

Winter 2024

# UCSF MAGAZINE



## The Road to **Rejuvenation**

Can science slow aging?

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A pharmacy professor and her students dove into documents from the opioid industry. What they discovered shocked them.



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# The Thrill of Progress

**One of the great privileges of my job is witnessing the arc of progress in science. Lately, it's been phenomenal.**

Take the three-dimensional models of organs and bones pictured in these pages. They are stunning not only visually but also for what they – along with new immersive technologies – are allowing our surgeons to accomplish: Reconstruct almost every bone in a young boy's face after it was shattered in an accident. See a way to make a complex heart repair, an approach that had remained elusive on CT scans. Train residents using augmented reality, allowing them to hold and examine virtual body parts.

Yet the physicians, imaging experts, and engineers in UCSF's Center for Advanced 3D+ Technologies, launched barely six years ago, are already envisioning moving into the fourth dimension. In this realm, the models will become even more true-to-life by integrating the motion of our bodies, like the beating of a heart. It's spectacular work that could revolutionize the field of surgery and other areas of medicine.

I am also awed by the discoveries emerging from UCSF's new Bakar Aging Research Institute (BARI). Scientists have long thought that the process of aging is irreversible.

No more.

As you will read in our cover story, BARI is revealing that aging is malleable. Researchers there are uncovering the biological mechanisms that help repair and rejuvenate



Pediatric cardiologist Shafkat Anwar (left) cofounded UCSF's Center for Advanced 3D+ Technologies. He and surgeons like Mohan Reddy (right), along with imaging specialists and engineers, are using 3D techniques to solve complex clinical cases.

cells. Their findings could eventually lead to age-defying therapies to help halt diseases like Alzheimer's, cancer, and diabetes. These efforts could propel us all into a healthier state, where we age with more vibrancy and vigor.

I have been at UCSF for more than four decades, and I still feel thrilled by the discoveries that continue to unfold here and by the progress they fuel. The advances we are making for our patients give me optimism for the future. I hope they do the same for you.

Sam Hawgood, MBBS  
Chancellor  
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PHOTO: ELENA ZHUKOVA

# Five Questions for Ryan Hernandez

**Ryan Hernandez, PhD**, whose trajectory led him from busboy to population geneticist, is helping propel a new era for science at UCSF by championing diversity, equity, and inclusion (DEI).

## Your early path?

Growing up, I was never drawn to science. Honestly, I was barely saved from cascading down the path toward gang life. Many friends weren't so lucky. I was the first in my family to go to college, and I only went so I could play football. But once I got there, I discovered research, and the rest is history!

## How does diversity strengthen science?

To me, the world of science is a better place when everyone has the opportunity to participate. People from different backgrounds and lived experiences bring different ideas, questions, and approaches to their research, which can help break down existing paradigms and open up new avenues of inquiry.

Hernandez is inaugural co-associate dean of DEI at the School of Pharmacy and a professor of bioengineering and therapeutic sciences.

## First steps as a new DEI leader?

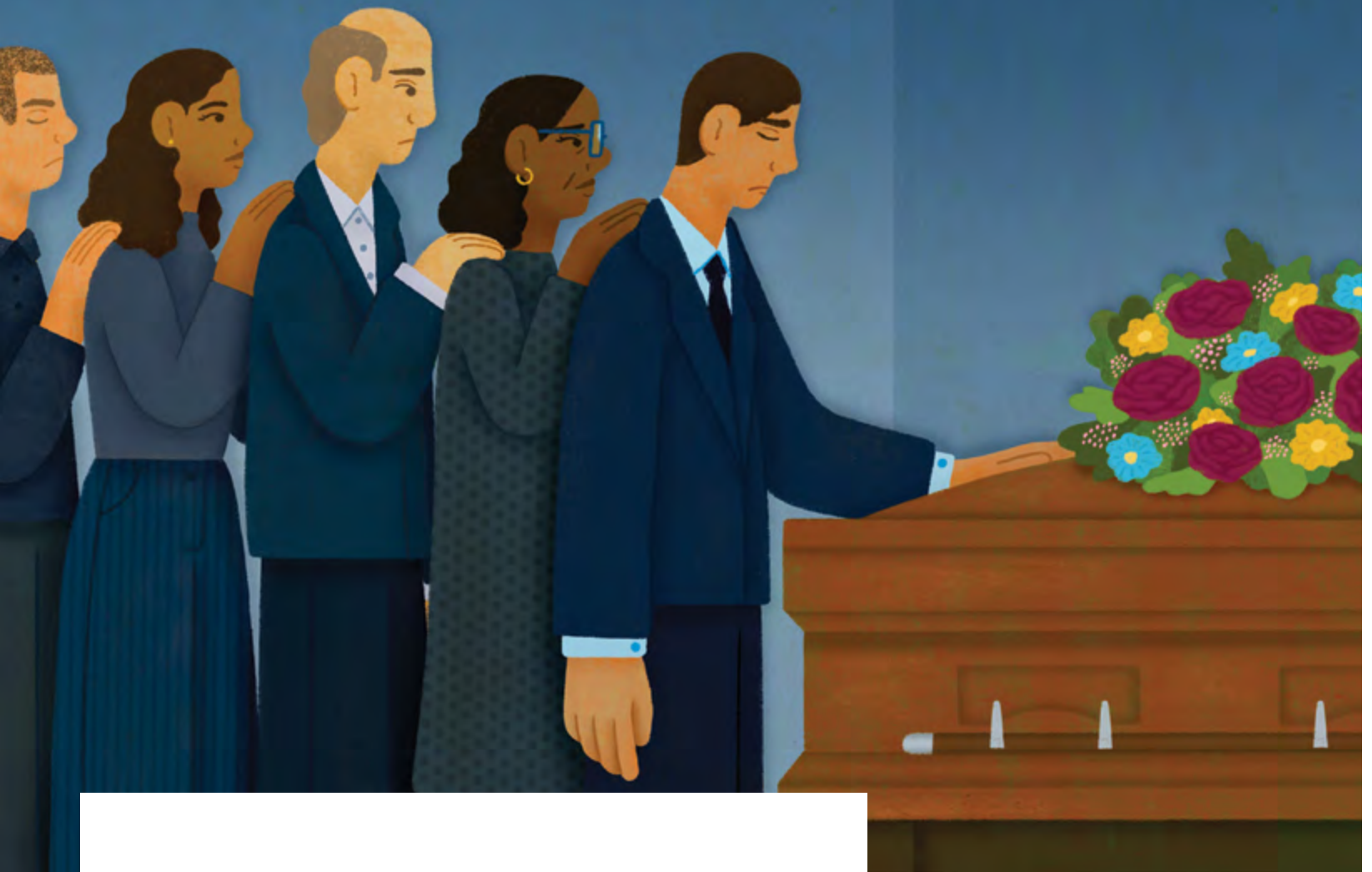
I want to listen to folks and give a voice to those who feel unheard. Once we establish a culture at UCSF centered on equity and inclusion, where people from historically excluded (HE) backgrounds feel welcome, supported, and sponsored, then we will really start making inroads toward increasing diversity.

## What excites you?

The community of scholars coming together to build a better future at UCSF. Many DEI efforts are siloed, inadequately supported, and insufficiently sponsored. That's why we're building ARCHES, a program that will support and sponsor our HE faculty. The potential is thrilling!

## What's another success?

Co-founding PROPEL, a postbac program that helps HE scholars gain additional experience before applying to graduate school. Since starting in 2021, PROPEL has admitted more than 160 diverse scholars who have been hired by labs in over 39 departments, 49 research institutes, and all of UCSF's schools. They work across the spectrum of biomedical research yet unite for community and support. I love it!



# How to Grieve – and How to Help Others Through Times of Loss

By Cyril Manning

The experience of death and loss is universal, but it's difficult to talk about end-of-life issues – even in hospital settings. We went to Jun Caole, DMin, a grief facilitator and the staff chaplain at UCSF Health's Mission Bay campus, for guidance on processing loss.

**Can you describe your work as a hospital chaplain?**

I care for people as whole beings. I still have patients who think they are dying when I see them, and I give them the last rites. However, palliative care chaplains do more than that. I consider my work holistic, addressing how people's existential needs affect their physical, emotional, mental, relational, and spiritual well-being.

**What question do you get asked the most?**

The question I get over and over again is: *Why me? Why am I suffering this way?* Instead of giving specific answers – because there is no right or wrong answer – I invite people to explore what they mean when they ask those questions. Existential issues often come up: guilt, forgiveness, fear, broken relationships, all sorts of things. Listening and helping people name and explore these things is what's most important.

ILLUSTRATION: PAGE STAMPATORI

### How can someone help a loved one who is experiencing loss and grief?

Be fully present. Really focus on the person and what they are saying – and don't be concerned about what you are thinking or what you're going to say. It's OK to say, "I noticed you're getting tearful while you're talking about this. Tell me more. How are you feeling right now?" Focus on validating and affirming them, not giving your own opinions or advice.

### How do you provide support that accommodates all belief systems?

I see people from many different religious traditions and with a range of philosophical beliefs and values, but they all share common emotions when faced with the death of a loved one. I am a firm believer that rituals are one of the most helpful ways of processing grief. While many of these are rooted in religion, nonreligious rituals can help folks, too. Nature walks, journaling, listening to a loved one's favorite music, talking to them after they are gone – these are just a few examples. I invite folks to create rituals that give them a sense of order. One participant in my grief support group said her brother's death brought chaos into her life. She created a ritual of making collages of his photos, and this helped her regain a sense of control.

### What are the healthiest ways to grieve?

Each person grieves differently. Grieving the death of a loved one usually comes with so-called secondary losses, such as a loss of meaning and purpose, normalcy and order, or identity and belonging. Acknowledging and honoring these losses is important. To some folks, this can be done by talking about their emotions with somebody they trust. For others, mindfulness practice is a better fit. Joining a grief support group is one of the best ways to process loss.

The truth is, most of us need to have our grief witnessed and validated by others. Ignoring or suppressing our emotions and thoughts can cause prolonged grief and a sense of suffering.

### Do some ways of grieving bring comfort faster than others?

In my experience, there are two kinds of griever. "Intuitive grievers" have no problems expressing their emotions or losses. "Instru-

mental grievers," on the other hand, do not talk about their emotions, but use tasks to process their grief instead.

For example, I have a relative who is an instrumental griever. After his mother passed away, he immediately returned to work and resumed his everyday life, including doing his favorite hobbies, as if nothing had happened. His lack of showing grief emotions struck me. I did not understand that this *was* his way of grieving. Years later he explained, "I went fishing, and that was how I processed my grief."

There is no *wrong* way to grieve, but people who are not able to talk about their grief emotions often have more difficulty.

### Talking about death and grief can feel quite taboo.

The reality is that we are surrounded by death, loss, pain, and suffering, but American culture is just so into the positive side of life. We are knowledgeable about so many things, but not grieving. We need to make talking about death and grief a natural part of discussions in public forums, and we need to teach young people, at an early age, that these things are normal.

In one of my grief support groups, I met a couple who lost their son when they were in their 70s. They said, "At our age, we should know how to deal with this – but we don't have any clue."

### What should someone do if their grief doesn't get easier with time?

When grief affects your ability to function daily, or when your physical reactions to it literally make you sick, grief may become clinical depression, and it is appropriate to seek professional therapy.

### What's your most important takeaway for readers?

When dealing with a grieving person, stay and make space for them to be heard and to be seen. It sounds simple, but it's hard to do.

To process grief, we need community. It could be a grief support group or a faith community, or it could be two people really listening and interacting. When grief is witnessed in a communal way, it helps people bear the weight of it. Grief shared is grief diminished. It helps us to know that we are not alone.

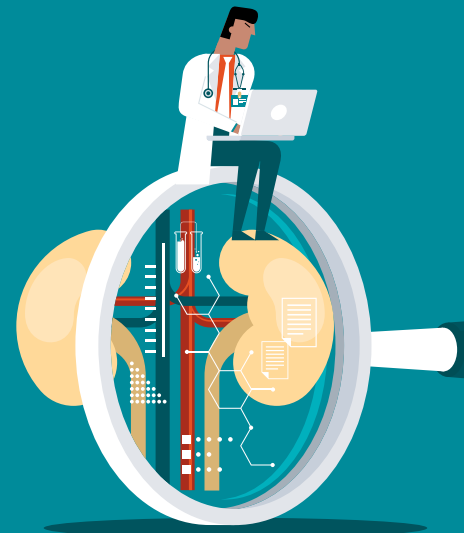
## Can an Artificial Kidney Finally Free Patients from Dialysis?

Half a million people in the U.S. must get dialysis several times a week because of kidney failure. UCSF researchers at the Kidney Project made a breakthrough with an implantable device called a bio-reactor, proving it can safely house kidney cells in large animals without triggering an immune reaction.

The cells, which balance electrolytes in the blood and produce vitamin D, remained healthy in the bio-reactor for a week.

Eventually, scientists plan to fill the bio-reactor with different kidney cells that perform vital functions – like balancing the body's fluids and releasing hormones to regulate blood pressure – then pair it with a device that filters waste from the blood.

"We are focused on safely replicating the key functions of a kidney," says Shuvo Roy, PhD, a UCSF professor of bioengineering and head of the Kidney Project. "The bioartificial kidney will make treatment for kidney disease more effective and also much more tolerable and comfortable."



# 12 Ways UCSF Is Exploring the Lungs

A world of science is examining the centerpiece of our respiratory system.

70+

Lung cancer clinical trials underway

21

labs studying lung biology

1,000+

Lung transplants performed since 1991

## Newly discovered impediments to breathing easy

Climate change is expected to increase lung cancer rates, due to escalating exposure to particulate matter in air pollution.

Workers making popular artificial-stone countertops are developing a potentially deadly, irreversible lung disease from toxic dust.

Lots of smokers show symptoms that are akin to those of tobacco-related diseases but that don't fit the criteria of any existing lung diseases.

Using race-based equations to evaluate lung disease (a common practice) may mean that severe disease in Black patients is classified as moderate.

## Blood factory

Over half of mouse platelets are made in the lungs, not the bone marrow. The finding may also pertain to humans and holds promise for treating certain blood disorders.

