UCSF MAGAZINE

Winter 2025

Evolution Revolution

Looking to the past to uncover the genetic roots of human disease

Contents

COVER AND TOP LEFT ILLUSTRATION: TIM O'BRIEN; MIDDLE LEFT PHOTO: ELENA ZHUKOVA; BOTTOM LEFT ILLUSTRATION: BRIAN STAUFFER; CENTER ILLUSTRATION: MARCOS CHIN; TOP RIGHT PHOTO: TOM SEAWELL

Last May, Amy Appelhans Gubser, a nurse at UCSF Benioff Children's Hospitals, swam 29.7 miles in frigid waters with no wetsuit from the Golden Gate Bridge westward to the Farallon Islands. She was the first ever to complete this feat.

Beyond Biology's Blueprint

In this issue, Shailee Jain, a talented computer scientist and postdoc in neurosurgeon Edward Chang's lab, shares an inside look at her effort to build a digital brain that mirrors the human mind. If she can create a model of a working human brain, researchers could one day explore treatments and interventions that would be impossible to test in human patients. This science could catapult our understanding of complex brain disorders and even the nature of cognition itself.

Computer scientist Shailee Jain is employing AI to unlock new possibilities for understanding the brain.

Dr. Jain's work exemplifies the promise of artificial intelligence in medicine. Across UCSF, researchers and clinicians are exploring its potential to reshape the way we care for patients, identify diseases long before they become apparent to the human eye, and speed the discovery of new treatments by revealing previously invisible patterns in disease.

Remarkable changes are already underway. UCSF scientists are at the vanguard with AI models aimed at helping radiologists detect early-stage cancers more accurately. They are refining predictive tools designed to alert clinical teams to the needs of patients at high risk for life-threatening conditions such as sepsis and heart failure, enabling earlier intervention. And they are using increasingly sophisticated algorithms to accelerate drug discovery by designing synthetic enzymes and screening massive libraries of compounds to identify promising new therapies.

Today, the world is striving to grasp the possibilities of our AI-enabled future. What we see clearly at UCSF is that AI's power lies not in replacing human insight but in amplifying it. When our clinicians and scientists partner with AI experts like Shailee Jain, they can analyze vast data sets, identify subtle patterns, and generate hypotheses at unprecedented speed and scale. I am convinced that the most transformative advances ahead will combine the analytical power of AI with the creativity, passion, and judgment of human brainpower.

Sam Hawgood

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

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Five Questions for Nicholas Holmes

Nicholas Holmes, MD, MBA, was recently named president of UCSF Benioff Children's Hospitals, which includes campuses in Oakland and San Francisco and 50 satellite locations across Northern California.

By Alexis Martin

We hear you're a big fan of superheroes and origin stories. What's yours?
Yes! I love origin stories. Part of mine begins right here in San Francisco. I was fresh out of medical school when I moved across the country to do my residency in urology in San Diego, followed by a fellowship in pediatric urology at UCSF. It was a pivotal time in my life: I met my husband and I found my calling – pediatrics.

Why pediatrics?
I was so inspired by my time at UCSF. Everyone I encountered had this deep, almost spiritual commitment to children. And the families I worked with put all their trust in me. It felt like an incredible privilege to be in service to them, and I couldn't imagine anything else I'd rather do.

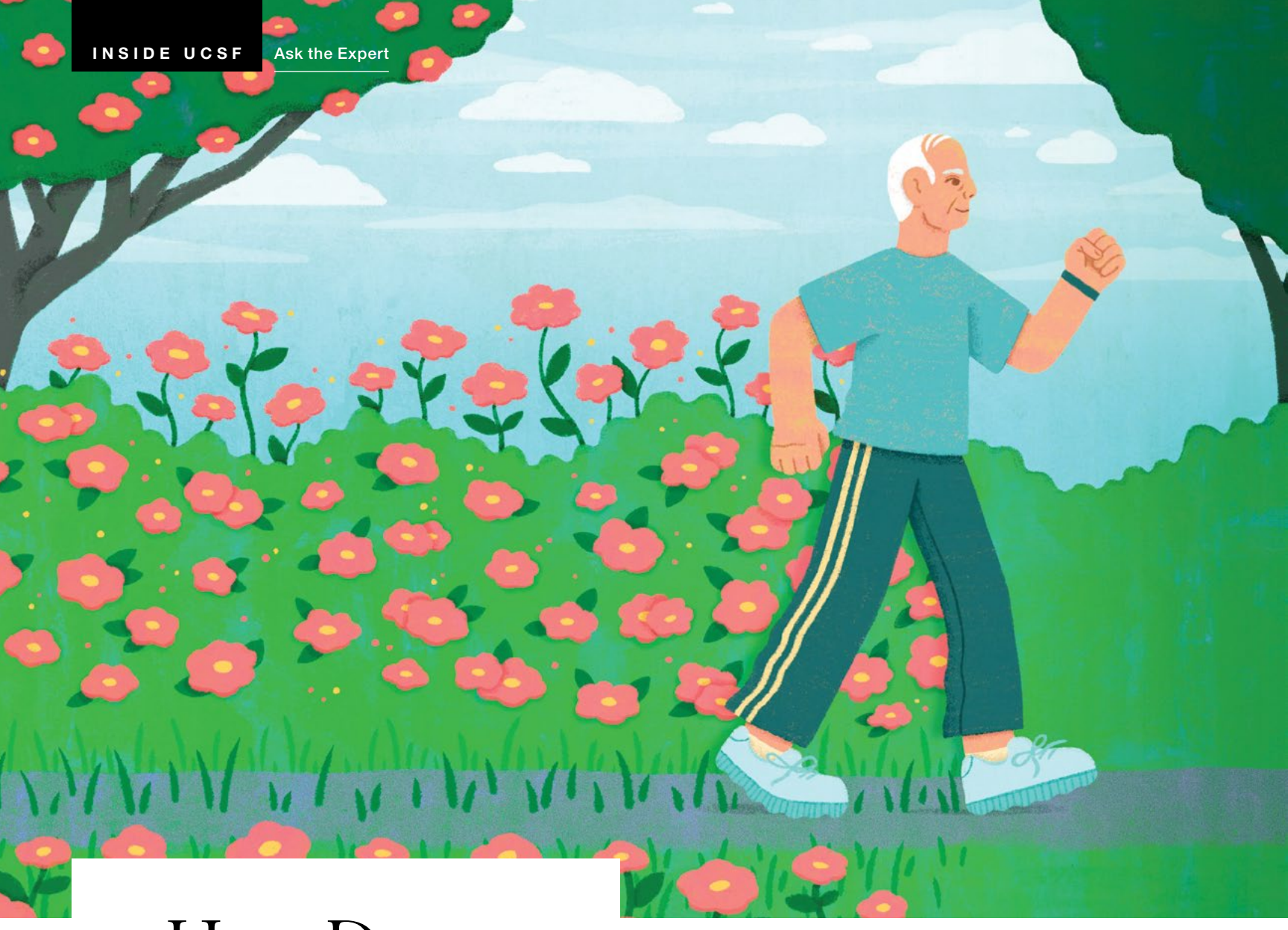
What are you most excited about?
The new hospital building in Oakland! The UC Regents recently approved constructing a $1.5 billion facility that will open in 2030. It's going to be transformative for our community. I can't wait to break ground.

You have served in the U.S. Navy and worked at other children's hospitals. What brought you back to UCSF?
We deliver some of the highest quality care and have some of the most recognized experts in the world. We have all the elements of a top children's hospital. We just need to weave those components together to create an integrated, comprehensive system of care. That's the project that pulled me in.

Top priority for year one?
As a leader, it's important to me to get to know this organization and have this organization get to know me. I want people to understand my vision, where I'm coming from, and how I hope to achieve our goals. By my one-year mark, I hope people feel like they know me, can communicate with me, can stop me and say "hi," and can give me feedback. That's how I've had success – by connecting with people.

Fun fact: In addition to running the Honolulu marathon with his husband, Gary, every year, Holmes surfs, paddleboards, and plays pickleball.

PHOTO: ANDREA ROWE/UCSFHEALTH.ORG



How Do I Prepare Today for Healthy Aging Tomorrow?

We asked UCSF's Louise Aronson, MD, and Courtney Gordon, DNP, how to plan for a vibrant future as we age. Aronson is a geriatrician and author of the *New York Times* bestseller *Elderhood: Redefining Aging, Transforming Medicine, Reimagining Life*, a finalist for the Pulitzer Prize. Gordon is a geriatric and palliative care nurse practitioner with UCSF's Care at Home program, which served 100 patients when she joined in 2011 and now serves 500.

By Katherine Conrad | Illustration by Paige Stampatori

How soon should I start planning for my older years?

ARONSON: It's never too early or too late. Even a 75-year-old lifelong couch potato can benefit from walking a bit and cutting back on processed foods. They'll have less pain, better-managed chronic conditions, and improved function and will likely live longer. You can start at any age, but sooner is better. Then you've got to keep it up, unfortunately. It's a bit like dusting or weeding. You do it, it feels good, and then there's tomorrow.

GORDON: If you know certain conditions run in your family, like high blood pressure, depression, or diabetes, you can be proactive now with diet, exercise, and appropriate medications. We've learned so much about nutrition, even in the past couple of years. The people I see who live long, healthy lives all practice moderation. They didn't cut things out, but they didn't overindulge either. It was a balance.

How should I prepare?

ARONSON: Address the fundamentals, which are pretty much the same at all ages. The earlier you pay attention to movement, nutrition, sleep, stress management, and social connections, the greater your chances of healthy aging and longevity. Obviously, life has stressors we can't control, but minimize those you can. For unavoidable stress, learn tools for lowering it because stress hormones lead to inflammation. Inflammation leads to chronic disease. Chronic disease leads to trouble, including death.

GORDON: In palliative care, we ask our patients, "What brings your life joy?" I'm not sure we ask that question in midlife because we're so focused on our careers or families. But I think we should step back and ask, "What *does* bring me joy?" Aging is a gift. If we're fortunate enough to keep aging, it's important to consider what brings us joy while we're still young.

Does it matter where I live?

ARONSON: Yes, it does. Where a person lives can correlate with their socioeconomic status and access to health care and community services. We live in a country that is rife with inequities. There are places in the Dakotas or even near Palo Alto, for example, where adjacent communities have a 15- to 30-year difference in lifespan. That shows this isn't about biology – it's about policy priorities and some people mattering more than others.

What if I don't have children to support me?

ARONSON: We're seeing many more "solo agers" these days. So I say: Pay it forward while you're young. Do things for older people now to create a culture where we take care of people, whether or not we're related. Also, make sure you have younger friends. If you're living into old age, a lot of your friends and family will die. If you don't start making new friends, you'll run out of support.

GORDON: Having children doesn't guarantee support. Many people think, "I have a kid, so I'll have a guaranteed caregiver." But I don't see that in my work. Children don't equal a qualified or capable caregiver. Whether you have children or not, planning for your future is crucial. How do you envision your aging process? Do you want to go to a retirement community, or do you want to stay in your home? Do you have a partner or friends you want to keep close to? It's all about thinking through how you see your later years and preparing yourself. Obviously, the financial piece is huge. The cost of aging, whether it's hiring care or moving into a facility, is so high. Plus, we're often on a fixed income as we get older. It's so important to be aware of all this.

> "It's a gift to be able to keep getting older. There's no magic pill."

What if I have limited resources?

ARONSON: With limited income, balancing your present versus your hypothetical future is tough. Many people will quite understandably pick the present. Start saving early and consider living in supportive communities, cohousing, or communal housing to reduce costs. Downsize sooner rather than later. Consider getting involved in your town. How can you help people age in place? How can we create the social and community support needed to get what most of us want – to age within the community, not segregated in a warehouse?

What are the biggest risks to my well-being?

ARONSON: Not moving, eating tons of processed sugary foods that cause inflammation, not getting enough sleep, using substances, and being constantly stressed without developing effective coping methods. It's best never to use tobacco or drink excessively. If you're going to use substances, do so rarely and in moderation. None and never are best, but few of us live up to that ideal.

Basically, it's things people don't do. I see people get arthritis and believe they must stop exercising, whereas the opposite is true. People need to take up strength training. If your balance was never your strong point, do balance-related exercises by 50 and strength training by 60 at the latest.

If you develop a chronic condition – be it arthritis, high blood pressure, or diabetes, or you gain weight in midlife as so many of us do – don't just say, "Oh well, this is aging." You can do things that will make a huge difference. Sometimes, you can reverse the condition. Even if you can't, you'll still be healthier. Investing in the fundamentals will reduce the adverse consequences on your ability to function in life.

Any surprising observations from patients?

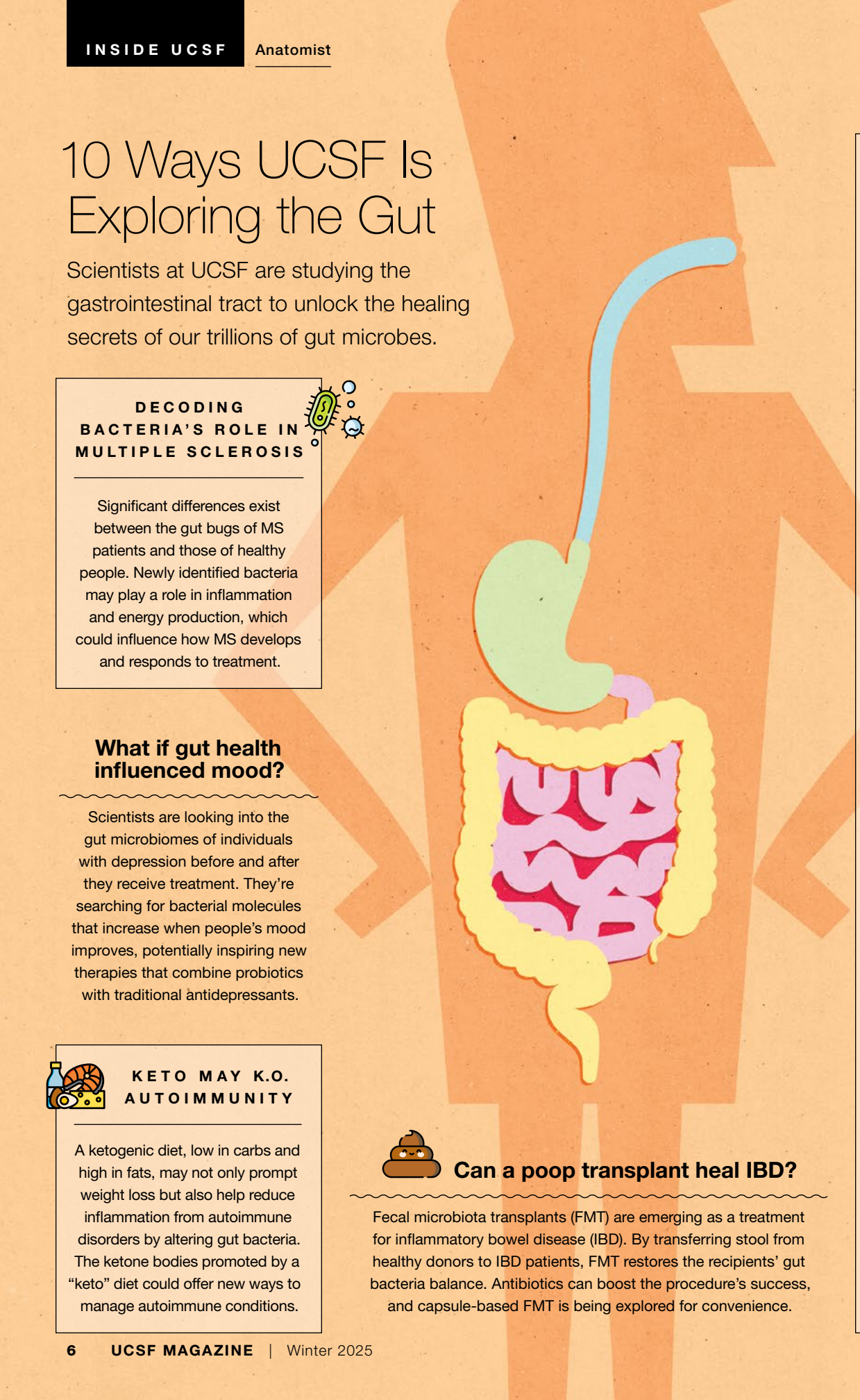
GORDON: Many people I meet say that where I'm at – two kids in school, a career, essentially the middle of my life – was the happiest, best time for them. Not necessarily the easiest, but the period they'd choose if they could go back. I find this fascinating because I'm always stressed out – as many of us are. But most folks say their lives were meaningful then, surrounded by friends, family, and work. So, pay attention to where you are right now – it may be the best time of your life. It's great to look forward, but let's also be in the moment.

So, what's the secret to aging well?

GORDON: In our caseload now, we have 14 folks over 100. I ask, "What's the secret?" Nobody has the answer, but there are some commonalities. Most were physically active. Many have a sense of humor, or they just don't take things too seriously. They enjoy life along the way, realizing it goes fast, and it's a gift to be able to keep getting older. There's no magic pill. I believe we shouldn't be so antiaging – we should enjoy it.

10 Ways UCSF Is Exploring the Gut

Scientists at UCSF are studying the gastrointestinal tract to unlock the healing secrets of our trillions of gut microbes.



