winning work changed the way that researchers studied HIV, and the animal test model he developed proved so useful, it is still used in preclinical settings to predict how anti-HIV drugs work in living systems.



TEAM LEAD: UNDERSTANDING

Warner C. Greene, MD, PhD, professor of medicine, microbiology, and immunology, UCSF; the director and Nick and Sue Hellmann Distinguished Professor of Translational Medicine, Gladstone Institute of Virology and Immunology; co-director, UCSF-Gladstone Center for AIDS Research

Greene saw his first AIDS patient in the summer of 1981 when he was a fellow at the National Cancer Institute. “This man with HIV/AIDS wasn’t my patient, but obviously, being trained in immunology with an interest in immunodeficiency, I carefully followed his case,” recalls Greene. “Essentially, we witnessed a complete meltdown of his immune system, followed by a deluge of opportunistic infections, ultimately leading to his death.”

Greene came to San Francisco in 1991 after serving as a Howard Hughes Medical Institute investigator and professor of medicine at Duke University. Upon joining Gladstone and UCSF, he began attending on the wards at SFGH. “My first month was disheartening,” Greene says. “Every patient on my medical service was infected with HIV. We had nothing to offer them other than treating one infection after another and providing supportive care.” These sobering clinical experiences drove his work in the laboratory studying HIV pathogenesis and new approaches to an HIV cure.

social services, which was soon emulated around the globe. In the face of growing fear of the virus, they accepted all patients who needed treatment, regardless of their means.

Volberding’s dedication has never ceased. Widely considered one of the world’s leading AIDS experts, he has worked on clinical trials for HIV-related malignancies and antiretroviral therapies (ARTs) and has supported research by other UCSF faculty members, who now investigate HIV/AIDS in more than 60 countries. He also co-directs the UCSF-Gladstone Center for AIDS Research. Ward 86 is now considered one of the top-rated medical care facilities for AIDS in the world, and the World Health Organization recently endorsed the San Francisco Model as the minimum standard for HIV care.

Today, Volberding is tackling what may be his toughest task yet: leading a team trying to eradicate the disease forever.

Shrewd virus still infecting millions

Although the global HIV pandemic has claimed an estimated 39 million victims, the advent of ARTs slowed the progression of the disease. HIV attacks the immune system, specifically its CD4 cells (T cells), making the body more likely to succumb to infection. ARTs have been highly

effective at keeping the virus from infecting new cells in HIV-positive individuals. But as soon as a patient goes off ARTs, HIV bounces back, giving evidence the infection hibernates within the system. AIDS was initially considered a disease affecting homosexuals, sex workers, and IV drug users. “They called it the ‘gay cancer,’” says Kerzner, referring to the early days of the epidemic.

But the face of AIDS has changed. HIV now infects mostly women and children. Women are twice as likely to acquire HIV during intercourse and today account for more than half of all people living with HIV. Despite all we know, in 2014 alone there were roughly 2 million new infections globally, 220,000 of which were of children infected by HIV-positive mothers. Seventy percent of the global HIV-positive population lives in sub-Saharan Africa, where people often must walk for a day or more to reach public transportation to treatment centers. More than 60 percent of those infected cannot afford treatment or are far from a treatment facility. Their plight makes clear the need for a safe, economical, orally administered, and transportable cure.

Driven by a sharper understanding of the nature of HIV infection and a growing population without access to care, many international AIDS organizations have launched concentrated programs to end AIDS. “We are at a unique moment in history. Over the next five years we have

TEAM LEAD: RECORDING

Satish Pillai, PhD, postdoctoral alumnus; associate professor of laboratory medicine, UCSF; associate investigator, Blood Systems Research Institute

Pillai wasn't always interested in studying HIV. He originally thought about astronomy but eventually settled on evolutionary biology. "My story is nerdier than the other folks," laughs Pillai. Through his interest in HIV as an evolutionary model, he became entranced with working on something that was immediately relevant to human health. "HIV is the ultimate evolver. Its rapid evolution and how that affected its clinical management fascinated me." HIV vaccines have proven impossible, largely because they rely on the immune system to attack invaders carrying particular proteins. "HIV's diversification and unpredictable protein-coding genes present a unique challenge," says Pillai.



a fragile window of opportunity to shift gears and put the global HIV response firmly on the fast-track to end the AIDS epidemic," Michel Sidibé, the executive director of the Joint United Nations Programme on HIV/AIDS (UNAIDS), recently declared.

Quickening the pace

Fully aware of the challenges ahead, the Foundation for AIDS Research (amfAR), which focuses on accelerating cure research by breaking down traditional barriers, launched its "Countdown to a Cure for AIDS." The initiative is strategically investing \$100 million in uncovering the scientific basis for a cure by 2020. The strategy looks not only at the brilliance of the science but also at the excellence of the collaboration.

Interested in finding the best team to uncover a cure, amfAR invited qualified individuals to submit proposals for funding. Among those invited was a San Francisco-based, self-assembled, multidisciplinary team of world-class scientists, clinicians, and industry experts with a phenomenal combined history clinically and in the lab. Many of the individuals have collaborated on HIV cure research for more than three decades. The team includes specialists from UCSF, the Gladstone Institute of Virology and Immunology, the Blood Systems Research Institute, Gilead Sciences, the Infectious Disease Research Institute, and other academic and industry partners.

On World AIDS Day 2015, December 1, amfAR revealed the cornerstone of its initiative: the establishment of the amfAR Institute for HIV Cure Research, led by Volberding and based at UCSF's Mission

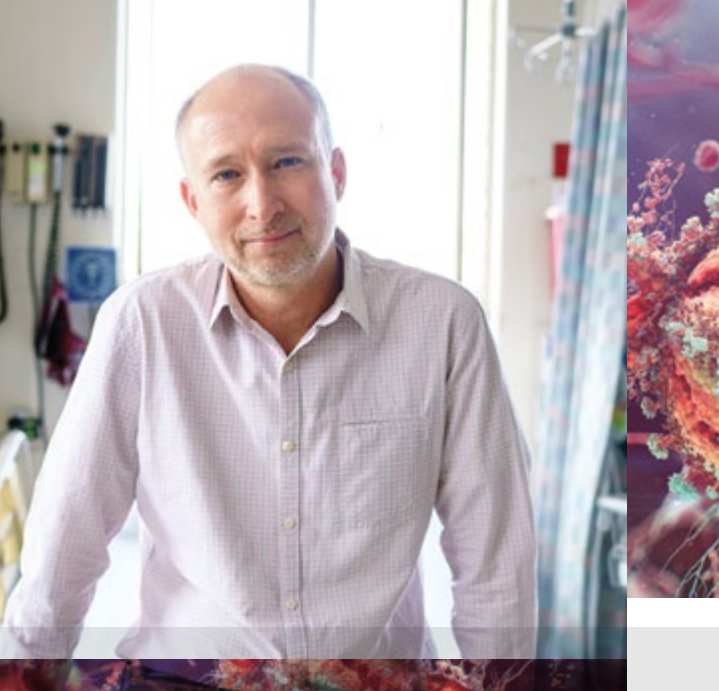
Bay campus. "The potential for this team of researchers to develop a cure is unparalleled" says Rowena Johnston, PhD, vice president and director of research at amfAR.

