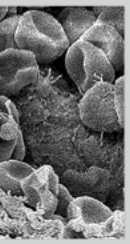
UCSF

MAGAZINE

Winter 2020



Special Issue
The Future

FEATURES

DEPARTMENTS

NEW HEIGHTS
In this artist's rendering of UCSF's reimagined Parnassus Heights campus, an open promenade replaces the steep, west-side staircase to Koret Way. Learn more about the vision for the campus's future at ucsf.edu/cphp.

UCSF MAGAZINE

WINTER 2020

COVER ILLUSTRATION: MIKE MCQUAID; THIS SPREAD: PERKINS EASTMAN

What will health look like in the future?

We are living in an age of biomedical disruptors: gene editing, artificial intelligence, machine learning, robotics, and many others. These new technologies have the power to transform health now and into the future in almost unfathomable ways.

But this is also an era of deep uncertainty, with escalating climate change, looming antibiotic resistance, and a widening gap between the wealthy and the impoverished both at home and around the world. These and other complex problems are sure to dramatically alter life on Earth.

To take a deep dive into that future, our *UCSF Magazine* editorial team interviewed dozens of faculty members who are confronting today's thorny challenges and are seizing disruptors to innovate for tomorrow. Their progress, perspectives, curiosity, and optimism embody UCSF's ethos and are captured in the pages that follow.

For instance, you'll read about several scientists, educators, and learners who are raising the alarm that the climate crisis is the biggest health challenge of the 21st century. They are passionately preparing tomorrow's clinicians, pursuing advocacy, and urging their colleagues to join them in acting – now – to thwart this global catastrophe.

PHOTO: STEVE BABULJAK

We also explore the ethical issues that all of us must grapple with, given the acceleration of gene editing and brain-machine interface technologies. These tools can forever change what many might argue make us human: our DNA and our minds. Where will they lead us 30 years from now? Where *should* they lead us?

The years and decades ahead will be an age of exponential change. While I can't predict what is to come, I am certain that UCSF will lead the way toward creating solutions for a brighter, healthier future.

Sam Hawgood

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

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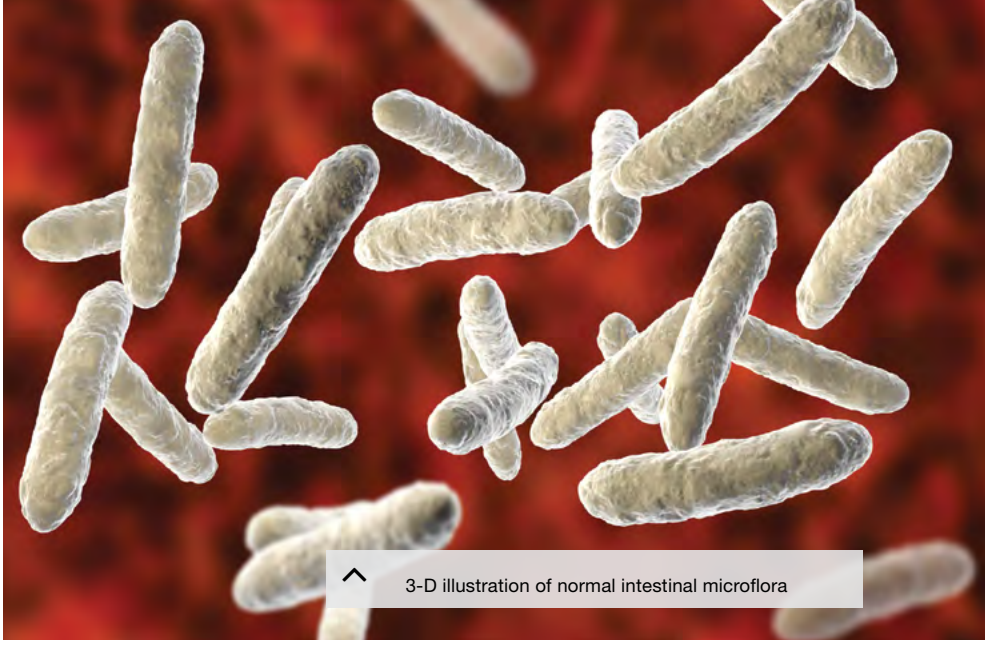
NEURON. IMAGE: TORSTEN WITTMANN

A Winning Glimpse Inside Young Neurons

UCSF's science imagery competition puts the beauty of science on display. This year's competition received over 210 entries from more than 50 labs across campus. The first-place image (above), submitted by Torsten Wittmann, PhD, a professor of cell and tissue biology in the School of Dentistry, depicts the cytoskeleton of neurons developing from induced pluripotent stem cells.

What Do Babies' Guts Reveal about Asthma?

Newborn infants with a certain microbial molecule in their gut may be especially vulnerable to developing asthma or allergies as they grow up, a recent UCSF study found.



3-D illustration of normal intestinal microflora

The researchers had previously examined a large cohort of 1-month-old babies and discovered that a small group of babies at high risk for asthma had different gut microbiota and much higher concentrations of a specific bacterial lipid in their feces. At higher concentrations, the lipid promotes immune dysfunction associated with allergic asthma.

Susan Lynch, professor of medicine

Their new study, according to senior author Susan Lynch, PhD, director of the new UCSF Benioff Center for Microbiome Medicine, identified the specific bacterial genes in the infant gut microbiome that produce this lipid. The team also showed that elevated numbers of these bacterial genes, or concentrations of the molecule in the feces of the infants, significantly increased their risk of developing childhood allergies or asthma. While the finding is just one component of a complex microbiome-immune interaction, Lynch notes that it's a first step toward early-life gut microbiome interventions that may prevent these diseases from developing.

FACULTY IN THE MEDIA

"We used to think that white meat was better than red meat for controlling blood cholesterol. What we found was there really was no difference."

Ronald Krauss, MD, a professor at the UCSF Cardiovascular Research Institute and at the Children's Hospital Oakland Research Institute and the senior author of a recent study that tracked the impact of various types of protein on blood cholesterol levels, to CBC/Radio-Canada. The key takeaway, Krauss said, is that if you want to lower your blood cholesterol, you should substitute plant-based proteins for both red and white meat.

"I hear from shelter providers, 'Gosh, we are set up for people who use drugs, but we have no idea how to manage dementia.'"

Margot Kushel, MD, director of the new UCSF Benioff Homelessness and Housing Initiative, on the increase in homelessness among older people and the lack of preparedness among shelters, hospitals, and law enforcement for dealing with the growing problem, in *Nature*