DECODING BACTERIA'S ROLE IN MULTIPLE SCLEROSIS

Significant differences exist between the gut bugs of MS patients and those of healthy people. Newly identified bacteria may play a role in inflammation and energy production, which could influence how MS develops and responds to treatment.

What if gut health influenced mood?

Scientists are looking into the gut microbiomes of individuals with depression before and after they receive treatment. They're searching for bacterial molecules that increase when people's mood improves, potentially inspiring new therapies that combine probiotics with traditional antidepressants.

KETO MAY K.O. AUTOIMMUNITY

A ketogenic diet, low in carbs and high in fats, may not only prompt weight loss but also help reduce inflammation from autoimmune disorders by altering gut bacteria. The ketone bodies promoted by a "keto" diet could offer new ways to manage autoimmune conditions.

Can a poop transplant heal IBD?

Fecal microbiota transplants (FMT) are emerging as a treatment for inflammatory bowel disease (IBD). By transferring stool from healthy donors to IBD patients, FMT restores the recipients' gut bacteria balance. Antibiotics can boost the procedure's success, and capsule-based FMT is being explored for convenience.

UCSF findings could guide treatments for:

Asthma
A link exists between the gut microbiome and childhood risk of asthma. Scientists aim to reduce this risk by precisely modifying asthma-causing genes in the microbiome without disturbing its beneficial functions.

Skin disorders
For colitis patients, gut inflammation may trigger skin problems by causing the immune system to mistakenly attack harmless skin bacteria.

Obesity and diabetes
Gut bacteria can vary significantly between ethnic groups, which might explain why some people gain weight differently, even on similar diets.

Osteoporosis and osteoarthritis
Studies in mice suggest that disruptions in gut health, such as from long-term antibiotic use, can lead to weaker bones.

Colon cancer
Certain gut microbes, including *E. coli*, can activate or deactivate chemotherapy drugs for colon cancer, impacting their effects.

STIs
Taking doxycycline after high-risk sexual encounters, a preventive therapy known as doxy-PEP, significantly reduces sexually transmitted infections (STIs) but may affect the gut microbiome.

ILLUSTRATION: KOTRYNA ZUKAUSKAITE

Could This New Drug Reverse Multiple Sclerosis?

Multiple sclerosis (MS) strips away a protective sheath, made of a substance called myelin, around the nerves in the brain and spinal cord; this leaves the nerve fibers exposed and causes problems with movement, balance, and vision. If left untreated, MS can lead to paralysis, a loss of independence, and a shorter lifespan. But now, researchers at UCSF and Contineum Therapeutics may have found a way to undo the destruction of myelin.

They've developed a drug called PIPE-307 that encourages the body to regenerate lost myelin. If it works in humans, it could help reverse some of the damage caused by MS. The drug targets a specific receptor on brain cells, triggering them to become myelin-producing oligodendrocytes. Once activated, these cells wrap around exposed nerve fibers, forming a new protective layer of myelin.

This breakthrough builds on a decade of work by two UCSF scientists – Jonah Chan, PhD, and Ari Green, MD. Back in 2014, Chan's team discovered that a common antihistamine, clemastine, promoted remyelination – something no one had thought possible until then.

Myelin (above) is illuminated in the brain using an antibody for a myelin gene. Myelin insulates the brain's neural wiring, axons, ensuring that electrical signals can be properly transmitted.

"Ten years ago, we found one way the body can regenerate myelin in response to the right molecular signals, effectively turning back some of the effects of MS," says Chan, a Rachleff Distinguished Professor of Neurology at UCSF and senior author of the paper. "Now, with this new drug, we've created a more precise therapy to activate this process."

PIPE-307 may herald a new class of MS therapies that help the body repair itself.

PHOTO: CHAN LAB

Does Too Much Salt Contribute to Eczema?

Eating too much salt might be linked to a higher risk of eczema, according to UCSF researchers. They found that consuming just one extra gram of sodium a day – about ¼ teaspoon, or roughly the amount in a Big Mac – could increase the chance of an eczema flare-up by 22%.

Eczema is a chronic condition that causes dry, itchy skin and affects over 31 million Americans. One in 10 people develop it at some point, and it's becoming more common, particularly in industrialized nations, suggesting that lifestyle and diet may be contributing factors.

While high sodium intake has long been known to increase the risk of heart disease and hypertension, scientists have now discovered that sodium can accumulate in the skin, possibly contributing to the inflammation that triggers eczema. Reducing salt intake might be a simple way to reduce symptoms.

Recommended:

Books, Videos, & Podcasts

READ

Relinquished: The Politics of Adoption and the Privilege of American Motherhood

In this decade-long study of adoption, UCSF sociologist Gretchen Sisson, PhD, sheds light on the often-overlooked experiences of mothers who put their infants up for adoption. Through their stories, she explores the intersection of adoption, reproductive justice, and inequalities that shape how families are created in America.

WATCH

Elena: The Courage in Being Human

When she was only 11, Elena Sweet received a life-altering diagnosis: a rare bone cancer. But through sheer resilience, creativity, and deep connections, this remarkable UCSF patient triumphed over adversity. This brief video makes it clear why Elena earned the 2024 Colin Powell Medal of Courage from UCSF Benioff Children's Hospitals. Visit: tiny.ucsf.edu/courage

LISTEN

Illuminating Health

Join experts from the UCSF School of Nursing as they delve into topics like postpartum depression, the healing power of music, and new ways to manage diabetes. Each episode of this podcast offers fresh insights to improve everyday health and well-being.

What's the Truth About Healing from (or Preventing) Injuries?

Common advice runs the gamut from spot-on to flat-out false. What's best for our bodies?

By Carin Moonin | Illustration by Farah Hamade

Recuperating from an injury involves many considerations, and determining the most effective approach can be confusing. Experts in UCSF's Department of Physical Therapy and Rehabilitation Science explain best practices in injury recovery and prevention.

MYTH #1: No pain, no gain.

"Pain is part of our lives. It's protective. If you step on a nail or touch a hot stove, pain kicks in to protect your body," says Megan Yamashiro, DPT '16, an assistant clinical professor. But if pain is ongoing or occurs without a clear trigger, it should be investigated.

Also, not all pain is the same. "Is it sharp or shooting pain? Is there numbness or tingling? Physical therapists will suggest different parameters to determine pain. If it's a green or yellow light, maybe we can forge ahead," she says. "If we are helping with an Achilles tendon issue, for example, some low-level pain can encourage healthy tissue changes to strengthen the tendon. But in some cases, like acute frozen shoulder or adhesive capsulitis, it's not helpful to push through pain. That's a red light, and we'll do something else instead."

Ivan Arriaga, DPT '18, an assistant clinical professor, says it's usually in people's best interest to begin moving soon after an injury, within tolerable limits. "If something hurts when you start doing it, and it feels better as you continue, your body's saying that's what you need. But if you experience ongoing pain and feel like you can do even less, that's counterproductive."

"When you start a new exercise program, some muscle soreness lasting a day or two is common," explains Richard Souza, PhD, a professor and the department's vice chair of research. "Providing that pain is gone by the next morning, you can probably progress slowly." But if you have persistent pain that occurs each time or gets worse, he suggests seeing a physical therapist.

"Listen to your body before it starts yelling at you," Yamashiro says. "If we pay more attention to those conversations, we can prevent a lot of problems."

MYTH #2: If I hurt my back, I should lie flat in bed.

Back pain can be scary. And people may fear they might not be able to regain mobility after a severe episode. But according to Luc Fecteau, DPT, an associate professor, the sooner you restart your daily activities, the smoother your path to recovery.

"During physical therapy, we'll watch how the back responds to different treatments. When the pain is acute, we use light movement and modalities to try to bring the pain down. Then, as soon as someone can tolerate a little more, we can progress," he says.

That said, a condition that causes numbness, weakness, or loss of bladder control is an urgent situation that requires further exploration, Fecteau adds.

A physical therapist may also serve as a de facto primary care provider. "Based on our training and education, we decide if each case is a treat, refer, or treat *and* refer scenario. It's never too early to get a consult if you're concerned about a more serious injury," Yamashiro says.

MYTH #3: You're ruining your neck by constantly gazing down at your phone.

"Using your phone isn't necessarily harmful to your neck – but not moving can be," says Yamashiro. "Try changing positions at least every 30 minutes. Vary sitting and standing. Use AirPods or headphones. The more you can change positions, the better."

Fecteau agrees. "We're not designed to stay static. We're designed to be moving. Our joints get nutrients through compression and

decompression cycles of our cartilage, which acts like a cushion protecting our bones. Without movement, the cartilage doesn't get the nutrients it needs. If we keep the same position for a prolonged period, we're asking for trouble."

MYTH #4: Running ruins your knees.

Souza would like to dispel this long-standing legend. It's simply false, he says.

"The biggest predictors of knee osteoarthritis are a high body mass index, knee malalignment, and a previous knee injury – for example, people who have torn their anterior cruciate ligament or their meniscus or had other major injuries within their knee," explains Souza. He does note that "one study shows that your odds are slightly higher if you were a very competitive, fast marathon runner. But for recreational runners, the evidence is definitely not there. However, if you've never run and at 50 or 60 want to start, you must do it very carefully. Your articular cartilage – the tissue that covers the ends of bones where they form joints – and other tissues aren't used to running, so injuries can occur. Slow transitions are the key to doing it safely."

MYTH #5: I can't improve my running or walking biomechanics.

It's never too late to adjust how we move. And it starts with gait modification, says Souza.

Walking and running involve complex actions at each joint, which affect your joint and muscle health, he explains. During gait analysis, a physical therapist assesses how your joints work together and your overall movement.

"Physical therapists can evaluate the alignment between your hip, knee, and ankle. We want to see proper alignment of the leg during loading phases. It's common for runners to have their knees collapse inward. That kind of form has been associated with injuries like iliotibial band – also called IT band – syndrome, kneecap pain, or stress fractures," notes Souza.

To address concerns like these, physical therapists work with patients to build strength, improve motor control, and train their muscles to contract with the right timing so they can move effectively and safely.

MYTH #6: I can't function without the latest newfangled shoes/gear/treatment.

The right tools can encourage people to move more, but one size doesn't fit all. And most of the evidence doesn't point to the latest gadgets making a measurable difference, say Fecteau and Souza.

"However, there's a lot in science we still don't understand," adds Souza. If you find something works for you, he says, but "research doesn't necessarily support it right now, that doesn't mean it's not effective."

MYTH #7: As I get older, I can't do as much.

You may not be able to complete the same workouts in your 70s as you did in your 20s, but that doesn't mean you should throw in the towel. All athletes benefit from improved strength. For example, runners who keep going well into their eighth decade may trade a couple of daily runs for resistance training, Souza says.

"One of the best things you can do as a runner are squats and lunges. They're multi-muscle, multi-joint exercises. If you do them correctly, with attention to form, you're exercising the exact muscles you need," he says.

Yamashiro also points out that any activity calls for adaptability in mind as well as body. She says she's met patients from 9 to 99 years old, and the ones who get to keep doing what they love share one asset: flexibility.

"Being able to evolve with your body is difficult. We see ourselves in the past, and we want to relive that feeling or athletic moment. It's OK to acknowledge your limitations while continuing to push the boundaries – maybe with a different activity. There's something beautiful about being able to change and adapt," she adds.

Healthy Diet with Less Sugar Linked to Younger Biological Age

UCSF researchers have found that sticking to a diet high in vitamins and minerals and low in added sugar is linked with younger biological age at the cellular level.

In the study, scientists analyzed how three different measures of healthy eating influenced an individual's "epigenetic clock" – a test that estimates biological age and can give insight into health and longevity. The results showed that the healthier people ate, the younger their cells appeared. However, even among those following a healthy diet, each gram of added sugar was associated with an increase in biological age.

"The diets we studied are in line with current recommendations for preventing disease and supporting overall health," says Dorothy Chiu, PhD, a postdoctoral scholar at UCSF's Osher Center for Integrative Health and the study's first author. She adds that the research highlights the powerful role of antioxidant and anti-inflammatory nutrients in slowing cellular aging.

Added sugar is present in

74%

of packaged foods, even in foods often tagged as healthy, like yogurt and energy bars.

Yifan Cheng, PhD (right), and Stephen Nishimura, MD, work with an electron microscope.

The Protein That Works in a Straitjacket

For years, scientists have thought that TGF-beta – a signaling protein that holds sway over an astonishing array of cellular processes, from embryonic development to cancer – could only do its work once it escaped a lasso-like "straitjacket."

But now, using cryogenic electron microscopy (cryo-EM), a powerful technique that enables scientists to make moving three-dimensional models of molecules at atomic resolution, UCSF experts have discovered that this protein is far craftier than they had thought.

It shakes and wiggles within its straitjacket, extending a few fingers to activate a neighboring receptor, despite being encased at the surface of the cell.

The finding upends decades-old dogma on how TGF-beta works. It could help scientists improve the many therapies aimed at controlling the protein, including an important new class of cancer therapies called checkpoint inhibitors that have not worked as well as expected.

"The field has historically focused on stabilizing these kinds of signals to get a high-resolution image, but doing that has ignored how flexibility could be part of their function," says Yifan Cheng, PhD, a UCSF professor of biochemistry and biophysics and co-senior author of the paper. "For TGF-beta, this flexibility plays a vital role, and we think it could explain how other poorly understood signals work – with implications for understanding and treating disease."

Scientists Discover Hormone That Builds Strong Bones

Researchers at UCSF and UC Davis have identified a new hormone, a maternal brain hormone called CCN3, that helps keep bones strong during breastfeeding and could also aid in healing fractures and treating osteoporosis. In studies with mice, the hormone was shown to increase bone density and strength, offering potential benefits for the general population. This discovery solves a long-standing puzzle – how females' bones stay strong during breastfeeding, even though calcium is drawn from their bones to produce milk.

PHOTO: NOAH BERGER

Breakthroughs and Other Buzz

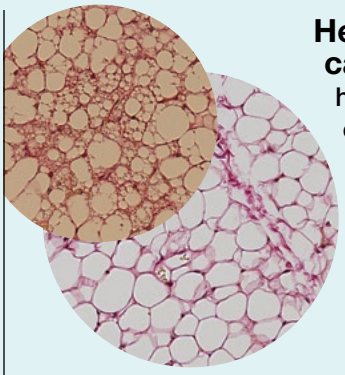
New clues to predict SIDS: UCSF scientists have identified metabolic biomarkers – substances in the body that reveal how well it processes energy – that may predict the risk of sudden infant death syndrome. This finding could open up new pathways for early detection and prevention.

Stroke care gaps in poor areas: UCSF research shows that hospitals in poorer communities are far less likely to offer certified stroke services, limiting their ability to provide critical, lifesaving treatment.

Predicting seizure risk: A team of UCSF epilepsy specialists has developed a method to predict a person's 24-hour seizure risk. This forecasting tool could help millions of Americans with epilepsy better manage their condition.

A-fib incidence higher: Atrial fibrillation, a rapid and irregular heartbeat, is three times more common than previously thought. New UCSF estimates suggest it affects nearly 5% of the population, or about 10.5 million U.S. adults. Although it's treatable, better prevention efforts are needed.

Tubes tied, pregnant even so: A UCSF study found that 3% to 5% of U.S. women who have had their tubes tied reported an unplanned pregnancy. The researchers said that contraceptive implants or IUDs could be more effective options for preventing pregnancy.



FAT CELLS: COURTESY LIANG LI, PHD, AND BRIAN FELDMAN, MD, PHD; KETO DIET: FUZULL HANUM

Helping fat cells burn calories: UCSF scientists have discovered how to convert white fat cells, which store calories, into beige fat cells, which burn calories to maintain body heat. This could eventually lead to new weight-loss medications.

Vision-saving discovery: Scientists have long known that blood vessels nourish the retinal cells that allow us to see, but the process by which these vessels form was a mystery. UCSF researchers have found a new type of neuron that guides their formation, which could lead to better treatments for several eye diseases.

ChatGPT overprescribes emergency care: If ChatGPT were cut loose in the emergency department, it might suggest unneeded X-rays or antibiotics for some patients and admit others who didn't require hospital treatment, a UCSF study has found. The researchers say it's still no match for the clinical judgment of a human doctor.

New pathway for spinal healing: UCSF scientists have uncovered a new molecular pathway that regulates scar tissue formation after spinal cord injuries. This discovery, based on mouse studies, could lead to the development of drugs aimed at promoting healing.

Keto stops cancer growth: UCSF researchers have discovered a way to stop pancreatic cancer in mice by pairing a high-fat ketogenic diet with a new cancer drug. The treatment blocks the cancer's ability to metabolize fat, its only fuel source, causing tumors to stop growing.

Transplant milestone: The UCSF Lung Transplant Program hit a major milestone by performing more than 100 transplants in one year, joining just a handful of U.S. medical centers to have done so.

Inflammation's toll on the brain: A UCSF study found that young adults with higher levels of inflammation – which is linked to obesity, inactivity, stress, and smoking – may experience reduced cognitive function by their 40s.

Ways to cut tween screen time: According to UCSF research, the most effective ways for parents to reduce excessive screen time in tweens is setting limits on screen use in bedrooms and during meals and modeling good tech habits themselves.

Trauma therapy can prevent disease: If young children experience significant trauma, psychotherapy sessions with a parent or other caregiver may slow their rate of biological aging and help prevent serious disease later in their lives, a UCSF study found.

