UCSF MAGAZINE

Summer 2025

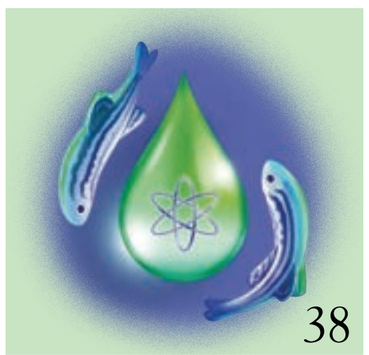
The **Plastic** Within

What scientists are discovering about the plastic inside our bodies

Contents

Experts are alarmed by emerging evidence that microplastics may damage the lungs and other organs.

Chronic pain can be crushing for patients and puzzling for physicians. But new ways to treat it are on the horizon.



A curious mix of AI, chemistry, and zebrafish is advancing the hunt for safer, smarter anesthetics.

For 25 years, a postbaccalaureate program at UCSF has helped aspiring physicians without traditional pathways to medicine, like Iván Piña-Cabanillas, find their future in the field.

COVER AND TOP LEFT ARTWORK/PHOTOGRAPHY: AURORA ROBSON/MARSHALL COLES; MIDDLE LEFT ILLUSTRATION: DANIEL LIÉVANO; BOTTOM LEFT ILLUSTRATION: ANA MIMINOSHVILI; CENTER PHOTO: GABRIELA HASBUN; TOP RIGHT PHOTO: STEVE BABULJAK

The Oscar of science: Stephen Hauser's dogged determination to defeat multiple sclerosis has earned him a Breakthrough Prize, one of science's top honors.

DEPARTMENTS

Science Is a Public Good

It is with immense pride that UCSF celebrates the extraordinary achievement of neuroimmunologist Stephen Hauser, a recipient of the 2025 Breakthrough Prize (page 22). His pioneering work in multiple sclerosis research has transformed our understanding of this devastating disease, shifting the paradigm from symptom management to targeted immune intervention. Through decades of meticulous investigation, Dr. Hauser's team identified the precise immune mechanisms driving MS progression, ultimately leading to treatments that can halt – and in some cases reverse – the course of the disease. This work exemplifies the power of persistent scientific inquiry and the profound human impact it creates.

UCSF Chancellor Sam Hawgood, photographed delivering last year's State of the University Address.

Even as we honor this achievement, we face unprecedented challenges in the scientific enterprise. Federal funding for the kind of research we pursue at UCSF is being eliminated in a rapidly shifting policy landscape, putting formidable pressure on laboratories and investigators across the nation and directly affecting our society. There is deep concern among the UCSF research community. And still our scientists look forward.

Groundbreaking science requires sophisticated technologies, specialized facilities, and teams of brilliant minds working collaboratively over years and often decades. These investments save lives and yield extraordinary returns – every dollar invested in basic biomedical research generates over $8.38 in economic output within eight years. UCSF's numerous contributions illustrate this impact, from Herbert Boyer's recombinant DNA work that launched the field of biotechnology to a new technique that can rapidly detect almost any kind of pathogen. Discoveries like these have been translated into therapies treating millions, have fueled private industry, and have made our country and world a better place.

The Breakthrough Prize is well known for its generous financial recognition, but such awards represent just a fraction of what's needed to sustain the scientific ecosystem.

At UCSF, we don't pursue discovery for prizes or recognition. We do it because a thriving society depends on the pursuit of knowledge, because innovation is essential to meeting our unprecedented global challenges, and because science is a public good worthy of sustained investment.

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

UCSF MAGAZINE
Summer 2025 | Vol. 14 No. 1

EDITOR
Anne Kavanagh

SENIOR CREATIVE DIRECTOR
Audrey Feely

ART DIRECTOR & DIGITAL STRATEGY
Stephanie Koch

SENIOR DESIGN ADVISER
Nada Hansen

COVER DESIGN CONSULTANT
Pentagram

VIDEO PRODUCTION
Walter Zarnowitz

CONTRIBUTING WRITERS
Jess Berthold, Eric Brooks, Carolann Clark, Victoria Colliver, Dora Dalton, Elizabeth Daube, Elizabeth Fernandez, Brandy Ford, Levi Gadye, Kira Goldenberg, Ashley Han, Paula Hermann, Suzanne Leigh, Laura López González, Robin Marks, Jared Marsh, Dana Mathes, Carin Moonin, Jeffrey Norris, Wynne Parry, Jaimie Seaton, Cameron Scott, Sarah C.P. Williams

COPY EDITORS
Dana Cook Grossman, Mark Goldstein

PRINTING
Lane Press

ASSISTANT VICE CHANCELLOR, EXTERNAL RELATIONS
Jane Feledy

EXECUTIVE DIRECTOR, ADVANCEMENT COMMUNICATIONS
Cyril Manning

UCSF Magazine is published twice a year by the UCSF Office of University Development and Alumni Relations.

CONTACT US
UCSF Magazine,
UCSF Box 0248
San Francisco, CA 94143
415-476-3480
alummag@ucsf.edu

WEB
magazine.ucsf.edu

PHOTO: NOAH BERGER

MIX
Paper | Supporting responsible forestry
FSC® C022085

Five Questions for Joanne Chun

Joanne Chun, PharmD '93, PhD '96, leads a new master's degree program – the first of its kind in the nation – focused on AI's transformation of drug discovery and development. The inaugural cohort in Artificial Intelligence and Computational Drug Discovery and Development (AICD3) started in fall 2024.

By Kira Goldenberg

What makes AICD3 so vital?
The way we approach medicine, health care, and research is really changing. Traditionally, scientific research started with a hypothesis. Now, the data can tell us where to start. I tell my students, 'The job you might be doing in 10 years might not exist yet.'

How will AI-based research benefit patients?
Humans can see three-dimensional things, but what about 500 dimensions? AI can recognize patterns that we could never see on our own. In areas like precision health, this means we can analyze vast datasets and fine-tune predictions to deliver more personalized treatments. It's a game-changer for patients.

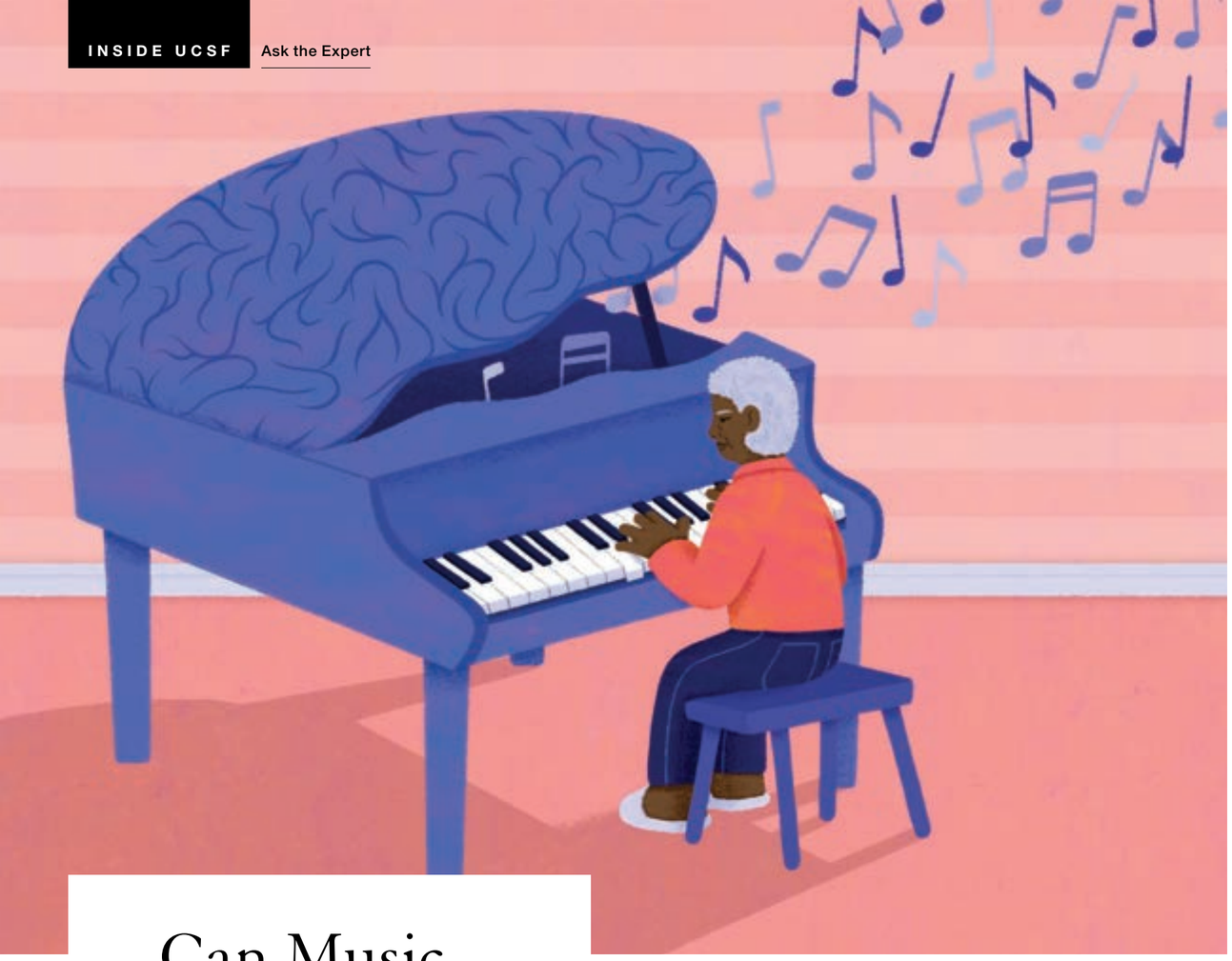
What do your students learn?
They study matters like machine learning, deep learning, pharmacokinetics, real-world data analysis, omics, and AI ethics. Then, they apply those skills in capstone projects with industry partners or within UCSF labs. Some will be developing a chatbot that helps access and interpret FDA drug labels. Others will analyze breast cancer patient data to uncover how race, prior treatments, or socioeconomic factors influence survival. Still others will train AI models to improve drug discovery.

PHOTO: ANASTASIA SAPON

What sort of students should attend this program?
We're looking for curious, motivated individuals who want to make a difference in drug discovery and development and who are excited about the potential of AI and machine learning. Our goal is to develop leaders who can think across disciplines and translate that knowledge into real-world impact.

How did you become such a leader?
I love learning and solving puzzles. To me, science is one big puzzle that pulls together ideas from different fields. With my background in pharmaceutical sciences, pharmacy, and computer science, I realized just how powerful it is to be able to think across disciplines. That's why I'm so proud to be part of this program – we're building something I wish had existed when I was in training.

Fun fact: Chun speaks more than five languages, including Portuguese, Spanish, and Cantonese, and a few coding ones like Python and JavaScript. She also knits, including the sweater she's wearing!



Can Music Benefit Our Brains?

Here's how music may help flex our neurons.

We asked UCSF's Julene Johnson, PhD, how music promotes healthy brain function. Johnson is an expert in cognitive neuroscience and music and a professor at the UCSF School of Nursing's Institute for Health and Aging. She also plays the flute, as well as a mean kantele – a plucked string instrument from Finland.

By Brandy Ford | Illustration by Paige Stampatori

What's the connection between music, language, and memory?
When I was a PhD student at the University of Texas at Dallas, I worked with the local Alzheimer's Disease Research Center studying how people with that condition retain musical memory. Sometimes, older adults can remember how to play music, read music, or sing better than they can speak. I learned that the brain's neural networks supporting music processing and production are slightly different from those supporting language production and understanding.

We know that music can stimulate language networks. For example, the melody in poetry or song lyrics can serve as a cue to help produce speech in people who have experienced a stroke. Research suggests that during speech rehabilitation, different parts of the brain can help take over language production.

How does musical improvisation boost brain health?
When you're improvising, you have to let go and be flexible. So some of the control and planning parts of the brain actually deactivate, and the more creative parts of the brain activate.

I'm collaborating with Charles Limb – a neuroscientist and the chief of otology, neurotology, and skull base surgery at UCSF – to study how piano improvisation training affects older adults. Though challenging, such training offers an accessible way to explore music, helping people practice cognitive flexibility while also learning fun and interesting new skills. Ultimately, we hope it encourages older adults to keep pursuing challenging cognitive activities throughout their lives. Music is not only pleasing and beautiful, but it also puts the brain to work.

Why the piano?
Learning basic piano skills is relatively easy, allowing study participants to improvise more quickly than they might on other instruments. Our participants are beginners with less than three years of piano experience. Many don't know how to read music, so we encourage them to learn by ear and experiment with piano improvisation.

Previously, I conducted a large clinical trial, with roughly 400 older adults living in San Francisco, on the benefits of singing in a choir. We found that group singing can reduce people's loneliness and significantly increase their interest in life. However, participants did not experience any cognitive changes. The benefits were social and psychosocial. On the other hand, piano training is linked to improved brain function, especially in problem-solving and attention.

How does playing music affect our brains differently from listening to music?
I often make the analogy of playing football versus watching it on television. Both are interesting, but the folks playing football are more committed physically, cognitively, and emotionally than those just watching it on TV. Also, we know that the more meaningful music is to someone, the more mentally engaged they'll be. For example, in people living with Alzheimer's, musical memory is often preserved even in the later stages of the disease.

Is listening to Beethoven more stimulating than listening to the Rolling Stones?
I know people who relax to rock music! The idea that there's a relaxing type of music is just not true. It comes down to how someone experiences music – what they find calming or energizing. Musical tastes are very personal. There's not some magical composition that has health effects. Music interacts with individuals' life histories, their experiences growing up, and what's meaningful to them.

How does music help people living with dementia and their families?
It can be a source of deep meaning and identity and can even help reinforce relationships and social connections. Integrating music into their everyday life brings people joy, facilitates relaxation, promotes bonding, and encourages singing and dancing. I am working with the AARP's Brain Health Action Coalition to promote music throughout the dementia journey.

Theresa Allison, a geriatrician at UCSF, is studying the effects of music in home settings for people living with dementia and their care partners. She has found that when older adults listen to music that is meaningful to them, they enjoy an improved quality of life.

5 WAYS TO MAKE LIFE MUSICAL

Share musical memories with friends and family.

Make your own music, whether you play an instrument or sing in the shower.

End your day with music to relax or fall asleep.

Build listening to or making music into your lifelong daily routines.