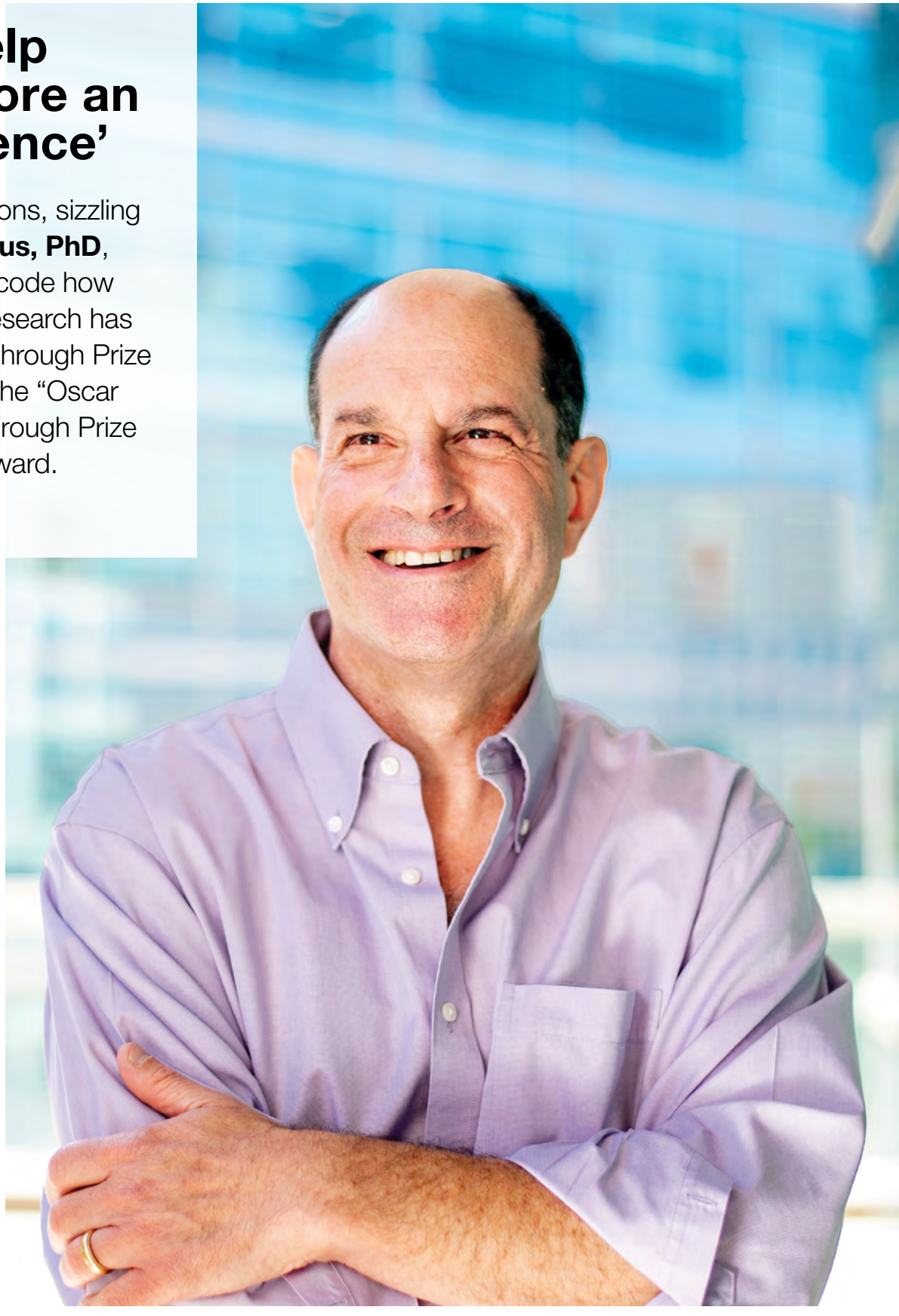
"We often have people who say, 'I wish I had never started down this path,' although I don't think people can really anticipate how they'll feel until they get there."

Perinatologist and medical geneticist **Mary Norton, MD,** director of UCSF's Division of Maternal-Fetal Medicine and the David and Kate Thorburn Professor, on the quandary of undergoing genetic testing when you're pregnant, on NPR's *Morning Edition*

ILLUSTRATION: DR_MICROBE

Scorpions Help Professor Score an 'Oscar of Science'

Venomous spiders, scorpions, sizzling chili peppers – **David Julius, PhD**, has tapped them all to decode how we sense pain. Now his research has earned him a 2020 Breakthrough Prize in Life Sciences, dubbed the "Oscar of Science." Each Breakthrough Prize comes with a $3 million award.



Julius, chair of the Department of Physiology and the Morris Herzstein Professor of Molecular Biology and Medicine, was honored for his groundbreaking work in deciphering the molecular basis of pain. During his years at UCSF, Julius has spearheaded some of the major advances in the field through his identification and characterization of a unique class of nerve-cell ion channels known as TRP (pronounced "trip") receptors.

In that work, Julius has used distinctive molecules from the natural world – tarantula and scorpion toxins and the compounds that produce the heat of chili peppers and the zing of wasabi, for instance – to gain an understanding of how signals responsible for temperature and pain sensation are transmitted by neural circuits to the brain. This work has stimulated significant research among scientists who aim to better comprehend and treat chronic pain, placing Julius among the world's most-cited scientists.

Julius's work was driven from the start by the great need for effective pain medications without the side effects and addictive potential of opioids. His research has led to significant interest in TRP channels as potential targets for new painkillers.

PHOTO: NOAH BERGER

Should You Take a Direct-to-Consumer DNA Test?

Since the human genome was completely sequenced in 2003, genetic testing has exploded into a multibillion-dollar industry. And with the rise of so-called "direct-to-consumer" tests such as those sold by 23andMe, which don't require a physician's sign-off, investigating your genes is easier than ever. But depending on your reasons, taking one of these tests may not be right for you, says Kathryn Phillips, PhD, a UCSF professor of clinical pharmacy who studies the use and value of new technologies for improving health care. She explains what you need to know before sending away your DNA.

By Lindsey Konkel

Kathryn Phillips is the founder and director of the Center for Translational and Policy Research on Personalized Medicine at UCSF and a professor of health economics and health services research in the Department of Clinical Pharmacy.

ILLUSTRATION: KEITH NEGLEY

What will you learn from a direct-to-consumer genetic test?

Many of these tests are geared more toward entertainment than clinical use. They report heritable traits like cheek dimples, earlobe type, and eye color, which may be fun but are not clinically important. They can also offer clues about disease risk, but such information is just a starting point. A physician would need to order you a more comprehensive, clinical-grade test if you want medical care based on your genetics.

How does a direct-to-consumer test compare to a clinical test?

Direct-to-consumer kits typically aren't testing at the same depth as clinical-grade tests. Take BRCA mutations, for instance. These are variants of the BRCA genes that may predispose a woman to breast or ovarian cancer. Direct-to-consumer kits only test for some of the most common mutations, so they can't tell you whether you're in the clear for every possible BRCA mutation. You'd need a clinical test for that.

What should you do if the results are unsettling?

Knowing what to do with a potentially confusing or unsettling finding can be a challenge. Imagine, for example, you tested positive for a gene that increased your risk of a disease for which there currently is no cure, such as Alzheimer's. A genetic counselor could help you navigate results like that. The good news is that for most health conditions, genetics is just one piece of your risk: Your genes aren't the only factor determining whether you get sick.

Will your genetic data be kept private?

Unfortunately, nothing is completely private these days. Most direct-to-consumer testing companies are in the business of selling the data they obtain – to pharmaceutical companies, for instance. These data typically are de-identified, meaning any personally identifiable information, such as your name and address, is removed. But your data may be used for purposes other than you intended, such as to help develop new drugs. Some people are okay with that, but others may not be.

Another issue you should be aware of is insurance. By law, health insurance providers cannot deny you coverage based on the findings of a genetic test, but those laws do not apply to other types of insurance. For instance, you could be asked to disclose the results of a genetic test when applying for life insurance, which could affect whether you're offered a policy and how much you're charged.

PHOTO: DAVID WAKELY; ALZHEIMER'S IMAGE: GRINBERG LAB

Hospital Top 10 in Nation, Best in NorCal

UCSF Medical Center has once again been recognized among the nation's elite hospitals in *U.S. News & World Report*'s annual Best Hospitals survey. This marks the 21st year that UCSF Health has been listed among the top 10 hospitals nationwide and the best in Northern California; UCSF was ranked seventh this year on the national Best Hospitals Honor Roll. In addition, UCSF Benioff Children's Hospitals was ranked among the nation's best children's hospitals in all 10 pediatric specialties assessed in the publication's 2019-20 survey.

Alzheimer's Disease Destroys Neurons that Keep Us Awake

Long before the memory problems associated with Alzheimer's disease begin to unfold, another phenomenon can develop: excessive daytime napping.

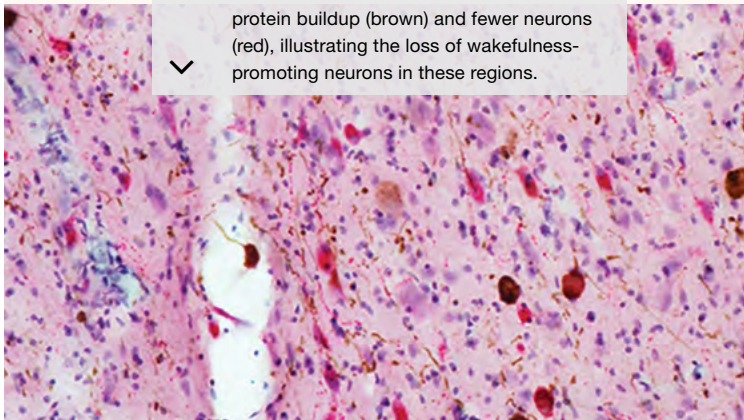
Lea Grinberg, associate professor of neurology and pathology

Some previous studies considered this napping to be compensation for poor nighttime sleep caused by Alzheimer's-related disruptions in the brain, while others have argued that the sleep problems themselves contribute to the disease's progression. But now UCSF scientists have shown that Alzheimer's disease directly attacks brain regions responsible for wakefulness during the day.