Breakthrough in targeting enzymes: UCSF researchers have figured out how to target GTPases, a group of 150 essential enzymes that act like cellular "switches." When mutated, these enzymes can cause diseases like cancer and Parkinson's. This breakthrough opens up new treatment possibilities.

What **Bold Steps** Are Needed to Lead UCSF into a **New Era**?

From the start, **Catherine Lucey, MD**, has defied expectations. While most of her peers pursued careers more commonly associated with women at the time, she was determined to become a physician. Forging a path in a male-dominated profession, she rose to become a respected leader who has shaped academic medicine. Now, as executive vice chancellor and provost, she's driving UCSF into a new era of research and education.

By Paula Hermann

PHOTO: BARBARA RIES

How do you begin tackling health care's most demanding challenges?

It requires looking beyond our institution – at our patient community, city, state, and nation – and asking, "What does the world desperately need from us?" It's about daring to think beyond incremental shifts and envisioning what could genuinely change the game. Asking big questions helps us think more expansively about what we can accomplish.

We are a small university. How can we make a big impact?

Transforming health care isn't about having just a world-class hospital. We also need a world-class discovery mission and educational environment. In addition, we need partners to help us develop or advance the best ideas into treatments for our patients. External partnerships with other academic institutions, foundations, and biotech and pharma firms have helped our researchers move discoveries into clinical trials and ultimately into therapies that hold great promise for treating and even curing diseases – biologic technologies like CRISPR and living therapeutics.

For example, our partnership with Thermo Fisher Scientific, located near our Mission Bay campus, will enable us to take cells from our patients and move them to commercial labs that then use technologies – discovered at UCSF – to develop targeted cell therapies. We may be a small university, but our faculty's creativity and our diverse partnerships allow us to punch above our weight.

Would you consider yourself a strategic disruptor?

I love that term! I think it's essential to examine systems and complex problems through a visionary lens and be willing to disrupt paradigms. My office supports people within UCSF in doing their best work, which sometimes involves what I call bureaucracy busting. Academia often clings to outdated systems or policies. We're actively working to find and modernize policies and systems to make work easier and more efficient for our people.

For example, we've improved UCSF policies around childbearing and child-rearing. When academic medicine first emerged as a field, it was a homogeneous population of primarily white men. Today, we have a diverse workforce representing different races, ethnicities, genders, sexual orientations, religions, and countries of origin. Our new programs include extended maternity and paternity leave benefits, enhanced lactation support services, flexible work arrangements, and increased on-site childcare availability. These programs better align with the needs of our current and future workforce. Systems improve when we're willing to question the status quo.

What is one radical change you'd like to see in medical education?

I'd love to see California invest in a strategy that ensures every person in every community in the state who needs care has access to a UCSF-quality health professional. That goal is one reason we're working with our colleagues at UC Merced and UCSF Fresno to launch a new medical education program. It's an example of how you can improve the health of communities by training people from those communities to be outstanding clinicians. Ensuring that every community in the state has access to exceptional care will require building on this pilot program and engineering others like it.

How do you manage the risk involved in advocating for unconventional approaches?

Risk is inherent in any innovative endeavor, but we lean on the scientific method. We plan, we test, and if things don't go as expected, we learn and iterate. A failure in our community of scientists and educators simply means that we need another iteration.

In my previous role in medical education at UCSF, a student from a historically marginalized group questioned the fairness and equity of our grading system. It led to a difficult and uncomfortable discussion, but we took the point seriously. A thorough internal investigation uncovered significant inequities that often favored students from majority populations. This led us to make substantial modifications to ensure a fairer grading system.

We published our findings in the peer-reviewed literature, sparking similar investigations and reforms across dozens of institutions and ultimately influencing national standards. This effort exemplifies our commitment to surfacing ideas, listening to concerns, and taking decisive action to create meaningful change.

What is the key to revolutionizing science at UCSF?

Transformational change thrives in an environment where idea-sharing is encouraged. I think the team spirit here is remarkable, and it's because of a culture of curiosity and a level of humility. We have always walked the walk in terms of collaboration, and team science is central to our reenvisioning of the Parnassus Heights campus, especially in the new UCSF Barbara and Gerson Bakar Research and Academic Building. The building is designed by scientists for scientists and strategically locates researchers from various disciplines adjacent to each other – for example, cancer, immunology, microbiota, and diabetes – to spur discovery. It's a revolutionary shift in how we do science and address significant issues in human health.

Catherine Lucey, a resident alum, began serving as UCSF's executive vice chancellor and provost in January 2023.

ON THE ORIGIN OF DISEASES

Insights from human evolution could change how we understand and treat illness.

BY ARIEL BLEICHER

ILLUSTRATION BY TIM O'BRIEN

For as long as life has existed, so has the potential for disease. Four billion years ago, as meteorites pummeled the planet and volcanoes spewed toxic gases into the primordial atmosphere, a molecule emerged that could copy itself – a kind of proto-DNA. This was the dawn of evolution. It also marked the beginning of genetic disorders, since replication inevitably leads to copying errors.

Soon, the first organisms were born, and the process of cellular reproduction laid the foundation for aging. Later, the genesis of multicellularity – which gave rise to bodies, limbs, and organs – paved the way for cancer. And when immune systems evolved to fight off pathogens, they set the stage for asthma and autoimmune conditions.

Eventually, evolution forged the human genome. When our ancestors diverged from other apes, they acquired extraordinary capabilities, including language and tool-building. But their larger brains, upright postures, and lack of body hair also left them vulnerable to certain neurological, joint, and skin ailments. As human populations spread around the globe, they faced new environments and evolutionary pressures. A great diversity of genetic variation arose – and with it, a great diversity of new disease risks, including diabetes, migraines, and sickle cell disease.

By looking to humans' evolutionary past, scientists at UC San Francisco are discovering not just *how* we get sick but *why*. They are finding that some of the same adaptations that make us uniquely human also make us uniquely susceptible to illness, particularly mental illness. They are learning how Neanderthals and other archaic human relatives passed along both advantages and disadvantages that many of us still harbor in our genomes today. And they are decoding the complex genetic legacy of humanity's growth and migration over the past 100,000 years.

These roots carry profound implications for modern medicine. Already, they are revealing possible origins of psychiatric disease, heart disease, and other human maladies whose causes have long remained elusive. They are also advancing our understanding of disease risk, showing how each human's distinctive ancestry can influence our health. This could all ultimately lead to new gene therapies and other personalized treatments inspired by ancient molecular innovations written in our DNA.

THE HUMAN CODE

When scientists published the first human genome in the early 2000s, Katherine Pollard, PhD, was a graduate student in biostatistics. To the untrained eye, the genomic sequence might have looked unremarkable – just a jumble of As, Cs, Ts, and Gs strung together like tiles in an impossibly long Scrabble rack. But Pollard knew those four humble letters, which represent the chemical bases of DNA, spelled out the instructions for life. She had long been fascinated by humans' origins. Now, with the blueprint for an entire person in hand, she was eager to compare it to that of our closest living relative, the chimpanzee. "I wanted to know what set us apart," says Pollard, who today is a computational genomicist at UCSF and the UCSF-affiliated Gladstone Institutes.

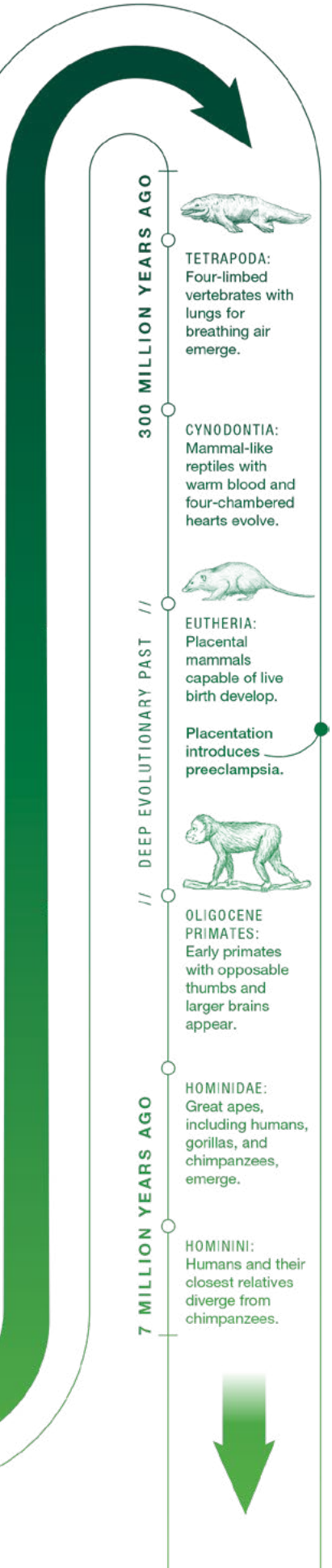
Humans' and chimps' development diverged around 6 million years ago, but remarkably, their genomes remain nearly identical – only about 1% of our DNA is different. Many of these differences are random, having little to no effect on our biology. Others hold secrets to human nature, and Pollard was determined to find them.

> Our archaic human relatives passed along both advantages and disadvantages that many of us still harbor in our genomes today.

During her postdoctoral fellowship, in 2005, she wrote a computer program that scanned the human and chimp genomes, searching for the segments that diverged the most. She found more than 200, each less than a few hundred letters long. In chimps, these DNA strings are similar to those found in other vertebrates, including mice, fish, and chickens. This implies that for millions of years of vertebrate evolution, the strings had been frozen in time. Then in humans, they suddenly transformed. Pollard called these fast-evolving parts of our genome "human accelerated regions," or HARs.

As the technology for sequencing and analyzing genomes improved, the list of HARs climbed to nearly 3,000. Pollard figured that because HARs had stayed the same in so many species before changing dramatically in humans, they must do something important – and that because they're important, they must be parts of genes. But as Pollard and others were surprised to learn, HARs turned out to be something else.

Investigating the human genome is like exploring a vast library. Perusing the stacks, you might spot a thick,



leatherbound volume – a gene. Inside is the recipe for a protein, a building block of living things. Browsing further, however, you might notice that such vital tomes are curiously scarce – a mere 2% of the library. Until recently, the remaining 98% – called noncoding DNA – was largely written off as junk, the evolutionary equivalent of credit card offers and campaign flyers that no one had bothered to toss.

This is where HARs reside. Their discovery helped convince the genetics community that such noncoding regions were worth a closer look. But if HARs weren't parts of genes, what *were* they?

Over the past decade, Pollard has been working with UCSF geneticist Nadav Ahituv, PhD. He directs the UCSF Institute for Human Genetics, and his lab had developed techniques to test hundreds of HARs in parallel. Their experiments using human and chimp cells have confirmed what Pollard and others had begun to suspect: Most HARs are regulatory sequences – manuals for how genes should operate.

Regulatory DNA tells a gene how many copies of a protein to make, in what cell types, and when. "It's how your cells know what kind of cells to become," says Yin Shen, PhD, an expert in gene regulation at the UCSF Weill Institute for Neurosciences and a collaborator of Pollard's in the effort to decipher what HARs do and how they work. Many HARs, for instance, sit near genes involved in brain development, leading researchers to conclude that they might play a role in psychiatric disease.

Humans suffer from an array of neurological conditions like autism, schizophrenia, and Alzheimer's, which chimps either don't get or experience much less severely. People with these diseases are also more likely to carry HAR mutations. "Psychiatric research has been laser-focused on genes," Pollard says. "There's a growing realization that we need to be looking at regulatory elements, too."

She and her colleagues have shown that HARs help orchestrate neural development, with about a third having unique functions in the human brain. Each HAR has between a few and a couple dozen DNA letters that changed during human evolution. Within a single HAR, some of the edited letters dial up protein production in human neurons, while others dial it down. These opposing effects suggest that many HAR edits evolved to offset others that had proven harmful. An edit that increased cognition, for instance, may also have raised the risk of psychiatric disease, leading to another edit that lowered the risk, like a game of tug-of-war.

"Evolution involves tradeoffs," says Alex Pollen, PhD, a neuroscientist at the UCSF Weill Institute for Neurosciences and another collaborator of Pollard's. His lab grows brain organoids, tiny models of neural tissue, from human and great ape cells. He's particularly interested in the genetic changes that drove the human brain's dramatic enlargement.

// HUMAN ACCELERATED REGIONS

Parts of the evolutionary genome that suddenly transformed in humans. Most are regulatory sequences – manuals for how genes should operate.

"One of the special properties of the mammalian brain is that when it expands, not all of it expands equally," Pollen says. He believes this uneven growth may have enabled cognitive advances but also created "vulnerable joints," where some neurons had to work harder to sustain more or longer connections. The brain may then have evolved mechanisms to compensate for those weaknesses.

Pollen's team recently found evidence for this theory in organoid models of Parkinson's disease. "We think there are adaptations that are partially protective," he says. "This may explain why we don't all have Parkinson's and could point us to new therapeutic targets."

OUR NEANDERTHAL INHERITANCE

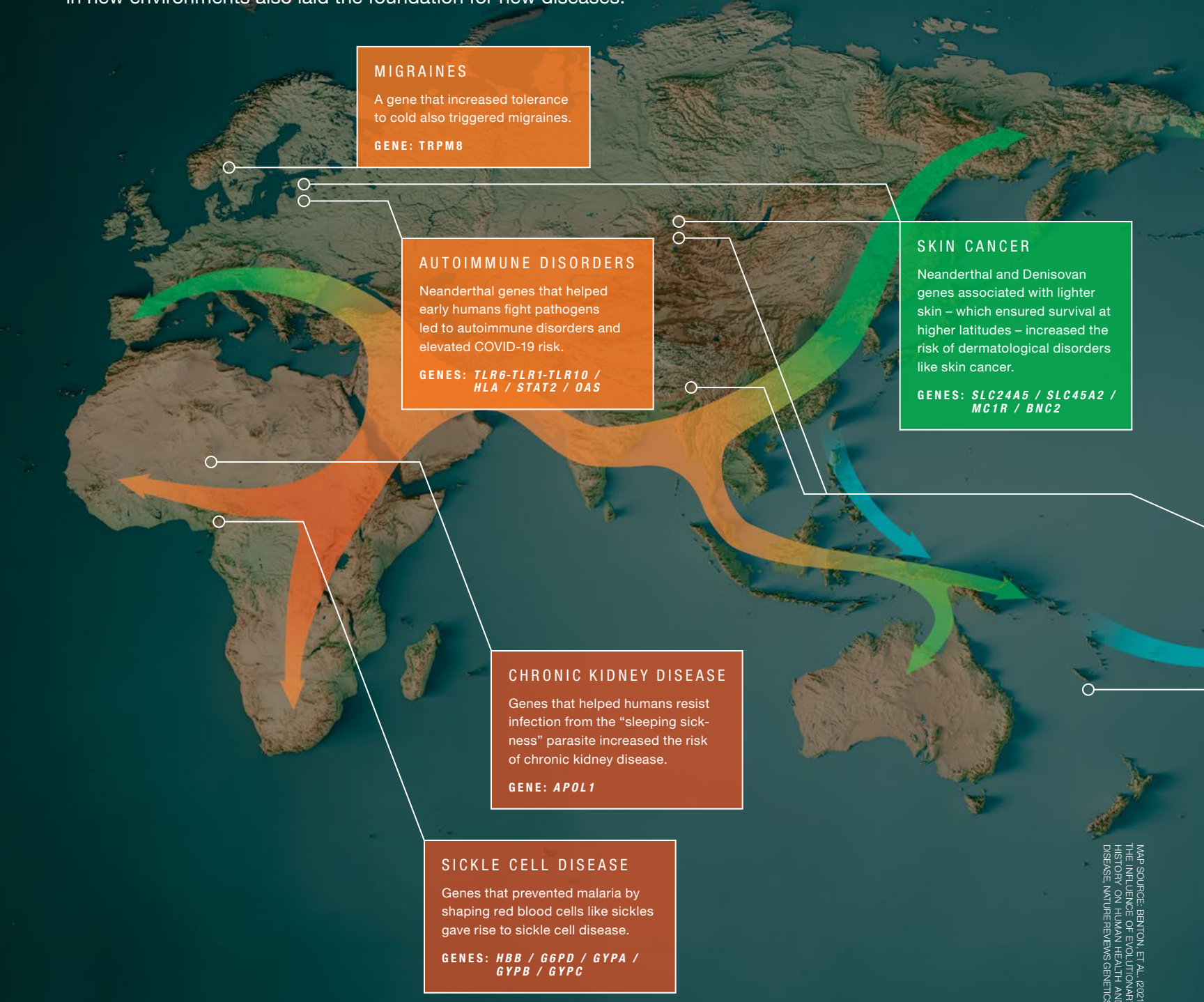
About 700,000 years ago in Africa, a branch of the human family tree split in two. One lineage stayed on the continent and evolved the anatomy of modern humans. The other migrated north, into Eurasia. Its descendants grew short and stocky, with big, wide noses, sloping foreheads, and prominent brows. These were the Neanderthals and Denisovans.

John "Tony" Capra, PhD, was a postdoctoral fellow in Pollard's lab shortly after scientists figured out how to extract and analyze ancient DNA from human fossils. Not long after, journals began publishing the genome sequences of Neanderthals and Denisovans who lived tens of thousands of years ago. When waves of modern humans eventually left Africa, they interbred with these archaic cousins. Neanderthals and Denisovans have since vanished, but, as researchers discovered, traces of their DNA live on in us. Depending on your ancestry, up to 4% of your DNA could be Neanderthal and up to 6% could be Denisovan.