amfAR awarded the team \$20 million to begin its investigations. HIV is adept at concealing itself within the body, making it harder to eradicate, so the team's main objective is to harness the power of the innate immune system to push the virus from its hiding places and eliminate or control the virus once it has revealed itself – a strategy referred to as "Shock and Kill."

amfAR identified four key scientific challenges – charting, understanding, recording, and eliminating (CURE) – which constitute a research roadmap of barriers to an HIV cure and also represent the four modules of the institute's research focus. Each of the four research modules has a specific purpose within the effort to locate, shock, and kill HIV wherever it is hiding.

HIV stealthily infiltrates and hides within the body, confounding researchers with its game of hide-and-seek. The Charting module seeks to identify and chart the "safe houses" where HIV hides, even in the presence of suppressive ARTs. Charting researchers will figure out which organs harbor the virus, in which cells and at what stage the virus hides, and whether these hiding places vary by gender. Using tissue samples, the team will then determine whether the virus found is "replication-competent." Although HIV reproduces at alarming rates, up to 90 percent of the viruses in infected cells have mutations or deletions, making them unable to infect other cells. However, even incompetent HIV cells produce inflammation and compromise immunity.

Capitalizing on that inflammation and then stimulating a T-cell response in an attempt to find an interaction that reduces toxicity yet



TEAM LEAD: ELIMINATING

**Steve Deeks, MD '90, resident alumnus;
professor of medicine, UCSF**

Deeks trained at SFGH between 1990 and 1993, the height of the local epidemic. “More than half of the hospital beds were occupied by young, previously healthy people who were dying of an incurable disease,” says Deeks. Given the obvious challenges of his inpatient work, Deeks found his muse in his outpatients. “When Paul Volberding offered me the chance to work in the outpatient clinic, I immediately took the job.” Planning on working for a few years on Ward 86 and then moving on to a fellowship, Deeks was motivated by caring for a highly engaged population and collaborating with like-minded scientific colleagues. Once he formed those collaborations, he couldn’t leave. “I have essentially had the same position for 25 years,” Deeks says.

allows for destruction of the hidden HIV reservoir, is the work of the Understanding module. Encouraging the inflammation in a way that is therapeutically meaningful without harming the patient is essential. “We are right on the knife’s edge. Too much stimulation can produce a toxic effect. Not enough, and we don’t rouse the virus out of its slumber,” says Warner C. Greene, MD, PhD, a professor of medicine, microbiology, and immunology at UCSF and the director, senior investigator, and Nick and Sue Hellmann Distinguished Professor of Translational Medicine at the Gladstone Institute of Virology and Immunology. With the majority of HIV viruses being defective, unveiling the lingering sleeping viruses that are able to spread is crucial.

PHOTOS: STEVE BABULJAK; ILLUSTRATION: ALEXEY KASHPERSKY

Using the immune response as a map, the Recording module will locate and determine the size of the dormant HIV reservoir by focusing on evolutionary and genetic insights to gauge the size of the reservoir and determine how it can best be destroyed.

The Eliminating module hopes to lure the virus out of hiding by stimulating toll-like receptors (TLRs). The TLR class of proteins plays an important role in the immune response and the body’s ability to recognize invading pathogens. With data from Gilead Sciences indicating that stimulating TLR-7 pushes HIV out of hiding and increases the effectiveness of vaccines, this module is focused on manipulating TLR-4, TLR-7, and TLR-9 to test the shock-and-kill curative hypothesis in preclinical and, eventually, human trials.

Collaborating for a cure

The ambitious five-year timeline means the CURE team will need to take risks and push boundaries, working closely to inform next steps in the discovery of a cure – a cure that would fundamentally change the lives of tens of millions of people and end one of the worst infectious disease epidemics in human history. “HIV research has evolved from a process of discovery to a technological challenge,” says amfAR’s Johnston. “And now it’s reached a critical mass. Bringing powerful new technologies, brilliant minds, and financial resources to bear, we believe it’s a challenge we can overcome.”

With the potential to help so many, the amfAR team is poised to discover the scientific basis for a cure. “UCSF has been there right from the beginning of HIV,” says Volberding, who holds the Robert L. Weiss Memorial Chair for HIV/AIDS Research. “We’ve been committed to this epidemic for a long time, many of us collaborating as a team for decades. Now we are bringing it full circle and coming together to find a cure. It’s a great UCSF story!”

Patients whose lives were changed by the advent of ARTs are also feeling a glimmer of hope. “What would a cure feel like? After a 30-year struggle with this disease myself . . . I wish it had come earlier,” says long-term survivor Kerzner. “But I can’t even think about a cure without remembering so many lives cut short by HIV. It would mean the end of a very dark era. A cure would mean a more hopeful future for so many people around the world.”

Weills' Extraordinary \$185-Million Gift Propels Neurosciences Research and Care

Joan and Sanford I. "Sandy" Weill had three people vividly in mind when they established the UCSF Weill Institute for Neurosciences in April: Joan's mother and Sandy's parents. Each family member, in his or her way, represents the Weills' deep interest in supporting the neurosciences and shaping their vision for the institute. Sandy's mother succumbed to Alzheimer's more than a decade after her diagnosis, and his father suffered from depression. Yet Joan's mother lived to 101 with her mind intact.

Powered by the couple's desire to help others, UCSF Weill Institute for Neurosciences (weill.ucsf.edu) will accelerate the development of new therapies for diseases affecting the brain and nervous system, including psychiatric disorders. It also provides the lead investment for the construction of a new 270,000-square-foot building at UCSF's Mission Bay campus that will serve as the institute's headquarters and will house state-of-the-art research laboratories, as well as clinics for patients with brain and nervous system disorders.

"Our gift to UCSF reflects an area of health care that is near and dear to our hearts," Joan says. "We want to keep healthy brains healthy, connect bench to bedside to make a bigger impact on neurodegenerative diseases, and help find treatments for those affected by mental illness, which is heartbreaking for so many patients and families around the world."