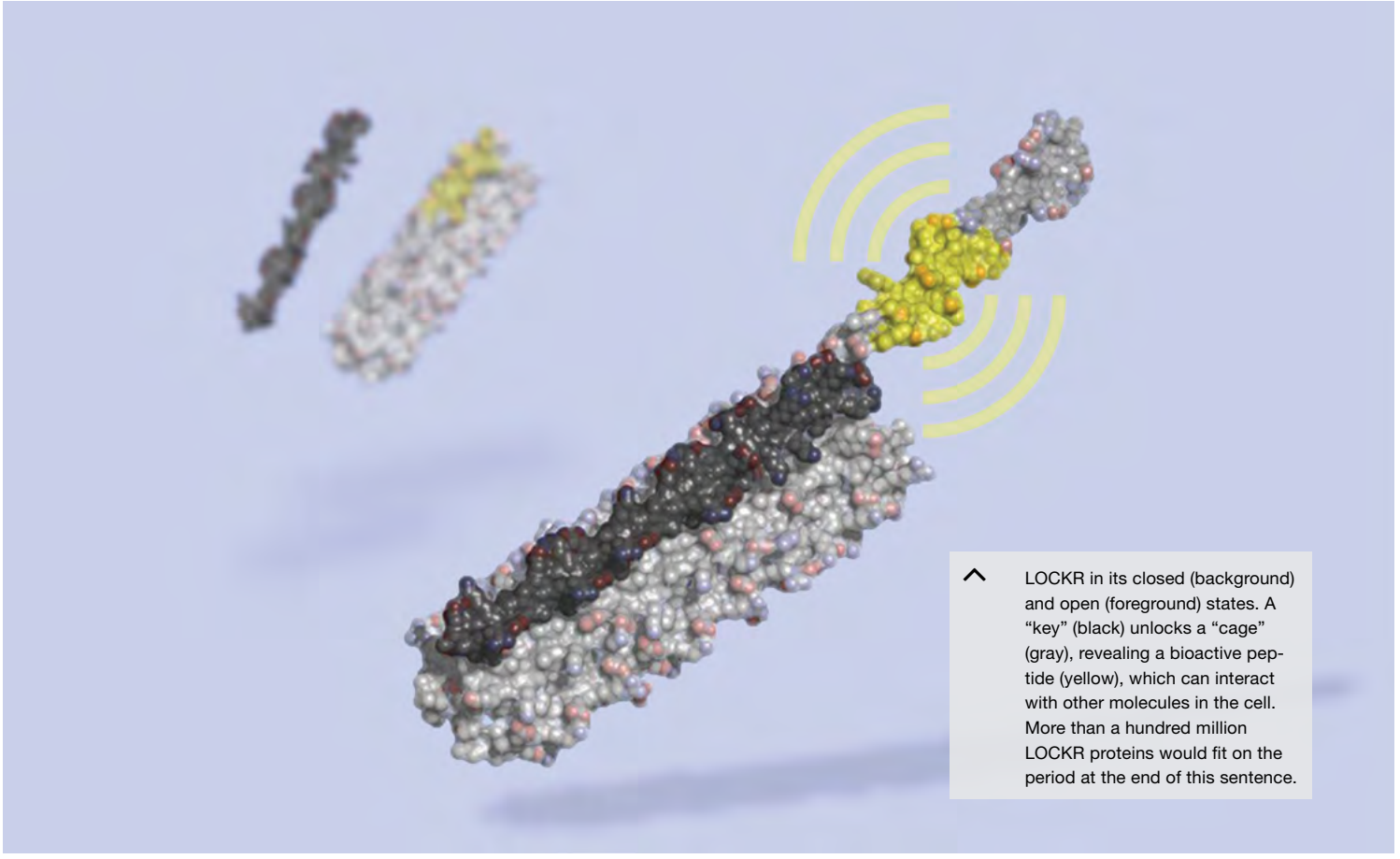
The new research demonstrates that these brain regions are among the first casualties of the neurodegeneration caused by Alzheimer's, and therefore that excessive daytime napping could serve as an early warning sign of the disease. In addition, by associating this damage with a protein known as tau, the study adds to the evidence that tau, rather than the more extensively studied amyloid protein, is responsible for the brain degeneration that drives Alzheimer's symptoms.

"Our new evidence suggests that we need to be much more focused on understanding the early stages of tau accumulation in these brain areas in our ongoing search for Alzheimer's treatments," says the study's senior author, Lea Grinberg, MD, PhD, an associate professor of neurology and pathology at the UCSF Memory and Aging Center.

Tissue from the brains of people with Alzheimer's disease shows increased tau protein buildup (brown) and fewer neurons (red), illustrating the loss of wakefulness-promoting neurons in these regions.



New 'Smart' Cell Therapies Offer Limitless Potential



LOCKR in its closed (background) and open (foreground) states. A "key" (black) unlocks a "cage" (gray), revealing a bioactive peptide (yellow), which can interact with other molecules in the cell. More than a hundred million LOCKR proteins would fit on the period at the end of this sentence.

Medicine has a "Goldilocks" problem. Many therapies are safe and effective only when administered at just the right time and in just the right dose; when given too early or too late, or in too large or too small an amount, medicines can be ineffective or even harmful. But in many situations, doctors have no way of knowing precisely when or how much to dispense.

Now, a team of bioengineers – led by UCSF's Hana El-Samad, PhD, and the University of Washington's David Baker, PhD – has devised a remarkable solution to this problem: "smart" cells that behave like tiny autonomous robots. In the future, these cells could be used to detect damage and disease and deliver help at just the right time and in just the right amount.

Amazingly, this can be accomplished without any direct human intervention, thanks to a first-of-its-kind artificial protein – designed on a computer and synthesized in a lab – that can be used to build brand-new biological circuits inside living cells. These circuits transform ordinary cells into smart cells that are endowed with remarkable abilities.

This new protein, formally known as the Latching Orthogonal Cage-Key pRotein, or LOCKR, was described in a pair of papers recently published in the journal *Nature*. And it's unlike anything biologists – or nature itself – have ever devised.

"While many tools in the biotech arsenal employ naturally occurring molecules that were repurposed for use in the lab, LOCKR has no counterpart in nature," says El-Samad, the Kuo Family Professor of Biochemistry and Biophysics at UCSF and co-senior author of the new studies. "LOCKR is a biotechnology that was conceived of and built by humans from start to finish. This provides an unprecedented level of control over the way the protein interacts with other components of the cell and will allow us to begin tackling unsolved – and previously unsolvable – problems in biology, with important implications for medicine and industry."

Hana El-Samad, Kuo Family Professor

LOCKR IMAGE: IAN HAYDON / INSTITUTE FOR PROTEIN DESIGN AT UW

Delaying Diabetes in At-Risk Young People

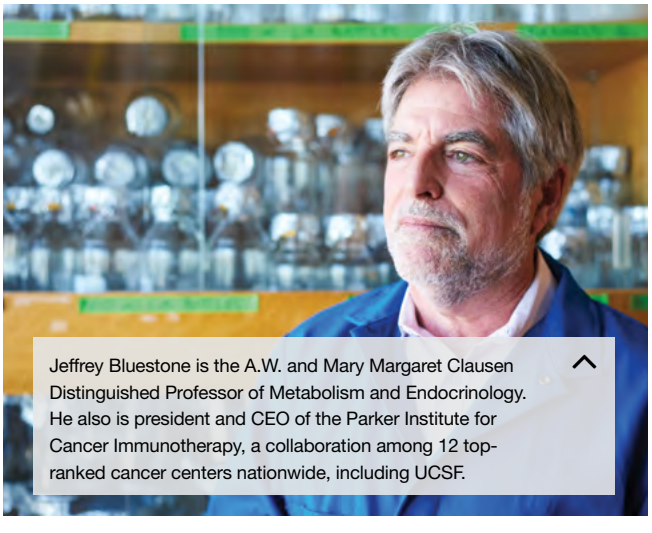
For more than 30 years, UCSF immunologist Jeffrey Bluestone, PhD, has believed that a drug he and his team developed in 1986 could stop the onset of type 1 diabetes – if given the right chance.

His research showed that the drug would target the body's out-of-control T cells before they destroyed insulin-producing beta cells in the pancreas and triggered type 1 diabetes, an autoimmune disease that afflicts more than 1 million people in the U.S.

But he had to wait both for the right drug strategy and for the pharmaceutical industry to catch up with the science. "It's not just something we threw at the wall and hoped would stick," says Bluestone, director of the Hormone Research Institute in the UCSF Diabetes Center. "The science told us this should work, so we kept at it."