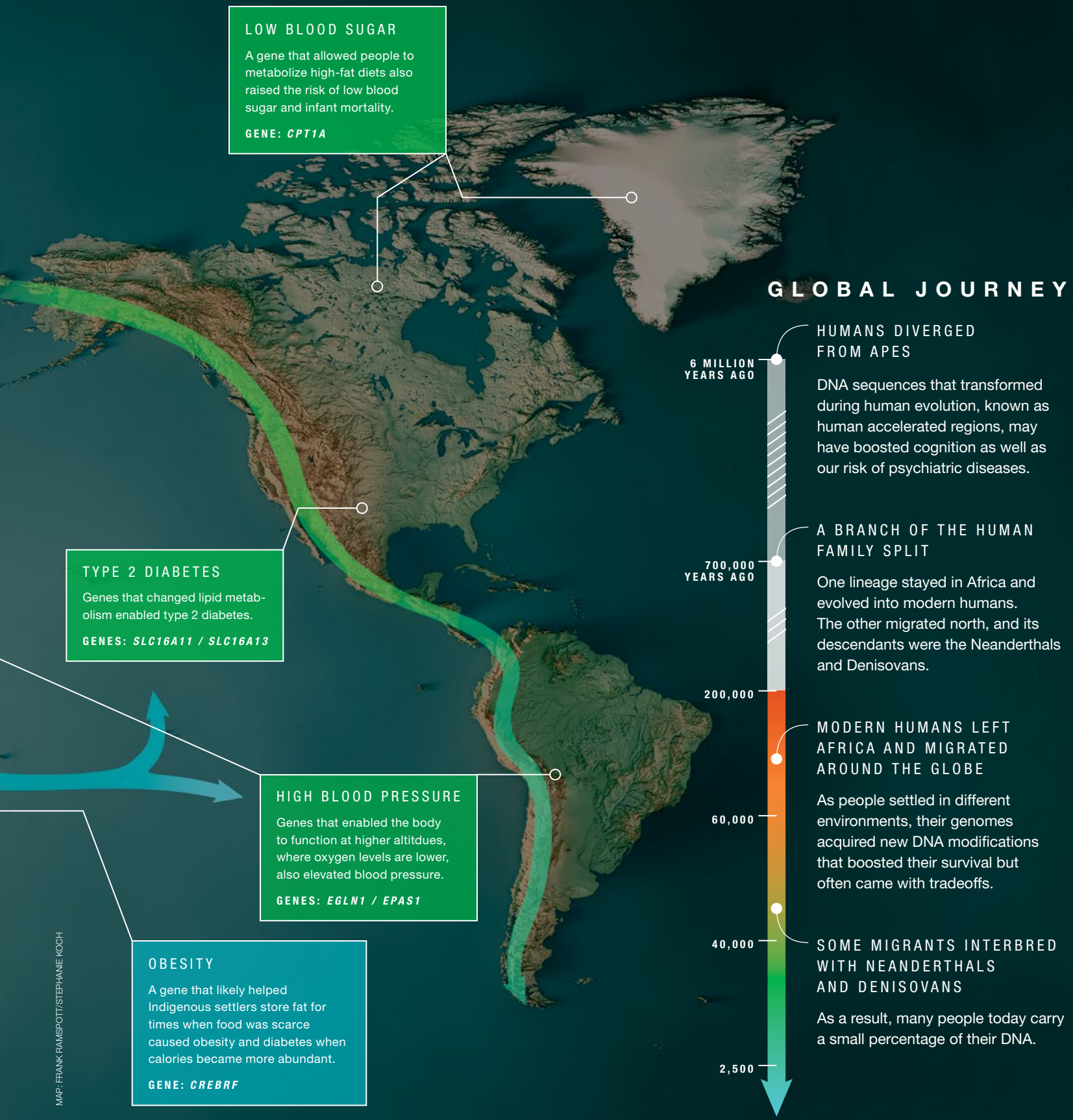
"That just blew my mind," Capra says. He began to wonder: How do the fragments of archaic human DNA still lurking in our own genomes affect *us*?

HOW ILLNESS EMERGED FROM ADAPTATION

As human populations spread around the globe, genetic changes that helped them survive in new environments also laid the foundation for new diseases.



MAP SOURCE: BENTON, ET AL. (2021), THE INFLUENCE OF EVOLUTIONARY HISTORY ON HUMAN HEALTH AND DISEASE. NATURE REVIEWS GENETICS



MAP: FRANK RAMSPOTT/STEPHANIE KOCH

// NOT SO DISTANT ANCESTORS AFTER ALL

Neanderthals and Denisovans split from the human family tree 700,000 years ago, but modern humans contain 4% to 6% of their DNA.

At Vanderbilt University – where Capra first ran his own computational genomics lab before moving it to UCSF in 2020 – he and his colleagues embarked on a groundbreaking study. The results, drawn from a database of 28,000 Europeans, linked snippets of Neanderthal DNA, called variants, to a variety of health conditions. They found that inheriting combinations of Neanderthal variants increased an individual's risk for depression and for getting skin lesions from being out in the sun. The team also identified specific Neanderthal variants associated with higher risk for tobacco use, malnutrition, bladder problems, and excessive blood clotting.

Other Neanderthal and Denisovan variants seem to be beneficial. Many people, for instance, carry archaic variants that affect immunity and metabolism, which may have helped their ancestors adapt to new pathogens and foods. Neanderthals also passed along variants for lighter skin and hair – a survival advantage at higher latitudes, where sunlight is weaker. And if you're an early riser, it might be thanks in part to your Neanderthal or Denisovan inheritance, Capra recently discovered. Scientists believe that this trait may help the body adjust to seasonal daylight changes and reduce the risk of mood disorders.

Most archaic DNA, though, no longer exists in humans living today. "When we look at parts of our genome that control certain traits – cognitive traits, for example – there is way less Neanderthal contribution than we would expect," says Capra, who is now a geneticist at UCSF's Bakar Computational Health Sciences Institute. Many Neanderthal variants, he explains, must have disadvantaged the modern humans who inherited them. As a result, they were less likely to survive and reproduce, and so the variants gradually vanished from the human population.

Researchers debate what this meant for Neanderthals themselves. By the time modern humans encountered them, their numbers were dwindling. Smaller populations are more susceptible to genetic drift, in which rare variants can become dominant simply by chance, even if they're harmful. Detrimental mutations could have easily piled up in the Neanderthal genome, Capra says. Neanderthals, he surmises, probably suffered from an array of ailments that could have led to their extinction. "I think they were a lot sicker than us," he observes.

Beyond illuminating disease genetics, archaic genomes could be "prime hunting ground" for gene therapies, Ahituv says. In addition to HARs, he is studying the tens of thousands of variants that differ in the Neanderthal and Denisovan genomes and our own. Like HARs, many of the DNA strings that contain these variants are in noncoding regions that regulate gene activity. Testing these strings in human cells, Ahituv has begun to assemble a catalog of variants that produced different traits in modern and archaic humans by changing how genes behave.

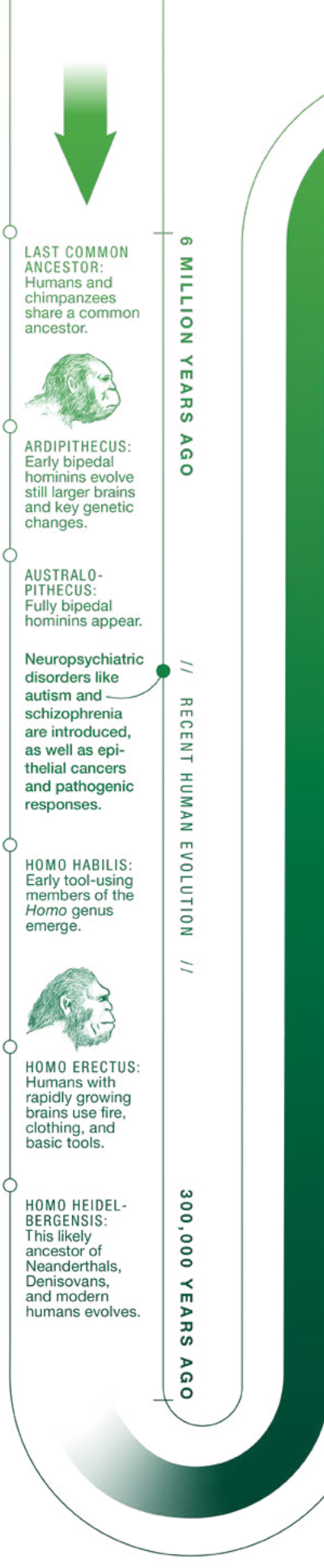
As an example, he points to a DNA string that controls a gene called *SATB2*. The version of this sequence that existed in Neanderthals and Denisovans was stronger than ours – that is, it caused *SATB2* to churn out more protein copies. The protein encoded by *SATB2* helps shape the skull and brain; having more of it gave archaic humans a more prominent face.

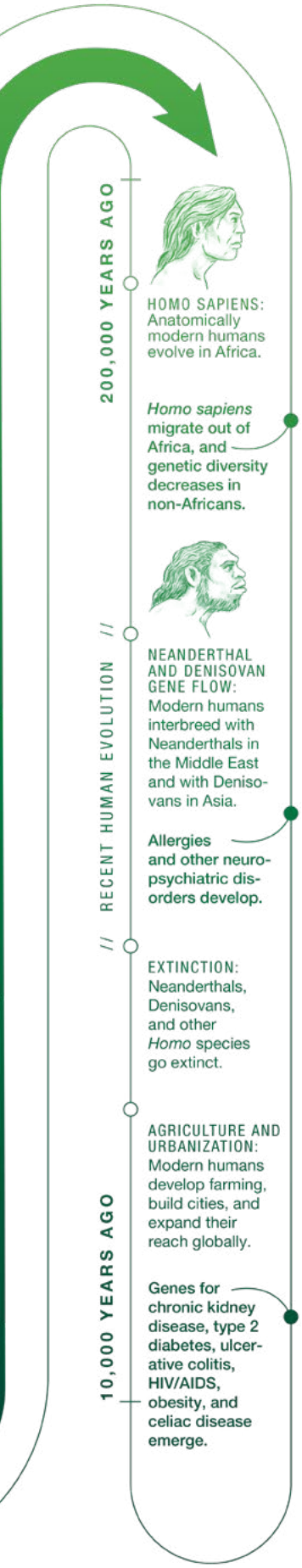
SATB2, Ahituv notes, is also implicated in Glass syndrome, which, among myriad other symptoms, causes the opposite outcome: a face that's unusually flat. If you wanted to create a gene therapy that reverses this effect – say, by designing a DNA sequence that boosts *SATB2* expression – the archaic sequence could be a good one to try, Ahituv says. "It's a crazy idea," he admits, "but it shows how evolutionary history could be useful for clinical discovery."

NEW ADAPTATIONS, NEW RISKS

Humans have come to inhabit nearly every environment on Earth – from frozen tundras to tropical rainforests to arid deserts. As ancient peoples settled all around the world, their genomes continued to shape-shift, acquiring new DNA modifications that boosted their survival. But, as throughout evolutionary time, these adaptations often incurred tradeoffs.

In west-central Africa, where malaria is rampant, a gene variant molded red blood cells into the shape of a sickle and prevented infection by malaria parasites – giving rise to sickle cell disease. In the Himalayas, another variant enabled humans to function on less oxygen – but also elevated their blood pressure. In Scandinavia, a variant that increased tolerance to cold also triggered migraines. Sometimes, variants that were once assets became liabilities when a population's descendants moved elsewhere or their circumstances changed.





Genes that likely helped early Pacific Islanders store fat for times when food was scarce, for example, became risk factors for obesity and diabetes when calories became more abundant.

Other times, different genetic variants brought about the same diseases in different populations. This is particularly true of complex diseases like asthma or breast cancer, which involve hundreds or thousands of genes and regulatory regions. Most of what's known about these diseases comes from genome-wide association studies (GWASs) – massive statistical analyses that compare DNA from many people to look for variants that are more common in those who have a particular condition than in those who don't. The findings can then be used to calculate a person's likelihood of developing that condition, known as their polygenic risk score.

Polygenic risk scores are often unreliable for people of non-European ancestry because most DNA samples available for research have come from Europeans. But that is beginning to change. In 2022, Catherine Tcheandjieu, DVM, PhD, a UCSF and Gladstone genetic epidemiologist, published the largest and most diverse GWAS of coronary artery disease and the first to include a large sample of genomes from Black and Hispanic populations. The study found 95 new DNA regions associated with the disease, which greatly improved the accuracy of risk scores for people across the board – except Black people.

> "My father is Mexican American, and my mother is white. My genome includes bits of DNA that came from Europe, bits from Africa, bits from American Indigenous populations. How the heck do I study *me*?"
>
> –RYAN HERNANDEZ, PHD

Tcheandjieu was puzzled. "You would think that if the biology of a disease is the same, you should be able to find the same mutations across populations," she says. But many of the genetic variants previously associated with coronary artery disease didn't show up in the Black population data. Maybe the problem was sample size: Did she just need more genomes to pick up a clear trend? Tcheandjieu didn't think so. She had a hunch that something else was going on.

She decided to look closer at one of the suspect DNA regions, known as the heart attack gene. Although we all carry a version of this gene, the letters in it can vary, like alternate spellings of the same word. In non-African populations, many people with coronary artery disease share the same misspellings.

But when Tcheandjieu examined the heart attack gene in people of African ancestry, she observed a much greater *variety* of spellings in that population overall. This makes sense from an evolutionary perspective, she says. Because African populations are evolutionarily older than other populations, they have had more time to accrue more genetic variation. Such diversity, Tcheandjieu says, could explain why it's been harder to find common risk variants in people with more African DNA.

Ryan Hernandez, PhD, a population geneticist at the UCSF School of Pharmacy, has found that Asian populations also have highly diverse genomes, but for a different reason. "In Asia, there have been massive population booms, where billions and billions of people have emerged over a very small amount of evolutionary time," he explains. Because each birth has supplied dozens of new mutations, rare variants have accumulated quickly.

Hernandez, who runs a lab with UCSF evolutionary geneticist Dara Torgerson, PhD, is working to understand the cumulative effects of rare variants and to develop new analytical tools to study genomes that don't fit the European mold. This is especially challenging in the Americas, he says, where many people have admixed ancestries. "I myself am admixed," he says. "My father is Mexican American, and my mother is white. My genome includes bits of DNA that came from Europe, bits from Africa, bits from American Indigenous populations. So I want to know: How the heck do I study *me*?"

The human story is still unfolding. Every baby born is a chance to tweak the genetic code. These revisions might be strengths, making the people who inherit them a little fitter or more resilient. Or they might introduce new disabilities or ways of suffering. Or possibly both at the same time. And as our environments and societies change, what was once beneficial might become harmful, or vice versa.

What remains to be seen is whether we can harness these evolutionary forces to build a healthier future.


FIGHT AIDS
SILENCE = DEATH
ACT UP
AID NOW
FIGHTING FOR OUR LIVES

HOW HIV CHANGED MEDICINE FOREVER

The quest to defeat HIV/AIDS didn't just turn a deadly virus into a manageable condition. It transformed science and health care.

BY SARAH C.P. WILLIAMS PHOTOGRAPHY BY ELENA ZHUKOVA
ILLUSTRATION BY MARCOS CHIN

“Today, many of the ethical principles that the HIV community shaped are used in every area of medicine.”

– Paul Volberding, who co-founded Ward 86, the country’s first outpatient clinic for patients with HIV, and later helped pioneer antiretroviral therapy

A FEW YEARS AGO, Steven Deeks, MD '90, was sitting at the back of a large lecture hall when the scientist on the stage mentioned his name. The researcher, speaking about the design of a new cancer immunotherapy, mentioned that Deeks had run one of the first trials. This came as a surprise to Deeks, who is an internationally recognized expert on HIV – not cancer. However, he learned that his decade-old study had paved the way for a new means of turning the immune system against tumors.

"It was the first time, and certainly not the last time, that I realized all this progress in other areas of medicine traces back to progress we made with HIV," says Deeks.

The impact goes well beyond cancer. The enormous amount of funding and intellectual capital spent on HIV research has led to many advances in science and health care – from clinical trials to infectious diseases to organ transplants.

At UC San Francisco, the ripple effects of HIV – the human immunodeficiency virus – are especially clear. In 1983, UCSF faculty members opened the doors to Ward 86, the country's first HIV clinic, at San Francisco General Hospital (SFGH). Over the four decades since, hundreds of physicians, nurses, social workers, and researchers have worked in Ward 86, across UCSF, and around the world to pioneer new ways of preventing and treating HIV. Today, many of them are using what they learned to help patients facing different diseases.

"With HIV, we had a problem that inspired a lot of people, and we had a lot of funding," says Deeks. "When you bring all these different stakeholders together and give them the right resources, you really start to make a difference in medicine."

When Community Voices Shape Clinical Trials

On July 1, 1981, Paul Volberding, MD, began his first day of work at SFGH, where he intended to start a new cancer program. But within days of Volberding's arrival, the wards had an unusual influx of patients. Young, gay men were coming in covered in purple blotches and rashes – Kaposi's sarcoma, a skin cancer usually only seen in older adults. As their disease progressed, these once-healthy men often developed other mysterious problems: diarrhea, blindness, constant sweating.