## Ending asthma

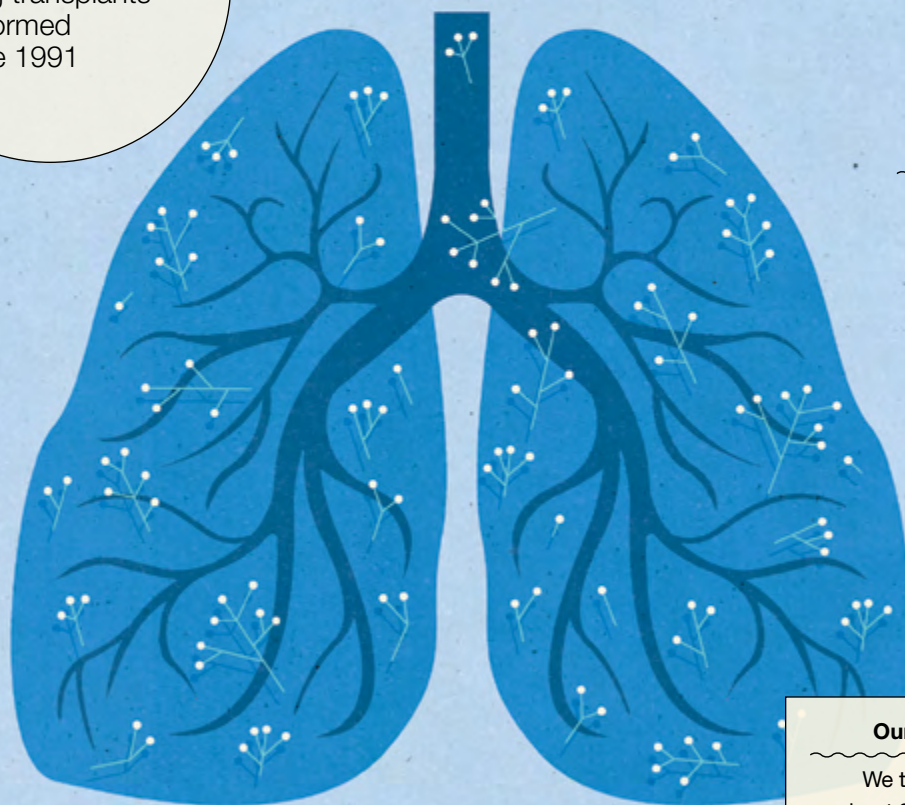
Experts aim to prevent asthma by editing the genes of microbes in the gut and airways that play a role in the disease.

## Curbing the deadliest cancer

Lung tumors are populated by a cornucopia of cancer cells. This makes lung cancer difficult to treat, as each type of cell responds differently to therapies – or not at all. But a groundbreaking study captured the genetic profiles of individual tumor cells and showed how the cells evolve during treatment. This knowledge could help thwart lung cancer drug resistance.

## Decoding inflammation

When an airborne virus is inhaled, the same molecular signals that trigger an immune response to fight off the pathogen can lead to dangerous lung inflammation. Researchers seek to unmask these mixed signals, which could lead to new ways to prevent damage.



## Why is smoke from wildfires so bad?

While the science is nascent, the secret may lie in the tiny particles the smoke contains. They can work their way deep into the lungs. This pollution can make respiratory conditions like asthma worse and increase the risk of respiratory infections, such as bronchitis and pneumonia.

### Our lungs by the numbers

We take about 20,000 breaths a day on average.

Our lungs have about 300 million to 500 million tiny air sacs called alveoli.

The surface area of our lungs is roughly the same size as a tennis court. The total length of the airways running through them is 1,500 miles.





## How AI Gave a Paralyzed Woman Her Voice Back

Ann worked with a UCSF team to train the AI algorithm to recognize her brain signals associated with phonemes, the subunits of speech that form spoken words.

UCSF researchers, in collaboration with the UC Berkeley College of Engineering, are harnessing the power of artificial intelligence to restore the voice of a paralyzed stroke survivor named Ann.

Through a pioneering brain implant, Ann can now express words and sentences using synthesized speech and a digital avatar, after 18 years of silence.

Tiny electrodes delicately placed on her brain's surface decode signals associated with Ann's attempts to talk. Advanced, custom-built algorithms recognize phonemes, the funda-

mental elements of speech, enabling Ann to construct words and sentences.

The team partnered with Speech Graphics, experts in AI-driven facial animation, to animate Ann's avatar, simulating lifelike facial expressions during a conversation.

"Our goal is to restore a full, embodied way of communicating, which is the most natural way for us to talk with others," says Edward Chang, MD '04, UCSF's chair of neurosurgery and the Jeanne Robertson Distinguished Professor. "These advancements bring us much closer to making this a real solution for patients."

PHOTO: NOAH BERGER

## Recommended: Books, Videos, & Podcasts



### North Woods

The *Washington Post* calls this novel "a time-spanning, genre-blurring work of storytelling magic." Written by Daniel Mason, MD '04, it's the tale of a house in the New England woods, told through the lives of its inhabitants across the centuries.



### Meet UCSF's Black Student Change-Makers

"You are here because you are a genius in every right," says Sydney Williams in this video about the graduate student organization BE-STEM (Black Excellence in Science, Technology, Engineering, and Math) and the exceptional leadership of Williams, Jaysón Davidson, and Christina Stephens. Find it on UCSF's YouTube channel.



### "Shame in Medicine: The Lost Forest"

This award-winning podcast series draws on the personal stories of more than 200 health care workers to explore how shame manifests in medicine. UCSF hospitalist and resident alum Emily Silverman, MD – who calls shame "the elephant in the room" – hosts the series, which is a collaboration between her *Nocturnists* podcast and the University of Exeter's Shame in Medicine project.

# What's the Truth Behind Popular Online Dental Myths?

Social media influencers are quick to share seemingly easy ideas and do-it-yourself dental hacks. But do TikTok trends save viewers a trip to the dentist – or cause tooth trouble?

By Tara Roberts

The bright-eyed young woman with the gleaming smile is eager to let her TikTok followers in on a secret: You don't need to go to the dentist to get your teeth whitened. Just follow her all-natural recipe – and don't forget to like and share the video!

Like many social media tips, dental hacks like these are too good to be true. But given the hundreds of such videos – and the thousands of views for each one – the myths keep spreading.

We asked Eva Bender, DDS, an assistant professor of preventive and restorative dental sciences and a clinician at the UCSF Dental Center, for the real story behind popular online oral hygiene advice.

## MYTH # 1: I can whiten my teeth with substances from my cupboard or fridge.

A scrub with products like lemon, strawberry, or papaya juice might deliver short-term sparkle to your smile. But they won't be as effective as proven treatments, and you risk damaging your teeth.

Smoking, chewing tobacco, or drinking beverages like coffee, soda, or red wine can stain the surfaces of your teeth. Plenty of substances can help remove such stains, but they aren't equally safe, Bender says.

Soaking or scrubbing your teeth with acidic substances, like fruit juices, invites cavities. The mouth is naturally slightly acidic because saliva's average acidity measurement, or pH, is about 6.7, compared to water's neutral pH of 7. The bacteria in plaque produce acid byproducts that further lower our oral pH. So bathing the mouth in even more acid diminishes saliva's natural buffering effects, causing enamel to begin to dissolve and creating cavities.

Other online influencers advise whitening teeth with activated charcoal. It's made of tiny, abrasive particles of porous carbon. However, just as a wire scrub brush might get gunk out of a dirty pan but also scratch the pan's surface, activated charcoal might deliver a quick polish but, says Bender, pointing to a 2023 study, cause microscopic damage to the tooth enamel, potentially making it stain more easily in the long run.



“Enamel is a precious resource,” Bender says. “Since no dental restorative materials are as good as natural enamel, I’m going to steer away from anything that’s going to irreversibly change its surface hardness.”

So what whitens teeth without unnecessary risk? Treatments in a dentist’s office and over-the-counter products from well-known brands, which are tested and shown to be safe and effective if used correctly. Bender recommends discussing your whitening goals with your dental professional.

## MYTH # 2: I'd better quit drinking carbonated water – it's bad for my teeth.

No need to throw out your favorite seltzer! Sparkling water is more acidic than still water because of the dissolved carbon that makes those delightful bubbles. But the pH of the average sparkling water isn't low enough to plunge your mouth into the danger zone of 5.5 and below, Bender says.

Tap water is typically the healthiest drink for teeth. Almost 75% of Americans get their water from community systems that are fluoridated, meaning the water has a small added amount of the mineral fluoride, in addition to naturally occurring fluoride. That helps protect teeth from decay – and even repairs some damage – by strengthening the enamel.

But if you want a different beverage for a treat, sparkling water is better than many alternatives, Bender says. In addition to carbonation, energy drinks and sodas also contain sugar and citric acid that feed

plaque and dissolve enamel. And diet colas may be sugar-free but are high in acidic flavoring.

Your best choice is sugarless, unflavored sparkling water. If you prefer flavored water, check the label for fruit flavorings, especially citrus, which contain citric acid.

### **MYTH #3: I can heal my cavities with a combination of vitamins and influencer-recommended toothpaste.**

Cavities in the outer enamel that haven't reached the underlying dentin can be repaired.

However, a magic-bullet toothpaste or vitamin regimen doesn't exist. You'll have to take a trip to the dentist to find and treat tooth decay. Strategic care can help heal and strengthen teeth by replacing lost minerals in enamel, a process called remineralization.

A bonus: Remineralized areas are harder to erode.

When a patient is practicing good oral hygiene, but X-rays show a high rate of decay, Bender starts a remineralization protocol. This includes fluoride varnish after dental cleanings and possibly more frequent office visits. For people with additional risks, such as cancer patients who received radiation treatments that dried up their salivary flow, Bender also prescribes MI Paste, a dental cream that contains the mineral building blocks of enamel.

Though MI Paste and some fluoride products are available online, Bender cautions against using them on your own. MI Paste is ineffective if applied at home like a regular toothpaste; in the office, a dentist applies it with customized trays to ensure it contacts the tooth surfaces that need repair.

Also, accidentally ingesting too much of a fluoride product can upset your stomach. While dentists can teach adults to properly apply fluoride treatments at home, children shouldn't be given fluoride varnishes unsupervised. The products often have appealing flavors, which puts kids at risk of ingesting unhealthy amounts of them.

"You do need to partner with your dental professional," Bender

says. "Find out if you are one of those high-risk patients, and ask what strategies could be useful in helping keep your individual rate of decay more manageable."

### **MYTH #4: I can order dental tools online and clean my teeth better at home.**

Don't risk it. Just because a tool works well in the hands of your dentist doesn't mean it's easy or wise to try it yourself – and you aren't going to learn how from YouTube.

Bender recalls a patient who noticed some residue left by fluoride varnish on his teeth and tried to remove it at home. He wound up in her office later that day with a broken front tooth that required a gigantic filling.

"If you're not trained in the morphology of teeth or how to hold the edges of the instrument against the tooth properly, you can damage the tooth," Bender says. "You can cause breakage and chipping. You can cause lacerations to the gum tissue, which can result in bleeding and infection. So it is very much not recommended."

Bender does encourage patients to use familiar and safe oral hygiene tools. Everyone should brush their teeth at least twice a day – or, even better, after every meal. Frequency is more important than the type of brush you use, Bender says. And you really do need to floss at least once a day. Flossing breaks up bacterial colonies between teeth that no toothbrush can reach.

And when you have a question about oral hygiene, turn to a professional, not someone promoting do-it-yourself "solutions" on social media.

Bender recognizes that the U.S. health insurance system often limits people's access to dental care, and they may not have their own dentist to call with questions. In that case, she recommends checking the websites of the American Dental Association or of tried-and-true companies like Colgate-Palmolive or Procter & Gamble, which manufacture Colgate and Crest toothpastes, respectively. Regional dental societies, like the California Dental Association, also offer free resources.



## **Genes May Explain COVID Super Dodgers**

How can some people be infected with COVID-19 without getting sick? These so-called super dodgers may have a genetic ace up their sleeve, according to a UCSF-led study. They're more than twice as likely as those who become symptomatic to carry a mutation in one of the genes for human leukocyte antigens, protein markers that signal the immune system. The variation appears to help virus-killing T cells identify SARS-CoV-2 and launch a lightning attack, even if they have never encountered it before. That's thanks to the novel coronavirus's resemblance to the seasonal cold viruses that T cells already recognize.

## Overwhelmed? Your Astrocytes Can Help

Scientists at UCSF have discovered a circuit in the brain that helps us calm down. The circuit involves a lesser-known type of brain cell, the astrocyte, which tunes into and moderates the chatter between overexcited neurons.

The researchers found that noradrenaline, a neurotransmitter that can be thought of as adrenaline for the brain, sends one chemical message to neurons to be more alert, while sending another to astrocytes to tamp down the overactive neurons. Until this study,

it was assumed that brain activity just quieted down over time as the amount of noradrenaline in the brain dissipated. “We’ve shown that, in fact, it’s astrocytes pulling the handbrake and driving the brain to a more relaxed state,” says Kira Poskanzer, PhD ’06, an associate professor of biochemistry and biophysics, UCSF’s Grace Boyer Junior Faculty Professor, and senior author of the study. The new brain circuit may hold a key to treating attention disorders like ADHD.

One astrocyte can connect to thousands of synapses, the connections between neurons.

## Makers of PFAS ‘Forever Chemicals’ Covered Up the Dangers



The chemical industry took a page out of the tobacco company playbook when it discovered and suppressed knowledge of health harms caused by exposure to PFAS (per- and polyfluoroalkyl substances), according to an analysis of previously secret industry documents by UCSF researchers.

Their paper examines documents from DuPont and 3M, the largest manufacturers of PFAS, and analyzes the tactics the companies used to delay public awareness of PFAS toxicity and, in turn, delay regulations governing their use. PFAS are chemicals widely used

in clothing, household goods, and food products. Called “forever chemicals” because they are highly resistant to breaking down, they are now ubiquitous in our bodies and the environment.

“These documents reveal clear evidence that the chemical industry knew about the dangers of PFAS and failed to let the public, regulators, and even their own employees know the risks,” says Tracey Woodruff, PhD ’91, MPH. Woodruff is director of the UCSF Program on Reproductive Health and the Environment, the Alison Carlson Professor, and senior author of the paper.

## Helping Teen Night Owls with Depression

School schedules aren’t built for kids who naturally fall asleep and wake up late, which may help explain why such teens are more prone to depression.

Now, researchers at UCSF have found a way to help these kids adjust to their innate sleep-cycle rhythms while still fulfilling their school responsibilities. The findings are a welcome sign for adolescents with depression, who are more likely than most to report staying up late.

While 40% of teens overall report being so-called night owls, in those with depression, 80% report late-night sleep patterns.

The key to success with the current intervention was teaching the night owls to structure their lives so they could sleep as late as possible, while gently training their bodies to fall asleep a little earlier.

“A big finding here is that there is a subgroup of teens for whom treating sleep is particularly important for improving depression symptoms,” says Lauren Asarnow, PhD, an assistant professor of psychiatry and a clinical psychologist at UCSF who specializes in sleep health. “And the other big finding is that they really need to be able to live a life that is more in line with their sleep-wake biology.”

# Breakthroughs and Other Buzz

**Triple benefit of tele-care:** A UCSF telecare program that both improves quality of life for patients with dementia and lightens the load for unpaid caregivers also has the surprising bonus effect of cutting Medicare costs, according to UCSF research. The program has been replicated across the country.

**Harms of tobacco plus cannabis:** People who use both cannabis and tobacco have a higher risk of depression and anxiety, highlighting the need for integrated support, a UCSF study found.

**Why such long ER waits?** Over the last decade, the number of emergency departments in California fell, while demand for acute care, especially from the sickest patients, rose. This finding from UCSF explains why ER wait times can be so long – a first step to improving emergency care.

**Zeroing in on chronic pain:** Pain is subjective, making it tough to treat. In a first, UCSF researchers identified individual biomarkers that may enable physicians to measure neural activity related to chronic pain. This objective measurement could help them personalize therapies for patients.