Get physical! Dancing, clapping along, and even swaying to a rhythm can connect you more deeply to music.

Can music be used to treat other cognitive challenges?
Yes, just as medications are prescribed for specific symptoms, music can be tailored to address different needs. For example, if a patient comes to our clinic and reports feeling lonely, their doctor might prescribe group singing. If a patient is concerned about their cognitive abilities, their doctor might recommend piano training.

So, does music have other health benefits beyond the brain?
Absolutely. If I had a crystal ball, I'd love to see music-based interventions in many different areas of health care. There's a wonderful story about an opera singer living with cystic fibrosis, a genetic disorder that can make breathing difficult. She started a nonprofit called Breathe Bravely, which helps others with cystic fibrosis discover the transformative connection between singing and breathing. It's really inspiring, and I'd like to see more of that in the future. I would also like to see music being used to help heal communities that have experienced trauma, whether from violence or chronic underinvestment.

7 Ways UCSF Is Exploring the Eyes

Researchers and clinicians are advancing the science of sight to ensure the health of these complex and crucial organs.

ANTIBIOTICS AND THE EYE'S MICROBIOME

The eye has its own delicate microbiome – a community of beneficial bacteria that plays a role in eye health. But common antibiotics can disrupt this balance. Researchers are studying how antibiotic use alters the eye's microbiome and contributes to antibiotic resistance, offering new insights into protecting vision at the microbial level.

Can light help stop seizures?

The human eye converts light into electrical signals that the brain can process. Researchers are drawing on this principle to treat epilepsy using optogenetics – a technique that controls neurons with light – to explore whether light-sensitive proteins can reduce seizure activity. This approach could lead to light-based treatments for neurological disorders.

STOPPING DIABETES-RELATED BLINDNESS

Diabetic retinopathy is a leading cause of blindness, but early action can prevent it. Researchers are now developing a tool to predict the disease's progression. By identifying key risk factors, such as age and blood sugar levels, physicians can intervene sooner, preventing irreversible vision loss.

Vision care that's accessible to all

Routine eye care is out of reach for many unhoused people, yet good vision is crucial for safety, mobility, and well-being. Since 2017, UCSF's Ophthalmology Shelter Clinic has provided free exams, glasses, and treatments for those in need.

Using stem cells to fight vision loss

Macular diseases and inherited retinal disorders slowly destroy vision and can lead to blindness. Researchers are using stem cell models to study how these conditions progress and to test potential treatments. Their work is ushering in more effective therapies to preserve sight.

AI THAT SPOTS EYE INJURIES FASTER

Retinal hemorrhages – bleeding in the back of the eye – can result from head trauma, high blood pressure, diabetes, or other conditions, but they're often hard to detect. Scientists are now training AI to analyze thousands of CT scans, building an algorithm able to flag possible hemorrhages with unprecedented speed and accuracy.

BONUS EYE-OPENING FACT:

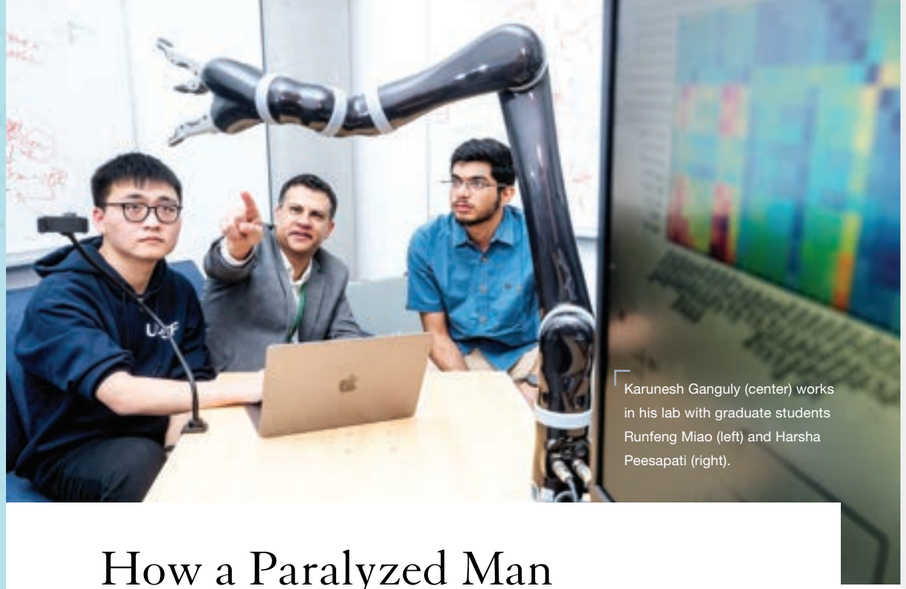
A UCSF-trained ophthalmologist pioneered the drug that became Botox

Starting in the 1960s, ophthalmologist Alan Scott, MD '56, spent years developing an injectable treatment to correct eye muscle disorders without surgery. The drug – Oculinum – was FDA-approved in 1989 and later acquired by Allergan, which rebranded it as Botox. Today, it's one of the most widely used drugs, with both medical and cosmetic applications. "I think that's a charming, slightly frivolous use," Scott told the *San Francisco Chronicle* in 2002 about its wrinkle-reducing appeal.

FIRST CENTER FOR RARE DISORDER

Gould syndrome, a rare genetic disorder, can cause serious eye defects. A surge in genetic testing has revealed that the syndrome – named for UCSF geneticist Douglas Gould, PhD, who discovered the mutation – is more common than once thought. Now, UCSF has opened the world's first clinical center dedicated to the disease.

ICONS: FLATICON.COM



Karunesh Ganguly (center) works in his lab with graduate students Runfeng Miao (left) and Harsha Peesapati (right).

How a Paralyzed Man Moved a Robotic Arm with His Thoughts

Researchers at UCSF have enabled a man who is paralyzed to control a robotic arm that receives signals from his brain via a computer.

He was able to grasp, move, and drop objects just by imagining himself performing the actions.

The device, known as a brain-computer interface (BCI), worked for a record seven months without needing to be adjusted. Until now, such devices have worked for only a day or two. The new BCI relies on an artificial intelligence model that can adjust to small changes that take place in the brain as a person repeats a movement – or, in this case, an imagined movement – and learn to perform the action in a more refined way.

"This blending of learning between humans and AI is the next phase for these brain-computer interfaces," says Karunesh Ganguly, MD, PhD, the Marjorie B. Hines Professor of Neurology. "It's what we need to achieve sophisticated, lifelike function."

Hungry Fat Cells Could Someday Starve Cancer to Death

PHOTO: NOAH BERGER

Liposuction and plastic surgery aren't often mentioned in the same breath as cancer. But they are the inspiration for a new approach to treating cancer that uses engineered fat cells to deprive tumors of nutrition.

Scientists at UCSF used the gene-editing technology CRISPR to turn ordinary white fat cells into so-called beige fat cells, which voraciously consume calories to make heat. Then they implanted the engineered cells near tumors, the way plastic surgeons inject fat from one part of the body to plump up another part. The beige fat cells scarfed up nutrients, starving most of the tumor cells to death. The approach worked even when the fat cells were implanted in mice far from the sites of their tumors. The fact that the injection procedure is common could speed the concept's development as a new form of cellular therapy.

Recommended:

Books, Videos, & Podcasts

READ

On Muscle: The Stuff That Moves Us and Why It Matters

Bonnie Tsui's latest book is a "celebration of musculature ... vivid, thought-provoking, undeniably fascinating," according to *Kirkus Reviews*. She researched it by visiting UCSF's Anatomy Learning Center with Amber Fitzsimmons, DPTSc '13, chair of physical therapy, as her guide, uncovering how the perception of muscle shapes cultural ideas of power and beauty.

WATCH

Finding HIV: A Swipe in the Right Direction

What do Tinder and the immune system have in common? Both swipe to find the perfect match, but instead of love, the immune system is hunting virus-infected cells. UCSF PhD student Sophia Miliotis explains it all in her clever, three-minute Grad Slam talk – and made history as UCSF's first-ever winner of the UC-wide competition. Watch it now on UCSF's YouTube channel.

LISTEN

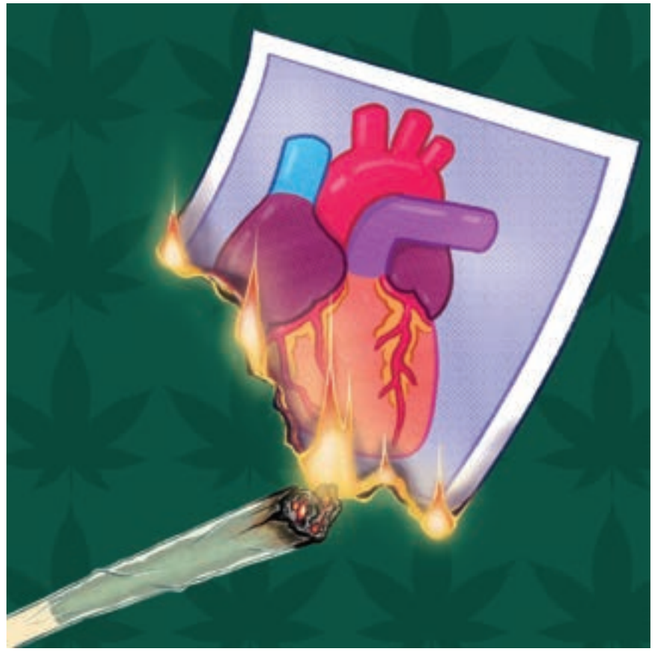
The Health Technology Podcast

Curious about the future of health care? This UCSF Rosenman Institute podcast explores big ideas like at-home tests for early cancer detection and the next wave of weight loss treatments. Hear insights from the front-line innovators and entrepreneurs tackling health's biggest challenges.

How Does Marijuana Affect Our Bodies?

UCSF experts shed light on persistent cannabis myths.

By Carin Moonin | Illustration by Farah Hamade



Marijuana has been a hot topic for years, but one often clouded by misperceptions. Many turn to it as a perceived panacea, hoping it will address health issues or enhance their well-being if other options have fallen short. But what scientists are learning about weed's health effects might come as a surprise.

MYTH #1: Marijuana smoke isn't as bad for me as cigarette smoke.

Although research studies on marijuana lag behind those on tobacco, smoke is still smoke, and it's never beneficial. Breathing any smoke can lead to cardiovascular disease or exacerbate respiratory conditions like asthma, say UCSF experts.

"There's a misconception that marijuana, being more 'natural' than highly processed cigarettes from tobacco companies, produces smoke that is less toxic," says Matthew Springer, PhD, a professor of cardiology. "But that's not the case. It's nasty stuff, with benzene, formaldehyde, and heavy metals you don't want to be exposed to, among many other substances."

MYTH #2: Edibles are safer than smoking marijuana.

"There's a mythology, popularized by the comedians Cheech and Chong in the 1970s, that marijuana is a benign product that doesn't cause significant intoxication. That's unrealistic today, with commercialized cannabis," says Laura Schmidt, PhD, MSW, MPH, a professor of health policy studies.

"We've never had cannabis this potent or abundant. We've never had cannabis commercialized or packaged like food. Many cannabis edible products mimic junk food. Bright colors, cartoon characters. They'll just change the name: Molly Ranchers versus Jolly Ranchers," she says.

Edibles, while lung-sparing, pose their own health harms, especially for the impatient. People who smoke marijuana feel the effects fast, so they know when they've had enough. But edibles take half an hour or more for the effects to kick in.

"Someone will take an edible and five minutes later they'll say, 'I don't feel it – I'm going to take more,' and end up taking way too much. They rush to the emergency room with panic, palpitations, and nonstop vomiting," Springer says.

MYTH #3: Marijuana isn't going to harm me long-term.

Even in less traumatic situations, experts are finding connections between marijuana and cardiovascular disease. UCSF research shows that marijuana interferes with the proper functioning of blood vessels and affects endothelial cells, which line blood vessels and are crucial for healthy circulation.

Leila Mohammadi, MD, PhD, lead clinical investigator for UCSF's CANDIDE study of cannabis use, has found that regular cannabis smokers have vascular issues similar to those of tobacco smokers, including atherosclerosis and endothelial dysfunction – early indicators of cardiovascular conditions like hypertension.

The study has also found that people who didn't smoke anything but did use marijuana edibles also had problems with their arteries; however, their blood didn't cause the same damage to lab-grown endothelial cells, suggesting that smoking and edibles affect blood vessel function in different ways.

"Using cannabis makes a 30-year-old's blood vessels resemble those of a 60-year-old," Mohammadi says.

MYTH #4: Marijuana can't hurt me since I'm young.

Our brains continue developing until about age 25, says William Burrough, MD, MPH, an assistant professor of pediatrics. It's one reason why substance use hits adolescents differently than adults.

"IQ tests are lower in people who use marijuana heavily, particularly during adolescence. Studies using brain scans have shown teenagers who frequently use cannabis have reduced brain matter and activity in the areas crucial for decision making and planning," he explains.

Fortunately, the brain is adaptable throughout life, Burrough adds. "While repeated cannabis use during adolescence can cause long-lasting changes, stopping or reducing it can lead to recovery and improvement in brain function. The body's ability to heal is remarkable."

MYTH #5: I can't overdose on marijuana.

Marijuana doesn't impact the body the way fentanyl and other opioids do, but people can become so intoxicated from it that they experience anxiety, paranoia, hallucinations, and sometimes psychosis, Burrough says.

"Anyone can be affected by substance use, but if you have a family member who has schizophrenia or psychosis, it can be particularly risky," he says.

MYTH #6: I can use marijuana to self-medicate.

"Many people are drawn to marijuana because it's easily accessible, and they can control how they use it," says Suzaynn Schick, PhD '01, an associate professor of occupational, environmental, and climate medicine. "If you've had bad experiences with Western medicine, that's appealing. I hear a lot of magical thinking around marijuana, often from people who feel they don't have better, safer alternatives."

Nhung Nguyen, PhD, PharmD, an assistant professor of general internal medicine, explains that although people may use cannabis to deal with health concerns like depression or anxiety, we still don't have clear evidence to support the presumed benefits. "It's hard to make conclusions about the effects without standardized product regulation."

Springer says research on the purported benefits of marijuana for medicinal purposes is an emerging and evolving field. But, he adds, "clearly, if a cancer patient can't keep food down, can't take oral drugs, and feels awful, and this is what makes them feel better, then to me that's a beneficial use."