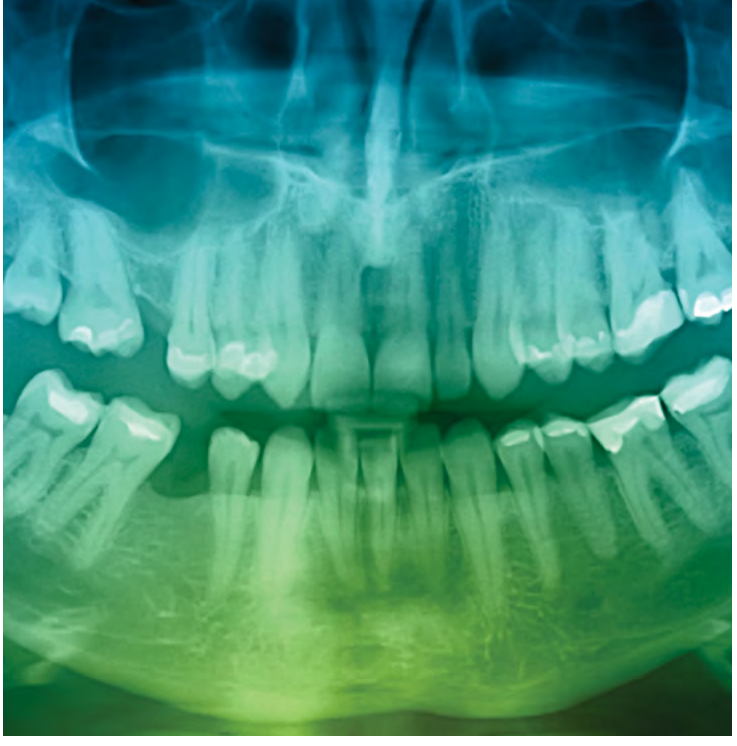
In June, Bluestone's research was validated when the American Diabetes Association announced the successful outcome of an eight-year drug trial conducted by Bluestone's collaborator, Kevan Herold, MD, of Yale University, in partnership with a national research network that includes UCSF. It turns out the key to the drug's success was to dose people at high risk for diabetes *before* their bodies succumbed to the disease.

Bluestone called the difference between the group treated with the drug – now called teplizumab – and the group given a placebo "profound." The trial showed that a two-week course of the drug delayed the onset of type 1 diabetes in study subjects by an average of two years and may have *permanently* delayed the disease's onset in some young patients.



Jeffrey Bluestone is the A.W. and Mary Margaret Clausen Distinguished Professor of Metabolism and Endocrinology. He also is president and CEO of the Parker Institute for Cancer Immunotherapy, a collaboration among 12 top-ranked cancer centers nationwide, including UCSF.

PHOTO: STEVE BABULJAK; X-RAY IMAGE: ZOKARA



Radical Action Needed to Stem Rampant Dental Decay

Almost half of the world's population suffers from tooth decay, gum disease, or oral cancers. Yet these diseases have been woefully neglected by the global health community, according to a recent series on oral health in the prestigious British journal *The Lancet*.

The authors implicate a system that prioritizes treatment over prevention, point to sugar's role in dental maladies, and call for radical reform of dental care systems to stem the tide of the problem. In an accompanying commentary, series co-author Cristin Kearns, DDS, MBA, an assistant professor of dentistry at UCSF, expresses growing concern that the dental profession will not make meaningful progress in combating the epidemic of oral ailments until it addresses the sugar industry's influence on dental research and professional bodies.

Cristin Kearns, a faculty member at UCSF's Philip R. Lee Institute for Health Policy Studies

"Dental research organizations have only recently woken up to the fact that their research activities haven't focused on sugars for many years, and very few people realize that these organizations have financial relationships with global candy, ice cream, sugary beverage, and snack companies," says Kearns. "While these relationships may be slightly less shocking when one considers these companies also sell oral health products, we can't lose sight of the fact that in many cases, these are the same companies that are opposing sugar-reduction policies, such as sugary beverage taxes."

Elderhood: Redefining Aging, Transforming Medicine, Reimagining Life

"Society has turned old age into a disease…a condition to be dreaded, disparaged, neglected, and denied," award-winning author **Louise Aronson, MD,** told the *Bay Area Reporter.* In her latest book, *Elderhood*, Aronson, a UCSF geriatrician, shares stories from her 25 years of caring for patients to weave a different vision – one that, as she puts it, is "full of joy, wonder, frustration, outrage, and hope."

Human Nature

How will the gene-editing tool CRISPR change our relationship with nature? Will it affect human evolution? This documentary explores these questions through interviews with the pioneering scientists who discovered CRISPR, the families whose lives are altered by this new technology, and the bioengineers who are testing it. UCSF alumna **Sarah Goodwin**, who earned her PhD in cell biology, is the leading science adviser on the film, as well as a producer.

Coping in Terrible Times

This NPR piece follows an unusual "pain rescue team" dedicated to easing the suffering of seriously ill kids in severe pain. The episode delves into the wrenching but powerful work of UCSF Benioff Children's Hospital San Francisco's integrative pediatric pain and palliative care team, which combines traditional pharmaceutical pain care with techniques such as acupuncture and massage. The program is one of just a handful of such teams in the nation.

Many Nurse Practitioners Are Thwarted in Treating Opioid Addiction

At least six states with high opioid abuse rates also have onerous work restrictions that hinder nurse practitioners (NPs) from prescribing medication that can help treat the problem, according to a study by UCSF researchers.

Joanne Spetz, associate director for research, UCSF Healthforce Center

These states, and others with restrictive scopes of practice for NPs, should reform their regulations, the researchers say, to take full advantage of the health care workforce in addressing the opioid crisis and meeting primary care needs.

"An important part of addressing the opioid crisis is helping people access treatment when they need it, and medication combined with therapy is the most effective approach," says corresponding author Joanne Spetz, PhD, associate director for research at UCSF's Healthforce Center and a professor at the UCSF Philip R. Lee Institute for Health Policy Studies. "NPs in states requiring that they practice under physician supervision or collaboration are much less likely to get waivers to prescribe these medications, and many of these same states have the highest rates of opioid overdose and addiction."

ILLUSTRATION: JING JING TSONG; ICONS: PICONS.ME

Are Workplace Chemicals Increasing Your Risk of Breast Cancer?

Millions of working women in California face exposure to chemicals that could increase their risk of breast cancer, including industrial solvents, antimicrobials, and phthalates.

A new web tool for the first time spells out those exposures. Users can search the database to see risk information on more than a thousand chemicals, sorted into 24 chemical groups, as well as which chemicals are likely to be present in various occupations.

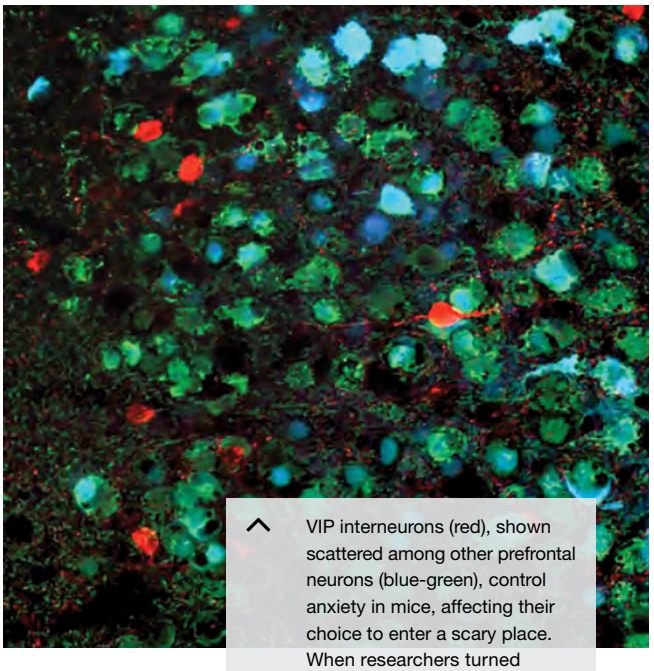
The tool, which was developed by researchers at UCSF and the California Department of Public Health, is part of an ongoing study focused on understanding potential breast cancer risks related to workplace chemical exposures.

View the tool at **cbcrp.org/worker-exposure**.