It would be months before their underlying disease was given a name – acquired immunodeficiency syndrome, or AIDS – and more than two years before the underlying virus, HIV, was discovered. In those early years, scientists weren't sure exactly how the virus spread. Across the country, some doctors even refused to treat AIDS patients because of concerns about catching their disease.

"When we started taking care of AIDS patients at the start of the epidemic, they were young people with serious and fatal complications that were just incredibly difficult to manage," says Volberding. "In many cases, part of the challenge was that [the patients didn't have] any kind of traditional family support."

Many of the men Volberding treated were his age, and he felt driven to do whatever he could to help them. Just two months into his new job, he co-founded the nation's first Kaposi's sarcoma clinic at UCSF Medical Center. By the time AIDS was recognized by the U.S. Centers for Disease Control, Volberding had immersed himself in research on the disease. He went on to help open Ward 86 and eventually became the co-director of the UCSF-Gladstone Center for AIDS Research. But he also became deeply involved in community organizations around San Francisco.

With few treatment options available beyond pain relief, Volberding worked to make patients comfortable, investigate what might be causing their disease, and start testing new interventions. In 1982, before HIV had even been discovered, Volberding began a trial of an immune drug to treat the Kaposi's sarcoma associated with AIDS. But to carry out these efforts, clinicians like him had to collaborate closely with the gay community, which was rallying behind HIV patients and providing a range of assistance.

"Without really planning it, a lot of physicians at San Francisco General found ourselves working side by side with community organizations," Volberding says.

As these support networks grew, academic researchers developing the first clinical trials for HIV maintained close ties with local organizations and family doctors, who were often treating patients after they left the hospital. For the first time, researchers were getting community input as they planned their research programs and clinical trials.

"We wanted to make sure the things that academic physicians were interested in studying were the same things that the community felt was important," says Volberding. "That input ended up being really critical."

Men with HIV, for instance, asked Volberding and his colleagues to turn more attention to preventing some of the secondary infections – like salmonella and tuberculosis – that often ravaged their bodies. Until that request, Volberding says, most researchers had been focused almost entirely on HIV itself. At the same time, the scientific community learned how to gain the trust of men likely to contract HIV, how to enroll them in trials, and how to design trials in an ethical way.

At the time, the only way for most men with HIV to receive any meaningful treatment was to enroll in clinical trials. But the way most trials had long been run meant excluding men who had other complicating conditions and assigning many patients to control groups that did not receive the new treatment. To maximize the number of HIV/AIDS patients who could receive experimental drugs, doctors and ethicists worked together to design trials differently. For example, some compared their results to previously collected data rather than to a control group, enabling more patients to access the experimental therapy.

"All of that seems commonplace now, but HIV really broke new ground when it came to the way researchers interact with community organizations and the way clinical trials are designed," Volberding says. "Today, many of the ethical principles that the HIV community shaped are used in every area of medicine."

The Race to Understand Immunity

By the 1990s, doctors knew the basics of how HIV was causing disease (by attacking the body's immune cells) and how the virus spread (through bodily fluids). New infection rates in North America and Europe were falling in the wake of public health campaigns. Yet patients already infected with HIV still struggled. By 1994, AIDS had become the leading cause of death for Americans between the ages of 25 and 44.

Deeks, who began caring for people with HIV during this time, recalls when he and his colleagues had just one drug to try to slow the progression of HIV. Called azidothymidine, or AZT, it blocked the ability of HIV-infected cells to make new copies of the virus. For a short time, the drug lowered virus levels in infected people. But HIV evolved quickly, eventually developing resistance to the drug in most patients. Other options were urgently needed.

"We knew we had to do something, so we started really pushing the envelope, trying whatever we could think of," says Deeks, who is now a professor of infectious diseases at UCSF.

He and other scientists pursued a variety of ideas. However, developing better treatments required a massive investment in basic research. In the 1990s, that investment happened: Federal funding for HIV/AIDS increased from millions of dollars per year to billions, hitting $10 billion annually by 1999. Researchers needed to understand exactly how the immune system was reacting to HIV and the details of its full life cycle. Thanks to the influx of attention and funding, many immunologists began devoting their labs to these questions.

"HIV blows up the whole immune system, which is terrible for patients but turns out to be really interesting for scientists," says Deeks. "You can essentially use this virus to see what happens when the immune system is shut down in a targeted way, and then what happens when you treat it."

The work of veteran HIV researcher and clinician Steven Deeks and others spurred foundational knowledge about the immune system and how viruses interact with it.

These experiments revealed a complex crosstalk between dozens of different immune cells and molecules – information that formed the bedrock of new immunology knowledge. It became the basis for many other studies on viruses, antiviral drugs, and vaccine development.

Eventually, researchers discovered that antiviral drug combinations targeting many different parts of the HIV life cycle could send HIV patients into long-term remission – successfully shifting the disease from a fatal diagnosis to a chronic but manageable condition.

Over the last couple of decades, the science pursued in the fight against HIV has proven valuable to many other efforts to improve health, particularly immunology. Although trial after trial of HIV vaccines has failed, the lessons learned in each attempt – including exactly how the human body produces antibodies and how to control those pathways – made the development of vaccines against other diseases easier.

"Even though we have not yet been successful at an HIV vaccine, the HIV community has gotten really good at tracking what a vaccine is doing in the body and whether it is working," says Susan Buchbinder, MD, a professor of epidemiology and biostatistics at UCSF and the director of HIV prevention research at the San Francisco Department of Public Health.

For example, a new vaccine against respiratory syncytial virus – approved for infants in 2023 – was possible largely because of knowledge gleaned from HIV research about how to target viral proteins. Similarly, when COVID-19 emerged, scientists quickly turned to methods for studying SARS-CoV-2 that had long been used to understand HIV and develop potential vaccines against the virus.

The innovations spurred by the rush to conquer HIV also led to Deeks' surprising connection to cancer. In the '90s, a small group of investigators developed a new way to genetically alter the immune system's T cells, letting them control what these cells recognized and attacked. They approached Deeks about trying to engineer these chimeric antigen receptor (CAR) T cells so they would destroy any HIV-infected cells in a person's body. Deeks readily agreed and launched one of the earliest clinical trials of a CAR T-cell therapy.

Liver specialist Jennifer Price (left) delivers care via a van to people with hepatitis C, an idea inspired by HIV community outreach efforts. Infectious disease physician Annie Luetkemeyer (right) says HIV's test-and-treat model is helping thwart hepatitis C.

"It almost worked," recalls Deeks. "We showed that these cells could effectively bind to HIV and that they could be used safely."

Years later, researchers realized that adding another immune molecule to the mix made the CAR T cells far more powerful. Building on Deeks' first trial, they found the therapy very effectively targeted cancer cells. Today, several CAR T-cell therapies have been approved by the U.S. Food and Drug Administration, and more than 30,000 patients with blood cancers in the U.S. have been treated with the therapy. It's now considered one of the most promising new ways to attack cancer, and researchers at UCSF and elsewhere are racing to extend its benefits to other areas of medicine.

A Blueprint for Hepatitis

Every Friday morning, a brightly painted van parks on a street corner in the Tenderloin district of San Francisco and opens its doors. Inside, staff members ready their supplies to screen people for hepatitis C, a virus that infects the liver and can lead to long-term disease and death. The team hopes to attract patients who are most at risk for the disease, including people using injectable drugs or experiencing homelessness. Rather than wait for these people to visit a clinic, they bring care to them.

The mobile van, dubbed DeLIVER Care, was the brainchild of liver specialist Jennifer Price, MD, PhD, a professor of gastroenterology at UCSF. Price says she took her inspiration from community initiatives to test for and treat HIV.

"The HIV community had been incredibly successful at reaching people who are less likely to interface with the traditional health care system," says Price. "We had a really good lesson, right here in San Francisco, for how to do that."

Launched in 2019, the van aims to make more people aware of their hepatitis C status and provide them with treatment. An estimated 2.6% of all adults in San Francisco are positive for the infection, putting them at risk of liver cancer and liver failure. But many people don't know they are positive.

Like HIV, hepatitis B and hepatitis C are viruses that spread through bodily fluids, cause chronic infections, and weaken the body over time. In the case of HIV, the virus attacks the immune system, while the hepatitis viruses target the liver. Many immunologists study both HIV and the hepatitis viruses because of the similarities in how they work and because about 10% of all people with HIV also live with one or both hepatitis viruses.

In fact, the viruses are so similar that several of the major HIV antiviral drugs also help control hepatitis B. Today, those drugs are used commonly in people infected with both viruses. In addition, the paradigms for testing and treating hepatitis are based on years of fine-tuning the protocols for HIV. Those years led to two takeaways: Test everyone and treat early.

For the first 20 years of the HIV epidemic in the United States, physicians recommended that only people with risk factors for the virus get tested regularly. But those risk factors mostly revolved around people's sexual behavior and injectable drug use – matters they might not be comfortable disclosing to a physician. The recommendation meant that people who didn't share this information, or didn't fit the risk profile, typically wouldn't be tested.

Annie Luetkemeyer, MD, a UCSF infectious disease physician, recalls a patient she treated many years ago who was being seen for severe headaches. A scan showed an area of damaged tissue in her brain, and doctors carried out an invasive biopsy to try to find the cause, suspecting a tumor.

"It ended up that she had toxoplasmosis, which is a classic infection associated with HIV," recalls Luetkemeyer, who was a trainee at the time. "Sure enough, she tested positive. If we had known her HIV status up front, we could have avoided the brain biopsy. But she was in a demographic where HIV didn't cross anyone's mind."

Because of stories like that, in 2006, the U.S. Centers for Disease Control and Prevention recommended routine HIV screening for all patients aged 13 to 64. In 2020, similar recommendations were issued for hepatitis C.

"It's the same story with hepatitis C," says Luetkemeyer. "There are so many people now diagnosed that don't know how they got it and don't have classic risk factors. But with hepatitis, I think we got to this place of universal testing more quickly because of HIV."

HIV insights also led to guidance to treat everyone with a hepatitis infection – even those without symptoms – and to begin treatment as soon as someone tests positive, without requiring a follow-up appointment. For years, clinicians worried that such an approach would lead to problems for patients. But studies on HIV showed that this tactic ultimately led to more patients receiving care than would have otherwise been the case.

In 2023, Price confirmed that this approach works for hepatitis C: 92% of people who received same-day treatment had undetectable amounts of virus in their blood at a later appointment. It was the first U.S. evaluation of a test-and-treat model for hepatitis C in a neighborhood setting.

"It's completely accurate to say we adopted the model that had been spearheaded for HIV," says Price. "And now it's helping us get rid of hepatitis C."

An Opportunity to Reshape Global Health

In most of rural East Africa, visiting a health care clinic was long seen as a last resort. Someone could go years without seeing a doctor, traveling to a clinic only for emergency care after a farming injury or because their family was sick with malaria. The idea of regular checkups or preventive medicine was foreign; most clinics were not equipped to follow patients over time or to prescribe medicines that would be taken for more than a few weeks.

In the late 1980s, that began to change. Countries like Uganda – where more than one in seven people tested positive for HIV by 1987 – organized new national health care clinics, trained community workers, and collaborated with funding agencies to support long-term treatment for HIV/AIDS patients. People who had rarely interacted with clinicians were suddenly being followed for years.

A MODEL FOR BEATING PANDEMICS

In 2020, many longtime HIV researchers found themselves reminiscing about 1981. A new virus was once again circling the globe. This time, though, they had decades more experience in identifying, understanding, and fighting viral illnesses. At many institutions, including UCSF, the first scientists and clinicians to steer their efforts toward the emerging COVID-19 pandemic were those who had focused their careers on HIV.

The infrastructure and expertise built to counter HIV laid the groundwork for a speedy response to COVID-19. Compared to the years it took to identify and isolate HIV, SARS-CoV-2 was isolated – and its genome sequenced – in just weeks.

"The whole reason the scientific community was able to come up with a vaccine for COVID-19 in less than a year was because of the backbone of HIV research," says Peter Hunt, MD, a UCSF professor of experimental medicine. "The way the vaccine was designed, the way we sequenced the virus, the way we measured the immune response to the virus and developed tests to quantify viral loads – it all leads back to HIV."

"In our country, we take for granted that there is an infrastructure for chronic health care," says Diane Havlir, MD, UCSF's Weiss Professor and chief of HIV, infectious diseases, and global medicine at Zuckerberg San Francisco General Hospital. "But before HIV, that was not true in most of the developing world, where there was no such thing as the lifelong treatment of any chronic disease."

Havlir realized about a decade ago that the public health infrastructure established in Africa to combat HIV could have major benefits for other areas of medicine. In partnership with local communities, she and her colleagues at SEARCH (Sustainable East Africa Research in Community Health) started testing the idea of integrating hypertension and diabetes screening and treatment into the HIV programs they were already working with in Uganda and Kenya. Havlir suspected that if these programs began advertising broad, preventive health care – rather than only HIV treatment – more patients would be apt to use them.

"For so long, HIV care was very siloed," says Havlir, noting that people didn't necessarily want to be seen walking into an HIV/AIDS clinic. "When you look at it from the patient perspective, it actually created some barriers and stigma."

When the expansion first launched in one rural Ugandan village in 2011, Havlir's group not only diagnosed many new cases of HIV but also hundreds of cases of malaria, tuberculosis, diabetes, and hypertension. Over time, the team found that they could manage chronic diseases over the long term, helping patients get their blood pressure and blood sugar under control. In 2022, they estimated their additional cost of diagnosing and treating hypertension was only about $11 a patient per year – hundreds less per patient than at other health centers in East Africa.

"We're able to leverage the existing HIV infrastructure in these places to deliver scalable, sustainable health care for many other conditions," she says. "When we first started trying to tackle HIV in the developing world, it was seen as a really bold move. But now, the benefits have multiplied beyond everybody's expectations."

“When we first started trying to tackle HIV in the developing world, it was seen as a really bold move. But now, the benefits have multiplied beyond everybody’s expectations.”

– Diane Havlir, who partnered with local communities in East Africa to successfully integrate the treatment of chronic diseases such as diabetes into HIV programs

Shailee Jain is a postdoctoral researcher in the lab of Edward Chang at the UCSF Weill Institute for Neurosciences. She is posing with scans of her own brain and a 3D printed model of her brain.

THE FUTURE OF NEUROSCIENCE

Building a Silicon Brain

BY SHAILEE JAIN, PHD, AS TOLD TO CYRIL MANNING
PHOTOGRAPHY BY ELENA ZHUKOVA

IMAGINE for a moment that we could create a model of the human brain so precise, so accurate, that it could mimic the brain's intricate neural patterns in real time. Imagine a "silicon brain," an artificial neural network so advanced that it could decode a human's thoughts, restore speech to those who have lost it, and – perhaps one day – even generate a personalized model of the unique brain activity of any individual.

This isn't science fiction. It's the future I'm helping to build.

My lifelong fascination with the brain's complexity sparked my interest in the intersection of neuroscience and artificial intelligence. I was drawn to the idea that AI can not only analyze massive amounts of data or help us write our emails or tell us which stocks to buy but also potentially mimic the fundamental aspects of being human – our ability to think, speak, and interact. In 2023, I joined the lab of Edward Chang, MD, at UC San Francisco to study brain-wide networks and even the activity of individual neurons in order to understand how our brains achieve a fundamentally human trait: language.

I feel incredibly fortunate to have entered this field when I did. For a long time, progress in neuroscience was slow because we didn't have the right technology. Then, in the 1980s

and 1990s, technologies for collecting brain measurements revolutionized the field. And now, particularly in the Chang lab, we have the ability to record the activity of single neurons in a person's brain while they are undergoing brain surgery. Just 10 years ago, we didn't think this was possible, but now we can track the activity of hundreds of single neurons, which is incredibly exciting. This will potentially revolutionize our understanding of brain circuits, especially those responsible for complex and uniquely human behaviors like language.

While this data is precious, to fully harness it, we also need powerful computational tools. This is where the recent surge in artificial intelligence and my background as a computer scientist come in. I'm hopeful that the fusion of AI and these new methods of measuring brain activity will transform neuroscience.

WE ARE AT A TIPPING POINT where AI's capabilities, driven by vast amounts of data and powerful computers, are unlocking new possibilities to understand the human brain. Over the past decade, we've successfully used AI to build models of brain data collected with various imaging technologies, including functional magnetic resonance imaging (fMRI), magnetoencephalography, and electroencephalography. These technologies have been instrumental in advancing our knowledge, but we are only now starting to experiment with AI-based models of single neurons in the human brain.

At UCSF, we have the singular opportunity to collect amazing, high-quality, and diverse types of brain data through our neurosurgeons, neurologists, and psychiatrists. For example, fMRI systems can tell us which parts of the brain are active in a patient at any given moment, and diffusion tensor imaging tells us how different regions of the brain are connected to each other. And thanks to a very recent technology unique to UCSF, called neuropixel probes, we can even collect data from individual neurons. Eddie Chang – my boss and the chair of neurosurgery at UCSF – pioneered the use of these probes in humans in a series of revolutionary brain surgeries in recent years. During these procedures, the patient is awake and performing different tasks in the operating room while the probe records how individual neurons in their brain are firing. Observing brain activity at this infinitesimal scale is almost unimaginable. It offers a never-before-seen glimpse into the brain's inner workings.