Burrough believes we could all benefit from being less dismissive about each other's points of view on pot. "These conversations get so caught up in people's personal feelings. There are legal, recreational, and medicinal aspects. It's a nuanced topic – never all or nothing," he says. "Maybe cannabis isn't as harmful as some other potential substances. At the same time, using it too often can lead to real harm. Ideally, I'd want people to talk to their doctor about their use."

MYTH #7: I can't talk to my doctor about marijuana.

Some people may fear they'll be stigmatized or shamed when talking to a provider about marijuana, but many clinicians are open to these discussions, says Meredith Meacham, PhD, MPH, an assistant professor of psychiatry and behavioral sciences. "They try to have nonjudgmental, open-ended conversations. They'll ask permission of a patient, like, 'Is it OK if we talk about cannabis? Tell me about your use. What do you like or not like about it?'"

If patients are debating between using marijuana or taking a drug for depression, for example, says Burrough, "I tell them we have strong evidence from randomized controlled trials showing which antidepressant medications are effective for moderate to severe depression and anxiety. We know what's in them. They are regulated and monitored."

MYTH #8: I can quit anytime.

Quitting marijuana isn't always as easy as people think – especially for heavy users. Those who use cannabis daily may try to stop but, within a day or two, experience heightened anxiety, disrupted sleep, and poor appetite. If that's happening, check with your provider – it's a sign you may have developed a cannabis use disorder.

Treatment options can include behavioral therapies to better understand triggers and teach alternative coping skills, medications to treat uncomfortable symptoms, or interventions to address underlying or co-occurring conditions like anxiety or depression.

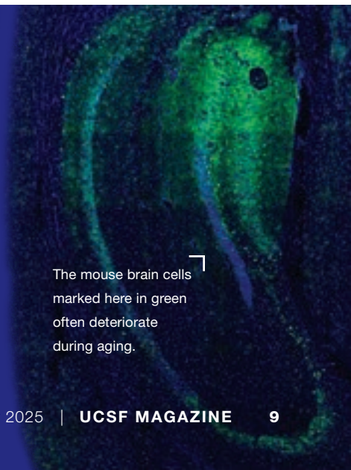
"Many things can be addictive – shopping, gambling, even social media," says Burrough. "Addiction happens when you lose control over that thing, when it's impacting your daily life in negative ways. The good news is, there are ways we can help. Like many treatment plans in medicine, it's often a combination of options, catered to your goals, that leads to success."

The 'Silent' X Chromosome Gives the Aging Female Brain a Boost

UCSF researchers studying aging in mice may have discovered how the female brain remains resilient with age, potentially answering a long-standing question: Why do most women outlive men and retain their cognitive abilities longer?

Females carry two X chromosomes. One of them is ensconced in an edge of each cell called the Barr body, where it can't express many genes, so scientists thought it didn't do much of anything. But the UCSF team discovered that as female mice reach the equivalent of about 65 human years, their "silent" second X starts expressing genes that bolster the brain's connections, increasing cognition.

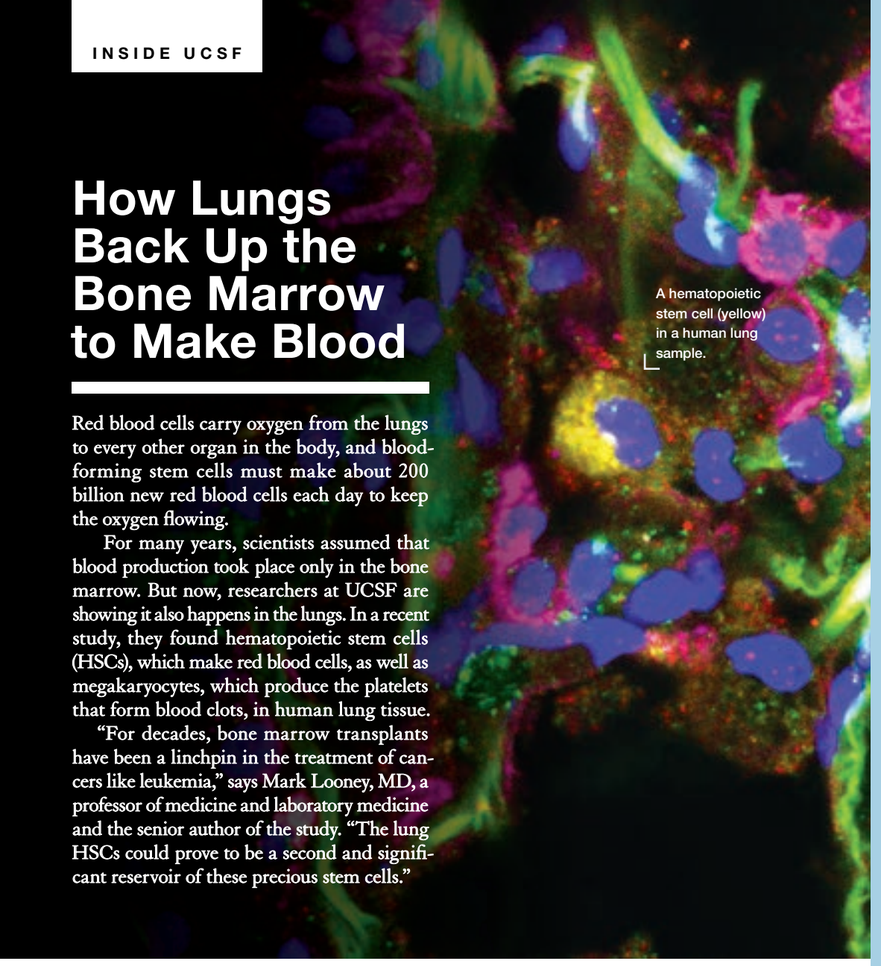
"In typical aging, women have a brain that looks younger, with fewer cognitive deficits compared to men," says Dena Dubal, MD, PhD, UCSF's Coulter Professor of Aging and Neurodegenerative Disease and the senior author of the new paper. "These results show that the silent X in females actually reawakens late in life, probably helping to slow cognitive decline."



The mouse brain cells marked here in green often deteriorate during aging.

IMAGE: GADEK ET AL., SCIENCE ADVANCES

How Lungs Back Up the Bone Marrow to Make Blood



A hematopoietic stem cell (yellow) in a human lung sample.

Red blood cells carry oxygen from the lungs to every other organ in the body, and blood-forming stem cells must make about 200 billion new red blood cells each day to keep the oxygen flowing.

For many years, scientists assumed that blood production took place only in the bone marrow. But now, researchers at UCSF are showing it also happens in the lungs. In a recent study, they found hematopoietic stem cells (HSCs), which make red blood cells, as well as megakaryocytes, which produce the platelets that form blood clots, in human lung tissue.

"For decades, bone marrow transplants have been a linchpin in the treatment of cancers like leukemia," says Mark Looney, MD, a professor of medicine and laboratory medicine and the senior author of the study. "The lung HSCs could prove to be a second and significant reservoir of these precious stem cells."

Most Children Use TikTok Against the Rules

A new UCSF study finds that most 11- and 12-year-olds use social media despite the platforms' age restrictions, with many showing signs of addiction. Underage social media use was linked to higher rates of depression, eating disorders, ADHD, and disruptive behaviors. Lead author Jason Nagata, MD '13, an associate professor of pediatrics, urges policymakers to prioritize children's health when addressing regulation of social media and advises parents to take an active role: "Parents can create strong relationships with their children by starting open conversations and modeling good behaviors."

Drinking Plenty of Water May Actually Be Good for You

Public health guidelines often recommend drinking eight cups of water a day, and many people assume it's a healthy habit. Now, UCSF researchers have systematically examined the evidence – and their findings support the benefits of staying hydrated.

They concluded that adequate water intake can aid in weight loss and help prevent kidney stones, migraines, urinary tract infections, and low blood pressure.

"For such a common and simple intervention, the evidence hasn't been clear, and the benefits were not well established, so we wanted to take a closer look," says Benjamin Breyer, MD, MAS '11, the Taube Family Distinguished Professor, the Hinman Distinguished Professor, and the chair of urology. "The amount of rigorous research turned out to be limited, but in some specific areas, we found statistically significant benefits," says Breyer, who led the study.

Besides aiding in weight loss, drinking water can help:

- Prevent kidney stones.
- Prevent migraines and recurring headaches.
- Avoid urinary tract infections.
- Control diabetes and blood glucose levels.
- Control low blood pressure.

CELL IMAGE: CONRAD ET AL., BLOOD; WATER: DELMONTE1977

Breakthroughs and Other Buzz

A better test for alcohol-related liver disease: A UCSF study has shown that a new blood test for a biomarker known as PEth could offer a more reliable way to assess alcohol-related liver damage than asking patients how much they drink.

First steps in building human organs: UCSF and Cedars-Sinai scientists have engineered "organizer" cells that guide stem cells to form organ-like structures, including one that mimics a heartbeat. This marks crucial early progress toward building customized human organs from scratch.

Estrogen and progesterone in chronic pain: Female hormones trigger immune cells to release natural opioids, UCSF researchers have found. This process blocks pain signals before they reach the brain. The discovery might lead to new treatments for chronic pain.

Monthly shots control HIV: UCSF researchers have determined that a monthly or bimonthly injection can help HIV patients who struggle with a daily pill regimen to achieve viral suppression, meaning the virus can't be transmitted to others.

One test, nearly any infection: A UCSF-developed genomic test can detect the cause of almost any infection – whether bacterial, fungal, or viral – in one day, using a single sample. The test could serve as an early warning system for pandemics.

The risks of radiation: CT scans could cause 100,000 cancer cases annually, UCSF researchers say. They found the risks are higher than previously thought, especially for infants and children. Reducing unnecessary scans and radiation doses could prevent many future cancers.

Prostate cancer rising: UCSF researchers found that from 2011 to 2021, advanced prostate cancer cases in California surged 6.7% annually. Death rates also stopped declining, likely due to reduced screening after federal guidelines warned against overtreatment of low-grade tumors. The findings underscore the need for early screening while avoiding unnecessary care.

Extended Paxlovid for long COVID: A UCSF study suggests that extended treatment with Paxlovid may help certain long COVID patients. The findings offer hope for people with lingering symptoms, though more research is needed to determine who benefits most.

REM sleep delay tied to Alzheimer's: A UCSF study suggests that taking longer to reach the rapid eye movement (REM) stage of sleep may signal early Alzheimer's. Delays in reaching the dream level of sleep were linked to more memory issues and higher levels of the amyloid and tau proteins implicated in Alzheimer's.

Neuroscience-based reading tool approved: More California schools will soon use a UCSF screening tool called Multitudes to detect dyslexia early. Developed over four years with 15,000 kids, the free screener is bilingual and guides interventions for children with reading challenges.

Turf fields jarring for joints: A UCSF study links artificial turf, especially on older or poorly maintained fields, to increased rates of lower-body injuries like ACL and Achilles tendon tears. Researchers recommend prioritizing natural grass or improving turf maintenance to reduce the risk of injuries.

A potential factor in preterm birth: UCSF scientists have discovered a molecular "timer" in mice that starts early in pregnancy and influences when birth occurs. The finding may help prevent preterm birth in humans and improve early detection of its likelihood.

T cells rewired to calm inflammation: UCSF scientists have designed immune "referee" cells that reduce inflammation without suppressing the whole immune system. The research may lead to better care for patients with transplanted organs, autoimmune diseases, or type 1 diabetes.

Brain evolution clues: UCSF scientists have discovered that fast-evolving regions of human DNA help neurons form more complex connections than is the case in chimpanzees. The findings could offer insights into humans' cognitive evolution and certain brain disorders.

How much B12 do you need? Vitamin B12 levels previously considered normal may not protect older adults from cognitive decline, according to a new UCSF study. The findings might lead to updated guidelines and supplements to better safeguard brain health.

Menopause may worsen MS: Walking, dexterity, and cognitive abilities decline after menopause in women with multiple sclerosis (MS), according to a new UCSF study. The findings raise the possibility that sex hormones could help slow the disease's progression.

CT SCAN: KORTYNA ZUKAUSKAITE/UCSF; ASTROTURF: EKATERINA KOMPALDI

Why Is **Discovery Research** So Important?

Over the past century, public support for science has led to rapid and remarkable milestones in medicine, from extending the average lifespan to decoding the human genome. But will that support be sustained? We spoke with **Grae Davis, PhD**, the Morris Herzstein Distinguished Professor of Medicine and director of UCSF's Kavli Institute for Fundamental Neuroscience. His team advances pioneering brain research and has a pressing new mission: fostering public understanding of science.

By Elizabeth Daube

PHOTO: ANASTASIA SAPON

What is the biggest challenge you face in talking about your work with nonexperts?
When I say I'm a scientist, people usually think of a teacher or a doctor. Everybody's walked into a doctor's office. Everybody's gone to school. Few have wandered into a laboratory.

Astrophysicists have perhaps done the best job communicating their science with the public. Most people know of Carl Sagan or Stephen Hawking. Everybody looks up at the stars. You start putting people in space, and this kind of science becomes part of our common experience. But a biologist or someone engineering on a nanoscale? There's nothing there for most people to identify with.

Just choosing the terms can be tricky. Basic science? Fundamental science?
The problem with "basic" science is it sounds simple, which it absolutely is not. Basic science involves the process of discovery. It's about posing a good question. Whether the answer is positive or negative, you learn something. The best experiments create *more* questions.

The more you know, the more you realize what you don't know, right?
Exactly. The ambiguity in science can be frustrating. There's a wonderful poem by Pablo Neruda that encapsulates this. A man sits at the edge of a well, fishing for light in a dark abyss. That's the image I have of science – patiently seeking information from a vast unknown.

How do you explain the value of discovery science to the public?
One way is to discuss the impact. Take a disease like amyotrophic lateral sclerosis, ALS. It is absolutely devastating. You can only treat the symptoms of pain or paralysis. There are ongoing clinical trials, but no one has discovered a way to stop ALS or even slow it down very much. And for most neurological disorders, including ALS, we still don't know the underlying causes.

Science is our only hope for these conditions, and it's important to unpack just how much work goes into a life-changing discovery. When you hear about a pharmaceutical company with a new drug, that drug was usually discovered through decades of scientific effort spanning many, many different laboratories. Creating a cure is like building a cathedral. Generations of workers pound nails and set stones, day after day, year after year.