A Few Insights

- About 1.7 million California women may be exposed in the workplace to solvents, to name just one category of chemicals.
- Nearly 200,000 of these women are so-called "informal workers" who may be especially vulnerable. Many black women, for example, work as personal care, nursing, or other aides – roles with the potential for exposure to risky chemicals in antimicrobials, fragrance ingredients, and combustion products.
- Cashiers – many of them teenagers – may be exposed to chemicals including bisphenol A in cash-register receipts and fragrance ingredients.

SCIENCE IMAGE: SOHAL LAB UCSF



VIP interneurons (red), shown scattered among other prefrontal neurons (blue-green), control anxiety in mice, affecting their choice to enter a scary place. When researchers turned these neurons off, animals became much bolder.

To Boldly Go or Anxiously Hang Back?

In a study involving mice, UCSF scientists have identified a particular group of neurons in the front of the brain that play an important role in anxiety's influence over behavior. They found that turning off signaling from these neurons can act as sort of a "chill pill," reducing the likelihood of anxious behavior driven by signals from another region of the brain.

Vikaas Sohal, associate professor of psychiatry

In a study led by Vikaas Sohal, MD, PhD, an associate professor of psychiatry, the researchers discovered that mice were more likely to decide to venture into an exposed part of an elevated maze – something they typically find quite scary – when cells in the prefrontal cortex called VIP interneurons were inhibited. Evidence from many studies suggests that such avoidance behavior in mice is a good analogy to anxious responses in humans, says Sohal. The new finding, he adds, could help lead to new treatments for anxiety disorders in humans.

Radical Investment in San Francisco's Future

Sociologist **Howard Pinderhughes, PhD,** has devoted his career to understanding racism, preventing youth violence, and creating healthy communities for all. Now, the professor of social and behavioral sciences in the School of Nursing is leading an effort to leverage UCSF's economic power to transform San Francisco's poorest and most vulnerable communities.

By Silver Lumsdaine

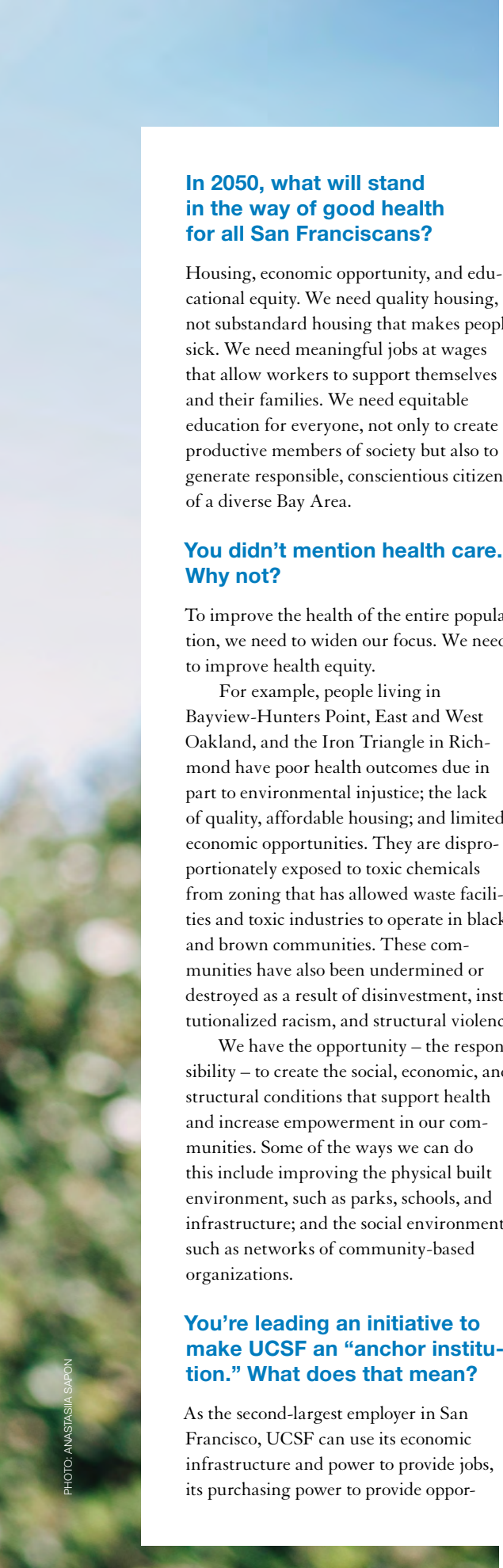


PHOTO: ANASTASIIA SAPON

In 2050, what will stand in the way of good health for all San Franciscans?

Housing, economic opportunity, and educational equity. We need quality housing, not substandard housing that makes people sick. We need meaningful jobs at wages that allow workers to support themselves and their families. We need equitable education for everyone, not only to create productive members of society but also to generate responsible, conscientious citizens of a diverse Bay Area.

You didn't mention health care. Why not?

To improve the health of the entire population, we need to widen our focus. We need to improve health equity.

For example, people living in Bayview-Hunters Point, East and West Oakland, and the Iron Triangle in Richmond have poor health outcomes due in part to environmental injustice; the lack of quality, affordable housing; and limited economic opportunities. They are disproportionately exposed to toxic chemicals from zoning that has allowed waste facilities and toxic industries to operate in black and brown communities. These communities have also been undermined or destroyed as a result of disinvestment, institutionalized racism, and structural violence.

We have the opportunity – the responsibility – to create the social, economic, and structural conditions that support health and increase empowerment in our communities. Some of the ways we can do this include improving the physical built environment, such as parks, schools, and infrastructure; and the social environment, such as networks of community-based organizations.

You're leading an initiative to make UCSF an "anchor institution." What does that mean?

As the second-largest employer in San Francisco, UCSF can use its economic infrastructure and power to provide jobs, its purchasing power to provide opportunities for minority businesses, and its community investments to increase community wealth and stability. With commitments like these, UCSF can anchor the physical and economic health of the poorest, most underresourced members of our community. This will radically improve health equity and help these communities to thrive by the year 2050.

You sound optimistic.

There's nowhere in the country that has the potential, the raw material, for an anchor initiative like we have here in San Francisco. UCSF contains tremendous brainpower, and we have a philanthropic infrastructure and community in the Bay Area that is second to none.

I am optimistic that our success will encourage other institutions in the Bay Area, and eventually statewide, to adopt an anchor strategy. This could profoundly increase health and decrease poverty in some of the most underserved communities and populations in the Bay Area. It is literally the only way we can have a dramatic impact on health equity in San Francisco.

How will this anchor initiative affect the private sector?

Improving the health and well-being of all members of a city improves the business environment. Businesses have a larger market for their products. We have a safer environment for everybody – from the standpoint of health and communicable diseases to issues around violence.

As one example, right now in San Francisco, we've got folks living in tents. We have folks who suffer from drug addiction and abuse. The tragedy is that we have the capacity and the potential to improve the health and well-being of the most vulnerable. What we need is the political, social, and economic will to take action.

Engaging private corporations and businesses as part of a citywide anchor initiative will be important. Collaborating with philanthropists will be important. For this initiative to succeed, it's going to take serious long-term commitment and some radical action not just by UCSF but also by members of the San Francisco community. We need people to get involved with this not just as a UCSF initiative but also as a citywide initiative.

Why focus on minority-owned businesses?

We should focus on minority-owned businesses in order to stop or reverse the decline of diversity in San Francisco. San Francisco's diversity has historically been an important part of our ethos – the sense of who we are as a city and as a community. However, gentrification and dislocation have dramatically decreased the numbers of African Americans. Working-class Latinos have flocked to the East Bay and to as far away as Stockton. Why? We've ignored and neglected the health and well-being of some of the most vulnerable communities in San Francisco. As a result, we are fast losing the diversity that we are so proud of and that we claim to value.

What do you hope and dream of for 2050?

I hope that the Bay Area in 2050 will still be a diverse mixture of many different communities. That our African American and Latino populations are thriving and living in quality housing, and that our schools are providing high-quality educational opportunity for everyone.

I hope that UCSF will be able to look back and say that we were responsive to the needs of the most underserved and underresourced communities, and that we were a catalyst for changing the corporate culture of the Bay Area. I hope we can say that we increased health equity so all residents of the Bay Area could live healthy, vibrant lives.

I dream of a future when a young, black girl who's born in Bayview-Hunters Point, East or West Oakland, or the Iron Triangle in Richmond has the same life expectancy, expectations for her health, and sense of possibility as a white girl who grows up in the Oakland Hills, San Francisco's Richmond District, or Nob Hill.