So in my work, I'm taking all these diverse sources of data and putting them into an artificial neural network. The goal is to produce the same patterns of "brain" activity in my artificial network that the patient's brain produces.

THE BIG CHALLENGE IN MY WORK is integrating all the data at our disposal into a single, working model. For example, fMRI is not a direct measure of neural activity but of how much oxygen different parts of the brain are using. The results tell us what's happening across hundreds of thousands of neurons. It's a very coarse measurement, but it is valuable for seeing patterns of activity across the entire brain. On the other end of the spectrum, neuropixels give us extremely high-resolution data from individual neurons, but we don't get a full-brain picture. I am trying to create AI models that can integrate the best of all worlds. By building models that process many different types of data modalities, we hope to develop a fuller picture of the human brain.

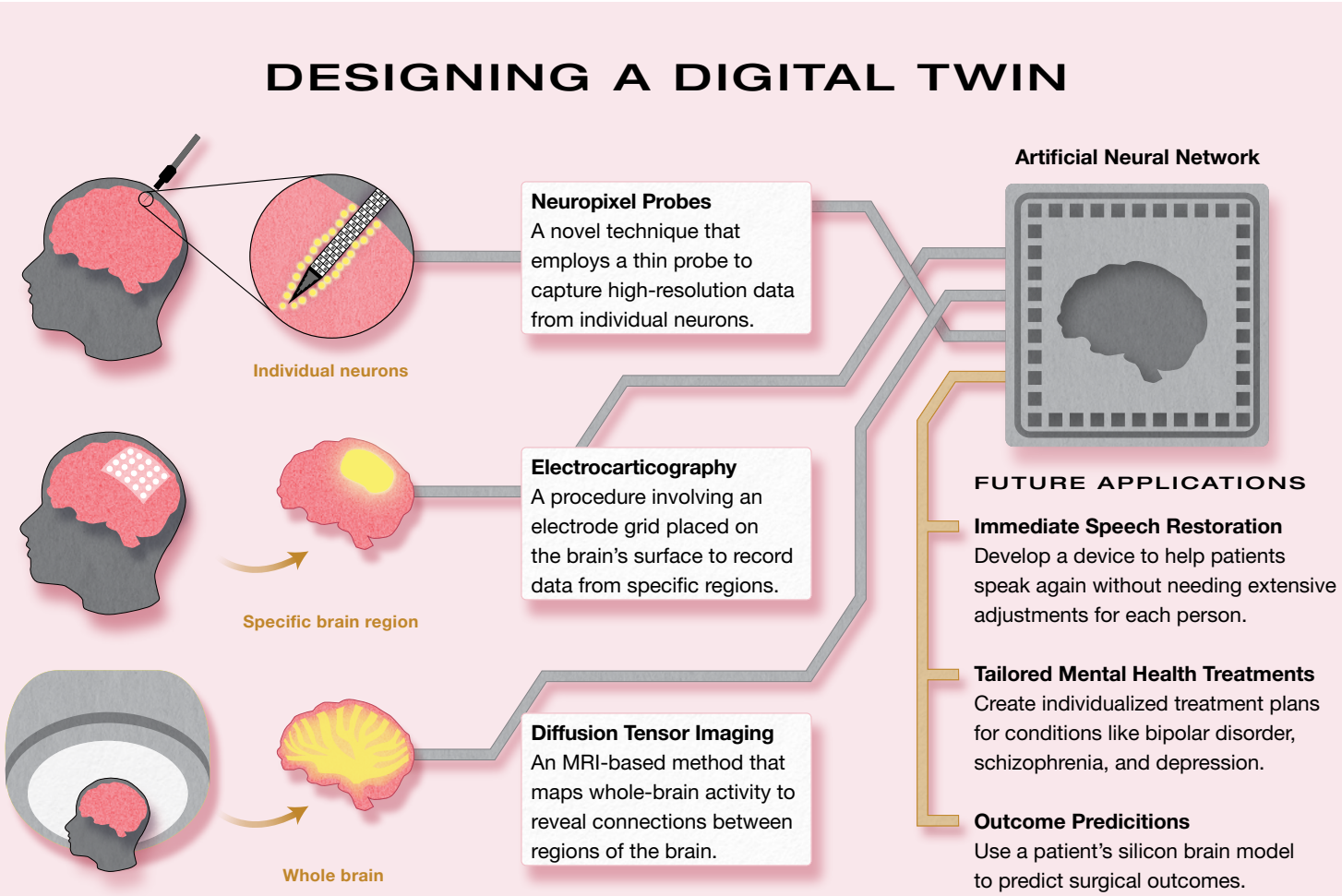
But we're looking not just at neural data; we're also incorporating text inputs that a patient might read or hear; the speech the patient produces or listens to; and behavioral data, such as how well the patient understands a specific sentence or can solve a math problem. By combining all these data sources into the same artificial neural network, we can create a "silicon brain" – a model that can produce the same patterns of brain activity as a human brain.

> **"An AI system trained on brain data could create a 'digital twin' of an individual human brain...enabling personalized insights into how that person's brain functions."**

ONE OF THE MOST EXCITING APPLICATIONS of this technology is in the development of new generations of brain-computer interfaces (BCIs). In recent years, Dr. Chang and his team have used BCIs to restore the ability to communicate to individuals who are paralyzed and can't speak. But while current BCI systems are powerful, they must also be highly personalized, requiring extensive training data from each new patient to function effectively.

This is where the concept of a silicon brain comes into play. By training an artificial neural network on vast amounts of neural data from many different people, I believe we can create a model that doesn't work just for one person but could be adapted to work "out of the box" for any patient. Imagine a device that could be deployed in any patient without the need for extensive calibration – a device that could restore speech or movement from day one. The implications for patient care are enormous.

IN THE REALM OF MENTAL HEALTH, the applications of this technology could be even more profound. For too long, our understanding of neuropsychiatric conditions has been limited by the tools at our disposal. Conditions like schizophrenia,



bipolar disorder, and depression are incredibly complex, involving multiple regions of the brain and intricate networks of neurons. While we can't dissect a living human brain to see how its components work, we could do this with an artificial brain model.

By feeding an AI system with data from patients with specific neuropsychiatric conditions, we could start to see patterns in how different parts of their brains interact and how these interactions may go awry. This could lead to new, more targeted treatments that address underlying neural mechanisms rather than just alleviating symptoms.

And as we move closer to simulating different brain disorders within an artificial model, we will be able to conduct experiments that would be impossible in a human patient. We can explore how certain stimuli or interventions affect neural activity in a controlled environment, allowing us to better understand and treat these conditions. In time, we could expand on this to study how the brain perceives the external world, retrieves memories, and ultimately produces thought.

Looking 20 to 50 years ahead, I believe an AI system trained on brain data could create a "digital twin" of an individual human brain. These AI-generated models could replicate not only general brain activity but also the specific neural patterns of an individual, enabling personalized insights into how that person's brain functions. Before undergoing brain surgery, for example, a patient's digital twin could be used to simulate the procedure and predict its outcomes. Or a clinician could build highly individualized treatment plans for neuropsychiatric conditions based on each patient's unique brain activity patterns.

WE ARE STILL IN THE EARLY STAGES of all this, and the journey ahead will involve not only refining these models but also ensuring that they are applied ethically and equitably in clinical settings.

There are huge ethical questions involved, especially when it comes to consent and data privacy. When working with human brain data, ensuring that participants fully understand what their data will be used for is crucial. We also have to consider the potential for misuse of the technology, especially if these models become advanced enough to predict individual brain activity. As these models become more mature, we'll need to have more conversations about ethical implications. We can start now by educating people about what these models are and what they are capable of.

These are provocative ideas. But technology is progressing quickly, and we might be closer to the future that I'm describing than we realize. By harnessing the power of AI, we are not just imagining the future – we are building it.

ILLUSTRATION: FARAH HAMADE

Nurse's Historic Swim

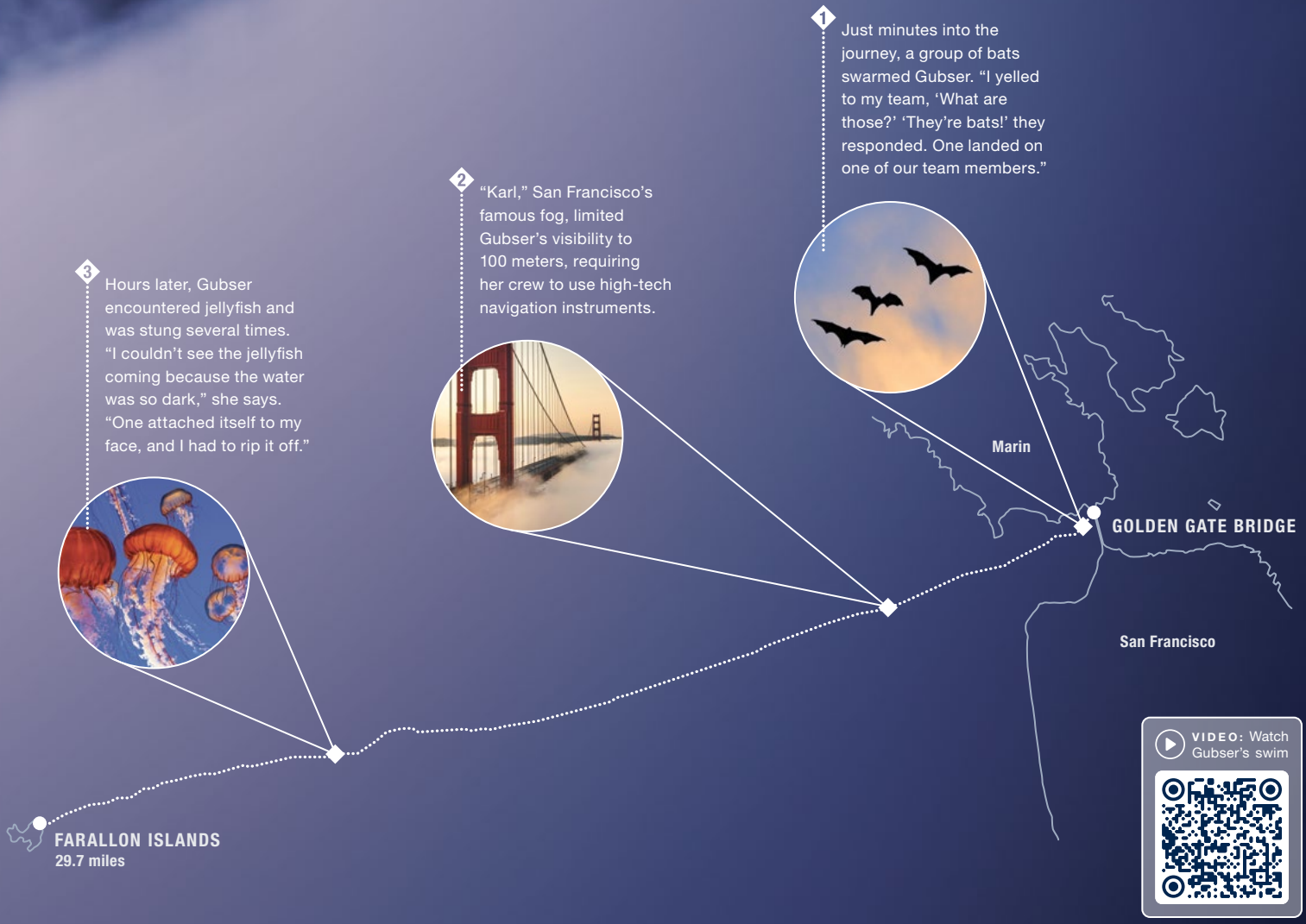
PHOTO: TOM SEAWELL; BATS: SERGEI URIADNKOV; BRIDGE: STEPHEN LEONARDI; JELLYFISH: GERALD CORSI

She has swum across the Strait of Gibraltar, Scotland's North Channel, and California's Lake Tahoe. And last May, Amy Appelhans Gubser, a fetal cardiology nurse at UCSF Benioff Children's Hospitals, became the first person, male or female, to make the 29.7-mile swim from the Golden Gate Bridge westward to the Farallon Islands. Furthermore, she did it without a wetsuit in 43-degree waters.

Along the way, the 55-year-old grandmother inspired people of all ages and backgrounds, from other nurses and swimmers to the governor of California. With 26 years of nursing under her belt, including many years caring for infants and children in intensive care, she sees open-water endurance swimming as a great stress reliever and "a very positive way" to ground herself – and credits her stamina to her job. "I don't think I could have accomplished this if I wasn't a nurse at UCSF," says Gubser. "When you're working in a critical care environment, you have to be able to prioritize. I knew I had the ability to compartmentalize and keep myself levelheaded enough to do this."

Throughout the arduous 17-hour swim, Gubser found strength in thinking about how her patients navigate their challenges. "I've seen my patients withstand things that I don't know if I could have the courage or strength to do, and they do it with such grace and poise," she says. "I channeled that and used that to propel me from mile to mile."

■ *Eric Brooks*



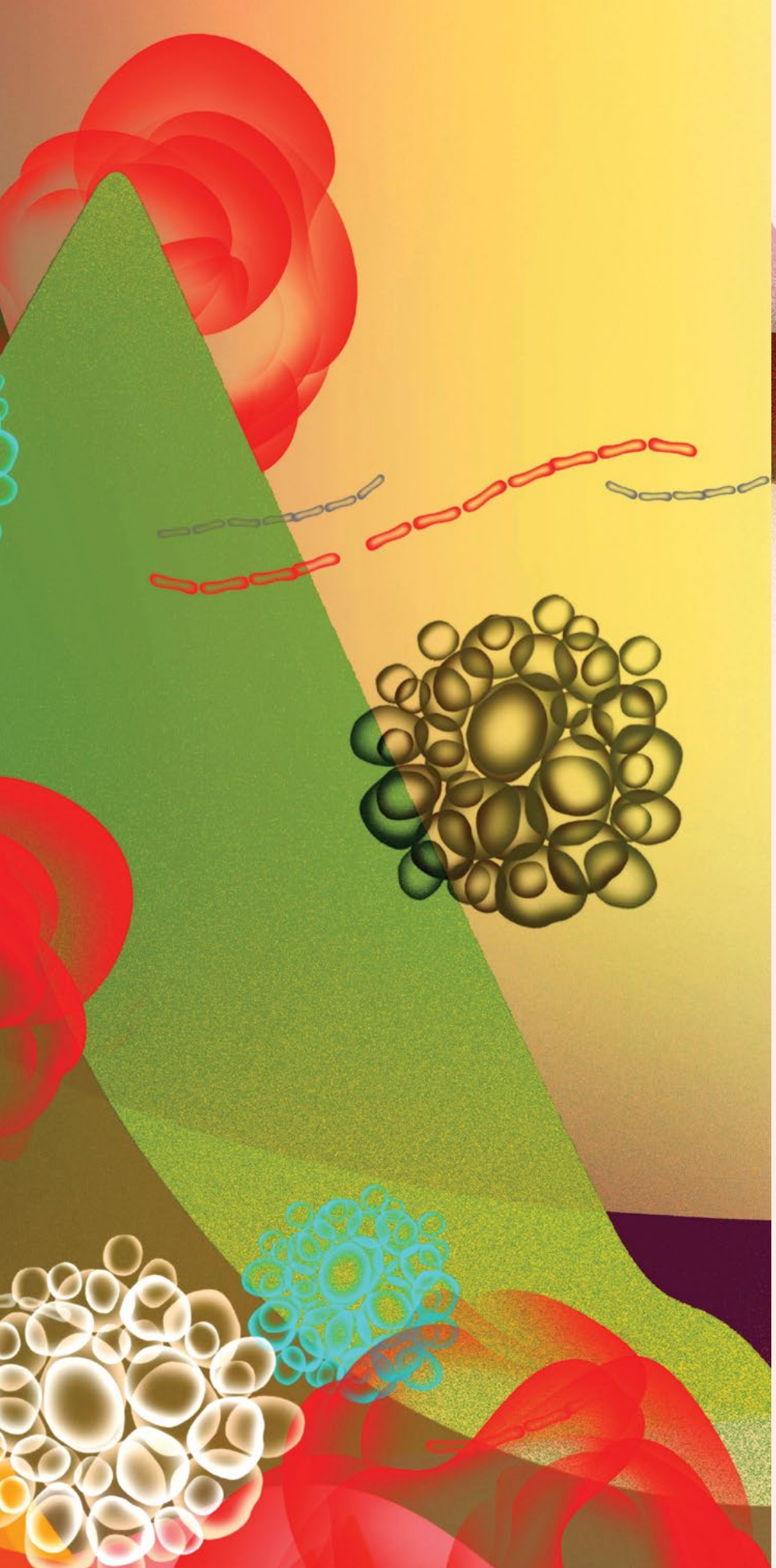
The trending health hazards you may not know about

ON THE RISE

By Elizabeth Daube *Illustrations by Brian Stauffer*

At the risk of spoiling all suspense, you already know about the biggest threats to your health. Statistically speaking, heart disease and cancer top the list of causes of death in the U.S. That's been the news year after year, for decades.

But what about the hazards on the horizon – the lesser-known afflictions that are occurring more often? UC San Francisco experts explain some of the health concerns on the rise right now.