Can you share an example from your lab?
Absolutely. We exist in a changing world. Our bodies must constantly adjust, counteracting disruptions that could cause harm. In my lab, we study brain resilience – how the nervous system detects and counteracts disruptions such as injury, infection, and neurodegeneration. Our goal is to discover how to promote brain resilience so we can create a therapy that can slow down or even cure neurological diseases like ALS. This new kind of treatment wouldn't depend on knowing the precise cause of ALS. It would be about making sure your body can resist degeneration, regardless of the underlying cause.

There are a lot of breakthroughs that started with curiosity, right?
Yes, this kind of science can lead to very tangible outcomes. Look at the success of gene editing, which is creating so many medical advances. We're seeing some of the first gene therapies emerge. That all came out of a paper from some scientists who were trying to understand how bacteria defend themselves from viruses. That research eventually led to CRISPR, an incredibly powerful gene-editing tool.

What happens when societies stop investing in science?
We give up hope for future cures. We need a constant flow of new ideas to fuel advances in biotech and pharmaceuticals. The most promising discoveries often fail on the path to drug development. The challenge is monumental. Truly, as a scientist, you get up every morning and you are *trying* to fail, to disprove your ideas. You may fail 5,000 times and then succeed once. But that one success might be an important step toward the next breakthrough.

Artificial intelligence can help us, but it works on information that we already have. It's not going to create the information we're missing. We still need expertise. We still need exploration.

What keeps you motivated to advocate for science right now?
In my lab, I often record the electrical activity of single nerve cells. I am amazed every time. You're watching the physics of life happen right in front of you. But that awe is not enough to sustain a career.

There's this notion of scientists standing on the shoulders of giants. And I don't think that's exactly right. I think we're standing on the shoulders of pioneers – generations of everyday scientists who went out into the unknown. They had to have resourcefulness and creativity and the belief that they were going to get somewhere better.

The scientific workforce is like that. We may or may not succeed on any given day, but we are trying to cure disease and alleviate suffering. And when some wonderful breakthrough does happen, we are standing on the shoulders of all those hardworking scientists who wandered into the wilderness and tried.

It comes down to hope. If you are the one diagnosed with ALS, it's not a rare disease anymore; it's yours. At that moment, hope is everything.

THE PLASTIC INSIDE US

TINY FRAGMENTS, MANY TOO SMALL TO SEE WITH THE NAKED EYE, HAVE INFILTRATED OUR BODIES.

by Wynne Parry
Artwork by Aurora Robson
Photography by Marshall Coles

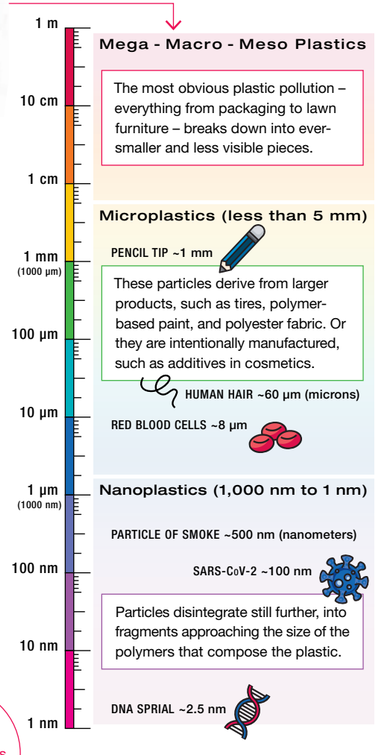
Every day, in a thousand ways, we take advantage of the utility of plastic. It's in our clothes, our cars, our cosmetics, and so much more. But eventually, these products turn into something else: tiny synthetic particles that spread quite literally everywhere – into our air, our food, our water, even inside of us. We are only beginning to tease out what the presence of these microplastics means for our health – and what we can do about it.

WHAT MAKES MICROPLASTIC?

Plastic comes in a dizzying array of forms. It is the acrylic in sweaters and paint, the polyvinyl chloride in water pipes and credit cards, the polyethylene in milk jugs and toothpaste tubes, and on and on. These diverse materials are made of **synthetic polymers,** which are long chains of repeating chemical units mostly derived from fossil fuels. The attributes that have made plastics ubiquitous in modern life – they are inexpensive, can be readily engineered for all kinds of uses, and are long-lasting – have also turned them into an environmental menace. Not only do we use and discard a massive amount of plastic, but this waste also will hang around for a very long time. While plastics haven't existed long enough for scientists to know for sure, they believe it could take hundreds to thousands of years for natural forces to break these materials down into ever-smaller fragments until **only small molecules derived from their polymers remain.**

DOWN TO SIZE

Microplastics are so small, we can swallow and inhale them. Some of the smallest particles, measuring perhaps one-thousandth the width of a human hair, can enter our bloodstream and pass through cell membranes.



Practical Products to Environmental Contaminants

Microplastic particles measure **less than 5 millimeters,** and many are even smaller.

Sometimes manufacturers intentionally add tiny plastic particles, such as microscopic capsules of fragrance in fabric softeners or compounds that enhance cosmetics.

Most form as a result of the disintegration of plastic products – when, for example, the asphalt erodes the rubber of your car's tires or the elements degrade litter on the roadside.

Or when the washing machine extracts fibers from your jacket.

DON'T COUNT ON RECYCLING

The global plastic recycling rate is a dismal 9%, according to the Organisation for Economic Co-operation and Development (OECD). But the problem likely runs deeper than just a lack of effort. California has sued the plastic maker ExxonMobil, claiming the company "falsely promoted all plastic as recyclable, when in fact the vast majority of plastic products are not and likely cannot be recycled."

ICONS: FLATICON.COM

JOURNEY FROM A JACKET...

Wear clothes made of synthetic textiles – like polyester, spandex, acrylic, or nylon – **and you're wearing plastic.** From the moment your soft fleece jacket, wrinkle-resistant dress, or trendy new top is manufactured, and every time you wear or wash it, these items release microplastics.

Manufacturing

Making synthetic fabric, including that used for clothes, creates microplastics. Microplastic fibers are present throughout the production of polyester yarn, for example.

Wear and Tear

Simply rubbing synthetic fabric produces plastic microfibers.

Environmental forces like the sun's UV rays help break polyester fibers into fragments.

Laundry

Washing clothing and other textiles made of synthetic fabric extracts microfibers that then travel down the drain.

MORE ON THE WAY

Global plastic use is projected to nearly triple between 2019 and 2060, according to the OECD.

Drying

Running synthetic fabric through the dryer produces microfibers that the machine then expels through its vents.

Packaging

Clear wrapping and other packaging for all types of apparel generate a massive amount of plastic pollution.

Disposal

After its useful life is over, synthetic apparel typically ends up as landfill, is incinerated, or is carried by rivers into the ocean.

...TO EVERYWHERE ELSE

Air
A cubic meter of air can contain over 1,000 particles of microplastic, especially indoors.

Water
While bottled water generally contains more microplastics, they also show up in tap water.

Soil
Microplastics have been detected in many types of soil – in cities, farms, and elsewhere.

Food
Microplastics have turned up in fruits, vegetables, salt, rice, and proteins, especially in highly processed foods.

JACKET: TARZHANOVA; CROPPED MICROGRAPH OF FLEECE FIBERS: © 2023 BARBORA PINLOVA AND BERND NOWACK. PUBLISHED BY ELSEVIER LTD.; USED UNDER A CREATIVE COMMONS 4.0 LICENSE

WHAT DO MICROPLASTICS MEAN FOR OUR HEALTH?

Microplastics have been found throughout the human body – in our brain and blood, in semen, and in breast milk. Science has yet to conclusively link these particles to any disease, but the emerging evidence alarms experts like **Tracey Woodruff, PhD '91, MPH,** director of UC San Francisco's Program on Reproductive Health and the Environment (PRHE) and the Alison S. Carlson Professor, who studies the health effects of environmental contaminants. To get a handle on what is known so far, she and colleagues at UCSF and the University of Sydney recently assessed studies of microplastics' health effects on three physiological systems – digestion, respiration, and reproduction – that sustain us as individuals and a species.

CELLULAR SHIFTS

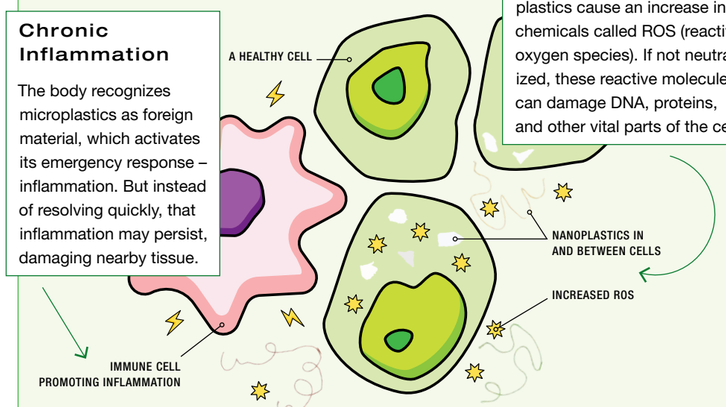
Once they infiltrate our body, our tissues, and even our cells, microplastics can trigger changes that may be harmful. These include:

Chronic Inflammation

The body recognizes microplastics as foreign material, which activates its emergency response – inflammation. But instead of resolving quickly, that inflammation may persist, damaging nearby tissue.

Oxidative (Chemical) Stress

Research suggests that microplastics cause an increase in chemicals called ROS (reactive oxygen species). If not neutralized, these reactive molecules can damage DNA, proteins, and other vital parts of the cell.



Should You Test?

TEST KITS PROMISE TO ASSESS THE MICROPLASTICS IN YOUR WATER, IN YOUR BLOOD, AND ELSEWHERE

Dimitri Abrahamsson, PhD, an environmental chemist and assistant professor of obstetrics, gynecology, and reproductive sciences at UCSF, cautions against test kits. He notes that plastics on your skin or in the environment where you collect a sample can contaminate it. "It is really challenging for us in the lab to get accurate measurements," he says. "I think it would be 100 times more difficult for someone at home."

ICONS: FLATICON.COM

STILL MANY QUESTIONS → Particles' size and shape, chemical additives, the polymer type, and other factors likely influence microplastics' biological effects. Researchers are trying to figure out how.

DIGESTION

Whether shed by takeout packaging or inadvertently introduced into food in other ways, plastic has become an inevitable part of our diet. To understand how these particles might affect the digestive system, Woodruff and her team focused on the intestines, including the colon. They reviewed the work of other scientists and found credible evidence linking microplastics to changes in these organs in animals. These included alterations to the immune system that may suppress its ability to properly protect the gut, while potentially promoting chronic inflammation. Although researchers don't fully understand the extent to which microplastics in the gut harm human health, such changes could increase the risk of disease, says Woodruff.

RESPIRATION

Just as they can sneak into food, fragments of plastic can linger in the air. Like bits of dust, smoke, or pollen, microplastics can travel into our airways and the deepest parts of our lungs. Studies in animals indicate that exposure to them may damage our lung tissue and impair our breathing, according to Woodruff's team. The damage associated with the particles includes scarring known as fibrosis. Microplastics appear to promote two related processes that drive fibrosis: chronic inflammation and oxidative stress. The latter, which is the biochemical equivalent of wear and tear, promotes inflammation and accelerates aging.

UCSF FINDINGS:

Cause for Concern

In both the intestines and the lungs, Woodruff's team categorized microplastics as a **"suspected" hazard.** This designation raises a red flag, but with the caveat that scientists don't fully understand the effects. But uncertainty doesn't mean we can dismiss the problem, notes Woodruff. "People will say, 'Well, your study said it was suspected.' That's true," she says. "But should we wait until it's too late? Because we are being exposed to them right now."

A Cancer Connection?

Certain biological changes – including chronic inflammation, immune suppression, and oxidative stress – promote the development of cancer. Evidence of these changes in the colon and lungs suggests microplastics **could contribute to malignancies** in these organs, Woodruff's team concluded.

NOT JUST PLASTICS

SCIENTISTS WORRY THAT MICROPLASTICS RELEASE HARMFUL CHEMICALS

Microplastics can physically interfere with biological processes – and that may not be all. Many plastics contain harmful chemical additives that researchers worry can leach out into our tissues.

These contaminants include plastic-softening substances called phthalates and PFAS compounds, which repel water and stains. Both are known to cause problems with fertility, development, and metabolism.

Well-known substances like these may just be the tip of the iceberg, however. UCSF's Dimitri Abrahamsson is more concerned about the chemical hazards that we have yet to identify.

Scientists haven't had much opportunity to study the health effects of some additives, such as those that protect plastics from ultraviolet radiation. And they are completely ignorant of the existence of others, since manufacturers in the U.S. are not required to disclose the substances they put into plastics nor to make them available for others to purchase for studies.

And because it takes a long time to conduct studies, scientists' findings may come too late, after the chemicals that concern them have already infiltrated the environment and our bodies.

He and his colleagues recently found elevated levels of 1,4-cyclohexanedicarboxylic acid – an understudied chemical used in plastic production – in the blood of mothers whose babies were born prematurely. Only limited studies in animals have explored the toxicity of this chemical, and Abrahamsson's lab could not find any research evaluating its effects on reproduction and development.

"We're trying to catch up with chemical production, but we just can't," Abrahamsson says. "If [some of these chemicals] are harmful and we're unaware of them, that's a little bit scary."

PHOTO: KRIENGSAK TAPASRI

HOW WILL MICROPLASTICS AFFECT THE NEXT GENERATION?

The accumulation of microplastics in our bodies could have consequences far beyond damage to own health. Early evidence suggests they may also impair processes necessary for conception and pregnancy, and potentially lead to lifelong difficulties for some children.

A THREAT TO FERTILITY?

Our intestines and lungs are, by the nature of their jobs, destined to encounter microplastics. While further from the onslaught, our reproductive systems are particularly vulnerable to disturbance. Research has already established that exposure to contaminants – such as synthetic chemicals that the body mistakes for hormones – readily interferes with fertility and fetal development. Based on previous work with animals, Woodruff's team found good reason to suspect that microplastics disrupt reproductive hormones and ovulation (the release of eggs). But they saw the most reason for concern with sperm, which appear to decrease in quality and quantity in the presence of these particles.

Plastic in the Placenta

IN HUMAN TISSUES AND CELLS, RESEARCHERS EXPLORE THE IMPLICATIONS FOR PREGNANCY

Pregnancy depends on the placenta. This temporary organ ferries nutrients and oxygen from mother to fetus, while also removing waste, protecting against illness, and secreting hormones essential for maintaining a healthy pregnancy.