The Climate Crisis is a Health Crisis

MEDICINE MUST RECKON WITH THE COMING CATASTROPHE

By Cyril Manning

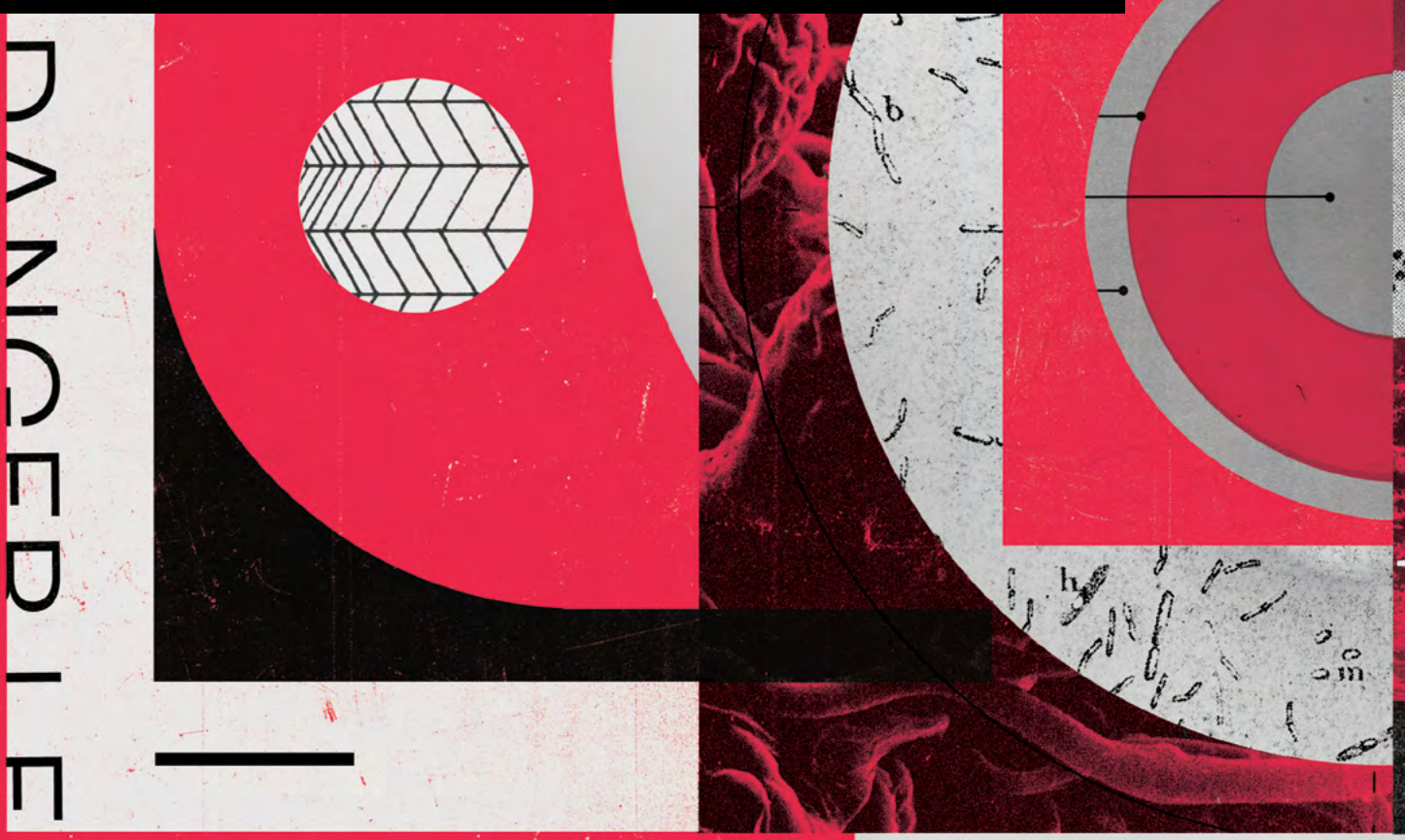


ILLUSTRATION: MIKE MCQUADE

On the morning of November 8, 2018 – as the skies above Paradise, Calif., sickened from a faint blue to ashy brown to blood red; as flames thundered and cracked through forest and town, incinerating homes and melting cars; and as thousands of terrified residents packed onto narrow, gridlocked roads – Amber Denna dashed into Paradise Drug, where she was a longtime employee. She snatched the pharmacy's computer server and threw it, along with a few personal possessions, into the back seat of her car.

On the phone with a colleague in nearby Chico, Calif., Denna had realized that the thousands of records stored on that server would be a lifeline for any nursing home patients, retirees, and families who'd manage to escape the devastation of the Camp Fire. Within just a few hours, most of the town's 26,000 inhabitants would lose everything. But those who survived would still need their medicine.

Owned and operated by Janet Balbutin, PharmD '68, Paradise Drug had been a hub of sorts for the community, as well as the first point of contact that many of its residents had with the medical system. With the data rescued from the fire, Balbutin ended up dispensing hundreds of free or deferred-payment medicines to those dispossessed residents. "Even now, we just stand back and say, 'What happened?'" says Balbutin. "To wipe out a town in three hours at the most.... We lost a lot of patients in the fire."

The Camp Fire was hardly the first, or even the worst, climate crisis-related disaster to upend human lives. The European heat wave of 2003, the first weather disaster to be widely linked to climate change, killed between 35,000 and 70,000 people, overwhelming hospitals and morgues. In 2012, unusually warm waters off the coast of Florida caused an algal bloom that resulted in $540 million in hospital admissions and emergency department visits. And when Hurricane Maria devastated Puerto Rico in 2017, it killed 3,000 people and wiped out countless Puerto Ricans' access to food, social services, and health care; in addition, it destroyed the supply chain for 44% of U.S. IV bags, creating months-long shortages at hospitals across the country and beyond.

"The climate crisis creates so many more human health impacts than we typically think of," says Wendy Max, PhD, a health economist in the UC San Francisco School of Nursing. In a recent study, Max and her co-authors looked at 10 climate change-fueled disasters in 2012 in regions across the U.S., including hurricanes, fires, disease and allergen outbreaks, heat waves, and spikes in ozone pollution. Far from a comprehensive list, these 10 events alone led to 917 deaths, 20,568 hospitalizations, 17,857 emergency department visits, and $10 billion in health-related costs. Such events kill, they pack ERs, and they leave lingering legacies of toxic pollution, pulmonary complications, and post-traumatic stress – but they are just a glimpse of what's to come unless the world makes an extraordinary course correction. "There's a profound human cost here and now," Max says. "Hopefully, seeing that helps elevate our understanding of the urgency."

If anyone feels that urgency, it's Katherine Gundling, MD.

A year ago, Gundling sat in her allergy-immunology clinic at UCSF's Parnassus campus, a stethoscope cupped to the ribs of a patient. The young woman's severe asthma had long been well controlled, but now her breathing was labored, with coarse wheezing audible all around her chest. Outside, smoke from the 2018 Camp Fire was choking San Francisco, and it had affected this woman so profoundly that Gundling's only recourse was to prescribe a powerful new medication. After years of seeing her patients suffer from ever-longer allergy seasons and "the increased nastiness of the pollens," this was the last straw. She was ready to get to the root of the problems she was seeing, and within a few months, Gundling had retired from her practice in order to focus on the relationship between climate change and human health. "I realized that I could not leave this planet without doing everything I could to affect what's happening," she says.

She dove in headfirst, learning about advocacy and joining the board of an international environmental group. She began reaching out to colleagues at UCSF and elsewhere – building a list of clinicians, health scientists, and corporate and nonprofit allies who shared her sense of urgency. Most notably, she connected with a group of UCSF students passionate about medicine and climate. "Students from all four schools were saying, 'Hey, why isn't everybody up in arms about this?'" Gundling says. Soon, she found herself mentoring them on career paths that could combine the health sciences with climate action, even accompanying several of them to Washington, DC, to educate legislators on the climate-health connection.

Inspired by these students, Gundling envisions a new medical career path, including a dedicated climate-medicine fellowship designed to equip health professionals with the expertise to prepare for and address climate-related medical disorders. "In 2050, the public health challenges will be much greater than today," she

PHOTO: NASA

Trying to help a patient severely affected by smoke-filled air drove physician Katherine Gundling to pursue a new career in climate medicine.