VALLEY FEVER

A Growing Threat in the Ground

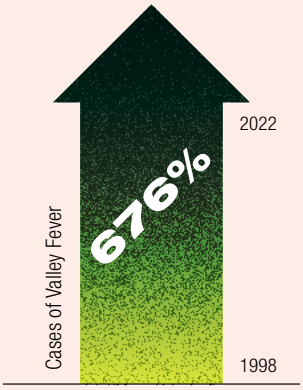
Meet coccidioides, the shape-shifting fungus that can turn from benign to deadly depending on its host.

Its unique ability to change form makes coccidioides, dubbed "cocci" by those who study it, dangerous. Traditionally, it's found in the soil of the American West – mainly California and Arizona – where it thrives as a mold. But when its spores are inhaled, they can transform into a yeast able to grow inside the human body. The result: valley fever.

"When we think of a yeast infection, it sounds benign," says Geetha Sivasubramanian, MD, chief of infectious diseases at UCSF Fresno. "But that's not the case with valley fever. The infection starts in the lungs and can spread to the skin, bones, and brain. I've seen young kids with infections in their spines, and they're paralyzed."

A dangerous mycological outbreak might call to mind *The Last of Us*, HBO's 2023 post-apocalyptic drama about a fictional version of cordyceps. That particular pandemic drives humans to bite each other, spreading disease in a rabies-like frenzy. Thankfully, cocci's got nothing in common with that sci-fi mushroom. Common symptoms of valley fever are akin to pneumonia: fever, cough, shortness of breath, body aches.

"It's not contagious from person to person," Sivasubramanian says. "If two people in the same family get it, it's because they live in an area where they're both inhaling the fungus. Valley fever affects animals, too, but you can't get it from your dog."



California cases of valley fever were once concentrated around the San Joaquin Valley, where UCSF Fresno is located. But cocci is spreading. Nationwide, the U.S. Centers for Disease Control and Prevention (CDC) logged 2,271 cocci cases in 1998. By 2022, that number had jumped to 17,612. Researchers believe climate change might be fueling cocci's spread, enabling it to venture into states like Oregon and Washington. During droughts, soil containing the fungus turns hot and dry. The resulting dust can carry cocci into the air – and deliver it directly to your lungs.

Some people inhale a few spores and never get sick. Others aren't so lucky. Having a compromised immune system or spending a lot of time around dusty soil increases your risk. After an outdoor music festival in Bakersfield, Calif., for example, 19 people contracted valley fever. Eight were hospitalized.

The fungus is a slow-growing pathogen, complicating diagnosis and treatment. Viruses can make you sick within days. Cocci? Think weeks.

"The test for valley fever relies on your body producing antibodies against the infection," Sivasubramanian says. "So it may take several weeks to get a positive result."

Because valley fever is often mistaken for pneumonia, some doctors prescribe antibiotics, which aren't effective. And in the rare cases when it spreads to the brain, patients don't always have obvious signs. Sometimes they only have a headache.

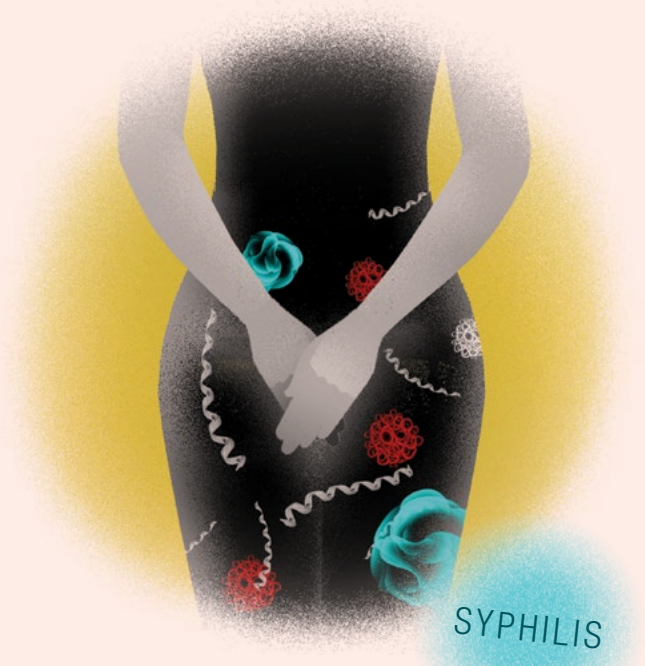
Cocci infections also take time to treat. Patients often need many months of therapy. And if cocci invades your brain, expect to stay on antifungal medication for life.

In high-risk areas of California, Sivasubramanian and her colleagues have been raising awareness of valley fever. To prevent infection, remember that the spores spread via dust – wet soil, not so much. Spraying down a garden, field, or construction site helps. Anyone who digs into dry dirt should wear a protective mask.

Sivasubramanian hopes to eventually establish a multidisciplinary center for treating valley fever at UCSF Fresno. In the meantime, she's studying health disparities related to the infection – especially among farmworkers – and helping to develop better, faster tests and treatments. In the coming months, UCSF Fresno plans to enroll patients with advanced valley fever into clinical trials for medications that might have fewer side effects.

Meanwhile, scientists like Anita Sil, MD, PhD – the J. Michael Bishop, MD, Distinguished Professor of Microbiology and Immunology – are exploring cocci's unusual response to temperature shifts and its ability to manipulate the human immune system. By understanding exactly how the fungus transforms and adapts in the lab, Sil hopes to find new ways to thwart it in the wild.

"Researchers are also looking at soil ecology and climate change," Sivasubramanian adds. "What's happening in California and Arizona? That could happen in other states. Every aspect of valley fever needs our attention right now."



The Resurgence of a Classic STI

"The French Pox." "The Spanish Disease." "The Italian Sickness." Slang for syphilis spans centuries – and countless attempts to blame outbreaks on someone else. Lately, the infamous bacterial disease is grabbing headlines again. Between 2018 and 2022, syphilis cases in the U.S. surged by almost 80%, reaching infection levels not seen since 1950.

One of the oldest sexually transmitted illnesses, syphilis often begins with a small genital lesion. This early, painless sign tends to go away, but over time, the infection damages distant organs like the heart and brain. Before antibiotics, some late-stage syphilis patients were marred by ulcers that eroded flesh and bone. Noses fell off. People died. It was grim.

By the time Ina Park, MD, MS, a UCSF professor of family and community medicine, first started seeing patients in 1999, syphilis had declined. After penicillin became available in the 1940s, public campaigns dramatically increased diagnosis and treatment. For a while, most U.S. states required couples to get tested for syphilis before marriage.

In the late '90s, the disease was rare enough that some physicians didn't encounter any cases at all. The elimination of syphilis seemed close at hand, according to Park, in part because so many people were using condoms as if their lives depended on it. "In the '80s, a lot of people were terrified of dying of AIDS," says Park, who is also the co-principal investigator of the California Prevention Training Center, which provides free training on HIV and STIs to health care professionals. "There were no good medications for HIV. People were associating sex with death, and they adjusted their behavior accordingly."

But as effective HIV/AIDS treatments emerged, safer sex practices began to wane. Park notes that attitudes toward condom use gradually shifted as the disease became more manageable.

"It wasn't a death sentence anymore," Park says. "People weren't afraid of other STIs in the same way they feared HIV/AIDS. Other things contributed, too, like the rise of smartphones. My patients say it's now easier to arrange a casual hookup for sex than it is to order pizza."

Eventually, as syphilis rates climbed once again, the CDC recommended routine testing for gay and bisexual men, who had the highest prevalence. But cases started rising among women and heterosexual men, too. Data suggests that people with substance use disorders contract syphilis at higher rates. A study of women and heterosexual men diagnosed with syphilis found that their use of injectable drugs or methamphetamine more than doubled between 2013 and 2017. Both kinds of drugs are linked to riskier sexual behavior, including transactional sex.

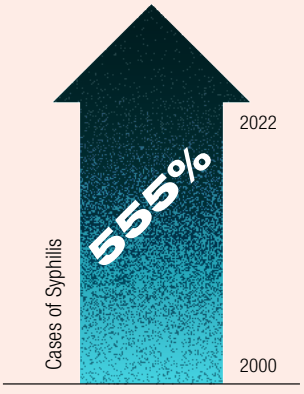
While Park hopes more awareness might prevent infections, she says the best way to reduce syphilis is to increase testing and treatment for everyone.

"Getting an STI is sometimes just a natural consequence of being sexually active," Park says. "All sexually active people need to get screened. STIs don't discriminate. They can happen to anyone. And most of the time, especially with syphilis, the symptoms can be so subtle that you don't have any idea. You can be completely asymptomatic."

Syphilis can also be acquired by a fetus during pregnancy. Congenital syphilis has increased tenfold since 2012, disproportionately affecting Black, Hispanic, and Native American babies. In 2022 alone, over 3,700 cases were reported, and nearly 300 infants died. While prenatal testing for syphilis is required in many states, some women still struggle to get any prenatal care.

Park says efforts are underway to make syphilis testing more accessible and convenient, including at-home tests that can be mailed to a lab. The Indian Health Service has also responded, deploying public health nurses who often drive hundreds of miles to offer testing and treatment on rural reservations. Locally, a team at Zuckerberg San Francisco General Hospital helps pregnant women with substance use disorders get prenatal care, STI screening, and addiction services.

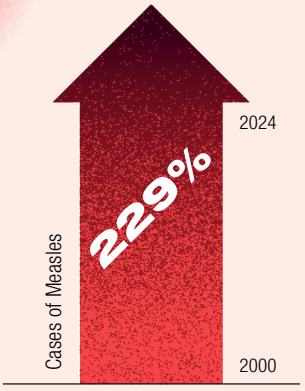
"For people who are not likely to come to us, we need to figure out a way to go to them," Park says. "This is such a tragedy because syphilis doesn't require a high-tech solution that costs millions of dollars. The public health price for a penicillin injection is less than 25 cents."



In 2000, the CDC reported 31,618 cases of syphilis – adult and congenital – the lowest annual total on record. By 2022, that annual total had jumped to 207,255.

MEASLES

An Almost-Overcome Malady



In 2000, after a year of zero transmission, U.S. officials declared measles eliminated. It was a success born of a decades-long effort to prevent the virus through widespread inoculation. The measles virus spreads readily through the air – lingering after a cough or sneeze for up to two hours – and the disease has no proven treatment. Infected people usually get a rash, fever, and respiratory symptoms, but complications can range from pneumonia to seizures to death.

Unfortunately, the American victory over measles hasn't held up.

"People should be worried about it," says Peter Chin-Hong, MD, a professor of infectious diseases at UCSF. "Vaccines have been one of the most impactful interventions in reducing childhood disability and death. But as vaccination rates go down, we risk reversing our progress and turning back time. Measles is a harbinger of things to come."

Rates of routine child vaccination plummeted during the COVID-19 pandemic, when many families skipped regular doctor's visits. But the ongoing drop in vaccination is more about a misinformation movement. Today, that movement is inextricable from politics. While most Democrats (85%) continue to support vaccine requirements for children, Republican support dropped from 79% in 2019 to 57% in 2023.

"There's been an infusion of politics into health care," Chin-Hong says. "They're so intertwined now. Choosing to vaccinate or wear a mask is almost like wearing a T-shirt with a [political] message.'"

Measles is just one of many threats that American children are traditionally vaccinated against. A recent polio case in New York caused alarm that that disease, which

Despite vaccine mandates in many states, childhood vaccination rates have dropped, and measles outbreaks have ticked back up. In 2024, more than 280 measles cases were reported in 32 states. Almost half of the patients were hospitalized, including 82 children.

permanently disabled about 35,000 people a year during its peak in the 1950s, might also be returning to the U.S.

To increase protection against preventable diseases, some advocate for ending nonmedical vaccine exemptions, which allow parents to opt out of mandatory child vaccinations due to religious, spiritual, or philosophical beliefs. After California enacted exactly this kind of law in 2016, a UCSF study found that it worked: Vaccination rates rose to 95% in most counties, restoring what public health experts call "herd immunity."

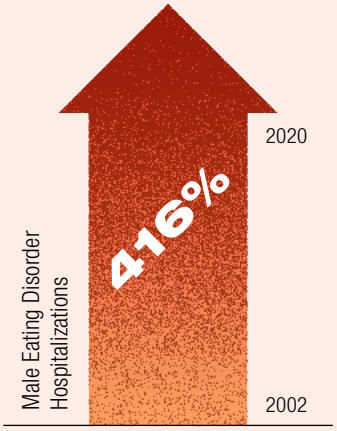
"It's easier for measles to find entry points in communities that are undervaccinated," Chin-Hong says. "Herd immunity is almost like a force field. Enough people have been vaccinated as children to keep everyone safe."

Chin-Hong thinks the U.S. would also benefit from a more centralized approach to immunization policy. While some states offer free childhood vaccines, funding and accessibility vary widely.

"This patchwork system and lack of a unified, national electronic health record make it challenging to keep track of people's immunization status," he says. "Where I grew up in the Caribbean, vaccines would just be delivered in schools. With health care here, you kind of have to find your own way."

For now, Chin-Hong fears American vaccine hesitancy might not shift until outbreaks grow and strike closer to home for more people.

"Vaccination rates go up when people feel more personally at risk," he says. "We all want what's best for the kids, but talking to parents about the disease only gets you so far if they're vaccine hesitant. Measles is just like, you know… who can really remember it? People born in the 1950s?"



Medical guidelines for eating disorders remain rooted in research on women and girls. Until 2013, the *Diagnostic and Statistical Manual of Mental Disorders* listed loss of menstruation as one of the criteria for anorexia nervosa. That's why Jason Nagata and other experts are leading efforts to make these guidelines more inclusive. Unfortunately, UCSF is still one of only a few institutions studying male eating disorders – including how many calories male patients can safely consume after periods of starvation.

MALE EATING DISORDERS

The Overlooked Image Issue

Eating disorders among women and girls have long drawn attention, prompting countless conversations about body image and how to overcome unhealthy expectations. In response, even Barbie, long critiqued as an unachievable ideal – if she were a real person, she'd have an 18-inch waist – has started to change. Mattel released its first "curvy" Barbie in 2016.

But recent research suggests that we've failed to notice a dramatic increase in body image issues among young men. A study of eating disorder hospitalizations between 2002 and 2020 found the largest increase in male patients, whose hospitalizations rose 416%.

"It's part of normal development during puberty to have some concerns about body image, but this has been recognized almost exclusively in girls and women," says Jason Nagata, MD '13, an eating disorders expert and associate professor of pediatrics. "These pressures also exist for boys and men, and there's more pressure today than decades ago. The idealized masculine body is now really big and muscular."

If a Barbie doll symbolizes female body standards, it's worth examining how male action figures have evolved over time, too. The Batman of the 1940s? He's this average guy with a mask and cape. Today, Batman has six-pack abs and crushing biceps. His legs look like tree trunks.

Ripped superheroes aside, social media might be the biggest driver of body dissatisfaction in the 21st century. Nagata says Instagram use among boys is associated with more disordered eating, less satisfaction with their muscles, and even anabolic steroid use.

"The impact of social media is pervasive," he says. "When I was growing up, most kids would never expect to be in a Hollywood movie or on TV or in a magazine. Now, anyone can be an influencer. And for many young people, their social lives revolve around social media."

Recent studies of adolescent boys find that a third want to lose weight and another third are trying to gain muscle. While some weight loss or muscle attainment can be healthy, Nagata warns that excessive exercise, strict diets, and risky behaviors tied to muscle growth tend to get overlooked in men and boys.

"Physicians screen for eating disorders, but they're typically taught to look for weight loss," Nagata says. "Doctors are trained to ask if patients are fasting, skipping meals, or using diet pills. But none of those questions capture any of the muscularity concerns.

"And to some extent," he adds, "extreme measures are normalized. My first male patient was a wrestler. He worked out six-plus hours a day and didn't eat enough. His disorder hadn't been recognized in part because everyone on his team was fasting for two days before their weigh-in. Even muscle-building substance use is relatively common in male athletes."

Muscle dysmorphia in particular – sometimes called "reverse anorexia" – can be tough to spot. People tend to consume a lot of protein and supplements as they try to bulk up, but it's not always clear when they've crossed the line into an unhealthy obsession. Those using anabolic

steroids usually keep it a secret, and they're focused on short-term muscle gains rather than long-term risks – like early heart attacks, strokes, and psychiatric problems. For those worried exclusively about looks and not longevity, note that anabolic steroids also cause male pattern baldness.

"We still need to do more research to improve care for these patients," says Nagata. "I followed that wrestler over the course of a year. He experienced so many struggles that girls wouldn't have faced. Many people still feel a sense of shame when they are diagnosed with an eating disorder. For boys, that stigma is often even greater because it's viewed as a feminine illness."

The Totally Unsurprising Trend

Spend time in any city, and you'll spot them: people zipping past on electronic bikes and scooters. Maybe you're one of them, off to run errands or get to work – no hunting for parking, no waiting for the bus! But surely you're not the jerk soaring down the sidewalk, expecting everyone to leap out of your way. Right?

Love them or hate them, the popularity of e-bikes and e-scooters keeps growing – and "micro-mobility" injuries are more than keeping pace. A recent UCSF study found that e-bike injuries doubled every year from 2017 to 2022, while e-scooter injuries jumped by 45% annually. And helmet use dropped. Predictably, cases of e-bike riders landing in the hospital with head trauma shot up 49-fold during the same period.

Benjamin Breyer, MD, MAS '11, senior author of the study, cites several likely reasons for the spike in injuries. First, many people opt for the convenience of renting bikes or scooters, but such services don't encourage helmet use.