Microplastics are now routinely detected in placentas. Joshua Robinson, PhD, a developmental and reproductive toxicologist and an associate professor of obstetrics, gynecology, and reproductive sciences at UCSF, is among those working to understand what this means for mothers and babies.

"We're concerned they could disrupt the placenta's normal function and cause stress, which may contribute to pregnancy complications," he says. "That matters because common complications can have traumatic, long-term effects on the child."

One such complication is preeclampsia, which has already been linked to certain chemicals used in plastics. In this condition, a poorly functioning placenta fails to supply the fetus with adequate oxygen and nutrition. This deprivation can lead to serious consequences, including stillbirth and lifelong neurological problems for the child.

Studies exploring the health effects of contaminants like microplastics often employ cell lines or lab animals, such as mice. Robinson's team takes a different approach, using real bits of human chorionic villi – the fingerlike structures in the placenta that form the interface between the maternal and fetal blood. "It's a little closer to what interests us," he says.

His lab has begun experiments exploring how the size of plastic particles affects their ability to infiltrate the chorionic villi. Once particles enter it, the researchers examine whether they alter the tissue's physical structure or molecular expression. He also hopes to learn how other variables, such as the type of plastic or the presence of chemical contaminants, influence the effects of microplastics.

Although early studies suggest microplastics may pose risks to the placenta and overall health, "there's just a lot more to unpack," Robinson says. "Scientists like me will have plenty of work to do in the coming years."

PHOTO: VALENTIN VALKOV

BETTER OFF WITHOUT PLASTICS?

No, says Woodruff. **Instead, "we have to consider what's really essential."** Plastics are crucial for some medical equipment, like IV bags, but toxic additives such as phthalates should be removed. **In many other cases, "there's a lot of plastics we don't need," she says.**

WHAT WE CAN DO

Plastic use is increasing, but that doesn't mean our fate is sealed like a single-use package.

Woodruff became interested in microplastics through her work on the toxic contaminants, like PFAS and phthalates, that have become deeply integrated into modern life. Through the programs she leads at UCSF, including PRHE and the recently opened Center to End Corporate Harm, Woodruff and her colleagues are studying the damage microplastics cause and advocating for change. For example, she and her team assessed their health effects to inform the state legislature, an effort sponsored by the California State Policy Evidence Consortium.

Over time, she hopes to see plastic use fall dramatically. But since most plastics are produced from oil and natural gas, she expects to encounter resistance from the fossil fuel industry.

"We will have to deal with a large, powerful financial incentive that's working against us," she says.

In the end, Woodruff envisions a shift away from disposable plastic products that would play out in many small ways. For instance, instead of serving food with plastic plates, cups, and utensils all meant for the trash, restaurants could partner with a contract business that specializes in collecting, cleaning, and returning dishes.

"You could create a whole new economy around just tableware," she says. "[Changes like this are] going to be more expensive in the beginning. But that's what we need: new infrastructure that's based on reuse."

"That's what we need: new infrastructure that's based on reuse." TRACEY WOODRUFF

REASONS FOR HOPE

WHY FIGHTING PLASTIC POLLUTION IS NOT A LOST CAUSE

Woodruff takes the most heart in the momentum the anti-plastics movement is picking up outside the U.S. Rwanda and Peru, for example, have called for a legally binding international treaty to end plastic pollution. Likewise, she notes that scientists in China have led research on microplastics. "It does give me hope that other countries see the importance of this issue and will elevate it," she says.

It's worth noting, too, that we've solved a big environmental challenge before: The hole in the atmosphere's protective ozone layer continues to heal, thanks to a global ban on ozone-depleting chlorofluorocarbons.

Although anti-plastics progress has been limited in the U.S., our nation has taken some steps in the right direction. These include an FDA ban on microbeads in toothpaste and certain cosmetics and a voluntary commitment by manufacturers to stop using grease-proofing PFAS in food packaging.

Meanwhile, states and municipalities are stepping up. California, for example, has mandated testing drinking water for microplastics and is considering banning microplastics in most cosmetics and cleaning products. And proposed legislation in Rhode Island would prohibit manufacturers from intentionally adding microplastics to their products.

Better materials may one day become widely available. In the past, regulations prohibiting certain substances have sparked innovation, according to Abrahamsson. For example, when leaded additives were phased out, gasoline had to be reformulated, leading to cleaner air and lower levels of lead, which can interfere with development, in children's blood.

And keep in mind that others share this concern. People don't want plastic particles and plastic-related contaminants accumulating in their bodies, Woodruff says. "No matter who you are or where you live in the U.S., people are concerned about their health."

5 Ways to Manage Microplastic Exposure (WITHOUT DRIVING YOURSELF NUTS)

Microplastics are everywhere. And while you can't completely avoid them or the potentially harmful chemicals they carry, you can take steps to reduce your exposure.

1

Don't microwave food in plastic. Heating a container causes chemicals from the plastic to leach into your food. Hot water in the dishwasher can also cause plastics to break down.

2

Avoid or gradually replace plastic products. Save glass jars for storage. Carry a canvas bag, metal or bamboo utensils, and a reusable water bottle. Buy natural textiles when possible.

3

Clean regularly. Microplastics can collect in dust. Vacuum with a high-grade HEPA filter, wet-mop, and dust with a particle-trapping microfiber rag to remove them.

4

Wash your hands and watch what you eat. Washing removes any unwanted substances. Eat more fresh, homemade food. Include lots of fruits and vegetables but less meat.

5

Take your concerns to work. Encourage your employer to reduce disposable plastic use by, for example, swapping plastic utensils in the office kitchen for metal ones from a thrift store.

Get more detailed advice by checking out PRHE's Toxic Matters site or UCSF's Western States Pediatric Environmental Health Specialty Unit.

ICONS: FLATICON.COM

He Discovered What Drives MS

Now countless patients benefit

Multiple sclerosis was long thought to be triggered by T cells – until one maverick scientist traced the disease to a different immune cell. Stephen Hauser, MD, uncovered the surprising role of B cells in fueling MS, paving the way for powerful new treatments that have transformed patients' lives. For this work, he was awarded the 2025 Breakthrough Prize in Life Sciences, often called the "Oscar of science." Hauser credits the many collaborators who made the discovery possible, especially the patients who participated in clinical trials. "Without them," he says, "this breakthrough wouldn't have happened."

Stephen Hauser is the Robert A. Fishman Distinguished Professor of Neurology and the director of the UCSF Weill Institute for Neurosciences.

PHOTO: STEVE BABULJAK

Can We Train Our Brain to Unlearn Chronic Pain?

Scientists are working to rewire the brain's pain pathways and unlock lasting relief.

BY JAIMIE SEATON

PHOTOS BY ANASTASIIA SAPON

ILLUSTRATIONS BY DANIEL LIÉVANO

SCIENCE ILLUSTRATION BY FARAH HAMADE

The orthopedist was yelling in Leeann Bongiorno's face: "There's nothing wrong with you! You just want drugs!"

But Bongiorno wasn't asking for drugs – she simply wanted help.

For two years, Bongiorno, 54, had been living with pain that she describes as a deep burning sensation far worse than kidney stones or natural childbirth. "They can give you a little something to take the edge off childbirth. I never had anything to take the edge off the leg pain."

By the time of Bongiorno's encounter with the orthopedist, she had been to four doctors seeking relief from her excruciating pain. They all asked the same question: What happened? The frustrating part was that Bongiorno couldn't think of anything that had set off the pain. One day it was just there.

"That's exactly what's complex about it," explains neurologist Cindy Chai, MD, a pain medicine specialist and associate professor of anesthesia at UC San Francisco. "People can have neuropathic pain from dysfunctions of the nervous system without an identifiable injury to the nerve. It can happen gradually or suddenly."

Stories like Bongiorno's are far from rare. She is one of 17 million adults in the United States, almost 9% of the population, who suffer from high-impact chronic pain – pain so severe it disrupts their daily life. Even more people, about a quarter of the population, suffer from chronic pain, which persists continually or intermittently over three months or more. And that number is rising. It went from 20% of adults in 2016 to 24% in 2023.

But pain isn't just a lingering symptom. It's a disorder of the nervous system – and UCSF researchers are looking for biomarkers to identify, measure, and predict pain while developing new ways to retrain how the brain experiences it.

Acute pain is so universal that it's the most common reason people seek medical care, and it's usually fairly straightforward. If someone has an abscessed tooth, for example, the cause of the acute pain is clear. Chronic pain can also have obvious sources, like arthritis. But with high-impact chronic pain, figuring out the cause is often more complicated. "Fundamentally, in chronic pain relief, we lack a lot of knowledge about which part of the nervous system is producing the pain," says neurologist Prasad Shirvalkar, MD, PhD, also a pain medicine specialist and associate professor of anesthesia at UCSF.

> "Pain can be a helpful, natural experience that is a protective mechanism for the body, but it can also be a pathologic condition of its own."
>
> CHRISTOPHER ABRECHT, MD

Even when the source *is* known, there's no guarantee that the available treatments will work. Anesthesiologist Christopher Abrecht, MD, the chief of pain medicine and medical director of UCSF's Center for Pain Medicine, says treatment is largely trial and error. The source of Bongiorno's pain turned out to be sciatica, and she did everything her doctors told her to do – physical therapy, acupuncture, and medications – but they didn't work. "Nothing could touch the pain," she says.

Finally, stymied as to how to help Bongiorno, the doctor who'd yelled at her suggested she go to UCSF. In 2020, orthopedic surgeon Sigurd Berven, MD, a professor of surgery, performed a spinal fusion to relieve Bongiorno's sciatica. The surgery was a success, and at last, after two years, she was pain-free – for about a month.

Pain wasn't finished with Bongiorno yet.

By pairing brain signals with deep brain stimulation, neurologist Prasad Shirvalkar and his team aim to interrupt pain as it flares – before it takes hold.

WHEN PAIN BECOMES THE DISEASE

Historically, pain was seen only as a symptom or warning of some other disease or as the result of an injury. "If you have pain in your arm from a fracture, the fracture is the problem.... And if you treat the underlying condition, the pain gets better," Abrecht says.

But sometimes the pain doesn't get better. For instance, a fractured bone could heal perfectly following treatment, yet the pain could persist. Or two people, similar in age and health, can have the same surgery, but only one might end up with lasting pain. Or a patient might undergo a successful surgery, only to develop chronic pain at the surgical site. "We don't know what's wrong – everything looks good – but the patient is having severe pain," Abrecht says. This was the case with Bongiorno. Her original pain had run down the back of her right leg; the new mystery pain ran down the front of her leg. Within six weeks of surgery, the pain was even worse than the sciatica pain had been.

When pain inexplicably persists, it ceases being a symptom and becomes a syndrome in its own right. "Pain can be a helpful, natural experience that is a protective mechanism for the body, but it can also be a pathologic condition of its own," Abrecht says.

IT'S ALL IN YOUR HEAD – LITERALLY

Whether it's a symptom or a condition, pain seems straightforward: A person steps on a nail and then feels pain. But pain is more complicated than that; it isn't actually experienced until it's processed in the brain.

Before a person feels pain, pain receptors in the body release neurotransmitters that send signals up the spinal cord and then to the thalamus, the brain's relay station. The thalamus processes the signals, which then travel to other parts of the brain (resulting in the

perception of pain), and the brain then sends messages back to the body. Here's where it gets complicated: These messages are shaped by a complex set of factors, including the person's genetics, memories of past episodes of pain, environment, and emotions – all of which influence how they feel the pain. Those factors can either amplify or mute the pain signals.

If the nail grazes the person's toe, for example, there might be some pain – but the *perception* of the situation is what drives the pain. If the nail sticks out of the person's shoe and has blood on it, they could think the nail had pierced their foot and perceive a great deal of pain. Or they could take off their shoe and see that the nail had only grazed their toe and perceive less pain. In both cases, the biology is exactly the same but the *perceptions* are different. And all of this happens in a nanosecond.

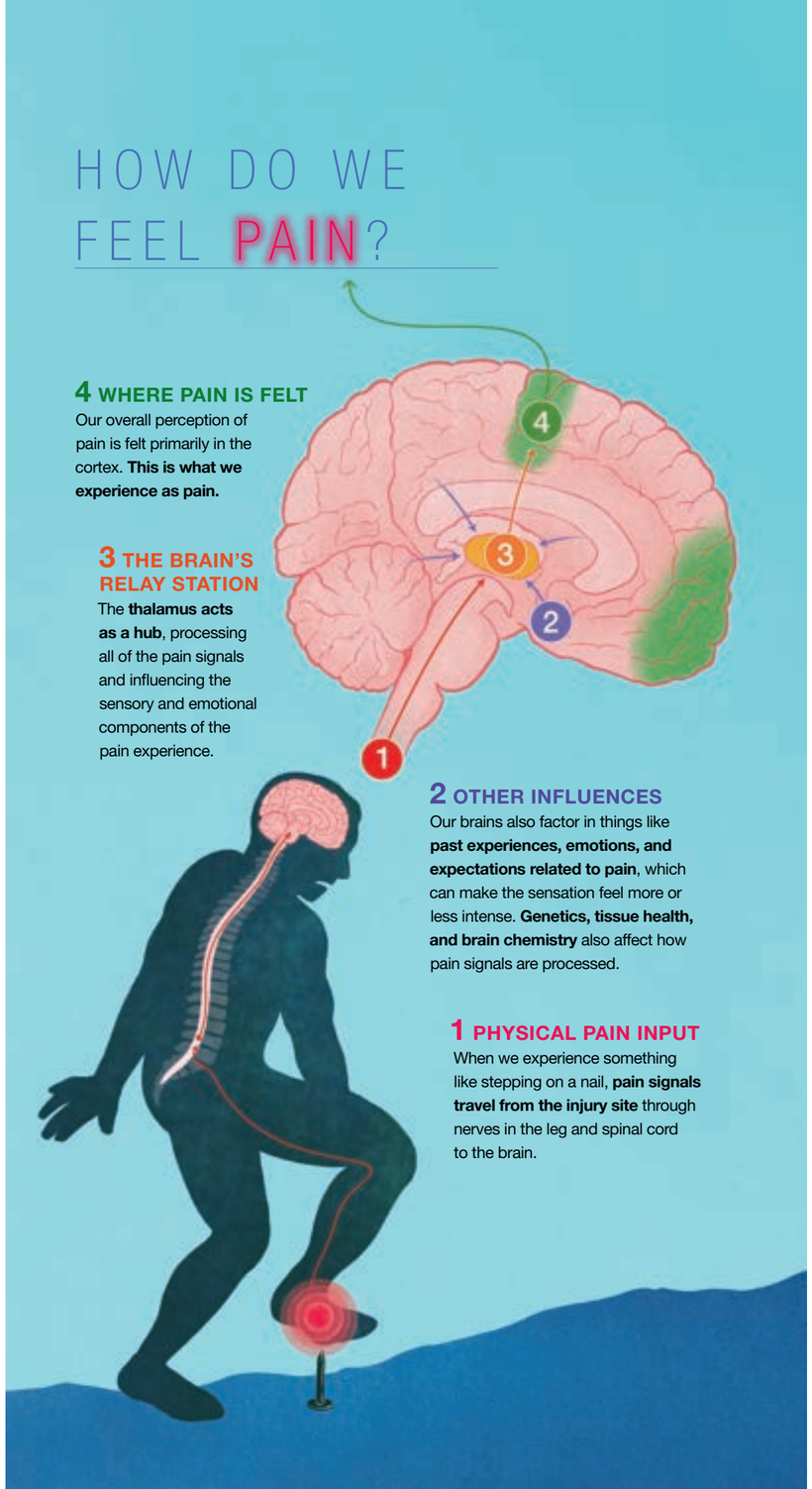
"It's in your mind, essentially," Abrecht says. "When you hear that pain is 'just in your brain,' that translates to people as 'You think I'm crazy and I'm making it up,' which is not the case. Pain is a complicated experience, and many factors are involved – and some of those are modifiable and some are not."