The Weills' gift of \$185 million is the single largest donation ever to UCSF and one of the most significant donations ever made to support

the neurosciences in the United States. Beyond the building, the gift provides support for graduate students and young investigators in the neurosciences and supplies funds for high-risk, high-reward research.

"Now is the moment for the neurosciences to begin making a real difference in the lives of patients and their families," says UCSF Chancellor Sam Hawgood, MBBS. "The Weills' unprecedented generosity will help make this possible."

The impact of the institute and the Weills' loving memories of their parents will be as enormous as the couple's lifelong generosity. The Weills were among the original signatories of the Giving Pledge, a commitment by the world's wealthiest individuals and families to dedicate the majority of their wealth to philanthropy.

With this gift, the Weills have made more than \$1 billion in gifts to educational, medical, cultural, and arts institutions during the last four decades, as well as a commitment of their time, energy, and passion. This has ranged from Joan's long stints on many boards, including as chair of the Alvin Ailey Dance Foundation and as a member of the board of Paul Smith's College of the Adirondacks for 20 years and as its chair for five years, and Sandy's multi-decade service as chairman of the boards of Carnegie Hall, Weill Cornell Medicine, and the National Academy Foundation. In recognition of their outstanding philanthropic work, the Weills were given the Carnegie Medal of Philanthropy Award in 2009.



PHOTO: SEAN DONNELLY

Alumni Hub

UCSF's All-Inclusive Alumni Community



At Alumni Weekend 2016, the six presidents of the alumni associations caught up with one another. They are elected by the associations of each UCSF school and the graduate division, and the Alumni Association of UCSF (AAUCSF) unites all of these school-based associations. Current presidents are (from left) Donna Barnes, BS '62, PhD '92, Graduate Division; Yao Heng, MD '87, resident alumna, Medicine; Donald Kishi, PharmD '68, AAUCSF; LaJuan Hall, DDS '94, Dentistry; Pauline Chin, BS '78, MS '92, Nursing; and Brian Komoto, PharmD '81, Pharmacy.

More than 65,000 individuals around the world are alumni of UC San Francisco. Whether they're in their mid-20s or their late 80s, they embody a multitude of talents and professions. They are dentists and orthodontists, physicians and surgeons, medical researchers and faculty, deans, nurses, and pharmacists. Others have taken paths you might not expect, like technology, advocacy, industry, diversity, government, medical publishing, administration, and many more.

In the following pages you'll meet just a few of these individuals, some who are seasoned professionals and others who have just recently completed their studies and started carving out their careers.

For all of them, UCSF has played an integral role in their lives, and all of them, no matter how long ago they got their degrees, are still members of the UCSF community.

You can connect with your UCSF alumni community through its Alumni Association, the umbrella organization that enhances and expands upon the offerings of each school-based alumni association. Check in at any time online to socialize with old friends, network with former classmates, or discover when the next alumni event will be in your area. The UCSF Online Alumni Community is available at your convenience; just go to www.ucsfalumni.org.

SCHOOL OF DENTISTRY

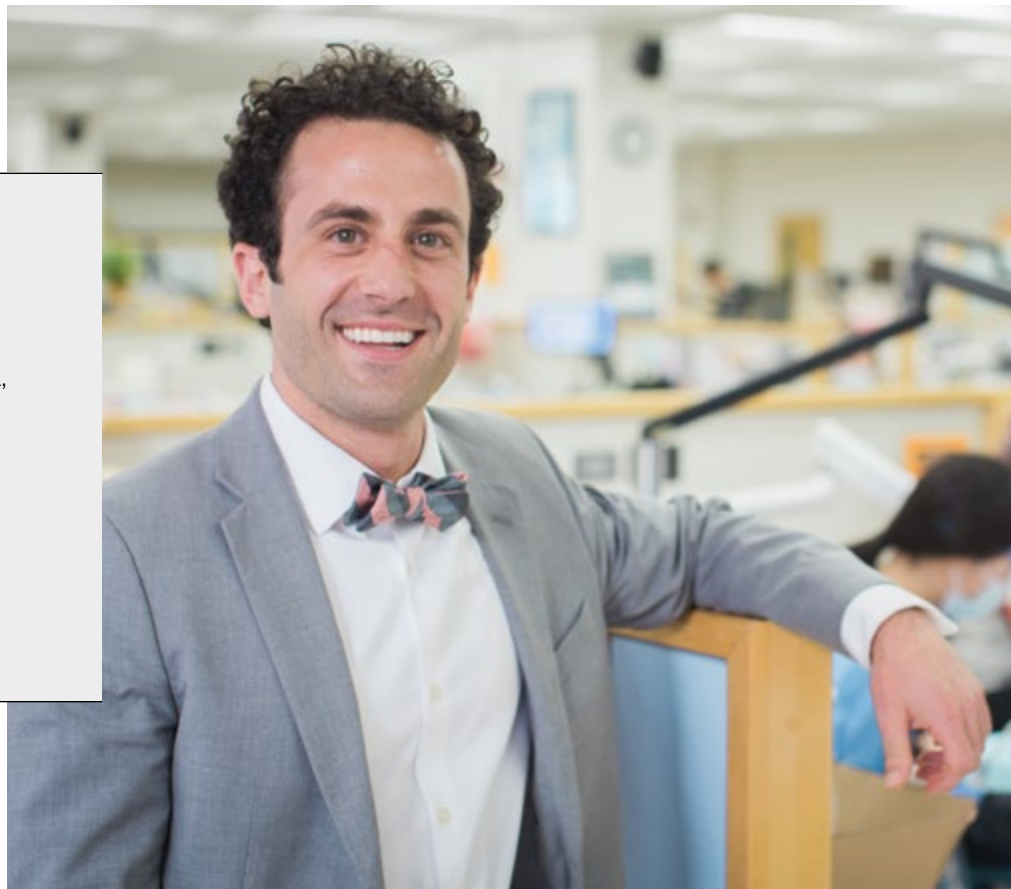
KJELD AAMODT, DDS '12, MS '15, POSTDOCTORAL ALUMNUS

Hometown: Carmel-by-the-Sea,
Calif.

Now: San Francisco, Calif.

Position: Director of
predoctoral orthodontics,
UCSF Division of Orthodontics

Hobbies: Sports, music, travel



Kjeld Aamodt surfs, skateboards, scuba dives, speaks fluent Spanish, plays jazz guitar and bass, and has his private pilot's license. But by day, he is an orthodontist, and for his dental education, he chose his dream school: UCSF.

“UCSF is inspiring,” he says. “It’s an incredibly creative tide pool, where leaders in medicine, nutrition, health care, dentistry, and every little microcosm can come together and leverage one another’s knowledge.”