"You have to bring your own helmet, and people don't like to lug them around," says Breyer, who is chair of urology and the Taube Family Distinguished Professor. "The rideshare companies could rent helmets, but there are a lot of logistical challenges, particularly around hygiene."

Another reason for accidents? Speed. E-bikes can hit up to 28 miles per hour without any pedal assistance. With greater haste comes less control, especially in urban settings where riders jostle with pedestrians and cars.

Intoxication also plays a role in some accidents. The UCSF study found that e-bike and e-scooter riders involved in accidents were more likely to have consumed alcohol compared to those injured on traditional bikes.

"I'm not sure why that is happening," Breyer says. "Maybe people think there's less potential for severe harm to others. But that's misguided. E-bikes can cause serious accidents. If you're too intoxicated to drive a car, you shouldn't cycle either. Especially in the age of Uber, just use a rideshare or walk."

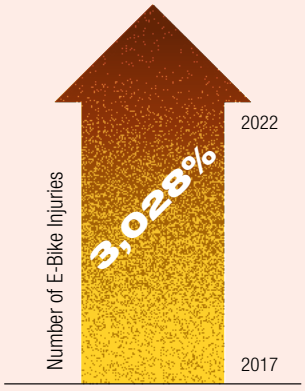
Breyer thinks expanding bike safety education and improving cycling infrastructure – such as protected bike lanes – would reduce injuries. But he also believes we need a cultural shift, especially around using helmets. Unfortunately, it can be tough to grab people's attention without, say, celebrity involvement.

"Think about skiing," he says. "Sonny Bono. Natasha Richardson. Michael Schumacher. They had these really bad skiing accidents. That helped raise awareness. It encouraged people to ski safely. Now everybody wears a helmet on the slopes."

While the surge in injuries is concerning, Breyer thinks banning e-bikes and e-scooters would be a massive mistake. Compared to cars, they're environmentally friendly and reasonably good for you, so long as they're used with some caution.

"I'm actually a big proponent of people riding e-bikes and e-scooters," says Breyer. "They are here to stay and play an important role in the transportation ecosystem. The research is sometimes doom and gloom, but these are very healthy activities if done safely.

"Knowing what I know, I still ride a bike. Just holding and navigating it requires core strength and balance. You're definitely getting a workout. And frankly, it's fun."



Some safety advocates are pushing for stricter regulations on e-bikes and e-scooters, but no national laws exist yet. Approved in September, California Assembly Bill 2234 enables counties to launch pilot safety programs that ban children under age 12 from operating an e-bike.

ALUMNI HUB

UCSF celebrates these Alumni Achievement Award winners for their contributions to practice, research, entrepreneurship, service, and mentorship, and for early-career success.

By Dora Dalton Illustrations by John Jay Cabuay

Alumni Mentor Award

SCHOOL OF DENTISTRY

William Carroll, DDS '80

A Mentor for Generations of Trainees

LASTING IMPACT

During his dental training, William Carroll learned a lot at UCSF – especially from how the institution responded to the then-emerging AIDS crisis. "It was one of the first health systems to implement universal, standard infection-control measures like gloves and masks," he says. After his graduation from dental school, he became an officer in the Navy – "the Navy life was the only thing I'd ever known," he says – and helped write infection-control guidelines for the entire command. "Thirty years later, while stationed in Hawaii, I noticed that some of the language my team wrote back in the '80s could still be found in the current infection-control instructions."

AN OFFICER AND A PROFESSOR

Carroll has lived all over the world – as a military kid, a UCSF student, and a Navy officer. "That was an asset for me because I developed an understanding that people are basically all the same everywhere," he says. Along the way, he's absorbed lessons about what it means to be a mentor, a teacher, and a team member. And at every point in his training and career, he found opportunities to lead others toward success. He spent 31 years in the Navy in numerous dental roles, including Pacific Fleet Dental Officer. Because teaching was his passion, that was how he wanted to spend the next chapter of his career. He's now a faculty member and associate dean for academic affairs at Roseman University of Health Sciences' College of Dental Medicine in Utah.

MENTORSHIP MAGIC

"I've learned how incredibly impactful a great health care team can be – and how important a mentor can be."

Alumni Humanitarian Service Award

SCHOOL OF MEDICINE

Laurel Coleman, MD '89, Resident Alum

A Global Volunteer in Palliative Care

FILLING A GREAT NEED

After she finished her training, geriatric and palliative care physician Laura Coleman moved to the central lakes region of Maine, where she became the medical director for a group of nursing homes, a hospice, and one of the first specialized residential memory care facilities in the country. After reading about a Gates Foundation-supported AIDS orphan care project in Otse, Botswana, she signed up for a stint there – a trip that began a new chapter in her career. "It opened my eyes to the great need there," she says. "HIV was still having a huge impact in Africa, and I had a skill set to help them cope and improve their quality of life." She's now been serving for many years on medical trips to Africa, Haiti, and Mexico, and with refugees on the Greek island of Lesvos. "Humanitarian volunteering – that's kind of in my DNA," she says.

SERVING THOSE ON THE INSIDE

When the COVID-19 pandemic hit, Coleman was a visiting clinical professor of palliative medicine at UCSF. Working with Brie Williams, MD, MS, the founder and director of UCSF Amend, which aims to change the culture in U.S. prisons, Coleman began caring for incarcerated men at San Quentin State Prison, where there was a major outbreak of COVID-19. "It was one of the most rewarding experiences that I have had," she says. "Each man had a different perspective on their situation that informed their health care decisions. Some died, some didn't, but we promised that we would walk with them through it."

COMPASSIONATE PRESENCE

"People tend to ostracize those who are dying. I am privileged to model compassionate presence, to help with symptoms even if we can't cure the patient."

Alumni Early-Career Award

GRADUATE DIVISION

Nicholas Hertz, PhD '13

A Scientist Inspired by Art and Nature

CHEMISTRY CURIOSITY

Nicholas Hertz grew up in an artist's commune in Malibu, overlooking the Pacific Ocean, and it was there, amid nature, surrounded by artists, that he fell in love with science. "I remember spending a lot of time running through the wilderness, creating paths, trying to find deer trails, and digging holes," he says. "Sitting there, looking at a tree, wondering, 'What is that tree made out of?' That was really what brought me into chemistry."

THRIVING UNDER THE RIGHT MENTOR

Hertz came to UCSF in 2007 to work with Kevan Shokat, PhD, the chair of cellular and molecular pharmacology. "What Kevan was doing at UCSF was applied to making new drugs and understanding biological pathways, and that's what I wanted to do – try to help human health." Hertz began looking at mutations in a mitochondrial kinase (a type of enzyme) dubbed PINK1 that is implicated in the development of early-onset Parkinson's disease. "I had a counterintuitive discovery, so I brought it to Kevan, who is so brilliant at interpreting findings," Hertz says. "And he said, 'If it's real, you just cured Parkinson's. Now go prove it.'" In 2013, Hertz and Shokat founded Mitokinin – the name comes from "mitochondria" and "kinase" – to develop a treatment for Parkinson's disease based on the mitochondrial dysfunction discoveries they'd made at UCSF. In 2023, Mitokinin was acquired by AbbVie for $110 million. Hertz launched his second company, Montara Therapeutics, in 2024 to pursue therapies for central nervous system diseases.

SURFING TO STAY HUMBLE

"I love seeing a piece of data that's really intriguing and then going surfing. It's definitely a way to come to a new idea. You realize how absolutely insignificant you are in the world. You can't have a huge ego if you're just getting absolutely pounded, destroyed by massive waves at Ocean Beach."

Alumni Entrepreneur Award

SCHOOL OF PHARMACY

Kelly Nguyen, PharmD '96

An Entrepreneur Empowering Patients

FAMILY INSPIRATION

When her father was a political prisoner in a "reeducation" camp in Vietnam, Kelly Nguyen's grandparents took care of her. "The cherished and loving foundation I had in my childhood was so powerful," she says. "I was broken so many times but kept on going because of the spirits of those who passed on that torch of love." After her graduation from UCSF, Nguyen started Mission Road Pharmacy, specializing in HIV and oncology medications and hard-to-find drugs. Her father was the inspiration for the project: He was diagnosed with cancer, and she cared for him through the end of his life. "That was the reason behind my first startup – for taking care of patients living with cancer, HIV, and other conditions of very high-touch care – providing what they needed to help them through the journey of their disease," she says.

FORGING NEW PATHS IN PHARMACY

Her latest venture is DrKumo, which empowers patients to verify, authenticate, and manage their medications using a smartphone and the platform's intelligent medication management guidance. Through telemedicine and remote monitoring, patients with chronic conditions like congestive heart failure and hypertension can measure their blood pressure or other health factors and share the data with care coordinators who can act on it. Due to its military-level cybersecurity protections, DrKumo was selected as one of just four firms to work on a $1 billion Remote Patient Monitoring and Home Telehealth contract for the U.S. Department of Veterans Affairs.

TEAMWORK MATTERS

"As long as you work really hard, then when luck strikes, you will be ready. Work hard on what you believe in and surround yourself with a team to help you along the way."

Alumni Practitioner Award

GRADUATE PROGRAM IN PHYSICAL THERAPY

Laura Keyser, DPT '08, MPH

A Champion of Maternal Health Worldwide

FROM BALLET TO PHYSICAL THERAPY

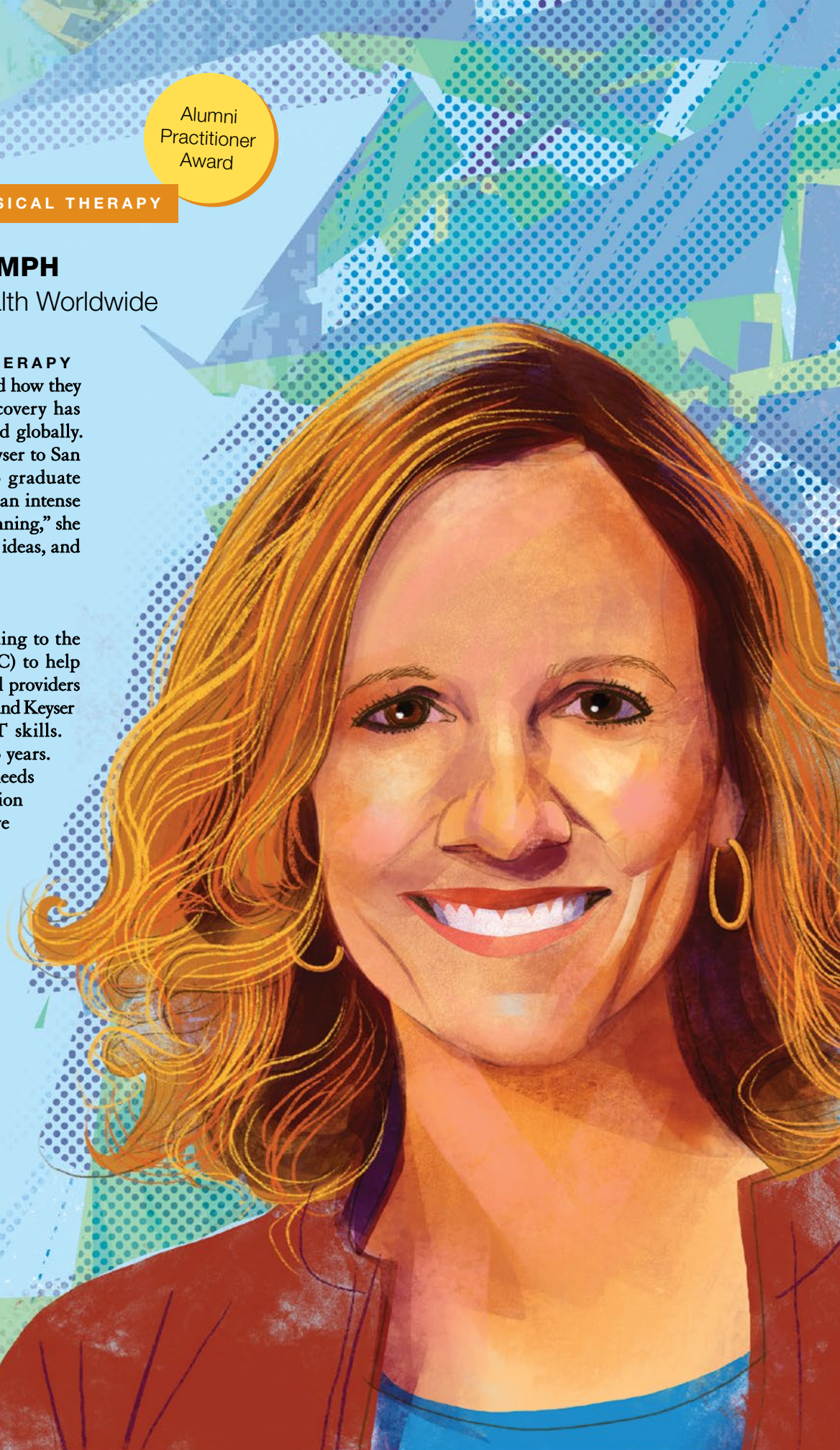
Laura Keyser's focus on women's bodies and how they cope with childbirth and postpartum recovery has taken center stage in her work locally and globally. Pursuing ballet professionally brought Keyser to San Francisco, but she ultimately pivoted to graduate training in physical therapy (PT). "It was an intense program, but I loved it right from the beginning," she says. "One of my favorite things is sharing ideas, and UCSF was a great place to do that."

HELPING MOTHERS HEAL

Keyser learned that a colleague was heading to the Democratic Republic of the Congo (DRC) to help build an orthopaedic rehab program. Local providers would be trained in basic surgery techniques, and Keyser and her colleague would teach them PT skills. A six-month commitment turned into two years. "It was a phenomenal experience, but the needs were massive," Keyser says. Her realization that improving maternal health could have an especially significant impact led her to co-found a program in the DRC to help women recover from obstetric fistula, an injury likely to occur after difficult labor without adequate medical attention. State-side, she co-founded Mama LLC to scale this work; a training guide that's now available in four languages has been down-loaded in over 25 countries. "We continue to grow our network so we can help more people," she says.

SCALING SPECIAL SERVICES

"I'm happy to say that the maternal health program we built has grown and is thriving. It's been great to see local clinicians take it and run with it."



Alumni Discovery Award

SCHOOL OF NURSING

Cheryl Cherpitel, BSN ’68, DrPH, MPH

A Public Health Researcher with International Influence

A SWEEPING STUDY

Cheryl Cherpitel did not spend her career in nursing, but the training that she received at the UCSF School of Nursing provided a springboard for her path into public health and epidemiology. Her nursing background also gave her credibility and comfort in the emergency rooms where she conducted the defining work of her career: studying the effects of alcohol consumption on injuries. Cherpitel developed the groundbreaking International Collaborative Alcohol and Injury Study, which included more than 40,000 patients in 101 emergency rooms across 33 countries. She also developed the Rapid Alcohol Problems Screen, which has been used nationally and internationally to identify alcohol-use disorders, create interventions, and inform policies to help prevent injuries and violence.

BIG IMPACT ON ALCOHOL ABUSE

Cherpitel says her work has resonated so widely because alcohol abuse is a huge problem. “It contributes a lot to the global burden of disease,” she says. “By focusing on the emergency room as a way to evaluate alcohol’s role in injury, I think conducting similar epidemiological studies has had a significant appeal to governments.” The World Health Organization became interested, seeking in the early 2000s to use her survey instrument in a dozen countries. The National Institutes of Health gave Cherpitel an R01 Research Project Grant, which was continuously renewed and funded her work for the next 17 years.

LASTING ECHOES OF NURSING

“What I found in so many of the countries is that people are just so appreciative. It’s really nice to feel like you might be making a little bit of a difference in their life. I guess the nursing persona comes out.”

Living My Most Joyful Chapter

By Sen Nguyen, MD

Since moving to San Francisco and joining UCSF, I've finally felt comfortable and safe expressing my true self.

It was during my time as a new faculty member that I began my social and medical transition, identifying as a genderqueer person and a transgender woman. A significant part of this journey was choosing a name that truly reflects who I am today.

My parents originally gave me an English name to help me assimilate while growing up in the U.S. South, but it was important for me to reconnect with my Vietnamese heritage. My chosen name, Sen, means lotus flower in Vietnamese, symbolizing a period of growth and transformation in my life.

The University of California recently rolled out a new policy that has been so meaningful to me. I'm able to use my chosen name at work and on formal documents across the UC system, which affirms my identity every day. As a health care provider in the UCSF Gender Affirming Health Program, where I care for transgender and gender-diverse patients, the opportunity to model what it means to feel affirmed in a professional setting is invaluable, both to me and to those I serve.

Growing up as a queer and trans Vietnamese American in the South, I faced many challenges, as many trans and gender-expansive people do.

However, by embracing all parts of myself, I'm now living the most joyful chapter of my life.

While there is often a lot of attention given to gender dysphoria – the distress experienced when one's gender identity doesn't align with their assigned sex – I want people to recognize that trans and gender-expansive individuals also experience gender euphoria. This is an overwhelming sense of happiness and well-being that comes when we are affirmed and celebrated in ways that align with our gender identity.

Every time we choose to embrace our authentic selves instead of living in fear, we choose love and fulfillment.

Sen Nguyen is an assistant professor of family and community medicine at UCSF.

PHOTO: ERIN LUBIN

UCSF Alumni

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