BREAKING PAIN'S VICIOUS CYCLE

Everyone feels pain differently, but one universality is that people with debilitating chronic pain are often consumed by it.

"One patient told me it feels like a million paper cuts – there's the pain component and then there's the suffering, the overwhelming weight of this unrelenting sensation that takes up all of their energy," Chai says. They're unable to do anything other than think about and manage their pain. "It's not unusual for patients to say, 'If you can just take away my pain for an hour, I will feel better.' It's this kind of oppressive burden," she says.

Many of those with chronic pain can't work or maintain relationships, which creates a vicious cycle. Without social support, someone



to care for them, or feeling valued in society, they can become depressed and anxious, which makes the pain worse. Chai explains that pain, mood, and sleep are intimately related, overlapping like a Venn diagram.

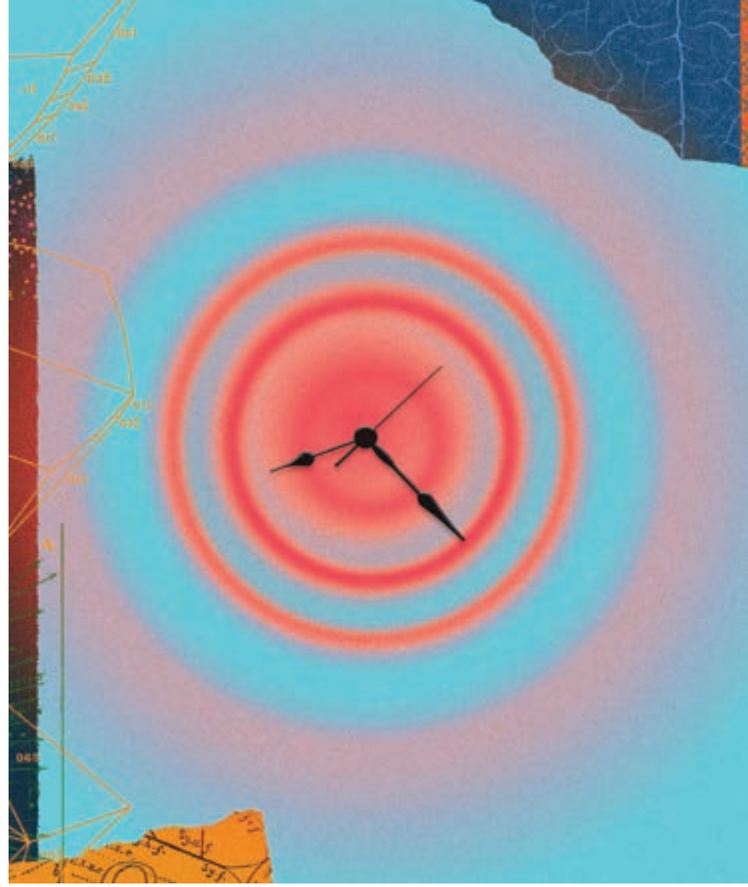
In some cases, chronic pain may lead to central sensitization, which is when the central nervous system becomes overly sensitive to stimuli. In other words, the brain learns pain too well, Chai says.

"Here's the thing. Acute pain is necessary for life because it's the alarm system to tell you that something is wrong," she says. "But in chronic pain cases, it's like the check engine light in your car that never turns off. The problem is not your engine – it's the light."

Pain psychologists help teach patients ways to unlearn their pain, to retrain their nervous system so they're experiencing sensation without the associated suffering.

"If you are sitting in a chair, if you want to, you can feel the sensation of the chair against your back," Chai explains. "But until I said that, you probably weren't thinking about it at all because our brains are wired to block out sensations that aren't useful."

For chronic pain patients, though, the brain interprets even neutral sensations as pain and suffering. In effect, pain psychologists help patients retune their sensitivity to their check engine light, giving them tools to reprocess pain, to get in touch with their nervous system and take control of some of the things we normally don't think about.



Chronic pain can feel constant and exhausting, like it never lets up. But pain psychologists can help patients retrain their nervous systems to feel sensation without the same level of suffering.

ATTACKING CHRONIC PAIN FROM ALL ANGLES

Chai says that patients who have chronic pain are best served in a comprehensive pain center with multidisciplinary providers. "And by multidisciplinary, I mean pain physicians with different training backgrounds, pain psychologists, and physical therapists."

Both she and Abrecht stress the importance of holistic, personalized care, which is a longtime hallmark of UCSF's Center for Pain Medicine. Treatments often combine medications, delivered in various ways, that can decrease inflammation and the sensitivity of the nervous system. Nerve blocks can also be used, both diagnostically and therapeutically, to target pain. Cognitive and psychological approaches, along with complementary therapies like massage, acupuncture, or aromatherapy, may be part of the plan as well.

The use of opioids presents a particular challenge. Many patients are afraid to take

them for fear of addiction, says Christine Miaskowski, RN, PhD, an expert in pain and symptom management and UCSF's Lamb Professor. She works with cancer patients and says that fear is a real challenge that must be overcome. "I tell people, 'You're not sleeping, you're not eating, you can't enjoy your family.… Would you tell me that you would be afraid to take your insulin if you were a diabetic and needed insulin?'"

THE SEARCH FOR A BIOMARKER

One of the biggest challenges in treating chronic pain is its invisibility: It doesn't show up on any scan, and there's no quantitative test to measure it. That's why finding a reliable biomarker – an objective signal that indicates how much pain someone is feeling in real time – is what Shirvalkar calls "one of the holy grails of pain research."

In his lab, he studies brain activity using tiny electrodes implanted in the brain to decipher which areas and circuits harbor important signals related to each patient's pain. This dual-purpose research allows his team to both study the fundamental biology of pain and develop potential treatments.

A breakthrough came in 2023, when Shirvalkar's team implanted electrodes in the brains of four patients who then tracked their pain at home. Patients reported the level and location of their pain and their other symptoms multiple times a day, while also capturing 30-second snapshots of their brain activity with the press of a button on a remote provided by the study. Using this data and machine learning, the team was able to predict, based solely on brain signals, when each patient would experience a high or low pain state.

Notably, they were predicting real-world chronic pain. They also discovered that the signals for acute and severe chronic pain are distinct – not just a more enduring version of the same thing, Shirvalkar says.

Leeann Bongiorno says she felt broken by her pain. She finally found relief through spinal cord stimulation, a technique that uses gentle electrical pulses to interrupt pain signals.

Now that they've shown they can track signals in the brain and predict when someone's going to be in significant pain, the team is developing a pain "thermostat" using deep brain stimulation (DBS). "We're taking those signals and, when the brain activity in real time indicates someone might be having a higher pain episode, we trigger the stimulator to turn on and short-circuit that activity," Shirvalkar says. His team is currently testing the feasibility and effectiveness of this approach, called DBS closed-loop therapy. "We're using this technology to try to develop biomarkers that might help predict who might respond to what therapy and what their long-term outcomes might be," Shirvalkar says.

The ultimate goal is to personalize DBS closed-loop therapy using these biomarkers while reducing the chance that the brain becomes desensitized to the effects. "Hopefully, by making it like a thermostat, we're delivering therapy only when it's needed and thereby preventing the brain from learning to ignore it," Shirvalkar says.

REWIRING RELIEF: HIGH-TECH HOPE FOR CHRONIC PAIN

Less than a year after Bongiorno's surgery, her mysterious new pain was so bad that her right knee would buckle when she stood. Eventually, she stopped leaving the house. "I lost friends. I was sitting on the sidelines as my life went by," she says. None of the treatments were working, so Bongiorno's team sent her to Shirvalkar.

Bongiorno says she walked into his office literally broken, like a kicked puppy. "I was thinking, 'Is this how my life is going to be? I can't live like this.' But Dr. Shirvalkar said, 'I'm going to stay here with you, and we're going to figure this out.' He gave me hope."

At that first appointment, Shirvalkar explained neuromodulation – a technique that uses electrical impulses to disrupt pain signals traveling along nerves. Nerves are like electrical cables that carry signals to the brain but that can transmit only so much information at once – just as bandwidth determines the amount of data that can be transmitted over an internet connection. So the idea is to overwhelm the *bandwidth* of the nerves to block or quiet the pain signals.

For localized pain, doctors might use peripheral nerve stimulation (PNS), placing a thin wire electrode less than a millimeter thick near the affected nerve. The electrode sends tiny, rapid electrical pulses that produce mild tingles which essentially replace the pain. For more widespread pain like Bongiorno's, spinal cord stimulation places two tiny wire electrodes in the epidural space of the spine. "It's like a pacemaker for your spine," Shirvalkar says.

Patients first try a temporary external device. If it reduces pain by at least 50%, permanent electrodes are surgically implanted. A small battery-powered generator is also implanted in the patient's abdomen or buttocks and then controlled by a remote.

"I was thinking, 'Is this how my life is going to be? I can't live like this.' But Dr. Shirvalkar said, 'I'm going to stay here with you, and we're going to figure this out.' He gave me hope."

LEEANN BONGIORNO

Bongiorno agreed to try spinal cord stimulation at that first appointment and received a temporary device just two weeks later. About a month after that, in early 2021, she received the permanent electrodes and generator.

Neuromodulation works for some people but not others, and experts don't have a good understanding of why its effects are so variable. Patients and clinicians work together to find the right settings.

For her first year with the stimulator, Bongiorno used a high frequency, which had no effect on her pain. "It was awful because you get your hopes up, you think this is the answer, and it's not working," she says. "You feel guilty and shameful for not getting better. It was frustrating because the trial worked for me. I assumed the permanent stimulator would be put in, and I would go about my happy life," Bongiorno says. But she didn't give up because she had faith in Shirvalkar, who was in constant contact with her as they adjusted the settings. "I would always leave his office more hopeful than when I walked in."

After about a year of no improvement, they switched her stimulator to a lower frequency – and, boom, that was it. "From my waist to my toes, I vibrate, and I can increase or decrease the intensity. I'm telling you, it sounds weird, but that works. I have zero pain."

Living pain-free for the past four years, Bongiorno is no longer sitting on the sidelines. She's back to playing tennis, walking, sailing, and playing with her grandchildren. In a recent note to Shirvalkar, she wrote, "In December, we completed our fifth solo sailing trip through the Grenadine Islands. I owe it all to you. [The spinal cord stimulator] literally changed and saved my life.… I am living my best life and enjoying it to the fullest. Words cannot describe."

"I never thought life would be this good," Bongiorno said in a subsequent conversation. "You can't keep me down."

"I never had the level of support I'm getting now," says Andre Codner, a student in the School of Medicine's postbac program.

BREAKING THROUGH

A transformative program is changing health care and lifting up communities, one future doctor at a time.

For some students, the road to medical school is obvious – paved by parents or teachers, smoothed by role models and mentors. But for many others – equally talented and often singularly inspired to serve – the path is not just harder to travel but also obscured from view. That's why, for a quarter of a century, the UCSF School of Medicine Post Baccalaureate Program (PBP) has been providing advanced coursework, MCAT guidance, and meaningful mentorship to college grads without traditional med school-ready resumes. The program kick-starts countless careers, bringing real benefits to the communities where these physicians eventually practice.

By Cyril Manning Photographs by Gabriela Hasbun

MENTORSHIP HIGHLIGHT:

Regular lunches, dinners, and texts with his mentor, Shieva Khayam-Bashi, who even showed him around San Francisco when he was new to the city.

RETURNING TO SERVE

After graduating from UC Santa Barbara, Iván Piña-Cabanillas had no idea what practicing medicine might look like, but he knew he wanted to apply his biochemistry degree to real-world problems. Without family money, he also needed a paycheck to help his older brother through medical school. So Piña-Cabanillas returned to his hometown of Salinas to work in the local hospital's emergency department, first as a scribe and then, as a second job, as a clinical assistant. "The ER wasn't what I expected," he says. "It wasn't like on TV. What stood out was just how many people were working together to make everything work." When it was finally his turn to try for medical school, he found the PBP. Through the program, he built a crucial relationship with Shieva Khayam-Bashi, MD, a professor emeritus of family and community medicine. Khayam-Bashi has provided him with mentorship that's "close to spiritual guidance," Piña-Cabanillas says. "It's so helpful, especially in those moments of self-doubt, to talk to someone who's been through it all." Looking ahead, Piña-Cabanillas' vision is clear: "I want to go back to Salinas and practice medicine there. There are so many people who need a lot of help. And if they don't have health, they can't do much else."