A NEED TO HELP: After winning the Reno Jazz Festival in high school, Aamodt imagined a career in music; then, after com-

pleting his bachelor’s degree in marine biology at UC San Diego, he considered that field. But he wanted to help people firsthand, and of all the health care professions, orthodontics seemed the best fit.

“Orthodontics combines health care with art,” Aamodt says. “Our patients’ faces are our canvases, and those faces are showcased every day.” He landed his UCSF job straight out of a three-year fellowship and now sees patients at four clinics in San Francisco and Monterey. He also has been tapped to incorporate emerging technologies into the curriculum and into clinical services.

NEW TOOLS FOR TEETH: The technology he’s currently focusing on is Invisalign, the teeth-straightening technique that replaces metal braces with clear aligners. Aamodt developed and is teaching didactic courses on the technique and is designing a clinical curriculum for orthodontic residents and general dental students. He’s also negotiating with suppliers to bring costs down and make the product more available and more affordable for patients.

“This is something that’s changing dental care, so it’s great for our students to receive mentorship with their training, before they’re out and learning it on their own,” he says. The nearly 300 students

who train in UCSF’s clinics every year soon will be able to offer the service to their patients.

Aamodt is also doing research on malocclusion by investigating how crooked teeth develop in isolated groups of indigenous peoples who don’t eat refined foods. In April, he traveled to Peru with a team of four students to initiate a long-term study on the teeth of the pre-Incan Uru people on the floating islands of Lake Titicaca.

“If you look at the archeological records, most people had straight teeth,” he says. “I’d like to discover why we have such a problem with crooked teeth today and how it developed in the first place.”



**MICHELLE HENSHAW,
DDS '93**

Hometown: Taunton, Mass.

Now: Taunton, Mass.

Position: Professor of health policy and health services research and associate dean of global and population health, Henry M. Goldman School of Dental Medicine, Boston University

Hobbies: Travel, reading, writing

As a first-year dental student, Michelle Henshaw saw how disease strikes early and hard in underserved communities. While performing screening exams at local elementary schools, she and her classmates peered into the mouths of youngsters and routinely spotted the unmistakable signs of tooth decay.

“It really opened our eyes to some of the challenges for children who don’t get regular dental care,” Henshaw recalls. She became passionate about providing dental care to underserved populations and scuttled her plans for a private practice career.

GLOBAL REACH: Today, Henshaw is a leading authority on oral health disparities. In fact, she served as an expert panelist on that topic at the UCSF 2016 Alumni Weekend Chancellor’s Breakfast Roundtable.

She’s had a 20-year career at Boston University, where she oversees a major initiative – Global and Population

Health – that’s working to eliminate inequities and enhance educational opportunities for dental students. Henshaw also codirects the Center for Research to Evaluate and Eliminate Dental Disparities, one of just five such federally funded programs across the country. (UCSF’s Center to Address Disparities in Oral Health is another.)

In addition to her roles as teacher and administrator, Henshaw is conducting research in Boston-area housing projects on the effectiveness of training local residents as oral health counselors to reduce the incidence of dental caries in small children. Working with her students on a similar project in rural Nicaragua, she is training nontraditional providers, in this case preschool teachers, to apply fluoride varnish to young patients’ teeth.

CHILDHOOD DREAMS: Henshaw grew up in and returned to historic Taunton, Mass., one of the nation’s oldest towns, south of Boston. She earned a bachelor’s degree in psychology

from Columbia University before heading to UCSF School of Dentistry. As evidenced by the Chancellor’s Award she earned and still proudly displays, Henshaw excelled as a dental student and stoked her scientific curiosity by working with UCSF Professor Richard Smith, DDS, on dental implant studies.

“I can’t pinpoint it, but from a very young age, I knew I wanted to be a dentist,” Henshaw says. “My time at UCSF focused my goals toward shaping the profession as a dental educator and improving the oral health of our global community.”

THEN AND NOW: BREAK TIME AT UCSF

What did our alumni do to blow off steam? “When we weren’t in the dental labs honing our skills,” Michelle Henshaw says, “we enjoyed the wonton soup at Beijing on Irving and the sunshine in Walnut Creek.” Kjeld Aamodt spent hours (and still does) at Golden Gate Park’s skate park and often went (and still does) to the Mission for eats, including Trick Dog’s awesome kale salad. “And I don’t even like kale,” he says.

SCHOOL OF MEDICINE



Born into a poor Hispanic family in Harlem, intermittently homeless, and a high school dropout, Richard Carmona enlisted in the U.S. Army in 1967 at the age of 17. His life could have turned out very differently, but he transformed youthful adversity and wartime suffering into a distinguished career that took him all the way to serving as U.S. surgeon general.

“War rarely solves anything,” Carmona says of his experience as a decorated Green Beret in Vietnam. “But for the first time, I was held accountable for my actions. Being a soldier taught me about discipline, duty, honor, camaraderie, and how to accomplish a mission.”

CATCHING UP: Following his military service, Carmona’s mission became his own education. He earned his AA in science at Bronx Community College on the GI Bill and held various jobs over many years, including ocean lifeguard, police officer, registered nurse, paramedic, SWAT team leader,

detective, and physician’s assistant. He arrived at UCSF in 1976 and graduated in three years with honors, earning the Gold-Headed Cane Award and serving as commencement speaker, an event he calls the highlight of his life. In 2002, he was nominated by the president as U.S. surgeon general and unanimously confirmed by the U.S. Senate.

LIFE AS EDUCATION: “My circuitous route actually paid off because all my life experiences – from soldier to emergency responder to health disparities to national preparedness – were an education unto themselves,” Carmona says. As the surgeon general, he focused on prevention rather than treatment, pushed for health literacy, and helped navigate the aftermath of 9/11, sometimes clashing with the administration on issues like stem-cell research, sex education, prison health care reform, and secondhand smoke.

Carmona and his wife, Diane, have a family of four, one biological daughter and three adopted children. Their oldest

son was born at San Francisco General Hospital, of an indigent and drug-addicted mother, while Carmona was a medical student. Now working all over the world, teaching, serving on boards, and designing policy, Carmona is still advocating for the public health. He owes it all to UCSF, he says, and remains one of UCSF’s most enthusiastic fans.

RICHARD CARMONA, MD '79, MPH, AND RESIDENT ALUMNUS

Hometown: New York, N.Y.

Now: Tucson, Ariz.