PHOTO: ELENA ZHUKOVA

says. “Our current medical training is not set up for this at all. We will require many more and larger facilities to treat acute and chronic climate-related illnesses. Students in the health professions will need to go out to these facilities, where senior physicians must provide proper training. Who will do this?” she says. “To complicate matters,” Gundling continues, “severe weather events will vary widely by location. For example, doctors in flood-prone Houston will need training related to mold, infectious diseases, and water contamination, while those in Northern California must respond to wildfire-related illnesses. Our need for public health specialists will also be much greater. And along with this is coordination with governmental services such as 911 during acute events. Could specially trained nurses or doctors handle these calls instead of police, who have minimal training?”

While these are daunting questions, the idea of incorporating climate change into medical education is already gaining momentum at UCSF and beyond. The changing climate will have profound implications for how tomorrow’s physicians must think about certain diagnoses. Infectious disease specialist Peter Chin-Hong, MD, notes that the students he is teaching today will surely encounter diseases that have never before been seen in California. “They need to know that with changes in climate, diseases have no borders anymore,” he says. “When somebody presents with something that looks like dengue, for example, the physician will need to be suspicious of that and be able to send the right tests, even though it’s not in the textbooks.”

HEALTH EFFECTS OF CLIMATE CHANGE

Heat-related disorders, including heat stress and heat-related kidney disease

Respiratory disorders, including those exacerbated by fine particulate pollutants, such as asthma and allergic diseases

Infectious diseases, including vector-borne diseases like Lyme disease and water-borne diseases like childhood gastrointestinal maladies

Food insecurity, including reduced crop yields and increased plant diseases

Mental health disorders, such as post-traumatic stress disorder and depression

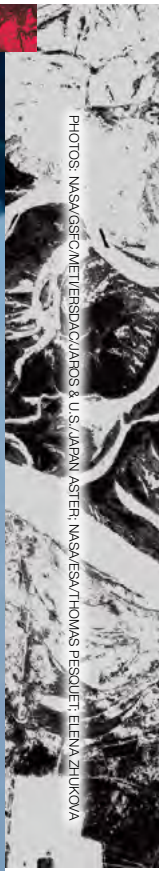
"Things are changing so fast," he continues. "We're not trying to teach the whole encyclopedia like we used to, but a way of thinking and a habit of mind. We need to give students the tools they need to solve the future problems we don't even know about yet."

UCSF's Sheri Weiser, MD, MPH, and Arianne Teherani, PhD, have shown how. Together, Weiser, an epidemiologist and practicing internist at Zuckerberg San Francisco General Hospital, and Teherani, a professor of medicine and education, developed a climate-health curriculum for learners across all of the health sciences. In addition, they've trained faculty members at all six University of California health campuses. Aside from an elective on climate change and health that's available to first-year medical students, their approach does not add stand-alone climate-science lessons. Instead, they train professors to integrate relevant knowledge and case studies into existing material. Professors of anesthesia, radiology, and pharmacy, for example, are encouraged to note that anesthetic gases, imaging technologies, and pharmaceuticals all have a significant carbon footprint. In psychiatry, students learn how most psychiatric drugs interfere with the body's ability to regulate temperature, creating life-or-death stakes for depressed or mentally ill patients during heat waves. Training in infectious diseases already covers the pathogens found in contaminated water and transmitted by insects; highlighting the health implications of increased flooding and expanded mosquito habitats is a simple, and essential, connection.

The approach is effective, and it has put UCSF's climate change education efforts ahead of those of most other medical and health professions schools, but Weiser and Teherani are eager to expand the program, both within and outside of UCSF. "Literally the biggest threat to human health ever seen is in front of us right now," says Weiser. "So why is this not front and center of everything? Why is it not being talked about all the time?"

Colin Baylen, a second-year medical student who co-founded the UCSF student group Human Health + Climate Change, puts it this way: "When I think about what my career might look like in 2050, I see climate change impacting any specialty I consider."

Infectious disease specialist Peter Chin-Hong says that his students will encounter diseases never before seen in California.



PHOTOS: NASA/GSFC/METI/ERSDAC/JAROS & U.S./JAPAN ASTER; NASA/ESA/THOMAS PESQUET; ELENA ZHUKOVA

Epidemiologist Sheri Weiser is training professors across the University of California health campuses to integrate climate health into existing coursework.

YEAR 2050

STUDENTS CONFRONT THE CRISIS

Second-year medical students Colin Baylen and Nuzhat Islam are fighting for the world's future. Hear from them and more UCSF students at: bit.ly/ucsf-climate-voices

The world, he says, will be a very different place when he and his classmates are at the peak of their careers. "Wherever I look," Baylen says, "I'll see climate change and its consequences."

Even the best-case climate scenarios for the decades ahead look pretty bleak. "There are only four scenarios that could actually kill hundreds of millions of people," says Sir Richard Feachem, DSc(Med), PhD, director of UCSF's Global Health Group. "Nuclear war, meteorites, and pandemics are all merely feasible. But climate change is already underway."

Between 2030 and 2050, climate change is expected to cause approximately 250,000 additional deaths per year worldwide from malnutrition, vector-borne diseases, diarrhea, and heat stress. By 2050 in the U.S., annual cases of West Nile virus – just one of the many infectious diseases that are projected to explode – will more than double. At least one projection estimates that by 2050, more than 3,400 additional Americans may die each year from heat stress. And the most vulnerable among us will suffer the most: poor people, the young, the old, pregnant women, and people with depression or mental illness.

Perhaps even more consequentially, climate change will displace hundreds of millions of people by 2100 – particularly near the equator, along coastlines, and in regions struck by drought. Extreme heat, food and water insecurity, rising sea levels, and natural disasters will uproot millions, isolating entire communities from the health systems they depend on and placing new burdens on health resources wherever those climate refugees end up. And this will happen not just in far-off places like India, Africa, and the Middle East; climate pressure in Central America is already adding fuel to the U.S. border crisis, and the World Bank projects that climate change will turn 1.7 million residents of Mexico and Central America into climate migrants by 2050.

> "There are only four scenarios that could actually kill hundreds of millions of people. Nuclear war, meteorites, and pandemics are all merely feasible. But climate change is already underway."
>
> —*Sir Richard Feachem*

PHOTOS: USGS EROS DATA CENTER; CHRIS VINAN; ELENA ZHUKOVA

On top of all this, the impacts of climate change on mental health are incalculable. Every hurricane, firestorm, flood, and deadly heat wave triggers waves of trauma and PTSD. Lost ways of life – whether in eroding seaside communities, on slowly dying farms, or in scorched mountain towns – exact an existential grief known as solastalgia. And acute and long-term changes connected to climate have been shown to elevate both interpersonal and intergroup violence, while undermining social identity and cohesion.

Ironically, the vastness of the problem is also connected to society's failure to adequately respond to it. "Climate distress often immobilizes us," says Elissa Epel, PhD, a professor of psychiatry and an expert on chronic stress and stress resilience. "We look like we don't care, but it's because we can't cope. The scope of our world's endangerment is so enormous that it makes us feel helpless. We become passive and collusive with what's happening."

The solution, Epel says, is to build personal and group resilience as a bulwark against the psychological toll of the climate crisis: "Part of dealing with climate distress is really letting ourselves have some space, support, and guidance" for processing our emotional reactions. "We've been looking at climate science to deal with climate change, but now, it's not about science. It's about human behavior and getting over our barriers."

Epel says that in the past, the way she has dealt with her own climate distress was "cheerleading others and saying, 'Let's see what's happening with the environmental activists, the climate scientists. What are *they* going to do?'" But now, she says, "I feel desperation about doing all *I* can in my own personal ecosystem." With that in mind, she recently agreed to co-lead a new UCSF task force on climate change and mental health, a group that's focused on research, training, and partnering on broader climate efforts at UCSF. Getting personally engaged in solutions is helping her live with her own climate anxiety. She hopes the task force will become a model for the world because "we have so much power as a university and as a health system."

"There's a profound human cost here and now," says health economist Wendy Max, who studies the impact of climate-change-fueled disasters.