THE POWER OF PERSISTENCE

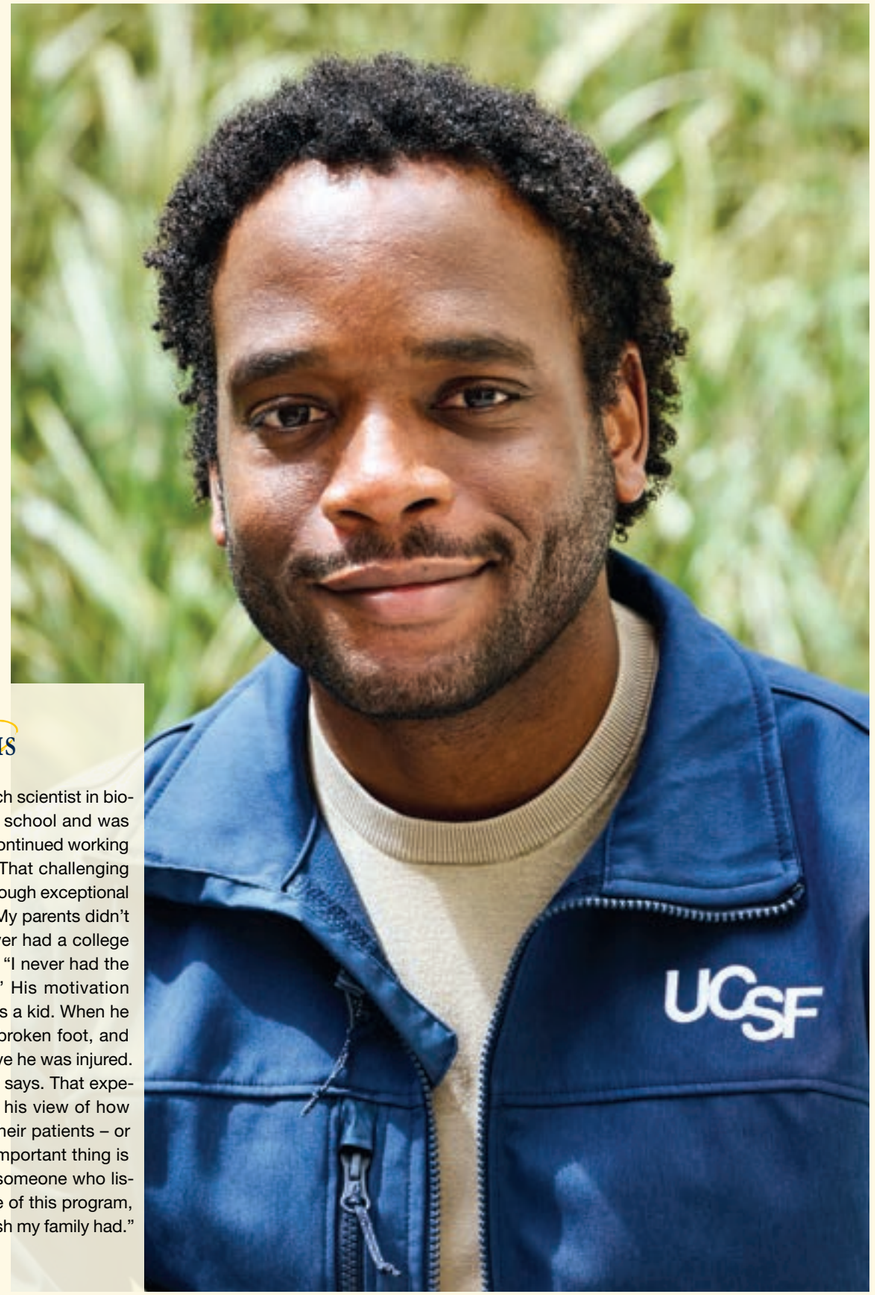
Olivia Waters was one of those kids who always wanted to be a doctor. As a kindergartner, she loved her pediatrician and decided to become one, too, and as she grew up, the dream didn't fade. So when Waters received no interview offers during the 2021 medical school application cycle, there was no way she was giving up. Instead, she discovered the PBP, which helped her tackle her greatest challenge: the MCAT. "Standardized tests have always been hard for me," Waters explains. The program's eight-week MCAT course, taught by UCSF medical students, made all the difference. "I took it again and finally got a score I was proud of. That lifted a big weight off my shoulders." Waters also found invaluable support in preparing her applications. "The staff was with us every step of the way, even after the program ended," she says. This continuity helped cement her decision to study at UCSF. Now in the PRIME-US program, which focuses on training future physicians to work in underserved urban communities, Waters envisions practicing medicine in her hometown of Oakland and focusing on maternal and child health in African American communities.

"Because of the PostBac program, I know that when I put my mind to something, I can do it."

CAREER CATALYST:

The clinical experience Waters gained through the PBP gave her valuable insight into hospital operations and strengthened her applications.

BARRIER OVERCOME:
Codner continued working full-time as a research scientist during his first semester to pay his student loans.



BEYOND THE SYMPTOMS

Andre Codner was already a research scientist in biotech when he set his eyes on med school and was accepted into the PBP. Initially, he continued working full-time to pay his student loans. That challenging balance was made possible only through exceptional support from the program's staff. "My parents didn't go to college in the U.S., and I never had a college adviser who was helpful," he says. "I never had the level of support I'm getting now." His motivation stems in part from his experience as a kid. When he was 11, he went to the ER with a broken foot, and the attending physician didn't believe he was injured. "He thought I was faking it," Codner says. That experience stuck with him and shaped his view of how impactful a doctor who listens to their patients – or who doesn't – can be. "The most important thing is that my future patients see me as someone who listens and cares," he says. "Because of this program, I know I can become the doctor I wish my family had."

"WHETHER IT'S MY PATIENTS OR THE YOUNG PEOPLE I'M NOW MENTORING, I WANT PEOPLE TO FEEL HEARD, SUPPORTED, AND SEEN."

BRIDGING LANGUAGE BARRIERS

Katrin Jaradeh, MD, a second-year resident in emergency medicine at UCSF, wasn't accepted to medical school on her first attempt. Thankfully, she found her way to the PBP, where the staff reassured her that getting in wasn't just possible, but that they also were personally invested in helping her succeed. Now that Jaradeh is a practicing physician, she carries that experience with her every day. "Whether it's my patients or the young people I'm now mentoring," she says, "I want people to feel heard, supported, and seen." It's a mission reflected in her ongoing research as well – studying the use of interpreters in the ER. "One big reason I went into emergency medicine is remembering how my grandfather, who speaks only Arabic, once went to the ER all alone. I've thought a lot about whether he understood what was happening – or if he was disoriented by it all. That focus on language-congruent care drives both my research and my practice."

PAYING IT FORWARD:
Jaradeh created two mentorship programs for students in the PBP, and she mentors medical students on their research projects.

The Quest to Reinvent Anesthesia

UCSF researchers are scouring millions of compounds – with help from tiny zebrafish – to create anesthetics safe enough to use without an anesthesiologist.

BY CAMERON SCOTT
ILLUSTRATIONS BY ANA MIMINOSHVILI

Before 1846, surgery was a crude and brutal undertaking, typically performed on conscious patients lashed to their beds. Then a Boston dentist publicly demonstrated that the highly flammable chemical *diethyl ether* – commonly called ether – could render a patient unconscious and insensitive to pain. Overnight, surgery became a major player in modern medicine.

Surgery has advanced dramatically since then, incorporating laparoscopes and lasers, titanium joints and transplanted organs. Anesthesia has changed much less, with just a handful of better drugs emerging. Ether gave way to less flammable chemical cousins. Barbiturates and dexmedetomidine were found by accident. And an intentional, decade-long hunt for safer alternatives produced propofol, which was approved in 1989 and remains the most commonly used intravenous general anesthetic.

Propofol and the other drugs used in today's operating rooms are safe when administered by specialists trained to manage their potentially life-threatening side effects. But anesthetics that don't require such expertise would open a brave new world in which surgery would be less onerous and less expensive for patients. It would also be more accessible in under-resourced environments, including rural areas, developing countries, and war zones, where a lack of anesthesiologists and their monitoring and life-support equipment often limits patients' access to needed procedures.

The prospect of portable surgery requiring fewer specialists and tools has motivated the Defense Advanced Research Projects Agency (DARPA) to fund a team of researchers based at the UCSF School of Pharmacy and UC San Diego who are seeking dramatically safer anesthetics. Pharmaceutical chemistry professors Brian Shoichet, PhD '91, and Jason Sello, PhD, are leading a project that combines artificial intelligence, molecule design, and innovative animal models to evaluate 6 million small molecules for anesthetic properties. The massive search spans a broad range of chemicals, raising the possibility that some may act through undiscovered, potentially safer biological mechanisms. The researchers expect to put about 10 drugs on the path to clinical trials, which would open the floodgates in a field that has moved at a trickle.

"We're at a moment where everything is coming together to accelerate progress. There is a consilience of multiple technologies," says Sello. "And at UC, we have the right group of people with the right skills and the right interests to bring them together."

A strange brew of methods working in sync

Computers using a technique developed by Shoichet will handle the largest swath of the 6 million chemicals. Large-library docking works like a high-speed virtual puzzle to determine which molecules in a vast library might interact with specific biological targets.

Most known anesthetics affect one of two biological mechanisms – propofol and benzodiazepines interact with the GABA-A ion channel, while dexmedetomidine interacts with alpha-2A adrenergic receptors. Shoichet is looking for other compounds that do the same. He starts with detailed models of these two cellular ports, including their shape and chemical properties. Then the computer program runs through similar models of millions of chemical compounds to identify which ones fit (or "dock") in those ports. Those that do are likely to have anesthetic effects.

Shoichet flags these for Matthew McCarroll, PhD, an adjunct assistant professor of pharmaceutical chemistry whose scientific workhorses are zebrafish larvae. As vertebrates, the fish have neurotransmitters similar to those in humans. But they reproduce quickly and develop organs within five days of fertilization. McCarroll and others have shown that these fish can help clear one hurdle that has slowed the search for better anesthetics: You can't start, as most research does, with fast-growing cells in petri dishes because cells aren't conscious. But at five days old, the fish are small enough to support the kinds of experiments researchers would otherwise perform with cells.

Larval zebrafish have another useful trait. They respond in specific ways to different types of neuroactive drugs, and McCarroll has uncovered a paradoxical reaction in anesthetized larvae: Knocked-out larvae whip their tails when they're exposed to vibration, while their awake compatriots show no response.

"The anesthetized fish don't react to any other stimuli, but they have this really robust acoustic startle response that we don't see with any other type of drug," McCarroll says. "It's super strange."

McCarroll has turned this curious behavior into a clever lab test: Put a small – and low-cost – amount of a test compound into 96 tiny wells, each one containing as many as eight larval zebrafish. Vibrate the tray and film the zebrafish. In every well with fish that twitch, you've got a potential anesthetic compound. McCarroll's postcard-sized tray can test 80 compounds at a time, with 16 control specimens to boot.

So far, about half the compounds identified by Shoichet's docking technique have caused McCarroll's zebrafish larvae to twitch in their telltale way. McCarroll is also dosing the larvae with other, randomly chosen compounds, to fish for one that works through a new biological mechanism that triggers fewer side effects than propofol or dexmedetomidine. New targets would also invite other researchers to join the hunt for better anesthetics.

McCarroll shares his hits with Sello, who looks at the compounds' chemistry, eliminating any with properties known to cause, for example, liver damage. Sello also adjusts some compounds' chemical makeup – say, to make them biologically soluble or more potent. (Molecule editing has become more precise in the decades since propofol was first made.) Sello sends the modified molecules to McCarroll so he can dose the fish, test their organs for damage, and even peer into their transparent heads to see how the drugs affect their brains.

"It's an iterative process," Sello says. "We'll try to create compounds that are more potent or that we would predict would have better pharmacological properties."

Candidates that pass all these tests will ultimately be evaluated in mice, putting the compounds on a more conventional path toward clinical trials. Extensive safety testing would still have to happen before any drugs could be tried in humans, says Michael Bokoch, MD, PhD, an associate professor of anesthesia who is also part of the all-star research team.

Hopes of revolutionizing surgery

A pilot project using the same unconventional method has already borne fruit. After screening 12,000 compounds, the team identified a candidate molecule. Through Sello's modifications, it became nidradine, a drug that has successfully anesthetized mice. Even more intriguing, it also has analgesic, or painkilling, properties. If nidradine makes it to the OR, it could reduce reliance on opioid painkillers.

"Its analgesic activity comes from binding to a sodium ion channel called NaV1.8, which is a hot target right now for the development of compounds to treat chronic pain," Sello says. "And our molecule came out of a random screen!"

The pilot has fueled the researchers' optimism that they may find as many as a dozen promising new drugs from the larger project.

The research's most ambitious goal is to revolutionize surgery itself, untethering it from highly specialized anesthesiologists. Safer drugs would allow nurses and medics to put patients under, sometimes without the bulky, expensive equipment that monitors and supports patients' vital functions in case of the depressed cardiorespiratory activity that many existing anesthetics can cause.

The ambition is grounded in a challenge: Anesthesiologists are in short supply in the military, in rural areas, and in lower-income countries. In war zones, wounded soldiers may wait precious minutes or hours for surgery while they are transported to a military medical center appointed with anesthesiologists and the tools they need. Similar situations arise in rural areas and lower-income countries. In fact, wait times in such locales can be indefinite, with millions of people going without needed surgeries every year.

Even if the search among the 6 million compounds finds just one that is incrementally safer than propofol, that improvement, extended across the hundreds of millions of patients worldwide who undergo surgery every year, would be substantial.

There would be benefits even at top-tier medical centers like UCSF, where dramatically safer drugs would allow anesthesiologists to focus on the most specialized and high-risk cases. For lower-risk procedures, hospitals could reduce their reliance on highly trained specialists, potentially lowering costs and making care more accessible.

"If the drugs were much safer, you might not even need an anesthesiologist for procedures such as cataract surgeries and endoscopies," Bokoch says. "That would extend our workforce and save patients money."

But even if the search among the 6 million compounds finds just one that is incrementally safer than propofol, that improvement, extended across the hundreds of millions of patients worldwide who undergo surgery every year, would be substantial. Currently, anesthesia contributes to death in a couple hundred people in the United States each year.

"We don't have to accept the status quo," Sello says. "We can do better, so let's try to do better."

ALUMNI HUB

Meet a few of UCSF's visionary Alumni Award winners, whose work is transforming health.

Illustrations by John Jay Cabuay

SCHOOL OF PHARMACY | Humanitarian Service Award

Maria Lopez, PharmD '01

Community Pharmacy Pioneer

PHARMACY REIMAGINED

Maria Lopez didn't just want to own a pharmacy – she wanted to redefine what one could be. As a first-generation college graduate and student-athlete, she knew the value of determination. With a passion for chemistry and patient care, she pursued her PharmD despite moments of doubt. "I considered dropping out when I realized many pharmacies operate like assembly lines," she says. "I wanted to create something different, something more personal." That vision led her to establish Mission Wellness Pharmacy, the first accredited specialty pharmacy in San Francisco.