Position: Distinguished professor of public health, professor of surgery and of pharmacy, University of Arizona; vice chair, Canyon Ranch; president, Canyon Ranch Institute

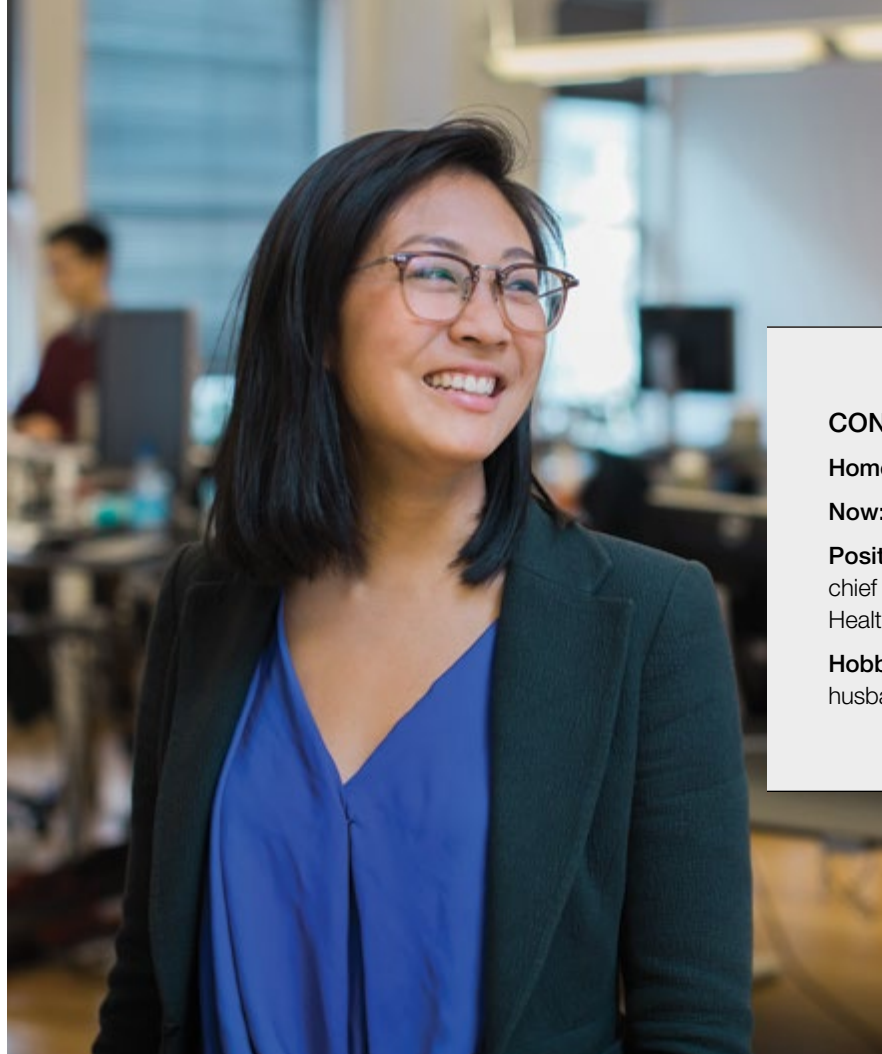
Hobbies: Daily workouts, travel, spending time with his kids and grandkids

“The further away I get from the university, the more I appreciate what a great education I received,” Carmona says. “It’s just the best place in the world.”

THEN AND NOW: BREAK TIME AT UCSF

During breaks, Richard Carmona says, “I would go to Millberry Union to work out and would often take my children there to swim and play. It was like the UCSF Country Club!” As a student, Connie Chen lived right on Irving Street and was an avid runner, so she spent lots of time running around the trails of Golden Gate Park and hanging out at Starbucks.

“Technology can’t replace medicine, but it can augment care and help empower patients.”



CONNIE CHEN, MD '12
Hometown: Pasadena, Calif.
Now: San Francisco, Calif.
Position: Co-founder and chief medical officer, Vida Health, Inc.
Hobbies: Hiking with her husband and dogs

With physician parents and lots of aunts and uncles who are MDs, Connie Chen grew up surrounded by medicine. “Family reunions are like grand rounds,” she quips.

Chen is pursuing a medical path, too, but she’s taking her skills in digital directions at Vida Health, the San Francisco startup that she and her colleagues created in 2014. Backed by such Silicon Valley investors as Khosla Ventures and Yahoo cofounder Jerry Yang, Vida uses a mobile app to connect patients with personal health coaches who provide support on everything from diet and fitness to managing medications and stress.

COACH IN A POCKET: The app can help individuals – especially those with chronic conditions like diabetes and high blood pressure – stay informed and healthier between doctors’ visits, Chen says. “I think we’re closing an access gap for people,” she adds, explaining that Vida’s coaches send daily text messages, check in with weekly video calls, and are available 24/7.

“Technology can’t replace medicine, but it can augment care and help empower patients,” Chen says. She also enjoys primary care medicine and works, as time permits, at St. Anthony’s Medical Clinic, seeing low-income residents of San Francisco’s Tenderloin district.

Chen graduated Phi Beta Kappa from Harvard University with a degree in economics and health policy and then headed to UCSF, where she landed such prestigious awards as a UC Regents Scholarship and a Paul and Daisy Soros Fellowship. Captivated by San Francisco’s tech culture, she began exploring the connection between health and technology. “I fell in love with the idea that problems create opportunities for breakthroughs,” Chen says.

TECH PERSPECTIVE: During medical school, Chen squeezed in many interests – serving, for instance, on the board of Universities Allied for Essential Medicines, whose goal is to

improve drug availability in developing countries, and working for HealthTap, an interactive health information startup. She was so drawn to technology that she took a leave of absence from her medical residency at Stanford University to support early-stage digital health companies at a Stanford-affiliated business incubator.

At Vida, Chen wears multiple hats. As she grows the company and conducts clinical research to measure her product’s effectiveness, she still gets excited about the promise of technology. “There’s so much opportunity to have an impact,” she says, “and to offer more compassionate care for patients.”

SCHOOL OF NURSING

**GINA INTINARELLI,
MS, PHD '13****Hometown:** Natick, Mass.**Now:** San Francisco, Calif.**Position:** Executive director, UCSF Office of Population Health and Accountable Care**Hobbies:** Golf, reading, wine-tasting

Gina Intinarelli never loses sight of her nursing roots. “If I come back to what’s best for the patient,” she says, “I can always make a good decision.”

Intinarelli crafts and implements innovative programs and tools to improve care for UCSF patients and advance overall population health. Her work supports UCSF Health, the new health care network encompassing UCSF Medical Center and seven regional entities.

In today’s evolving health care environment, launching interventions that integrate services, produce positive health outcomes, and control costs is a vital assignment. Intinarelli’s

to-do list stretches from coordinating extended care for Medicare patients with new hips and knees to rolling out an automated phone program that checks on the wellbeing of freshly discharged patients as it frees up busy nurses’ time.