**A gene therapy first:** UCSF Benioff Children’s Hospital Oakland was the first hospital in the western U.S. to administer a newly approved gene therapy to treat the blood disorder beta thalassemia. It could eliminate the need for lifelong blood transfusions.

**Top rankings for UCSF:** UCSF Medical Center ranked among the country’s best hospitals in adult care in U.S. News & World Report’s prestigious Best Hospitals honor rolls for 2023-2024. In addition, the publication ranked UCSF Benioff Children’s Hospitals among the nation’s best pediatric medical centers in all 10 specialties it assessed in its 2023-2024 ranking.



**Long COVID’s wily ways:** Long COVID can persist for at least a year after the acute illness has passed, or appear months later, according to the most comprehensive look yet at how symptoms play out over a year. The findings stem from a sweeping collaboration between the U.S. Centers for Disease Control and Prevention, UCSF, and seven other health systems.

**Psychedelic helps heal trauma:** A clinical trial showed that MDMA, the psychedelic drug known as “ecstasy” or “molly,” can be a powerful new tool in treating people with moderate to severe post-traumatic stress disorder. The UCSF-led study puts MDMA on the path to be the first psychedelic to seek approval from the U.S. Food and Drug Administration.



**African plant inspires depression drug:** Scientists at UCSF, Yale, and Duke developed two new drug candidates to combat addiction and depression based on an African psychedelic plant called ibogaine. Their targeted molecules outperformed fluoxetine (Prozac) in blunting symptoms in mice – but avoided dangerous side effects common with ibogaine itself.

**Chemicals and cancer:** Researchers found that women who developed breast, ovarian, skin, or uterine cancers have significantly higher levels in their bodies of endocrine-disrupting chemicals like PFAS and BPA. It’s a strong signal that the chemicals may be playing a role in cancer risk and should be studied further, say the investigators, who are from UCSF, the University of Southern California, and the University of Michigan.

**Improving Alzheimer’s care for Asians:** UCSF is helping to create the first large group of Asian American study participants to bolster Alzheimer’s care for Asian populations in North America, a cohort that’s significantly underrepresented in research on the disease.

**Better prostate cancer detection:** Genetic factors can cause normal variations in men’s levels of prostate-specific antigen (PSA), even if they don’t have prostate cancer, according to research by UCSF and Stanford. Accounting for these genetic determinants when men are screened may improve detection accuracy.

**Hope for halting MS:** In a study of more than 20,000 people with multiple sclerosis led by UCSF and the University of Cambridge, scientists discovered a genetic variant – after sifting through more than 7 million possibilities – associated with some patients becoming disabled faster than others. The breakthrough could spur new treatments that prevent the disease from progressing.

# Artificial Intelligence: A **Revolution** for **Health Care**?

Electronic health records promised big improvements in health care but ended up making extra work for physicians and nurses. **Kay Burke, MBA, RN**, works on solving those challenges, helping UCSF Health improve the digital tools that nurses use every day. Could artificial intelligence make their jobs – and our health care – better?

By Elizabeth Daube



PHOTO: ANASTASIA SAPON

### **Why is everyone talking about artificial intelligence (AI)?**

We're seeing more generative AI – ChatGPT is a great example. You can ask a question, and the tool searches an almost infinite database of information. Then it summarizes a logical response. So you as a user are not researching a bunch of different sources. You're just asking a question.

Interest in AI in health care has exploded because there's a nursing shortage and a lot more burnout. Clinicians need support, and more sophisticated technology – namely, AI – could help.

### **What's behind the burnout?**

Clinicians have experienced increased stress since the pandemic. In the U.S., over 100,000 nurses left the profession between 2020 and 2021 – the largest drop in 40 years. I surveyed about 7,500 UCSF nurses and allied health professionals, and they attributed their feelings of burnout to constantly being on the computer. Technology has proliferated.

We didn't really put work phones in the hands of all nurses four years ago, but now? The number of digital messages they are receiving from patients and other clinicians has exploded. They're constantly bombarded by alarms and alerts, and their ability to respond to all of them just isn't the same by the end of a shift. And nurses are getting called in to work more often because staffing is so short. It ends up being a very hectic environment.

### **How could AI reduce that stress?**

AI could help nurses handle the additional documentation tasks. Say I have to give a patient report to the next nurse at every shift change. What if I could prompt the electronic health record with, "Look back 12 hours on Mr. Jones and provide a summary," and then AI populates a report with food and water intake details,

medication reactions, upcoming MRIs or other imaging, estimated date of discharge, and so on.

All the emerging AI trends are in some way alleviating cognitive burden. Right now, nurses are typically hunting and pecking to find and input this information. Often, some of it is missing or forgotten. The AI's summary might not be fully accurate, but generative AI isn't purporting to be. It's providing a response to a prompt and then allowing the expert clinicians, the humans, to manipulate that summary.

### **What about patients? Will AI help us?**

When electronic health records were implemented, patients complained that their clinicians stopped looking them in the eye. They were always looking at the computer. Nurses and other clinicians went into the profession to care for patients, right? They don't want to be entering data constantly. In the future, natural language processing could help with that by capturing the provider's voice and documenting information about a patient in their record. AI could even suggest a medical intervention that should happen based on that conversation.

Also, companies are already developing cameras that can see something clinical – a wound, for example – and the technology can tell if the wound is becoming infected. Machine learning can then suggest that the nurse call the physician. Or let's say a patient is deteriorating, and a nurse hasn't observed that yet, but the monitors and cameras are capturing clinical data. The AI sends an alert to the nurse saying, "Check on this patient." The AI is not taking away the work of the nurse or the clinician, but it's augmenting their decisions. Your outcomes as a patient might improve.

A few vendors are offering this kind of technology to UCSF Health to explore. But we have to be very careful as we decide whether to use it. We have to know what kinds of data are being considered.

### **Why do you need to understand the kinds of data the AI is using?**

There's a big difference between explainable AI, which is very transparent, and black-box AI. With black-box AI, you're not sure exactly which data are going into the algorithm. There's a saying: "Garbage in, garbage out." If the data going in is not reliable or relevant, the output coming out might not be useful, whether the output is a patient care summary or a suggested medical intervention. That can be very dangerous. If we cannot explain how we made a medical decision as a result of AI, that could be a regulatory or privacy violation, or worse, lead to a poor clinical outcome. With transparent AI, you can lift up the hood and see everything the algorithm considered to, say, recommend a certain blood test. But we're not there yet.

### **What is your biggest concern about AI?**

As AI increasingly enables care delivery, we need to make sure that it's not misused – for example, that it won't exacerbate inequality. The black-box AI could examine not just clinical data but also social data that contribute to health outcomes. For instance, is the patient housed? Do they have access to transportation? This social data is in the electronic health record. And if it's brought into the algorithms, we have to make sure the AI isn't potentially incorporating bias into the output – the clinical recommendations it makes.

Consider an organ transplant list. You, a patient, said three years ago that you are food-insecure. Is an algorithm going to suggest that you be bumped down the list because food insecurity could affect your transplant result? I'm making up this example, but it's a concern. We can't let that happen. Ethics are at the heart of the AI conversation in health care.

Kay Burke is the chief nursing informatics officer for UCSF Health.





# THE ROAD TO REJUVENATION

By Christina Hernandez Sherwood

Illustrations by Matthieu Bourel

Fortified stem cells. Enhanced memory. A longevity hormone. UCSF researchers are finding out whether we can cancel – or at least delay – old age.

# W

hen laboratory mice are born – pink, with their eyes shut tight – they’ve already begun to age. In about eight days, their gray-black fur starts to show. By two months, the mice are grown up but young – their coats full and shiny, their bodies slender. Like humans, they reach a natural, physical peak.

This stage doesn’t last long. They lose the ability to reproduce by their first birthday. By age 2, mice are considered older adults – the rough equivalent of 70 human years. They’re filling out in the middle. Their fur is dull and flecked with white.

But they’re not too old to change. If researchers give them a running wheel or cut their calorie intake, the mice become healthier and more energetic. The researchers aren’t particularly surprised; we have long known that certain habits are beneficial to aging bodies, including our own.

Now researchers want to understand *why* – and they’re making fascinating discoveries that could transform human aging and tackle a host of ailments, from heart disease to dementia. At UC San Francisco’s new Bakar Aging Research Institute (BARI), 70 scientists and clinicians are all trying to answer the same question: How can we slow, or even reverse, aging?

## A BRAIN-BOOSTER IN THE BLOOD

In Greek mythology, Clotho is one of the Fates. She spins the thread of life, determining when we are born and when we die. When researchers discovered a naturally occurring hormone that regulates aging, they named it *klotho*. The amount of *klotho* in your body declines with age, and people with higher levels of the hormone tend to live longer, healthier lives.

“In science, we have long thought that when we age, we age,” says Dena Dubal, MD, PhD, UCSF’s Coulter Professor of Aging and Neurodegenerative Disease. “But aging is malleable. There are actually molecules behind aging more slowly. What if we could just replenish our *klotho* levels periodically? Maybe *klotho* could be a treatment for Alzheimer’s, for Parkinson’s.”

Dubal has made it her mission to learn more about how *klotho* works and uncover its potential as an age-defying therapeutic.

A decade ago, she found that giving mice shots of *klotho* improved their cognition and made their brains more resistant to age-related degeneration. Since then, she’s been investigating *klotho*’s potential as a therapy for aging brains. Her team studied *klotho* in rhesus macaques, primates with brains similar to those of humans. After a shot of the hormone, the macaques could more quickly and accurately remember where to find a food treat.

How does *klotho* provide this brain boost? The hormone itself doesn’t cross the blood-brain barrier. In her most recent work, Dubal found that *klotho* can stimulate platelets, which are produced by bone marrow and help form clots. Platelets are known for their ability to stop bleeding so the body can repair injuries. When mice are injected with *klotho*-stimulated platelets, their bodies release platelet factors that travel to the brain. One in particular, platelet factor 4 (PF4), acts as a cognitive enhancer. It appears to strengthen the connections between brain cells.

“It’s a really unconventional role for platelets,” Dubal says. “PF4 can do what *klotho* does. Understanding how it does that is a high priority for us.”

Dubal’s PF4 finding became even more notable when she realized she was not the only researcher to identify its cognitive enhancement capabilities. Two other teams, one of them also at UCSF, have reached the same conclusion: PF4 seems to cause a brain boost in mice. All of the researchers are continuing their work on PF4, in the hope of one day testing the molecule as a therapeutic in humans. An early challenge: ensuring that PF4 doesn’t cause harm, given its potential to increase blood clotting. So far, Dubal says, her team hasn’t observed any negative side effects.

Just one in five people has a genetic variant that produces high levels of *klotho* (and, presumably, PF4) in the body. But Dubal points out that everyone has some level of *klotho* – and the power to change it.

“Age-related cognitive dysfunction has become one of the biggest biomedical problems for which we have no effective medical therapies,” she says. “There’s nothing that can be done about whether I have the variant. But I know exercising and stressing less can increase *klotho* levels, so I focus on what I can influence.”

## LOWER OXYGEN, LONGER LIFE?

It's almost impossible *not* to live an active lifestyle in Denver. Protected bike lanes line the streets. The surrounding mountains offer a playground of hiking trails and ski slopes. But Isha Jain, PhD, a UCSF assistant professor of biochemistry and biophysics, thinks there might be another reason why Rocky Mountain residents have a longer life expectancy than inhabitants of almost any other area of the U.S.

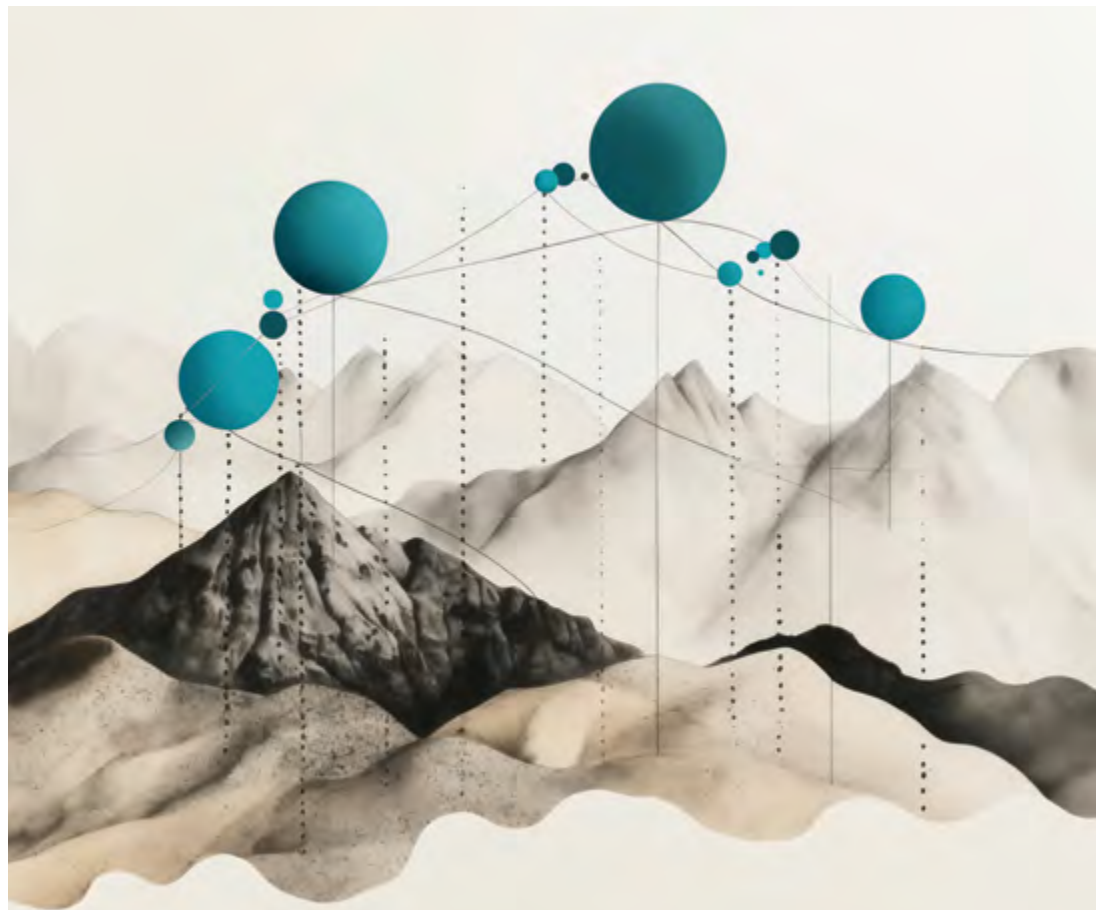
Denver is known as the Mile High City for its extreme altitude; sit in the 20th row of the upper deck at Coors Field, home of the Colorado Rockies baseball team, and you're a whopping 5,280 feet above sea level. (San Francisco's average elevation: 52 feet.) That means Denver's air has less oxygen than lower-lying cities. Jain is studying how low-oxygen environments protect our bodies from age-related cell damage.

"If you do a heat map of altitude and longevity in the U.S., the overlap is striking," she says. "But there isn't a proven association between altitude and increased longevity. Epidemiological studies can be confounded by factors like diet and exercise. We're hoping, in the lab setting, to dissect out the contribution of oxygen versus other lifestyle variables."