LOCAL IMPACT TO NATIONAL CHANGE

For nearly two decades, Lopez has innovated clinical services in her Mission District business, creating models now used nationwide. Hers was the first independent pharmacy in the U.S. to provide hepatitis C testing and one of the first to obtain treatments – delivering medications to patients in homeless shelters and under bridges. Mission Wellness Pharmacy was also the first in the state to offer on-site testing for HIV and other sexually transmitted infections. Lopez's pioneering practices led to legislation enabling pharmacists to prescribe HIV prevention drugs, a policy since adopted in more than half the states. These early firsts laid the groundwork for her responses during the COVID-19 pandemic, including setting up the nation's first pediatric vaccination clinics and training pharmacists nationwide in COVID-19 pediatric vaccination protocols.

STRENGTH, SERVICE, AND HEART

Building a thriving community pharmacy hasn't come without challenges. "For women entrepreneurs, and even more so for Latinas and other women of color, doors close constantly. But resilience means learning that if one door closes, another is meant to open," she says. Her grit and compassion have served her and her patients well. "The pharmacy is their extended family. They trust us to explain their medications in a language they understand. They are not just a number."

■ *Paula Hermann*

SCHOOL OF MEDICINE | Entrepreneur Award

Ken Song, MD '00, Resident Alum

Curiosity Rover

OFF THE BEATEN PATH

While his medical school classmates rushed into residencies, Ken Song charted an unconventional course that would ultimately redefine what a medical education could achieve. "It was highly atypical for someone to go through medical school and not go straight into residency," says Song, who, upon graduation, took an opportunity in the business sector. After two years as a management consultant, Song returned to UCSF for a residency in internal medicine, followed by further training at the University of Washington and Fred Hutchinson Cancer Center. But he was itching to return to entrepreneurial pursuits.

INSTINCT FOR INDUSTRY

Over the past 15 years, Song has rapidly launched a series of visionary startups in multiple sectors – diagnostics, life science tools, and drug development – that have led to billion-dollar acquisitions. He's not only demonstrated a sort of sixth sense for promising ideas but also possesses the leadership to bring them to fruition. A common thread in his work is a desire to make a difference in people's lives. Among his many innovations is the low-cost Harmony prenatal test, which has established a new standard for prenatal screening. The test detects fetal chromosomal anomalies noninvasively, using a pregnant woman's blood sample. Now, as president and CEO of Candid Therapeutics, Song is developing novel, easy-to-administer therapies for autoimmune diseases. "I see my value in getting into emerging areas where things are not yet defined and helping to shape those industries," he says.

BUILDING WHAT'S NEXT

His unusual career path shows where exceptional medical training, combined with curiosity and courage, can lead. "If you look at my history – where I've been and what I've done – it looks quite disorganized and random. And that's because it is," he says. "But I think to myself: Wow, if I wasn't doing this, would these things even exist? Probably not. That's what motivates me and keeps me going."

■ *Dora Dalton*

SCHOOL OF NURSING | Jan Norbeck Distinguished Service Award

Jian Zhang, MSN '92, DNP
Chinatown's Champion

CULTURALLY ROOTED CARE

When Jian Zhang arrived in the U.S. as one of just 15 students selected by the China Medical Board for advanced nursing education, she was surprised to learn there was a hospital in San Francisco dedicated to serving Chinese patients. Zhang found her calling at Chinese Hospital – the nation's only medical center of its kind. "I felt like I could impact the Chinese community most there," she recalls. "It's a safe place for healing, where patients receive culturally and linguistically appropriate care." This early connection blossomed into a lifelong commitment to uplift an underserved population and provide care that respects Chinese traditions and values.

CREATING A COMMUNITY LIFELINE

During her training at Chinese Hospital, and while working there since her graduation, Zhang has built relationships and honed leadership skills. Early on, she taught breast cancer prevention classes, raising funds to sustain them and cover mammograms for uninsured immigrants. This work laid the foundation for her decades-long effort to address the unique needs of San Francisco's Chinese community. Zhang stepped into the CEO role at Chinese Hospital in 2017 and, three years later, faced an unprecedented challenge. "During the pandemic, we went door-to-door providing education, testing, and vaccines," she says, "and we achieved an 88% vaccination rate." Under her leadership, the city's only independent community hospital – though it's faced financial pressure – has expanded services and created partnerships with UCSF to bring specialty care to its unique population.

BLUEPRINT FOR INCLUSIVITY

By championing bilingual services, health education, and insurance access, Zhang has created a model for culturally inclusive care. "This hospital is the community's heart, where people can gather, heal, celebrate, eat familiar foods, and have conversations about their health in their native language. I want to ensure we can continue to meet our community's most pressing needs."

■ *Ashley Han*

GRADUATE PROGRAM IN PHYSICAL THERAPY | Alum of the Year

Benjamin Boyd, MSPT '02, DPTSc '08
A Driving Force in Holistic Pain Care

THE ART BEHIND HEALING

As a child, Benjamin Boyd spent hours sketching skeletons in his father's pediatric physiatry office at Children's Hospital Oakland. His fascination with the human body, coupled with a cousin's muscular dystrophy diagnosis, inspired him to pursue a career in physical therapy. He uses art – creating storyboards to visualize his patients' experiences – to help ease their pain and restore their independence. "I've always been artistic and use it to problem-solve and understand situations," says Boyd.

SEEING THE WHOLE PERSON

Boyd has over 20 years of specialized experience in pain management, including conducting research on neuropathic pain in people with diabetes and those recovering from breast cancer treatment. "In physical therapy, it's essential to look at all factors that could influence the body, overall health, and mind," Boyd says. "We need to look beyond the physical experience." He integrates biological, psychological, and social factors to provide holistic care. Boyd is also the author of an influential book, *Bodily Relearning*, that reimagines pain management for both patients and clinicians. Drawing from his dual roles as a clinician and an academic, his work offers tools to incorporate whole-person care. "Many patients appreciate a holistic approach because … they're not being treated just as a diagnosis or pathology," Boyd says. "It's important to validate their lived experience."

THE NEXT-GEN PAIN SPECIALISTS

Boyd's influence extends beyond the clinic to the classroom, guiding future health care professionals in evidence-based, compassionate pain management. "Physical therapists are at the forefront of helping people productively navigate their lives, and we should never lose sight of capturing the person in front of us."

■ *Ashley Han*

SCHOOL OF DENTISTRY | Practitioner Award

Ronni Brown, DDS, MPH, Resident Alum

Transforming Care in Jails and Beyond

UNCOVERING LINKS TO METH MOUTH

When Ronni Brown first looked into a patient's mouth at the Sonoma County Main Adult Detention Facility, the incarcerated 20-year-old needed full-mouth extractions. "Every single tooth was blackened with decay," she recalls. In case after case, a troubling pattern emerged: the devastating oral effects of methamphetamine use, a condition sometimes referred to as "meth mouth." Her work in correctional facilities gave Brown a front-row seat to a crisis that her peers in private practice weren't identifying. "I realized that perhaps my colleagues didn't know what they were seeing," she says. This discovery led her to pursue a dental public health residency at UCSF, where her groundbreaking research on what she'd observed became an essential resource, helping dentists worldwide recognize and respond to the oral implications of substance use disorders.

CARING FOR THE INCARCERATED

For 27 years, Brown provided emergency dental services to thousands of incarcerated individuals. "From the beginning, my focus was on ensuring that every patient felt cared for and understood," she reflects. "In a place where uncertainty and stress are constants, it was important to create a safe space where they could receive the care they needed." Her dental suite became a state model for correctional facilities. Now, as senior community health planner with San Mateo County Behavioral Health and Recovery Services, Brown leads overdose prevention initiatives that build on her decades of experience working with vulnerable populations. "It is transformative work," she says of her efforts to improve lives affected by substance use and reduce the associated stigma.

HUMANIZING ADDICTION IN DENTISTRY

Brown has trained thousands of dental professionals internationally, equipping them with practical tools to identify substance use disorders and connect patients with resources. Her book, *A State of Decay*, makes her research accessible to professionals and the public. "I hope I've inspired the profession to understand the complexities of addiction and their role in treating it with compassion and care. I hope they see the person in the dental chair – not just a disease, but someone's mother, father, brother, or sister."

■ *Paula Hermann*

SCHOOL OF MEDICINE | Alum of the Year

Stephanie Chao, MD '06

Children's Wellness Warrior

PIONEERING VR IN THE OR

For many children, medical procedures are terrifying, sometimes leaving lasting trauma. Pediatric surgeon Stephanie Chao has found a way to change that through virtual reality (VR). "Being in a medical environment can cause trauma with lifelong consequences," says Chao, the trauma medical director at Stanford Medicine Children's Health. Instead of relying on general anesthesia, which may have effects on developing brains, she now uses VR headsets, along with a local anesthetic, during minor surgical procedures. "It transforms what was once a fearful experience into something they can comfortably endure with little to no side effects," she explains. "Often, they don't even realize the procedure has started or ended because they are so engaged in the virtual reality experience. Patients who return regularly actually look forward to it."

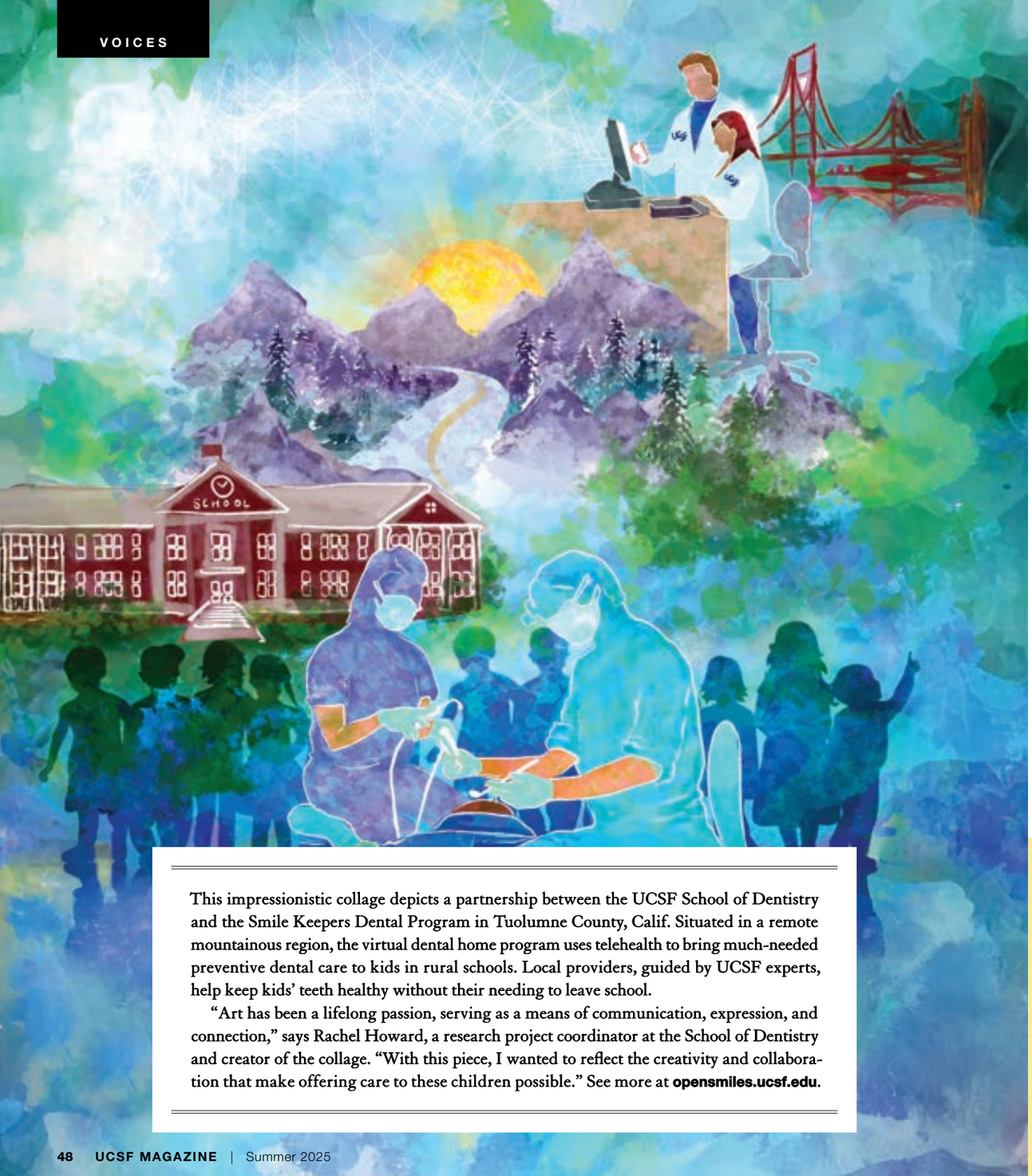
ADVOCATING FOR GUN SAFETY

Chao's commitment to improving children's lives ranges from bedside innovation to nationwide advocacy. Her translational research lab focuses on injury prevention, mainly tackling the leading cause of death among U.S. children: gun violence. She developed a nonpartisan K-12 curriculum, PLEDGE, to teach gun safety, secure gun storage, and mental health awareness. "Our goal is to empower children to become agents of change by educating them about gun responsibility and making their communities safer," says Chao, who has advocated for gun safety legislation on Capitol Hill, at the White House, and in schools across the country. "I'm going to keep working until no child dies from gun violence."

MOBILIZING THE VILLAGE

"I know improving children's health globally will take a whole society working together, but each of us has a role to play, and I'm committed to doing my part."

■ *Paula Hermann*



This impressionistic collage depicts a partnership between the UCSF School of Dentistry and the Smile Keepers Dental Program in Tuolumne County, Calif. Situated in a remote mountainous region, the virtual dental home program uses telehealth to bring much-needed preventive dental care to kids in rural schools. Local providers, guided by UCSF experts, help keep kids' teeth healthy without their needing to leave school.

"Art has been a lifelong passion, serving as a means of communication, expression, and connection," says Rachel Howard, a research project coordinator at the School of Dentistry and creator of the collage. "With this piece, I wanted to reflect the creativity and collaboration that make offering care to these children possible." See more at **opensmiles.ucsf.edu**.

0906
University Development
and Alumni Relations
UCSF Box 0248
San Francisco, CA 94143

Nonprofit
Organization
U.S. Postage
PAID
UCSF

UCSF
University of California
San Francisco
advancing health worldwide

magazine.ucsf.edu