PASSION FOR INNOVATION:

“You’re constantly learning and trying something new,” says Intinarelli, who arrived at UCSF in 1990 as an East Coast transplant and recently minted ICU nurse. She was also the first in her large family to go to college.

“The bedside work was so incredible,” she says of the cardiothoracic surgery patients she cared for. “Frequently the

patient gets better before your eyes.”

One day, she discovered that a patient who had recently recovered from a massive heart attack had resumed his three-pack-a-day smoking habit. Seeing the relapse as a failure of the health system and not the patient himself, she started a hospital-based smoking cessation program.

NURSE AS ACTIVIST: Eager to make an even greater impact by tackling problems before people get sick, Intinarelli entered the nursing school’s new health policy doctoral program, directed by tobacco industry critic Ruth Malone, BS ’89, MS ’91, PhD ’95 (see opposite page).

“I learned what it means to be a nurse activist,” Intinarelli recalls. Joining a group called Nightingales Nurses, she bought single shares in tobacco companies to earn herself the right to attend shareholders’ meetings, where she talks about the hazards of tobacco. At such a meeting last year, she got Walt Disney Company CEO Robert Iger to agree to ban images of smoking in films oriented to young people.

Above all, Intinarelli says, UCSF’s policy training empowered her to view health issues broadly and create solutions for entire patient populations. “It’s about the ability to zoom out and see the big picture and zoom in again to move programs along.”



RUTH MALONE, BS '89, MS '91, PHD '95

Hometown: Portland, Ore.

Now: San Francisco, Calif.

Position: Professor and chair, Department of Social and Behavioral Sciences, and Nursing Alumni and Mary Harms Endowed Chair, UCSF School of Nursing

Hobbies: Hiking, cooking, reading

Ruth Malone considers tobacco-caused diseases “an industrially produced epidemic” and has dedicated a large part of her academic career to understanding how that epidemic was created and sustained.

“Today, if a company introduced a product that killed one out of two users prematurely, perhaps

more, you wouldn’t allow it on the market,” Malone says. “But cigarettes are still available on virtually every street corner. There is a disconnect there.”

Malone started out as a nurse in Oregon and came to UCSF in 1987, hoping to expand her skills with a bachelor’s degree. Before long, she was encouraged to get her doctorate and has been at

UCSF ever since. “Once you have a foothold here, you don’t want to leave,” she says with a smile.

BEYOND THE CLASSROOM:

An award-winning teacher and mentor, Malone is internationally recognized for her research on the tobacco industry’s corporate strategies – and how they have contributed to causing nearly 500,000 deaths each year in the U.S. alone, according to the Centers for Disease Control and Prevention.

“Tobacco companies actually see public health as a competitor,” she says. Delving into UCSF’s Truth Tobacco Industry Documents, an archive of 14 million internal tobacco company papers, Malone and her research team have shed light on the impact of the industry’s advertising, manufacturing, research, and political activities.

“Even so, we have just scratched the surface,” says Malone, whose work has explored such tobacco industry exploits

as campaigns targeting African-Americans, the gay community, and even the mentally ill, as well as one company’s secret plan to provoke contention among public health advocates.

END IN SIGHT? Malone is now developing work focused on an “endgame” to stop the epidemic rather than just control it. “My goal is that we look back one day and clearly see tobacco disease as a 20th-century phenomenon and wonder how people let it go on for so long,” she says. “If we can end the smallpox epidemic, why can’t we end an epidemic created by tobacco companies?”

Her full schedule includes serving as editor-in-chief of the international policy journal *Tobacco Control* and helping direct the health policy program she co-founded at the School of Nursing. One of her favorite activities, though, is interacting with students.

“It’s fun to see light bulbs go on,” she says, “and to watch people blossom.”

PHOTOS: SONYA YRUEL

THEN AND NOW: BREAK TIME AT UCSF

She says she didn’t have much time for fun, but Ruth Malone misses trolling the library stacks to find the odd book that would plant great ideas in her head. “Now you have to choose one search term, which really limits your results,” she says. Gina Intinarelli says she has more fun now, visiting the Sonoma County home where she and her husband play golf, go wine-tasting, entertain, and take hikes and walks with their “canine child.”

SCHOOL OF PHARMACY

**JAMES KNOBEN,
PHARM D '71, MPH****Hometown:** San Diego, Calif.**Now:** Silver Spring, Md.**Position:** Drug information consultant, National Library of Medicine**Hobbies:** Reading, writing, choral singing, travel

In pharmacy school, Jim Knoben noticed that his classmates were constantly jotting down tidbits of practical information about drugs they were studying. Thinking he had a better idea, he began assembling a handy guide of these clinical pearls.

Much to his surprise, Knoben wound up launching a classic in pharmaceutical literature that became a required text for generations of students and an indispensable resource for pharmacists and physicians worldwide. His *Handbook of Clinical Drug Data* described the mechanisms, drug interactions, pros and cons, and other characteristics of more than 1,200 drugs. “There was nothing else on the market at the time,” says Knoben, who served as coeditor with two classmates for 10 editions of the book.

THINKING NATIONALLY: Knoben was always fond of organizations and, during his student years, served as president of the pharmacy school’s student body and alumni association. After graduating, he embarked on a

career with the U.S. Public Health Service while continuing to juggle his editorial responsibilities.

During a 45-year career at an array of federal agencies, Knoben emerged as a pioneering pharmacist in government service. He won accolades – including three U.S. Surgeon General’s Exemplary Service Medals – for improving access to drug information, introducing a new breed of doctors of pharmacy to policy-making, and supporting the U.S. Public Health Service.

PHARMACISTS’ ADVOCATE:

As the first pharmacist to direct the Food and Drug Administration’s Division of Drug Information Resources, Knoben demonstrated that pharmacists could contribute valuable expertise to drug information and new drug application reviews. “There was a need and a role for pharmacists trained in much more than dispensing,” says Knoben, who routinely hired clinical pharmacists and offered summer jobs to PharmD students.

Today, Knoben is helping millions of patients, practitioners, researchers, and others tap into a wealth of information at the National Library of Medicine, the world’s largest medical library. Now semiretired, he serves as a drug information consultant and manages electronic databases focused on liver-damaging drugs and medications for breast-feeding women.

Looking back, Knoben is grateful for the opportunities UCSF gave him. In fact, his first job was as a special assistant in the Public Health Service to the late Donald Brodie, PhD, a nationally recognized clinical pharmacy theorist and former UCSF professor.

“Getting into UCSF,” he says, “was one of the best things in my life.”