In Jain's early work, lab mice with a disease that caused them to age prematurely resided either in a cage with sea-level air or a "hypoxia hotel," a large box in which the oxygen was diluted to about 11%. That's the equivalent of air at an altitude of about 14,800 feet, such as the mountain regions of Nepal and Peru. The mice breathing sea-level air – with double the proportion of oxygen – died at about 50 to 60 days old, a typical lifespan for mice with their condition. Mice in the hypoxia hotel lived three times as long.

"Oxygen has always been considered to be a beneficial gas," Jain says. "We've been challenging that premise by showing that moderate hypoxia – a low-oxygen environment – is actually beneficial. We call this the Goldilocks Oxygen Principle: Both too much oxygen and too little oxygen can be toxic."

Jain hypothesizes that a low-oxygen environment prevents and reverses oxidation, a process that damages cells and increases over time. Nutritional research also explores whether certain foods and supplements might safely limit oxidation in the body – and how their absence might speed up the damage. A newer arm of Jain's research focuses on how specific vitamin deficiencies can affect aging and age-related diseases. "We are identifying sets of age-associated conditions that are benefiting individually from each vitamin," she says. "We're trying to turn that into targeted therapies, almost like a personalized medicine approach to vitamins."



In the future, Jain hopes to offer clinical trials of inhaled hypoxia as a therapy for children with severe mitochondrial disorders, who age rapidly and have few treatment options. If inhaled hypoxic therapy is found to be safe, Jain says it could be delivered through a portable hypoxic tank – like the oxygen tanks that patients with limited lung function use, but with the reverse effect – so patients aren't confined to hypoxic rooms. For now, though, it's not easy to put this research to use.

"Extreme hypoxia can be dangerous," she says. "We really do need to do the clinical trials before applying this concept to ourselves."

## THE INFLAMMATION-AGING LINK

Inflammation in the body has been linked to some of the most devastating diseases of our time: Alzheimer's, cancer, diabetes, and more. But controlling "inflamm-aging" – the chronic, low-grade inflammation that increases in our bodies with age – is complicated, according to Ari Molofsky, MD, PhD, an associate professor of laboratory medicine. The body sometimes *needs* inflammation to fight off infections or heal wounds.

“Inflammation is not all bad,” he says. “Most of it is our body trying to do what it thinks is right. It tries to repair damage and limit infection. In many cases, there is a complete repair back to baseline. But sometimes we don’t quite get back to where we began, and a lifetime of this process alters our immune state and can create inappropriate inflammation, which is part of what’s pushing folks toward diseases associated with aging.”

Researchers have known about the inflammation-aging connection for some time. Now, they’re exploring ways to safely reduce the inflammation in our bodies – from the heart to the brain and even the skin – to slow the aging process and extend good health as long as possible.

Molofsky’s work aims to build a deeper understanding of the immune system and how we might modify and direct it. For example, a stroke often causes damage and inflammation around the brain. Molofsky recently found that fibroblasts, cells that help form connective tissue, contribute to the rebuilding of the brain’s borders after a stroke. It’s a surprising finding given that, until recently, technology wasn’t advanced enough to provide a detailed rendering of these “builder” cells at the blood-brain barrier.

“We think immune cells are talking with the builders and remodelers of the tissue,” Molofsky says. “Understanding that crosstalk is going to be critical.”

His lab is mapping out the cellular pathways behind normal body processes to better understand what goes wrong in age-related diseases. He hopes to manipulate fibroblasts so they work in a way that regenerates damaged tissue but stops unnecessary inflammation.

“We want to make the builders build for us,” he says. “Our goal is to use them across diseases of the central nervous system and other organs to reinforce a healthy structure.”

Some inflammation solutions could emerge merely from fixing chronic conditions. In a recent collaboration with radiology colleagues, Aric Prather, PhD, a professor of psychiatry, found that people with insomnia have higher levels of vascular inflammation – a process linked to plaque buildup in the arteries and cardiovascular disease – compared to people without sleep problems. The upside? Data from other researchers suggest that when a person with insomnia is treated, their levels of systemic inflammation may decrease.

Another chronic condition worth treating? Dry skin. The body’s largest organ, the skin is also prone to age-related inflammation. Research suggests this could be more than just a cosmetic concern. Inflammation in the skin might spread throughout the body and contribute to other health problems, says Katrina Abuabara, MD, an associate professor of dermatology. In a 2022 paper, she reported that adult patients with eczema have a 27% higher risk of dementia.

Preventing or easing mild skin inflammation might be surprisingly simple. Research by Peter Elias, MD ’67, a UCSF professor emeritus of dermatology, suggests that applying petroleum jelly to the skin of older adults might reduce levels of inflammation in their blood.



## BETTER SLEEP

If you’re among the older adults whose sleep quality has declined over the decades, Prather says there are some proven steps you can take to mitigate the problem. First, establish a sleep schedule you can stick to by stabilizing your wake-up time. Then, make lifestyle choices that optimize your likelihood of getting a good night’s sleep. These include monitoring caffeine use, getting light exposure when you wake up, managing stress, winding down before bed, and designating the bedroom for just two activities: sleep and sex.

## STEM CELLS: THE BODY'S MASTER REGENERATORS

If scientists can find ways to safely use and enhance stem cells, they could be the ultimate antiaging agent. Embryonic stem cells have the remarkable ability to transform into any type of cell in the body, from liver to bone. Later, adult stem cells help maintain our bodies, constantly replenishing their reserves to support regeneration and repair. For example, specialized stem cells in your bone marrow make blood cells – not just once, but throughout your life.

Unfortunately, stem cells aren't immune to the aging process. Stem cell biologist Leanne Jones, PhD, UCSF's Stuart Lindsay Professor of Experimental Pathology and the director of BARI, is working to understand how the functions of adult stem cells break down as we get older.

"It's important to know how aging impacts stem cells," Jones says, "because we want to utilize them for regenerative medicine. Some researchers are already exploring ways to use stem cells to, say, reverse age-related macular degeneration in the eyes or replace dysfunctional dopaminergic neurons in the brains of Parkinson's patients."

One way to protect stem cells might be ensuring that they have enough of the right kinds of energy sources to function properly, while also getting rid of byproducts the cells generate. Jones's team found that when certain adult stem cells contained too many lipids, they lost the ability to renew themselves and generate specialized cells over time. Further study is needed, but Jones is investigating whether enzyme-targeting therapeutics might ensure the right balance of lipids in cells and improve tissue maintenance in older adults.

Physical exercise appears to be a practical way to slow the decline of stem cells. In other research, Jones found that older mice that exercised voluntarily for six weeks had an uptick in cell division in their small intestines. The result was so striking that the cellular composition of the intestine of an older mouse that exercised looked similar to that of a younger mouse. Jones is still working to understand why exercise stimulates cell division in the digestive system, which typically doesn't function optimally as we age. She hypothesizes that exercise could be causing changes that enable us to better absorb the nutrients needed to fuel physical activity and recovery.

Having a cellular-level understanding of how exercise spurs rejuvenation in the body could help scientists mimic the response with a therapeutic, Jones says. In the intestine, for instance, such a medication could counter digestion problems in older adults who are too ill or weak to exercise.

"We want to get people living more healthily for as long as possible," Jones says, "That's our goal."

## CUT CALORIES, SHARPEN MEMORY

Need inspiration to pursue a healthy lifestyle? For Saul Villeda, PhD, associate director of BARI and UCSF's Endowed Professor of Biomedical Sciences, it's laboratory mice. Years spent watching the older mice in his lab exercise regularly or restrict calories – then appear to grow younger before his eyes – have changed Villeda's own behaviors for the better.

"When I saw this old, fat mouse with gray hair start to look shinier and fitter, even I started exercising," he says. "I never did that before. And I'm more mindful about what I'm eating, of not being like that mouse at the all-you-can-eat buffet."

Villeda's latest research involves short-term, late-in-life caloric restriction in mice. His team gave mice unlimited access to a high-fat, high-protein food mix for two weeks, while researchers weighed their intake. Then they gave the mice about 30% less food. After the calorie restriction, the mice were tasked with a series of cognitive-behavioral tests, like navigating water mazes to reach a dry platform.

"It's similar to us finding a car in a parking garage," Villeda says. "When the mice are young, they're really good at the mazes. When they're old, they're pretty bad. It takes more time and they make more errors." By tallying those errors and timing the mice, Villeda found that calorie-restricted older mice had memory recall as good as their younger counterparts.

Villeda hypothesizes that this kind of memory improvement is a stress response – the body's way of maintaining health in the face of limited resources, whether taking in fewer calories or burning more of them. Finding out exactly how this response occurs will be no easy task, Villeda says, but it would pave the way to developing drugs that mimic it.

"We're fascinated with identifying how we can trick the body into thinking that it's calorically restricted without actually doing it," he says. "We know this extends health and life span. But caloric restriction is not sustainable as people age. We want the benefits without the struggle. I still want to eat brownies and bacon."



# THE WONDERFUL WORLD OF **3D+**

How a suite of advanced 3D technologies is ushering in surgery's most sophisticated era yet.

By Alexis Martin

Photographs by Elena Zhukova

Shortly after Alexander Lin, MD, joined UCSF Benioff Children's Hospitals in 2022, a 12-year-old boy was flown in for emergency surgery. The child had been run over by a vehicle, and nearly every bone in his face was shattered.

As co-director of UC San Francisco's Craniofacial Center, Lin was the lead plastic surgeon on the case. He had his work cut out for him. The child had suffered severe fractures to his eye sockets, cheeks, nose, and jaws. His eyebrows and lips were torn apart. His forehead bone – which surgeons elsewhere had removed when his brain began to swell – would need to be reconstructed entirely. He'd also lost vision in his left eye, and ophthalmologists suspected that one of his optic nerves had been injured. The vision loss could be permanent.

"It was a difficult, difficult case," Lin says. "Reconstructing this child's face bones would be like fixing a broken egg that's covered by a blanket. I can't just cut open his skin to see the fractures and fix them. I have to make little hidden incisions under his eyelids, mouth, and

lips. I'm basically making holes in the blanket and then trying to fix the egg through the holes."

The mystery of the optic nerve made the case even more complex. Computerized tomography (CT) scans didn't show exactly what was crushing the nerve. Without that knowledge, any attempt to repair it could cause further, possibly irreparable, damage.

Lin needed to see more. He printed a three-dimensional (3D) model of the boy's skull – a physical replica constructed from the patient's CT scans that would allow him to examine the eye socket by hand. Deep within the orbital cavity, he found the culprit: A small piece of broken bone had jammed the optic nerve.

"It was so far back," Lin recalls. "There were all these tiny pieces of bone, much further back than most eye socket fractures. But when I held the model, I saw that I could reach down with my finger and move this one piece of bone away from the nerve. I don't know how I could have visualized that without 3D printing."

Hours later, Lin was in the OR. A student



held up the 3D model nearby so Lin could refer to it during the procedure. “It was like having X-ray vision,” he says. On the model, the “blanket” covering the boy’s injuries was gone and the cracks in the “egg” were in plain sight, with color-coded landmarks guiding his every move. One by one, Lin repaired the multiple fractures.

The optic nerve was next. Peter Sun, MD, the Chen Professor of Clinical Neurosurgery, stepped in to assist. Sun gently lifted the child’s brain, and Lin lowered his finger into the back of the eye socket. Even amid so much bone and blood, he was able to see his target. His muscle memory guiding him, Lin placed his finger on the fragment of bone, rotated it away from the nerve, and attached it to the skull.

Eight weeks later, the patient’s vision returned to his left eye. “With a result that extraordinary,” Lin says, “it’s hard to imagine how we could have done it any other way.”



UCSF’s 3D printers live in a small, cluttered lab on the Mission Bay campus. The large, black machines sit side by side amid stacks of boxes, tools, and other equipment.

On a recent day, one of the machines was whirring steadily. A printhead the size of a car battery moved back and forth above a pale, yellow shape. From left to right, it deposited a thin layer of liquid plastic atop the object; from right to left, it shone green ultraviolet light over the liquid, hardening it, before depositing the next layer. Over the next 10 hours, hundreds of these layers came together to form a 3D model of 12-year-old Samantha Rodriguez’s heart.

Three-dimensional printing transforms computerized images into tangible objects. “It’s like raised topographical maps of the 19th century,” says orthopaedic surgeon Alan Dang, MD ’06. “Layers of material are stacked on each other, some forming islands, some mountains. When it’s done, you have a three-dimensional map.”

In medicine, 3D modeling can merge hundreds of individual slices from a scan such as a CT or magnetic resonance imaging (MRI) to form a three-dimensional replica of anything from a vital organ to a skeletal structure to a cardiovascular network. The resulting model can be explored virtually on a computer screen or be printed and examined physically.

“This technology literally lets me put the anatomy into the surgeon’s hand,” says Shafkat Anwar, MD, medical director and co-founder of UCSF’s Center for Advanced 3D+ Technologies (CA3D+). “It lets us take a newer, deeper look at what’s happening and make much more sophisticated decisions about what to do next.”



Established in 2018, CA3D+ represents a unique collaboration between surgeons, imaging experts, and engineers – applying advanced 3D visualization and manufacturing techniques to solve some of the most complex clinical cases at UCSF. In the past six years, CA3D+ has produced more than 700 3D models and become a national leader in using the techniques in medicine.

Before Anwar co-founded CA3D+, the technology was still relatively new in medicine. It was just over a decade ago that specialists in radiology, like Jesse Courtier, MD, started harnessing the power of three-dimensional augmented reality in medical modeling, and Alan Dang and his brother, Alexis Dang, MD ’04, also an orthopaedic surgeon, created UCSF’s first anatomical 3D print.

The Dang brothers had always loved to tinker with computers – they built motherboards in middle school and programmed computers in college. So as 3D printing began to take off in the popular interest, their curiosity was piqued: How might they use 3D technology in orthopaedics?

“There was all this hype,” Alan Dang says. “Even Martha Stewart was developing a line of 3D-printed products. So I bought the cheapest 3D printer I could find. We didn’t even know what we could do with it. We just thought, if anybody can make this work, it’s us.”

With no user manual for how to replicate broken bones, the brothers applied trial and error and scoured message boards for tips. “We ended up learning a lot from hobbyists, including those in the ‘maker’ and right-to-repair movements,” he says, referring to recent technology-based extensions of the do-it-yourself ethos.

Their first model was of a broken clavicle. It took a few attempts to get the print right – the computer kept trying to correct the fracture as an error in the data – but when the object finally took shape, the brothers were immediately struck by its potential.

“With a CT scan, your brain is integrating about 300 images to create that model in your mind,” says Alexis Dang. “With 3D printing, you can hold the model in your hand. Rotate it. Get a sense of scale, of where you need to be – a thumb or a finger’s breadth away from some anatomical landmark. You’re preparing your muscle memory for the actual surgery.”



## EXAMINING TINY PATIENTS

Three-dimensional modeling can be a powerful tool in pediatrics, given the small size and delicate nature of fetal and infant anatomy. Scans of a fetus at 29 weeks’ gestation, for example, revealed a tumor the size of a soccer ball that was compressing the unborn baby’s airway. Several institutions declined to operate due to the complexity of the case. But the UCSF team used a 3D model to identify an airway they could access during a surgical delivery. The procedure was a success, and the child is doing well today.



**T**he CA3D+ office is across campus from the printer lab. Anwar shares the space with Michael Bunker, the center's 3D printing engineer. Bunker has not only spent years building medical devices from scratch but he's also a seasoned gamer, a hobby that gives him a strong feel for 3D work.

In between Anwar's and Bunker's desks is the center's "library": an astounding array of colorful organs, bones, muscles, and molecules. There are walnut-sized infant hearts revealing complex structural defects; knotty tumors buried deep within labyrinths of vital organs; and curvy spinal cords joined by teal, fuchsia, pink, and purple vertebrae.

Drawing on his expertise as a pediatric cardiologist and cardiac imaging specialist, Anwar works closely with Bunker to design models that reduce the mystery of interpretation for surgeons. The models transform unique anatomy into detailed, manipulable road maps indicating the path a surgeon should take inside the body and revealing which biological landmarks show the way.

Anwar scans the library and pulls out a tangle of blood vessels resembling a deciduous tree in winter, with colored branches giving the structure a psychedelic effect. "This one isolates out the blood vessels so they're easier to see," he says. "We color-coded the vessels and told the surgeon, 'This is what you need to go after,'" he says as he touches the blue and pink branches. "Collect these vessels and bring them here. You'll find them in front of this landmark." He points at a knob jutting off a yellow branch.

In other cases, a model can reveal the feasibility of a risky procedure. That was the case for Samantha Rodriguez, who was born with single-ventricle heart disease, a rare defect that left her with only half of her heart to pump. By the time she was 6, Samantha had already endured three open heart surgeries. In the years that followed, her health stabilized, but her long-term prognosis remained precarious. Pediatric heart surgeon Mohan Reddy, MD, who specializes in repairing congenital cardiac defects, had to decide whether to perform a fourth, extremely delicate and high-risk procedure to cure the disease – or do nothing and hope for the best.

Using data from high-resolution 3D imaging, Anwar and Bunker printed a model that put Samantha's malformed heart into sharp relief. Reddy took the heart in his hand, opened it up, and explored its inner workings. He could see a clear way to construct a two-ventricle repair, a pathway that had remained elusive on CT scans prior to the creation of the 3D model.



#### ◆ TACKLING COMPLEX CASES

This is one of multiple 3D-printed skull models created of Lin's 12-year-old patient. In this version, the jaw has already been repaired, and the colors each depict separate fragments of broken bone to guide Lin's work during surgery. The bone fragment impinging on the optic nerve is represented by the lighter shade of pink. Over the past six years, CA3D+ has produced more than 700 3D models like this one to shed light on some of the most complex clinical cases at UCSF in cardiology, plastic surgery, orthopaedics, neurosurgery, and other specialties.

The surgery was a success, and Samantha is feeling better than ever. In September, Anwar presented her heart model at the World Congress of Pediatric Cardiology and Cardiothoracic Surgery to illustrate the enormous potential of 3D technology in heart medicine. At UCSF, surgeons now use 3D modeling to evaluate nearly every child who is born with complex congenital heart disease and faces high-risk surgery.

A heart model like this one was used to design Samantha Rodriguez's surgery.



“You can see the variation between these models,” Alexis Dang says, pointing to where the humerus meets the shoulder socket. “And you can feel it. When you move the humerus, you can tell how stable it is or how easily it falls out of place. Being able to feel it and touch it makes a big difference. These prints tell me how and when to treat the patient.”

The Dangs hope to continue demonstrating the versatility and breadth of 3D modeling as a surgical planning tool. “There are so many applications out there that we never would have thought of,” Alexis Dang says. “At the beginning of the pandemic, we used 3D printers to address supply chain issues by printing face shields and replacement parts for our air purifiers. We never would have thought to do this if not for the unique circumstances.

“Our goal is to get as many people as possible from across the UCSF community – not just clinicians but also researchers and students, and beyond medicine, in dentistry and nursing – to use the models so we can discover even more applications for our patients.”



Over the years, the Dang brothers have become convinced that 3D printing isn't just for complex medical problems. They believe that every surgery – no matter how unremarkable the case – can benefit from 3D modeling.

Take recurrent shoulder dislocation, an injury that Alexis Dang, a specialist in sports medicine, sees often. Doctors determine the appropriate treatment – whether a nonoperative intervention like physical therapy, an arthroscopic surgical procedure, or more invasive open surgery – based on the amount of bone loss at the edge of the glenoid, the socket portion of the shoulder joint.

For years, orthopaedic surgeons relied on CT scans to assess bone loss. “But the problem with CT scans is that they just give you an image of a slice of anatomy,” says Alexis Dang. “When you're imaging these slices, if you're slightly off in your orientation, it can skew your measuring. When it comes to bone loss, the amount of loss might appear differently based on how you cut the slice.”

He lines up three glenoid prints on his desk, each about the size of a fist. The models conjure up his brother's analogy of raised topographic maps: the layers of plastic forming the joint look like sedimentary rock.

## ◆ 3D'S WAVE OF THE FUTURE

In 2020, CA3D+ performed the first virtual fit test of a ventricular assist device (VAD) at UCSF. The device pumps blood from the heart to the rest of the body. VAD procedures are risky, but they can increase a patient's chance of survival. In the past, surgeons had to test the fit of a VAD during open surgery. Today, it's standard practice for UCSF teams to test the fit virtually, using 3D modeling of the patient's body and the device in mixed reality to ensure an ideal fit before surgery.

Three-dimensional modeling is also becoming a powerful educational tool. Anwar is using augmented reality technologies – an interactive experience that overlays 3D digital content onto real environments and objects – to teach trainees about cardiology. Using an app called Sira, developed by UCSF radiologist Jesse Courtier, holographic 3D models allow students to hold and explore a virtual heart and gain a deeper understanding of congenital heart disease.

**F**or Anwar, too, surgical planning is just the tip of the iceberg.

Back at the pediatric craniofacial center, a few months after regaining his eye sight, Lin's 12-year-old patient underwent another surgery to replace his missing forehead and eye socket, which were destroyed in the accident. This time, Lin used sterile guides 3D printed in an external laboratory to cut precise pieces of bone from uninjured parts of the child's skull to create a new forehead and eye socket.

What makes these prints unique is that they were sterilized for safe use in the patient's body during surgery. In the near future, Anwar and Lin hope to bring this sterilization process in-house. This will include making sterilizable 3D parts in UCSF's current facilities and adding a new facility at UCSF Benioff Children's Hospital Oakland for building these tools.

Anwar even has his sights set on eventually moving into four-dimensional anatomical modeling. "Our hearts and our bodies are moving through time and space," he explains. "We want to build models that show us how our bodies perform when they're in motion – that's the fourth dimension."

He takes a heart model in hand. "This is the heart when it's still, but what will it look like when it's contracting? How will blood flow through it? If we can integrate that physiology into our modeling, we can learn so much more. We can predict the outcome of one surgery compared to another."

For now, Anwar is excited to nurture the exponential growth of 3D printing in medicine, and the groundbreaking subspecialty that he, the Dang brothers, Lin, Courtier, Bunker, and others have built at UCSF.

"Ten years ago, I never could have imagined that we would be here," he says. "We've gone from talking about cardiac 3D printing as a cool new tool to showing that it's possible, across multiple disciplines, to support an entire health system and hundreds of patients with this technology."

Meanwhile, back in the lab, the 3D printers are churning out another one of Anwar and Bunker's models. They will use this one to discern if a tiny neonate's circulation can be rerouted to correct a complex malformation. Anwar can't wait to get his hands on it and start visualizing the surgery.



A  
PRESCRIPTION  
FOR LONELINESS

What a tiny grassroots program  
in the Tenderloin is teaching  
doctors about healing through  
human connection.

BY ARIEL BLEICHER

ILLUSTRATION BY HOLLY STAPLETON

PHOTOGRAPHS BY ANASTASIIA SAPON



In the winter of 2015, at the beginning of his first term as surgeon general of the United States, Vivek Murthy, MD, embarked on what he called a “listening tour of America.” In cities and towns across the country, he sat down with people from all walks of life – parents, teachers, business owners, philanthropists, community leaders – and asked what health issues troubled them most.

As the nation’s doctor, he was prepared to hear about problems like diabetes, mental illness, infectious outbreaks, and the opioid epidemic. And he did. But he also picked up on a common complaint that he hadn’t anticipated. This affliction, he later wrote, “ran like a dark thread through many of the more obvious issues that people brought to my attention.” Most people didn’t identify it as a health concern, but Murthy understood that it was causing them great pain and, in some cases, making their other ailments worse.

What unites so many Americans, he realized, noting the irony, is loneliness.

We’ve all felt it from time to time – that ache of wanting to be close to other people, to belong, to be loved. When it persists, it strains our hearts and spreads inflammation, damaging our tissues and blood vessels. And the impacts on our health can be profound.

Research consistently shows that prolonged loneliness and isolation (a distinct but similarly fraught experience) increase our risk for cardiovascular disease, immune dysfunction, insomnia, stroke, dementia, depression, and anxiety. It’s no wonder that lonely or isolated people are also more likely to die young. According to a massive analysis of 70 studies with more than 3.4 million participants, loneliness and social isolation raise the chance of early mortality as much as smoking and obesity.

Ashwin Kotwal, MD, MS, a geriatrician at UC San Francisco, is one of a growing number of physician-scientists who have been calling on health systems to address patients’ fundamental need for human connection. “A lot of us have been screaming from the rooftops for a while that this is important,” he says. When I visited him earlier this year at the San Francisco VA, he was still dealing with the fallout of the pandemic lockdown. “When patients didn’t see their family members for many months, they really declined,” he told me. “Their dementia got worse. They developed pressure injuries because they weren’t getting out of bed as much. The use of antipsychotics increased a ton.”

As a palliative specialist, Kotwal often helps patients prioritize meaningful social activities, such as attending a daughter’s wedding or a grandson’s graduation. “What people care about at the end of life is not being alone, probably more than not being in pain,” he says. Only recently, though, have health care providers at large begun to see loneliness as a serious health concern. “Many clinicians didn’t understand how it was our responsibility to do something,” he says. “The feeling was, ‘This is outside the scope of our clinical practice.’”

Kotwal’s UCSF colleague Carla Perissinotto, MD, MHS, a fellow geriatrician who helped train him in the field, was one of the first researchers to get a paper on loneliness accepted by a medical journal. Her landmark study, published in 2012 in the *Archives of Internal Medicine* (now *JAMA Internal Medicine*), found that loneliness predicts worsening disability and death in people over age 60. “There was a lot of skepticism in the medical community,” she recalls, even though social scientists had been documenting the phenomenon for decades. Often, when she would present her results at scientific conferences, physicians in the audience would dismiss them, saying “This isn’t a big deal” or “It’s just depression.”

Perspectives have shifted as evidence of a loneliness epidemic has mounted. The prevalence of loneliness has risen steadily since the 1970s, when Americans began consuming more digital entertainment – such as television, and later, social media – and participating less in social and civic activities, such as going to church or joining a labor union or bowling league. Today, almost half of U.S. adults say they are occasionally lonely, and about 1 in 10 are frequently lonely – far more than the number with other chronic conditions, including heart disease and cancer.

After his national tour, Murthy sounded the alarm, as did several prominent health organizations. COVID-19 drove home the urgency of their message. As rates of loneliness spiked because of social distancing, many physicians saw for the first time how isolation could exacerbate frailty in an elderly patient or erode the mental health of a young one. “If there’s a silver lining to the pandemic, it’s that there’s now an explosion of interest in addressing this problem,” Kotwal says.

Yet even as doctors increasingly recognize loneliness as a public health crisis, they face a thorny question: How, exactly, do you help a patient who is lonely? “It’s much easier as a physician to say, ‘Oh, you have high cholesterol. Here’s your statin,’” Perissinotto says. But what do you prescribe for social distress?

## BETTER THAN A PILL

Last July, Perissinotto hosted a retreat at the UCSF geriatrics division for a half-dozen employees of the Curry Senior Center, a community nonprofit in San Francisco’s Tenderloin district. Her husband, who is a chef, had prepared a lunch of roasted chicken and cauliflower, a kale and wheatberry salad, and hand-rolled pasta made with flour he had milled himself. “The shape is *stroz-zapreti*, which means ‘strangled priest,’” she delightedly informed the group.

Nearly a decade ago, Perissinotto, a natural socializer, began building relationships with the Curry Center and other Bay Area organizations that foster social connections. These hard-earned partnerships have allowed her, together with Kotwal and others, to start studying loneliness intervention programs alongside the people who run them. “As medical academics, we often forget that the answers are in the communities we serve,” she says. Her goal is to identify the strategies that work and determine how to replicate them.

The assembled Curry employees included former salespeople, tech workers, insurance agents, and social service administrators. They now staff a program that pairs them with elderly residents in and around the Tenderloin who are lonely or socially isolated. Because the staffers share some of the same interests and experiences as their clients – they might be part of the LGBTQ+ community, say, or also be coping with mental health issues – they refer to

“I just kind of thought we were this old hippie, granola program... And then Carla comes along, and the next thing you know... we were able to translate granola into diamonds.”  
— DANIEL HILL



“As medical academics, we often forget that the answers are in the communities we serve,” says Carla Perissinotto, a professor of geriatrics. She collaborates with Daniel Hill to study the impact of a peer-support program that he manages in the Tenderloin district.

themselves as peers. That's not to say that just anyone with a common background can do this work. Although the positions don't require formal qualifications, most of these Curry employees are trained in peer support, a specialization newly recognized by the state of California that entails skills like conflict resolution and trauma awareness.

As the food warmed in the oven, Perissinotto introduced herself. The peers have been working with her team to collect data on the Curry program for several years now, sharing their reflections and surveying each other's clients every six months, but this was the first time that many of them had met her or heard the backstory of the UCSF-Curry collaboration.

"I became interested in loneliness really by chance," she told them. "Obviously, I knew about it because we all experience it at some point our lives, but I'd never asked about it in a clinical setting." Then one day, during her residency, she stumbled upon a questionnaire developed by researchers at UCLA to measure loneliness, and she had an epiphany. "It was like, 'Why aren't we talking about this in medicine?"

And what do we do about it?' Fast-forward to seven years ago, when I met Daniel."

Daniel Hill, a Gandalf-like figure in his early 60s, has managed Curry's peer program since its inception in 2015. Before that, he'd been employed at a homeless services organization, but after a shooting at his office, he became afraid to leave his house and stopped going to work. He eventually took another job, in AIDS hospice care, then was laid off and "sunk right back into that place of depression and isolation." Nevertheless, he "went through the motions" of applying for jobs in order to get unemployment benefits and ended up landing the one at Curry.

The role was a perfect fit, though it took Hill a while to realize it. "Me being a peer is one of the closets I've had to come out of," he later told me. "I don't know if it was shame so much as a recognition that PTSD and major depression weren't things you talked about in the workplace. But then I saw how my staff was using their experiences to uplift others, and I was inspired. I started saying, 'Yes, I'm a peer too.'"