THEN AND NOW: BREAK TIME AT UCSF

Jim Knoben recalls San Francisco’s picturesque Chinatown restaurants, as well as pubs that served fish and chips wrapped in newspaper. Robert Schoenhaus and friends hung out and studied in the Informatics Research Center, the pharmacy school’s 24/7 state-of-the-art computer lab, which sometimes required fueling up on pho and $C_8H_{10}N_4O_2$ (i.e., caffeine).

“We’re able to . . . spend enough time with patients to figure out the barriers to their use of medications.”



ROBERT SCHOENHAUS, PHARMD '03

Hometown: San Francisco, Calif.

Now: San Diego, Calif.

Position: Director of pharmacy benefits administration, Sharp Healthcare

Hobbies: Keeping up with daughters Emily, 5, and Leah, 3

Robert Schoenhaus is a product of UCSF in more ways than one: after all, he was born at UCSF Medical Center in 1976.

Graduating from UC Santa Cruz with a bachelor's degree and a hankering to study pharmacy, Schoenhaus had practical reasons for choosing UCSF. His father was stationed in Bosnia with the U.S. Army, he explains: “It was important for me to be close to home to help take care of things.”

TEAM PLAYER: UCSF introduced Schoenhaus to lifelong friends and the impact of team-based care. One of his most powerful experiences was helping organize the Children's Health Hut (CHH), a free health fair for

underserved kids. CHH drew volunteer students from every discipline and is still going strong after 18 years. “We did good work for people who didn't have access to health care,” he says.

Upon entering practice, Schoenhaus quickly began charting new directions for his field. In 2005, he helped create the first position in applied pharmacoconomics at UC San Diego Medical Center and demonstrated how different medication regimens and less-expensive drugs saved money without sacrificing quality. He also co-founded an ongoing, biannual forum at UC San Diego exploring fresh approaches to cost-effective pharmaceutical care.

POTENT RX: Setting his sights on even greater challenges, Schoenhaus completed the UCSF-run California HealthCare Foundation Leadership Program in 2012. He's now a leading voice for change in the profession; his contributions have been recognized with such honors as UCSF's 2015 150th Anniversary Alumni Excellence Award and the 2013 Albert B. Prescott Pharmacy Leadership Award.

For too long, Schoenhaus says, pharmacists have been isolated from primary care teams, dispensing medicine without knowing why. He envisions pharmacists as “medication navigators,” working alongside patients and doctors to ensure

that the best drugs are prescribed and taken.

“We're able to ask the right questions and spend enough time with patients to figure out the barriers to their use of medications,” Schoenhaus says. He supports measures like California's recently enacted Senate Bill 493 that expand the scope of pharmacy practice and address the looming physician shortage.

Along with serving as a preceptor to pharmacy students, Schoenhaus never stops innovating. His latest effort is a texting program to help improve medication adherence. “It won't be punitive,” he says. “Our goal is to motivate the patient.”

GRADUATE DIVISION



**MICHAEL PENN JR.,
PHD '00, MD '03**

Hometown: San Francisco, Calif.

Now: Emeryville, Calif.

Position: Vice president of diversity, outreach, and mentoring, Gladstone Institutes

Hobbies: Hiking, working out, music, travel, meditation

Always a high achiever, Michael Penn excelled at San Francisco's Lowell High School and graduated with top honors from Morehouse College. His deep interest in health and science drove him to UCSF School of Medicine, where he landed a slot in UCSF's elite MD-PhD program. The only African-American student in his cohort, he had visions of becoming a clinician-scientist.

ALTERNATIVE PATH: "If you'd told me then that I'd now be working in diversity, or with a tech startup, I'd never have believed you," Penn says. He joined Gladstone in 2012; his mission there is growing inclusion – especially for women and people of color – and building respect for emotional intelligence, leadership skills, and atypical careers in the high-powered world of science. He says it's the hardest job he's ever had. As CEO of startup *terma.io*, he is also developing cutting-edge, artificial intelligence technology designed to enhance interpersonal communications.

His UCSF years weren't easy. "I exceeded my expectations," Penn says. "But I also realized that clinical medicine was not for me." He went through a humbling nine-month depression and subsequently launched a search, both inward and outward, for his true calling. Thanks to supportive mentors, colleagues, and his own perseverance, Penn completed the MD-PhD program.

BREAKING THROUGH: "My UCSF training opened infinite doors for me, beyond academics," Penn says. All signs pointed him in new directions: his longstanding interest in business, his summer at biotech giant Genentech, and a UCSF panel discussion on alternative careers in science. After briefly serving as a San Francisco health commissioner, he spent eight years at Genentech. There, he first played a critical role in marketing Herceptin, a targeted drug for treating breast cancer; and then worked in business development, sourcing a variety of novel drug development technologies. That experience offered him insight

into the business of biotech, where he believed he could have the greatest impact.

Along the way, he partnered with colleague Frederick Moore, PhD '02, to create a nonprofit, Building Diversity in Science, to break down barriers for both minorities and those seeking nontraditional

careers in science. An outgrowth of that work is their book *Finding Your North*, for anyone interested in a science career.

"The book speaks to everyone, not just to people of color," Penn says. "That's the irony of my inclusion work: it reveals that we're alike in more ways than we are different."

THEN AND NOW: BREAK TIME AT UCSF

Michael Penn has fond memories of a great Thai restaurant on Irving Street and enjoyed hanging out with friends at the Starbucks on Parnassus Avenue. The restaurants Carla Washington once frequented have changed, she says, but one thing that hasn't changed is the Millberry Union gym. "I still see the same people there I've been seeing for 20 years," she says, a statement that reminds her of what UCSF stands for: "U Can Stay Forever."

“The potential this drug has. . . is what gets me up in the morning – and working evenings and weekends.”



**CARLA WASHINGTON,
PHD '95**

Hometown: Cleveland, Miss.

Now: San Francisco, Calif.

Position: Senior director of clinical pharmacology, Global Blood Therapeutics

Hobbies: Travel, photography, hiking, working out, listening to music

Carla Washington, who grew up in the pint-sized town of Cleveland, Miss., has come full circle. Years after winning the seventh-grade science fair for her project on sickle cell disease, she is now a clinical pharmacologist working on a treatment for that same life-threatening blood disorder.

“I’ve always been attracted to unmet medical needs,” says Washington, who leads clinical pharmacology studies for GBT440, a potential sickle cell drug, at Global Blood Therapeutics, a South San Francisco biopharmaceutical company. She hopes GBT440 will help some 100,000 Americans

with sickle cell disease, plus millions more worldwide.

Sickle cell disease, which often affects people of African ancestry, turns red blood cells into a sickle, or crescent, shape, which can block the flow of oxygen-rich blood and cause severe pain and organ failure. “The potential this drug has to be a disease modifier and change the course for people living with sickle cell is what gets me up in the morning – and working evenings and weekends,” Washington says.