In 2017, the Curry Center was looking to evaluate the impact of Hill's program to help raise funding, which is how he got put in touch with Perissinotto. "I just kind of thought we were this old hippie, granola program run out of a basement in the Tenderloin," he explained at the retreat. "And then Carla comes along, and the next thing you know..."

"...I'm bringing you coffee and lunch," she interjected with a laugh.

Ashwin Kotwal, an assistant professor of geriatrics, has been calling on health systems to address patients' need for human connection. "A lot of us have been screaming from the rooftops for a while that this is important," he says.





“And we start talking about validated measures, and then the questionnaires come out, and all of a sudden we were able to translate granola into diamonds, you know what I mean?”

By diamonds, Hill means data. For two years, the research team had surveyed 74 participants in the Curry program who ranged in age from 59 to 96. After the team tallied the input, the results were unequivocal: Peer support increased social interactions and reduced feelings of loneliness and perceived barriers to socializing, such as physical ability, cultural difference, and mood. By the end of the study period, the incidence of depression had dropped from 38% to 13%.

“I knew we were helping people,” said Hill, who is a co-author on the 2021 paper reporting the finding. “But this was like, ‘Whoa.’ And Carla – I love her – she goes, ‘Show me a medication that will do *that*.’”

## A PROFESSIONAL FRIEND

A few weeks after the retreat, I met Alessia Furlow, one of the Curry Center peers and Hill’s assistant manager, at her office in the Tenderloin. Though it’s known for seediness and crime, the neighborhood is a place of multitudes. Vibrant, stories-high murals adorn its drab brick facades, some of the last refuges of affordable living in the city. Children shoot hoops, dealers hawk fentanyl, and old men play dominos and practice tai chi. Commuters jostle past shoppers and parents pushing strollers, while people down on their luck slump under storefronts advertising pupusas or money orders or bánh mì or live jazz.

Furlow, who is in her 30s, had agreed to introduce me to one of her clients, a 73-year-old named Maggie Hosmer. Despite the age gap, Furlow says she finds it easy to connect with older residents. “I love to laugh,” she says. “So I think I just come across as open and fun.” She will join clients for coffee or lunch, stroll with them to a park, or just sit and chat with them in their homes – whatever they’re up for. “There’s no agenda,” she says. “It’s about cultivating trusting relationships.”

On our way to Hosmer’s apartment, Furlow took a detour to show me the Cadillac Hotel, where many of the seniors in Curry’s peer program live. When it opened in 1907, the Cadillac was billed as San Francisco’s “most select” luxury inn, featuring 180 rooms and a grand ballroom. But after the neighborhood declined in the 1960s, the building became a residential community, with staff providing social services to tenants – a role now filled by Curry Center case managers.

In the lobby, an eight-piece swing band was setting up for a concert. “Oh, hey, Sonya, how are you doing?” Furlow greeted a case manager in a Warriors T-shirt.

“I case manage everybody on the fourth floor,” Sonya Lister told me, adding that she refers tenants to the peer program whenever they seem cut off from the bustling community around them. “It’s a phenomenal program,” she said. “It really helps people come out of their shell.”

When we arrived at Hosmer’s place, a small sunlit studio in the nearby Fillmore district, she welcomed us wearing a blue turtleneck, black slacks, and slippers. Her gray hair was cropped short, and she wore tiny gold hoop earrings. Hanging by her bed was a popular 20th-century print by Maxfield Parrish that

depicts a naked figure bending over a young woman in a dreamy Grecian scene. “A lesbian classic,” she quipped.

Gay culture is something that she and Furlow had quickly bonded over. Before they met in 2021, Hosmer was spending her days holed up at home reading. She’d lost touch with her family, and most of her friends had died or moved away. “So I’d go to the library every month and get lesbian novels and whodunits, and I’d just read them from eight in the morning to six at night,” she told us. “I’d get real lonely, but I didn’t recognize what it was.”

Then one day, she went to the Social Security office to check on her benefits, and the door was boarded up. Same thing at the bank. She waited for the bus, but all the drivers refused to stop. “Finally, somebody came along and said, ‘You don’t have a mask. That’s why the bus keeps going by you.’” She hadn’t known that a pandemic had broken out or that businesses were shuttered due to protests over the killing of George Floyd.

She called the Curry Center so she could read the news online and heard they had a technology program. “I said, ‘I want a tablet and a lover,’” Hosmer recalls.

“So I got the tablet,” she says, and then grins. “I’m still working on the lover.”

What Curry did offer was a peer. Furlow was one of the first people Hosmer had hugged in a long time. She helped Hosmer sign up for dating sites and warned her about romance scams. They binged on *The L Word* and

watched *Screaming Queens*, a documentary about a little-known uprising by drag queens and trans women in the Tenderloin in 1966. They sat on Hosmer’s bed eating mango strips and Thai chili almonds and talked like girls at a slumber party.


Lately, Hosmer has been reaching out to more people. She started going for walks and out to eat with another client of Furlow’s. She invited a former coworker to join her for a haircut and reconnected with an old friend who shares her love of music

and poetry. And she got a cat, a gray-and-white tabby named Sheba. “Right now, my life is kind of settled,” she said. Rarely does she feel the twinge of loneliness anymore.

Before we left, I asked Hosmer how she thought about her relationship with Furlow. Who was this warm, supportive person to her?

She turned to her peer. “I consider you a friend,” she told Furlow. “Would that be weird if I said, ‘This is my friend Alessia?’”

“No, that’s not weird at all,” Furlow replied. “I mean, it’s part of my job, right? But I definitely feel like there’s a companionship. There’s that intimacy of friendship, for sure.”



“There’s  
no agenda.  
It’s about  
cultivating  
trusting  
relationships.”

— ALESSIA FURLOW

## WHAT DOCTORS CAN DO

Curry's peer program works precisely because it's so informal. When the UCSF team analyzed in-depth interviews with clients and peers, they found that almost all the participants used the word "friend" to describe their peer. The program's flexibility and agenda-free ethos, the researchers wrote, "facilitated trust and gave clients a safe space to build skills and confidence." Clients felt that the peers genuinely cared about them and didn't judge or condescend to them, as other service providers sometimes did. (As one peer put it, "I'm not a doctor talking down to you, like, 'Oh, you need this and that, and here's your problem because I say so.")

The program's creators had assumed that would-be clients were isolated because they weren't getting services like counseling and mental health care. But that wasn't the case. "What we discovered was that everybody's connected to services," Hill says. Most clients, it turned out, already had doctors and therapists and case managers, and they didn't want any more. ("I have enough," one client said.) The problem, in other words, wasn't that lonely people weren't being referred to providers; it was that their providers weren't referring them to programs like Curry's.

One reason is stigma. "No one wants to raise their hand and say, 'Hi, I'm Daniel. I have no friends,'" Hill says.

And most providers don't ask. Clinicians often worry that bringing up loneliness and isolation will make patients uncomfortable, says pediatrician Matt Pantell, MD '13, MS, who studies social drivers of health at the UCSF Center for Health and Community and with the UCSF Social Interventions Research and Evaluation Network.

But that fear is probably unfounded. In a 2021 study of more than 250 patients recruited from primary care clinics nationwide, Pantell and his colleagues reported that 94% of subjects said they wouldn't mind being screened for social isolation. "In general, patients are very open to being asked about social factors in clinical settings," he says.

Of course, asking is just the first step. Some physicians might be hesitant to discuss loneliness and social isolation, Pantell says, because they don't have good answers. "There's no perfect solution for everyone," he acknowledges. But helping a patient find one starts with getting to the root cause, something doctors are well-trained to do. And the fix might be surprisingly simple. Maybe a quiet grandmother just needs a hearing aid so she can talk with her grandkids. Maybe a shy tween needs a ride to play sports with his friends. Maybe the patient has their *own* ideas about what they need.

Meanwhile, social prescribing – recommending community resources or activities that can help address social needs – is burgeoning. A prescription for loneliness could be a referral to a peer program like Curry's, a support group, an after-school club, or even a robotic pet (google "Paro the seal"). To make referrals easier, UC hospitals and other medical centers are starting to link databases of community service organizations with electronic medical record systems, Pantell says. "There are a ton of amazing interventions that most clinicians have no idea exist."

Elena Portacolone, PhD '11, MPH, MBA, a sociologist at the UCSF School of Nursing's Institute for Health and Aging, says that health care providers could also do more to prevent patients from becoming severely lonely or isolated in the first place. Patients are particularly vulnerable after being diagnosed with a serious illness, she says, especially if they live alone.

In her own research, Portacolone has interviewed nearly 100 older adults living alone with cognitive impairment, a reality for 4.3 million people in the U.S. Many of them have become so withdrawn that they are difficult to find, and she's learned to rely on tips from emergency responders, librarians, and even cockroach inspectors. Suicidal thoughts among her subjects, she says, are sadly common.

"These people are struggling with chronic uncertainty and frustration about not knowing what's going on or what to do," Portacolone says. "The diagnosis should be a moment where providers can help create or foster a deeper support network."


## GOOD MEDICINE

Five years ago, just as the project with the Curry Center was getting off the ground, Ashwin Kotwal called on a patient at an assisted living facility. "She was an older woman in her 90s, a veteran," he recalls. He'd been summoned because she wanted to use the End of Life Option Act, a California law that allows people who are terminally ill to request an end-of-life drug from their doctor.

This was surprising because the woman wasn't terminally ill. Although her vision was waning and she used a wheelchair, she was otherwise in fair health. She had children and grandchildren who visited her often.

"But as we talked, I learned that she had completely lost her sense of belonging because her disabilities had prevented her from being able to volunteer in her community," Kotwal says. Helping people had given her a sense of purpose, of connection. So instead of a pill, he prescribed her a gig taking calls for Friendship Line, a California hotline that lends a sympathetic ear to older adults feeling lonely or depressed. Over time, and with more care, her spirits lifted, and she no longer wished to die.

"When we start to recognize the value of human connection, we can make a huge difference in the quality of people's lives," Kotwal says. Programs like Curry's have long understood this. But they're tiny, underfunded, and under-professionalized – "granola" ventures scraping by on the sidelines of medicine's shiny arena. "People outside of health care have developed a tremendous amount of expertise," he says, and it's time that physicians catch on. "It's actually good medical care."



“When we start to recognize the value of human connection, we can make a huge difference in the quality of people’s lives.”

— ASHWIN KOTWAL, MD, MS

Maggie Hosmer (left) and her Curry Center peer, Alessia Furlow, share an easy rapport. The two enjoy watching shows together and just talking and laughing. Hosmer calls Furlow a friend and says she rarely feels lonely anymore.

## DANGEROUS BEAUTY

These cancer cells are on the march: They are migrating away from the human breast cancer tissue where they originated, in search of other tissues to invade. Cell biologist and engineer Matthew Kutys, PhD, and his team harness organoids – living tissues derived from patient tumors – to study how cancer spreads. The striking images they capture show how cells' own mechanisms of locomotion are hijacked to enable metastasis.



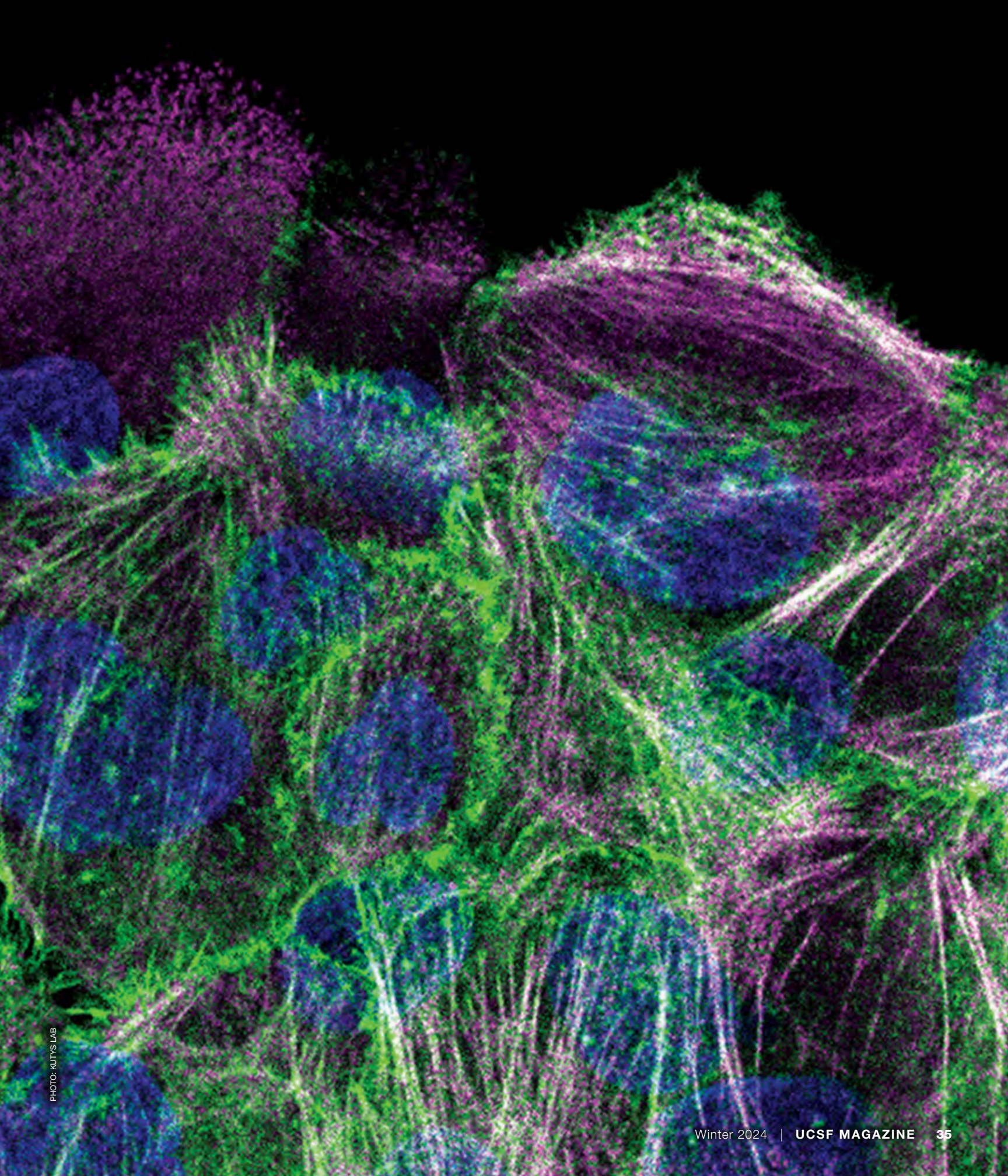


PHOTO: KUTYS LAB

Plaintiff's Exhibit  
**PX-FL-1647**  
 Case Number:  
 2018-CA-001438



07/06/2010 11:08 AM

To "Pharmacy Manager 03166"  
 cc  
 bcc  
 Subject Re: Question about Fla board holding rph's liable for excessive c2 rx's

No, we will not refuse to fill scripts for large quantities. you are a pharmacist not the C2 police.