RESEARCH CALLING:

Washington originally planned to be a hospital pharmacist but entered UCSF’s doctoral program

when she realized she missed the thrill of research. Her passion for bringing discoveries from the lab bench to the patient’s bedside has taken many forms. Since graduating, Washington has designed and guided clinical studies for several Bay Area firms exploring therapies for hepatitis C, HIV, cancer, and other diseases.

Last May, she jumped at the chance to join Global Blood’s staff. “These memories came back from when I was 12 and working on my sickle cell science project,” Washington says. “I was surprised to learn that few advancements had been made in the treatment of the disease, and I was immediately intrigued.” It also stirred

memories of her late grandmother, Leola, who supported the young girl’s scientific curiosity.

GIVING BACK: Grateful for her wonderful experience at UCSF, Washington recently joined the board of the Graduate Division Alumni Association. She is also an honorary board member, after serving nine years on the board, of Larkin Street Youth Services, a San Francisco organization that assists thousands of homeless and at-risk young people. “I felt I needed to get involved,” Washington says of her work there. “The organization provides a continuum of services that empower these kids to pursue their dreams.”



It's a Bird, It's a Plane ...

Holy costume party! If you happened to be at UCSF Benioff Children's Hospital San Francisco last fall, your "spidey sense" might have been tingling. The "grime fighters" of Mastercare Window Washing put on quite a show for the kids, rappelling down the sides of the

building in full costume – and leaving the windows sparkling clean, to boot. The washers, who swoop in periodically, even took the time to visit young patients. As Spider Man once said, "With great power there must always be great responsibility."

Thank you for making a difference.

UCSF is grateful to its many patients, faculty, alumni, and friends who have remembered UCSF in their wills and trusts.

Your confidence in us and your financial support inspire us to be the best at what we do every day in our patient care, education, and research programs.

If you would like to make a gift through your estate, make a lifetime gift of special assets such as real estate or securities, or fund a life income plan for yourself or a loved one, please contact the UCSF Office of Gift and Endowment Planning at 415-476-1475 or giftplanning@ucsf.edu.

To learn more about planned giving or to make a gift today, please use the attached envelope.

Patient Brylee Hutcherson catches up with one of her caregivers after a follow-up visit to UCSF Benioff Children's Hospital Oakland.

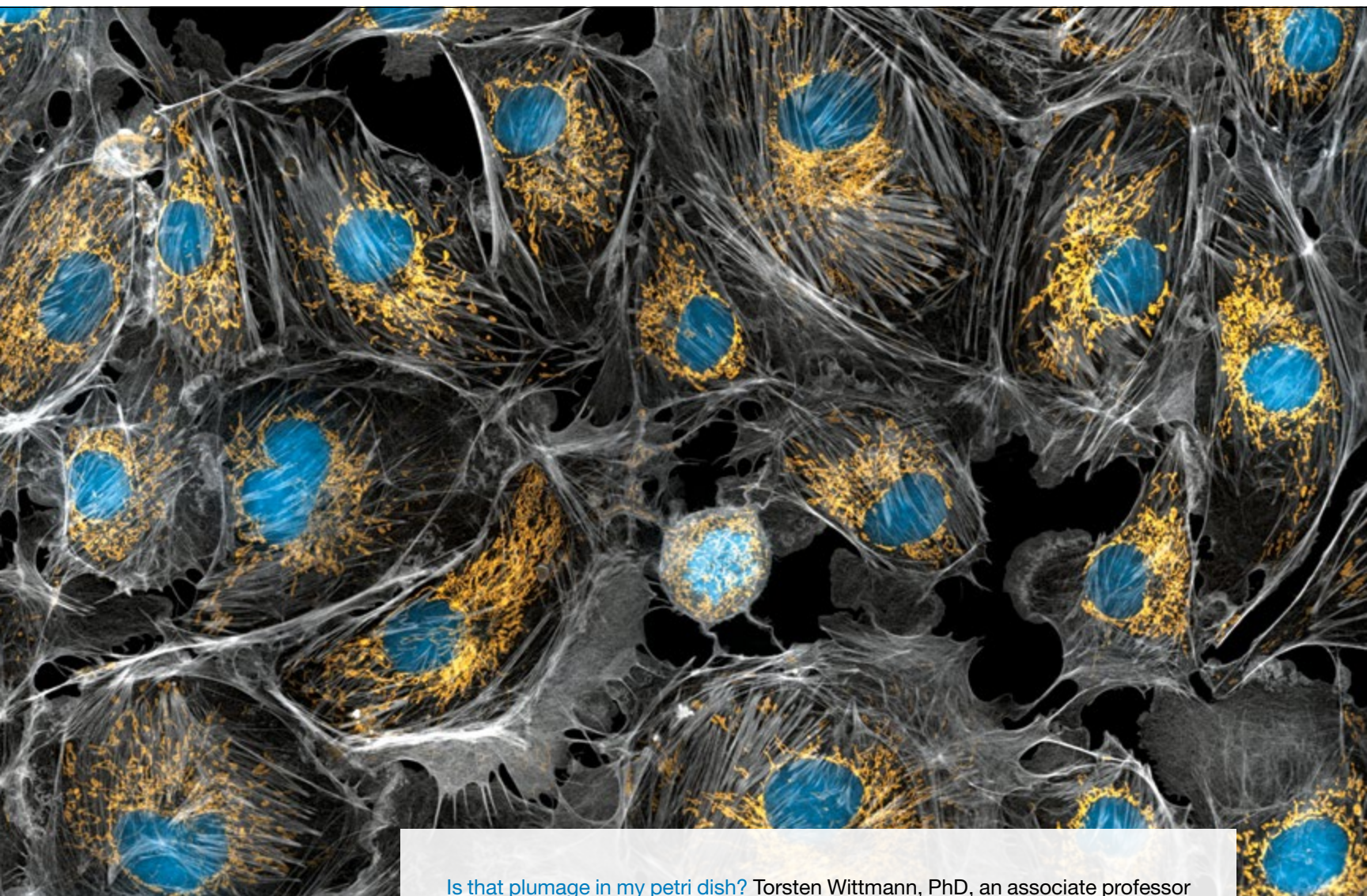


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Is that plumage in my petri dish? Torsten Wittmann, PhD, an associate professor in the School of Dentistry, took home the grand prize in UCSF's Sci-Resolution contest with this image of endothelial cells, which line our blood vessels. Called mitochondria, the yellow thickets are the power plants of the cell, and the blue eyes are their nuclei. View more stunning contest images at bit.ly/ucsf-contest.