Thanks  
 District Pharmacy Supervisor  
 "Pharmacy Manager 03166"

07/01/2010 04:2



Do you think we should start refusing rx's for quantities of 180 or 240? What should we do to protect our licenses?....

EXHIBIT # 10  
 DATE \_\_\_\_\_  
 DEPENDENT \_\_\_\_\_  
 PROFESSIONAL REPORTERS (800) 376-1000

<p>Acute Publication #1          (DIORTAP-07-02133):          Causes and Consequences of Under-managed Acute Pain</p>	<p>Responsibilities</p>		<ul style="list-style-type: none"> <li>Journal update 2/26, 3/31, 4/21, 4/28, 5/12, 5/19, 6/27...manuscript still under review</li> <li>Contacted [redacted] for his assistance</li> <li>Balliettes left multiple messages with journal</li> <li>IPC contacted also on 6/17</li> </ul>	<ul style="list-style-type: none"> <li>Following journal acceptance, create reprints for sales rep distribution (TBC)</li> </ul>
<p>Acute Publication #2          (DIORTPUB-09-03397):          Understanding the Role of Neuroplasticity in Pain Progression</p>	<p>Being Misdiagnosed</p>		<ul style="list-style-type: none"> <li>Revise and resubmit manuscript</li> </ul>	<ul style="list-style-type: none"> <li>Following journal acceptance, create reprints for sales rep distribution (TBC)</li> </ul>

✓ **Media Outreach-TARGETS: YOUTH, VETERANS, PUBLIC**

•Chronic Pain is the #1 public health problem



# CORPORATE STRATEGY, NATIONAL TRAGEDY

By Robin Buller \_\_\_\_\_ Photo Illustration by Chris Burnett

**Fudging numbers. Targeting children. Paying professors. UCSF's industry archives expose the marketing tactics that fueled the opioid epidemic.**

**H**anna Yakubi sat stunned. On her screen was a marketing plan from the Pain Coalition, a front group – masquerading as a patient advocacy organization – funded by major pharmaceutical companies implicated in the opioid epidemic. In plain language, it laid out high-pressure tactics aimed at getting people to use more pain medication, including one that Yakubi hadn't seen before: targeting kids.

One slide told drug sales reps to reach out to youths “early,” at the “elementary school level,” and to use wording that a 6-year-old could understand: “Pain is your body telling you something important.” Bullet points even suggested that salespeople connect with respected channels, like Little League coaches and school nurses, and essentially turn them into mouthpieces for the merits of medicated relief.

It was March 2020, and while much of the world was hitting pause on work and school, Yakubi and her colleague Brian Gac – then students at the UCSF School of Pharmacy – were sinking their teeth into a nascent subcollection in UCSF's Industry Documents Library. More specifically, they were sifting through 500 previously unexamined court documents from a landmark case brought by the state of Oklahoma against Johnson & Johnson, Purdue Pharma, and 11 other opioid manufacturers. The case accused the companies of having employed deceptive marketing tactics for opioid products, thereby perpetuating the nationwide opioid crisis. With all the documents available digitally through the UCSF Library, Gac and Yakubi could work virtually and in tandem during the pandemic lockdown.

At the time, most of the trials against opioid drug manufacturers were still underway. Many verdicts had yet to be declared. The Oklahoma case, decided in the state's favor in 2019, “was one of the first big decisions ever made, even at the state level, and we were able to dig into it,” says Gac, PharmD '21, now a fellow at the U.S. Food and Drug Administration.

While the document cache was slim, it was rich in information. From emails in which executives floated marketing plans targeting veterans to announcements that incentivized pharmacists to ignore concerns about filling too many opioid prescriptions, the documents laid bare the profit-driven intentions and willful negligence of the opioid industry. They revealed a problem that scholars, politicians, and the general public were just beginning to understand and that has contributed to the death to date of more than 600,000 Americans.

Under the supervision of Dorie Apollonio, PhD, MPP, a professor of clinical pharmacy, Gac and Yakubi went on to publish the first studies of opioid industry practices grounded in materials from the collection, which today boasts more than 3 million documents. Looking back, the two see that they were just scratching the surface of a trove that holds vast scholarly potential for researchers studying topics ranging from the legalization of psychedelics to the appeal that vaping products hold for young people to the power of authority figures in the workplace. “There is an endless supply of information in that archive,” says Yakubi, PharmD '21, now a resident in oncology pharmacy at UC Davis.

What's more, the documents present an opportunity to prevent future drug industry injustices by allowing researchers to look at the opioid crisis through the eyes of those at the center of commercial wrongdoings.

## From tobacco to opioids, UCSF has a long history of documenting industry practices

Established two decades ago to house millions of documents that surfaced from lawsuits against the tobacco industry, UCSF's Industry Documents Library is a rich repository of sources that reveal the inner workings of various commercial sectors, including fossil fuels, chemicals, pharmaceuticals, and food. Research into the tobacco files, much of it led by UCSF's Center for Tobacco Control Research and Education, has provided unprecedented insight into that industry's cynical tactics and helped foment sweeping changes in tobacco laws. Additional studies have exposed troubling practices in other industries as well.

It was an opportunity to work in the tobacco archives that first brought Apollonio to UCSF as an American Legacy Foundation postdoc two decades ago. As a master's student at Harvard, she had researched syringe exchange programs, and as a doctoral student at UC Berkeley, she had studied tobacco industry lobbying. Since joining the School of Pharmacy faculty in 2006, she has investigated topics ranging from the way the sugar industry obscured the health dangers of sucrose to how the use of tobacco and recreational cannabis products overlap. “My interest in substance use goes way, way back,” Apollonio says.

Through her research, she developed deep relationships with the archivists at the helm of the Industry Documents Library, who first encouraged her to dig into their holdings from the drug industry five years ago. At the time, the materials had received little scholarly attention.

But Apollonio needed students to help, and most showed little interest in documents research – a field that is just now gaining traction in pharmacy. As she was about to give up, Gac and Yakubi walked into her office and were instantly enthralled with the idea. “It was a miracle of timing,” she says.

## Pharmacy students make disturbing discoveries



Gac and Yakubi could barely contain their excitement when Apollonio first suggested that they explore the internal communications of some of the biggest players of the pharmaceutical industry – and biggest culprits in the opioid epidemic. “If I don’t do this project now, I may never have an opportunity like it outside of pharmacy school,” Yakubi recalls thinking.

Apollonio’s decades of experience in the tobacco archives gave the team a running start. Gac and Yakubi moved through the files quickly – in part because they weren’t doing much of anything else during the pandemic lockdown, but also because the material was so captivating. Working methodically, they identified core themes, such as how companies sought to target children and other vulnerable groups, manipulate statistics, and downplay opioids’ addictive properties.

They found, for instance, that Johnson & Johnson actively used ghostwriters to write academic papers that both overstated the efficacy of opioids and downplayed their addictive properties. In fact, the company designed studies and drafted entire journal manuscripts internally before sending the papers to scholars who were later named as primary authors. Often, those individuals were prominent professors who received sizable consulting fees in exchange for the use of their names.

In another example, a social media networking site called “Growing Pains,” which was funded by Janssen and Medtronic, seemed to the researchers designed to market prescriptions to teens with chronic pain.

Both students can recall key moments, as they sorted through the files, when they made disturbing discoveries. For Gac, it was reading the internal marketing plan for OxyContin and realizing that executives had pulled not only sales strategies but also slogans directly from Big Tobacco. For her part, Yakubi was astounded by emails revealing that companies had targeted Afghan war veterans, a group that is already at high risk for substance misuse. Leaning into the population’s emotional vulnerability, marketing executives sought to make veterans and their physicians believe that opioids were the only recourse to treat trauma.

Federal agencies like the Department of Veterans Affairs and the Department of Defense were identified as “strategic customer segments” by Janssen. Executives from Purdue Pharma lobbied for federal legislation like the Military Pain Care Act of 2008, which called for all active military personnel, veterans, and their dependents to be preemp-

tively and regularly assessed for pain. And slides from a 2012 Janssen training program encouraged public relations specialists to use slogans like “those who have served, need to be served” as a means of encouraging doctors to prescribe more opioids to veterans coming home from Iraq and Afghanistan.

“That one bothered me because my parents were affected by the war in Afghanistan,” says Yakubi, who is the child of Afghan refugees. “I could see that kind of methodology working so efficiently within my community, as well.”

A large part of what made the marketing techniques so problematic was that many campaigns were unbranded, meaning it wasn’t always clear that companies – which stood to profit from sales – had paid for the endorsements. Plans for a 2008 unbranded campaign orchestrated by Janssen said outright that the ideal outcome of the initiative would be for primary care providers to “state that they will be more aggressive in their treatment and use more opioids.”

**“I’ve read industry documents for a long time, and I should stop being shocked, but I always end up finding a moment where I’m still shocked by what someone has written down.”**

<Dorie Apollonio, PhD, MPP>

Even Apollonio, who had made her fair share of startling discoveries over the years, remembers leaving meetings with Yakubi and Gac feeling aghast. “I’ve read industry documents for a long time, and I should stop being shocked,” she says, “but I always end up finding a moment where I’m still shocked by what someone has written down.”

## Setting the stage for a burgeoning new field

Before long, the team realized they were looking at enough material to produce more than one – possibly as many as three or four – substantial academic papers. Those publications laid the groundwork for Apollonio’s next group of students.

Using Gac and Yakubi’s work as a model, four current third-year pharmacy students, including Clever Chiu and James Chhen, dove into a case involving the national pharmacy chain Walgreens. Focusing on specific retail spaces enabled them to ask new questions, like what role distribution centers might have played in enabling the opioid crisis, and whether issues of negligence spanned the entire company or were specific to individual stores.

Chiu was struck by what the documents revealed about the behavior



# TARGETING KIDS, VETERANS, AND OLDER ADULTS

*Finding Relief: Pain Management for Older Adults* 12.29.2008 FINAL  
Video Script

8

VIDEO	AUDIO CONTENT	COMMENTS
Walking, looking out at horizon with Vets hat on	It was during his real-life service in the Vietnam war that Byron first injured his back...training as a paratrooper.	:07
	For years, he worked through chronic back pain. He even ran his own business servicing heavy aquariums.	:06
	Meeting with Dr. Gallagher	His efforts to self-medicate were not a success. Eventually Byron found his way to the V.A. - and a pain management center. With his doctor, he started setting realistic goals.
	Byron	7/2:35:09-:12 The first thing I had to do, was to get my pain to a manageable level.

## Scripts for Vets

Opioid manufacturers sponsored unbranded campaigns positioned as public health or disease awareness initiatives to promote opioid use among military veterans and older adults. These are video script segments from one such campaign.

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Confidential

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Pain Non-Branded Campaign\_ROUND2\_MTC

- Physicians report many patient types as undertreated. These include: the elderly, younger patients, post-operative and post-trauma patients, and new patients

Attempt to include these patient types in the undertreatment Message

## Media Outreach Initiatives

Reaching out to: **Youth**

- reach early: elementary school level; via respected channels, e.g., coaches
- deliver a practical message: Pain is your body telling you something important.

Reaching out to: **Returning Veterans**

- where do they get their information about pain management
- change the paradigm of stoicism: the positive side of pain management

Reaching out to: **Media**

- capture venues that the media want to cover, e.g., art created by

Slide 5 of 7

## Bad Influencers

Opioid manufacturers sought to recruit coaches and school nurses to encourage kids to use opioids. The slide at left is from a meeting of the Pain Coalition, a group of leaders in pain management and Janssen professionals that aimed to influence how children, veterans, and other vulnerable groups perceive pain. The document at the far left is from an internal Janssen presentation that identified target groups for an unbranded initiative.

# PAYING PHYSICIANS TO PROMOTE PRESCRIBING

Tapentadol Team Status - 6/24/2009 - Acute Pain Publications

**EXHIBIT**  
Deem-Eshleman  
6  
1/25/19

Project Title	Author	Journal	Past Steps	Current Status
Acute Publication #3 (Job # 01ORTPUB-08-03625) Pain pathways and the mechanisms of analgesia	Charles Argoff	Journal of Family Practice	<ul style="list-style-type: none"> <li>Conference call with Dr. Argoff 12/3</li> <li>Outline sent to Dr. Argoff for review 1/30</li> <li>Outline approved by Dr. Argoff 2/8</li> <li>Follow-up call with Author 2/26</li> <li>1st draft sent to author 4/16</li> <li>2nd draft with author 5/15, approved draft with minor</li> </ul>	<ul style="list-style-type: none"> <li>Revised draft with alternative journal target sent to Dr. Argoff</li> </ul>
Acute Publication #4 (01ORTPUB-08-03284): Appropriate Pain Management: Matching the right drug and dose to your patient's pain	Hill Mc...	Mayo Clinic Proceedings		

Greetings and Question - Message (HTML)

From: Heins, James James.Heins@pharma.com  
 Subject: Re: Greetings and Question  
 Date: October 23, 2014 at 6:24 PM  
 To: Charles Argoff pargoff@optonline.net  
 Cc: Barbarotto, Gina Gina.Barbarotto@pharma.com

Great. Thank you

Sent from my iPhone

On Oct 23, 2014, at 6:00 PM, "Charles Argoff" <pargoff@optonline.net> wrote:

Excellent  
 Well done  
 I have no suggested changes

Sent from my iPhone

On Oct 23, 2014, at 4:04 PM, "Heins, James" <James.Heins@pharma.com> wrote:

Here is the press release and the note I sent yesterday. I apologize if you didn't receive it. Can you please confirm receipt?

## Ghostwriting

In many cases, opioid company employees designed, wrote, or revised studies and then sent them to listed authors for review. Above is a partial list of manuscripts that Johnson & Johnson tracked for publication in academic journals. At right is an email from a neurology professor at Albany Medical College approving his quote in an opioid-related press release drafted by a Purdue Pharma public affairs director. Researchers noted that the professor, Charles Argoff, MD, received over \$1.6 million from opioid makers and other drug companies between 2013 and 2021.

Thanks for jumping on the call this morning to discuss the ISP (INSYS Speaker Programs), which we will be starting in the next 6 weeks. We have to start our planning now with these programs. Make sure that you prioritizing the physicians you want at these programs (high decile) and where and when will be the best way to impact them.

## Bribing Doctors

The archivists at UCSF and Johns Hopkins University also uncovered troubling tactics. A speakers bureau launched by the pharmaceutical company Insys was at the core of the federal trial against Insys executives, who were convicted of conspiring to bribe doctors. These documents provide a window into the company's aggressive tactics to increase sales. For example, one is from a sales manager instructing his team to prioritize speaker candidates who are "high decile" – the company's top prescribers of its opioid product.

program for your district is: \$4,000. Your Q2 Budget is: \$80,500  
 In compliance with the speaker bureau SOP, in order remain active, all active speakers complete 2 programs per year. The following fall who were not scheduled programs in Q1 and are not tracking to requirements.  
 ectly if you have any concerns; in the meantime, we will add Speaker Status Updates" email. This should assist you with us.

All documents are available at: industrydocuments.ucsf.edu/opioids



## Enticing research possibilities, in academia and beyond

of individual store managers in response to company incentives that rewarded teams for distributing more opioids. “Store managers were giving bonuses to pharmacists who were filling more prescriptions,” he says, meaning the pharmacists had little motivation to flag problematic patterns of substance use.

In fact, the group found that pharmacists would be singled out and subjected to disciplinary action for raising suspicions. In internal complaint filings, a Walgreens corporate employee firmly reprimanded a pharmacist after she raised concerns about the quantities of opioids prescribed by her store. “No, we will not refuse to fill scripts for large quantities,” the email read. “You are a pharmacist not the C2 [narcotics] police.”

Chiu was floored: “I was just like, ‘Wow, I can’t believe they’re writing these things.’”

### A document pipeline opens

Since Gac and Yakubi first dove into the 500 documents in March 2020, the archive has veritably exploded in content and use. In 2021, the UCSF Library forged a partnership with Johns Hopkins University (JHU) to help manage and facilitate engagement with the Opioid Industry Documents Archive (OIDA), which is now its own entity. “We’ve had a lot more help,” says Rachel Taketa, MLIS, of the collaboration; a processing and reference archivist at UCSF, she has worked closely with Apollonio and her students.

Recently, Kate Tasker, MLIS, director of the Industry Documents Library, and Caleb Alexander, MD, MS, a professor of epidemiology and of medicine and the OIDA lead at JHU, led the charge to collect materials from numerous opioid settlements that have taken place around the country. They’ve reached out to attorneys general in Massachusetts, Minnesota, New York, and other states to ensure that documents are properly preserved.

“Sometimes, internal company documents that are turned over during the discovery phase of lawsuits become public, but historically, the vast majority either go back to the company, get shredded,...or get deleted,” explains Tasker. “So it’s really significant for these discovery documents to be made public.”

“I guess efforts to get documents to go public finally reached the right ears,” says a relieved Taketa, who also credits Stanton Glantz, PhD, the retired UCSF professor seen by many as the founder of the tobacco industry archives, with having written an influential op-ed about the public’s right to know the contents of settlement disclosures.

Thousands of new files are added to OIDA every month, and another 10 million or more may be coming down the pipeline. With every new acquisition, the UCSF and JHU team must diligently comb through each file to ensure that sensitive information is redacted and that the documents are thoughtfully organized. The library recently won a prestigious award for those efforts. “This isn’t just a WikiLeaks-style project where we’re...throwing documents on the internet,” says Tasker.

She and her JHU colleagues hope that such a wealth of untapped information will draw in new researchers – including from beyond the walls of their own institutions.

The archive has limits, of course. It reflects only internal industry perspectives, for instance, and some material remains inaccessible because of privacy concerns. “I’d be cautious using opioid industry documents exclusively,” says Apollonio. But its takeaways, the researchers say, are invaluable.

Scholars of law and business as well as medicine may gain insights from the material. From questions of legal liability to duties of care to ethical shipping and distribution practices, the range of topics reflected in the archive is vast. “Industry malpractice didn’t start with drugs,” and it won’t end with them, Gac says, pointing to other sectors that have engaged in harmful marketing tactics, like the food, firearms, and social media industries. Beyond academia, journalists and filmmakers have also found the collections fruitful. Their work has increased the public’s awareness of how major companies, like the consulting firm McKinsey, helped to bolster opioid marketing. It has also spotlighted how hundreds of thousands of Americans turned to street drugs when doctors reduced or discontinued their opioid prescriptions in response to the overuse crisis.

For pharmacists, the repository’s contents teach the importance of care and diligence. “The archive has given me a better understanding of the true clinical utility of drugs,” says Yakubi, emphasizing that opioids can and do play an important role in treating pain. Today, Yakubi works with cancer patients, whose need for opioids is undisputed. “We use opioids a lot, but we use them appropriately,” she says. To her, that makes the manipulative tactics on display in the documents that much more nefarious.

Chhen walked away with a new appreciation for the many roles that individuals and groups can play in perpetuating a public health crisis at ground level. “The opioid crisis was multi-factorial,” he says. “It involved a whole group of organizations.”

But there is still more work to be done to prevent future addiction epidemics, says Apollonio – especially on the regulatory side. “They are not doing the job that people hoped that they would do,” she says of laws that predate the opioid epidemic and that penalize unbranded campaigns and other dangerous marketing tactics. “They’ve been kind of a blunt instrument. There’s absolutely no reason that another addictive medication isn’t going to have the same kind of trajectory in the future.”

That’s where internal documents research can be a valuable tool that can lead to meaningful change and help prevent future catastrophes, she hopes. By learning where opioid industry insiders took wrong turns, researchers can help to expose gaps in drug policies, as well as ways in which additional regulatory oversight may be beneficial. As a result, the drug industry might be better positioned to prioritize patient well-being over profits.

“How do you keep them from marketing in problematic ways while still making medications accessible to people?” Apollonio asks.

Going forward, that search for balance – one that appreciates the dangers of deceptive marketing tactics, as well as the fact that pharmaceuticals save lives – will serve as her guide.

# ALUMNI HUB

Meet five recent alumni who are outstanding mentors to a new generation of aspiring health scientists, including teens from underserved communities and trainees who are people of color.

Illustrations by John Jay Cabuay

## SCHOOL OF NURSING

### Amber Bell, MS '19, CNM

#### Returning an Age-Old Vocation to its Roots

As a child, Bell was in awe of her mother's pregnancies, believing childbirth attended by midwives was the "most beautiful thing in the world." She had no idea how rare her mother's experience was. Before the early 20th century, giving birth at home with a midwife – often a woman of color – was common. But as medical education was formalized, doctors touted pain relief to persuade mothers to labor in hospitals, where midwives were unwelcome. In the 1960s and '70s, the women's movement campaigned to train midwives as nurses, resulting in midwifery becoming a mostly white profession. Today, less than 5% of midwives in the U.S. are people of color.

#### RE-DIVERSIFYING

Seeking change, Bell – a UCSF assistant professor of family health care nursing – is one of many people now helping UCSF "do the hard work of re-diversifying the midwifery profession." Co-leader of the Midwifery Mentoring and Belonging Program, founded in 2019 at UCSF and Cal State Fullerton, Bell pairs Black, Indigenous, and people of color (BIPOC) midwifery students with working midwives as mentors and preceptors.

#### TURNING THE TIDE

Traditionally, BIPOC students have struggled at academic medical institutions largely due to racism in classrooms, textbooks, and hospitals. "Consider a Black student walking into a hospital where preceptors are white, but patients are Black. Comments are made about who's having babies – and why. How awful for students to hear preceptors speak poorly of patients who look like your family." The tide, however, is turning. Twelve of 13 students in the program's class of 2023 identify as BIPOC.

#### MIDWIVES AS LIFELINES

"You see the beautiful moments, and then you see utterly devastating moments when babies die unexpectedly. Mentorship becomes a lifeline by offering reassurance that you're not alone. It's having someone who can stand by you. They might not have the answers, but they've been through it."

#### HOPE

When Bell decided to follow her heart into midwifery, she interviewed at top schools and soon discovered that UCSF champions the values she holds dear. "I was blown away by UCSF's commitment to reproductive and social justice." She believes UCSF's dedication will ensure that future preceptors look like the community they serve: "That's the hope."

■ *Katherine Conrad*



## SCHOOL OF DENTISTRY

## Rubin Sorrell II, DDS '21, MPH

### Improving Oral Health in Bayview-Hunters Point

#### NEIGHBOR TO NEIGHBOR

Even before Sorrell was a dentist, the lifelong Bayview-Hunters Point resident was advocating for healthier teeth in his community. In 2015, he created Dental Robin Hood to distribute toothbrushes, toothpaste, and floss to more than 300 local families and to barbershops to disperse. The organization also educates members of his San Francisco community about dental health. Now a nonprofit, Dental Robin Hood partners with the city's public health department to improve oral health for kids and runs a program that has introduced about 50 local high school students to careers in dentistry. Additionally, Sorrell mentors dental students through UCSF's First-Generation Mentorship Program. "I'm just doing what somebody did for me," he says.

#### LIGHTING THE FLAME

As a child, Sorrell rarely saw a doctor who looked like him. He decided to become a dentist after some UCSF dentistry students spoke at a Black Student Union meeting when he was in 10th grade. "It lit the flame," he says. Though his journey was circuitous – Sorrell spent a decade in the military and got a public health master's en route to achieving his dream – he now works in the same Bayview-Hunters Point building where the neighborhood's first Black physician, Arthur Coleman, MD, established a community clinic in the 1960s.

#### A HELPING HAND

"Where I'm from, a lot of people didn't make it to even be my age. I'm no different; I just got lucky. I'm hoping to be that person who helped somebody make it."

■ *Kira Goldenberg*



## Hugo Aguilar, PharmD '20

### Lightening the Load for Future Pharmacists

#### AT YOUR SERVICE

As an oncology pharmacist, Aguilar supports patients and their families through harrowing experiences. But he is just as dedicated to another role: mentoring budding pharmacists. While at UCSF, he helped sustain First Generation to College (FG2C), a UCSF organization that has connected 160 students with resources and professional mentors in their chosen fields since 2018. Once a student participant in FG2C, Aguilar now offers informed advice to aspiring first-generation pharmacists. “I see the value of passing on my knowledge and my experience to others,” he says. “If it’ll lighten their load and help their path become a little clearer, I’m all for that.”

#### A DREAM DEFERRED

Aguilar’s own career goal was clear from the time he got a summer job in high school as a pharmacy clerk. But as the first person in his family to seek higher education, the path to his goal was less clear. He was accepted into a degree program right out of high school but joined the Marines instead. “At the time, I had the fear that I wouldn’t make it – I wouldn’t complete it,” he says. After a four-year tour, he completed college in San Diego before heading to UCSF to achieve his long-held vision. He credits his success to support and guidance from mentors along the way.

#### WITHOUT A MAP

“The whole path was a scary unknown, always having imposter syndrome hanging over my head – not knowing, not hearing firsthand from close relations how things would go. I was always bracing myself for the unknown, every step of the way. I learned early on: Seek mentorship.”

■ *Kira Goldenberg*



**Taia Wu, PhD '23**

## Sharing a Sense of Scientific Wonder

**OPENING DOORS**

In 2018, far from her Washington state home, Wu was a second-year grad student searching for ways to connect with San Francisco when she found A Home Away from Homelessness and began tutoring teenagers struggling with schoolwork. Realizing that the experience helped her as much as the teens, Wu successfully encouraged her UCSF peers to get involved. “I saw that a synergy could exist between UCSF and these kids, where grad students could open doors to research for local students who might not get these opportunities otherwise.”

**A CALMING PRESENCE**

Mentoring taught Wu a lesson she didn't see coming. As she tutored, she saw how stress affected students' ability to learn and recalled how stress had stood in her way. “Math or science is rarely the hard part, it's the emotional context, the ability to tune out the message that you aren't smart enough. As a tutor, I can provide an emotional container where people can become calm enough to think straight.”

**CHANGING WHAT IS POSSIBLE**

“I love mentoring because science is boundless, and these students are not only experiencing it for the first time but also realizing they can build their futures in it. Scientific discoveries change what is possible for society, and we all have the right to find our place in that transformation.”

**LAUNCHED**

Earlier this year, Wu helped a student she had mentored since she was 15 move into her dorm at UC Merced, becoming the first in her family to attend college. Watching students overcome so many obstacles to pursue their dreams reminds Wu of her own path. “I found my place in science because mentors told me [that] exactly who I am is exactly who we need.”

■ *Katherine Conrad*



## Abdikarin Abdullahi, MD '23

### Increasing Equity in Med School Admissions

#### BEING THE CHANGE

The process of applying to medical school was intimidating for Abdullahi, a first-generation student, so he decided to help those following in his footsteps. He created Bridging Admissions, which began in 2018 as a student campaign to pair aspiring doctors with mentors who could guide them through the application process. It has since blossomed: The program has mentored over 1,000 applicants, and it offers about 10 participants annually a \$2,500 fellowship to cover application-related costs, from tech assistance to interview clothes. The vast majority of these fellowship students are accepted at prestigious medical schools, and Abdullahi and his team aim to continue supporting them.

#### REMEMBERING HIS ROOTS

Abdullahi was raised in San Diego. As the child of Somali-refugee parents, he knew firsthand “how lower-income status interfaces with health,” he says. “We relied on Medicaid for our health insurance and Section 8 housing to help make ends meet.” After completing a college-prep program that helped ready him for higher education, he decided to pay it forward, returning to the program as an educator. “That’s when I fell in love with teaching and mentorship,” he says. He sees his career in medicine as another way to increase equity in communities like the one where he grew up.

#### PHYSICIAN ASSISTANCE

“The best part of being a doctor has been all the little moments, just holding a patient’s hand as they’re getting their blood drawn and seeing the comfort it brings them.

It’s empowering – and a reminder that being someone’s physician is an incredible privilege.”

■ *Kira Goldenberg*

## The Light and Shadow of Life

By Vilma Reyes, PsyD

The saying “*Todo tiene solución, menos la muerte*” (“Everything has a solution, except death”) was instilled in every fiber of my being by my courageous parents, who always found a way forward. I am the product of the best of them – their persistent love, sacrifice, and generosity. From my mother, I learned “*Se pone mas agua a la sopa*” (“You can always add water to the soup”) as she shared her heart, her home, and her cooking with our large family. From my father, I learned to find humor in life, to marvel at the depth of the universe and the mind, and to trust in the benevolence of people.

When I was 11, terrorists attacked our family farm in Huacho, Peru. As my family ran away to hide, we saw men with rifles on the roof shooting at us and later heard bombs reducing our house to rubble. We miraculously survived, and my parents fled with me and my three brothers to the U.S., where we sought asylum. To this day, I am in awe of the courage and optimism that experience called for. Over 30 years later, I still recall the shock and horror, as well as my father’s strong hand holding mine, reassuring me that we would be OK. Light and shadow – the *chiaroscuro* of life.

It is no surprise that since 2009, I have devoted my career to child-parent psychotherapy, a method that restores a child’s

sense of security through the parent-child relationship. I am honored to have learned from Dr. Alicia Lieberman, the developer of this model, at UCSF as well as from all the families who have entrusted me with their care. Their stories of overcoming and thriving after experiencing frightening violence and injustice teach and humble me. They echo a similar thread: Relationships are the greatest buffer to mediate harm.

The only thing my father could not find a solution for happened last year, when COVID-19, meningitis, and cancer took down this mountain of a man. To his dying day, he was steadfast with humor and optimism, dreaming of a farm he wanted to buy for his grandchildren. You will still find my mother living in the mountains, her skin weathered, her eyes brimming over with stories, *boleros* in the background, and plenty of hot chicken soup for anyone we bring to her home. I lean on the wise words of my parents, and my career mentors, as I now embark on the great adventure and honor of parenting my two young children with my wife. Light and shadow – the *chiaroscuro* of life.

Vilma Reyes is an associate clinical professor and a psychologist in the UCSF Child Trauma Research Program.

A photograph of a woman with curly brown hair, wearing a white shawl with fringe and a brown sweater, looking out over a coastal landscape with greenery and the ocean. The image is the background for the top half of the page.

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