One important player flexing that power at UCSF has been Naomi Beyeler, MPH, who is both the staff lead for the Global Health Group's climate change and health initiative and a PhD student focused on researching the impacts of climate change on health care delivery in low-resource settings. In 2018, Beyeler organized a global forum that drew nearly 300 government and global health leaders to UCSF. The event culminated with a "call to action" endorsed by more than 100 of world's most respected health organizations. Beyeler was the key author of that rallying cry, which frames two ways that the health sector must engage with the issue:

She calls one approach "health action for climate," noting that the health sector – which accounts for a stunning 10% of the U.S. carbon footprint and 5% globally – can play a significant role in reducing greenhouse gas emissions by greening its own practices (see sidebar). On the flip side, Beyeler says, there is "climate action for health." Essentially, this means that health scientists and caregivers should embrace the role of climate messengers because "every policy in the climate space is going to affect health." She notes that "some of those pathways are going to benefit health more than other

TO FACE THE FUTURE, THE HEALTH SECTOR MUST:

Commit to low-carbon buildings and facilities

Prioritize sustainability when purchasing pharmaceuticals, medical devices, food, and other products

Invest in renewables and energy efficiency

Minimize waste and enforce sustainable waste-management processes

Embrace sustainable transportation and water-consumption policies

Plan ahead to withstand extreme weather events

PHOTOS: USGS/NASA/LANDSAT 7; USGS EROS DATA CENTER; ELENA ZHUKOVA

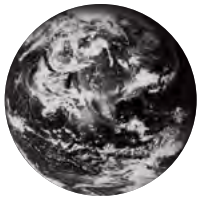
alternatives, so the health sector has a real stake in being engaged in climate policy."

For example, shutting down dirty power plants, investing in local food systems, and creating green urban spaces all cut carbon emissions while also making communities – particularly underserved ones – healthier. "When we as a society finally choose to intervene, we can not only prevent many of the worst scenarios from happening," says Katherine Gundling, "but we can also address health disparities in the process."

"I'm an optimist because there are so many things we can do," she says. "The question is, are we going to define the future, or are we going to react to it?"

Health professionals could play an outsized role in defining that future because, according to Gallup, people trust them more than those in any other profession. "When physicians and nurses get out there and talk about something, people sit up and say, 'Let me pay attention. These are people I respect and believe,'" says Wendy Max, the health economist. Leveraging that trust to illuminate the health impacts of climate change elevates science above politics. And, of course, it shifts the stakes from abstract, seemingly distant ideas like sea level rise to deeply personal, universal concerns for our own well-being and that of our kids.

In September, Karly Hampshire, Nuzhat Islam, and Sarah Schear made exactly that argument to some of the most powerful people in Congress. On the same day that 7 million people across the globe were striking for climate action, these three UCSF medical students joined more than a dozen physicians to lobby California Senators Kamala Harris and Dianne Feinstein; Speaker of the House Nancy Pelosi, from California's 12th district; and Representative Barbara Lee, from California's 13th district, on climate issues. "We encouraged them to link climate change to human health whenever possible, allowing people to internalize climate change and make them realize that it is not about someone else, somewhere else," says Hampshire. "It's their kid's asthma, their best friend's fire-related PTSD, their dad's heat stroke."



YEAR 2050

A CALL TO ACTION ON CLIMATE AND HEALTH

In 2018, more than 100 health organizations endorsed a climate and health call to action spearheaded by UCSF's Global Health Group. Find the full call to action at bit.ly/ucsf-climate-health

Graduate student Naomi Beyeler authored a "call to action" for climate-change engagement that more than 100 of the world's most respected health organizations endorsed.

> "The question is, are we going to define the future, or are we going to react to it?"
>
> —*Katherine Gundling*

Like most of the people in this story, Hampshire has vivid recollections of the day in 2018 when Paradise burned and of the weeks that followed. Soupy, noxious air choked the city. Everywhere, faces were hidden behind N95 masks or tightly wrapped scarves. "It was such an eerie time, as if out of a sci-fi movie," she says. "I remember thinking: Is this what the world is going to look like all the time? Is this the type of place I'm going to raise my children?"

For many in the Bay Area and beyond, the hazy, toxic glow of the Camp Fire-polluted skies seemed to illuminate the truth most of us have known but, as Epel puts it, are too "frozen" to grapple with: The climate is changing, here and now, and San Francisco is no less vulnerable than Miami, Damascus, or Manila.

That knowledge can feel bleak, but it comes with one tremendous upside: It can catalyze action. "We know what's ahead of us," says Gundling. "But we also know we can bend the curve. Some people may see addressing climate change as a moral imperative. But as health care professionals, it's much more tangible than that. The moral imperative to engage with the climate crisis grows out of the consequences we see for our patients."

PHOTOS: USGS/NASA/LANDSAT 7; NASA GODDARD RETO STÖCKLI; ELENA ZHUKOVA

*T*echnology will soon give us precise control over our brains and our genes. *W*hen we can govern the very biology that makes us who we are, what will it mean to be human? *A*nd who will we want to be?

By Ariel Bleicher

This is a story of another time, of a plausible future 30 years from now, give or take, in which the human experience of life and health (and perhaps even of who we are) will unfold unlike anything known before.

The citizens of this future will learn early in life – through some combination of next-next-next-generation genetic testing and intelligence gleaned from their smart accessories – whether they are heading toward disease: depression, dementia, diabetes, what have you. More importantly, they will be offered an exit strategy.

Some future citizens will take a familiar route: medications, behavioral therapies, or lifestyle modifications. But for others, the path to well-being will require novel interventions. For example, those genetically predisposed to certain disorders might opt to get any risky DNA snipped out of their genes or rewritten. Those with neurological diagnoses, meanwhile, might be prescribed a brain implant – a clingwrap-like electrical film laid on the brain's surface, perhaps, or a network of thinner-than-hair wires snaked within its anatomy, to keep its neural circuits firing properly.

One might think, assuming these procedures have been shown to work safely and well, that future societies will have everything to gain and little to lose. Who wouldn't divert the course of their own health, or their children's, to avoid suffering down the road? And yet our neurons and our DNA are more than the origins of illness. They are also the substrates of our being: our identity, our humanity, arguably consciousness itself. Once we begin to manipulate these elements for medical purposes, do we not risk altering who we are?

If a gene therapy or brain implant erased, say, a person's propensity for depression, would it also erase possibly related facets of their personality, such as introversion, pensiveness, or melancholia? Would they recognize strange thoughts or behaviors as side effects or mistake these changes for a "new normal"? And if they chose not to have these treatments, or couldn't afford them, would they be passed over for jobs, for health insurance, for social acceptance? Who would they be? Would they still be themself?

ILLUSTRATION: MIKE MCQUADE

> "*T*hese devices are part of an evolution of thinking about the bionic human."
>
> —*Edward Chang*

EDWARD CHANG

UCSF professor of neurological surgery and member of the UCSF Weill Institute for Neurosciences

JENNIFER DOUDNA

professor of chemistry and of biochemistry and molecular biology at UC Berkeley

PHOTOS: NOAH BERGER; BARBARA RIES

*T*he *B*ionic *H*uman

Since before the first *Homo sapiens* walked the Earth 200,000 years ago, we humans have been shaped by our own inventions. Fire control, stone tools, eyeglasses, the cotton gin, electricity, antibiotics, the atom bomb, the heart transplant, in vitro fertilization, the internet – for better or for worse, technology has long fashioned us as individuals, as societies, and as a species. Still, there is something exceptional about the prospect of gaining mastery over our brains and genes.

First, consider brain implants. In the past couple of decades, surgeons have installed them in hundreds of thousands of patients with epilepsy, obsessive-compulsive disorder, and movement disorders, including Parkinson's. The implants relieve symptoms like seizures or tremors by sending electrical pulses to culpable brain areas – a technique known as deep brain stimulation. Many experts believe its use will only expand as implants get smaller and more sophisticated and as implantation surgeries become less invasive. "I wouldn't be surprised if, in 20 or 30 years, such devices will be as ubiquitous as cardiac pacemakers," says Edward Chang, MD '04, a professor of neurological surgery and the William K. Bowes Jr. Biomedical Investigator at UC San Francisco. He and some of his colleagues have even begun to refer to implants in the brain as "brain pacemakers."

Unlike heart pacemakers and other synthetic body parts, however, brain implants could challenge the typical ways we think about human augmentation. "There's no question these devices are part of an evolution of thinking about the bionic human – how we can modulate and tinker with ourselves to replace or restore functions," says Chang, who, together with UCSF colleagues, is now testing several applications for the technology, including whether it can help treat mental-health problems and restore movement and speech to patients with paralysis. "But now we're talking about directly interfacing with the brain, which is much more salient than something like a hip replacement or an artificial kidney, because it has to do with the mind."

Gene therapies, too, carry a special philosophical weight, bearing upon not the human mind but our genome – the complete set of DNA whose molecular code, and how it's expressed, give rise to a singular life. These therapies insert or modify DNA in human cells to overcome genetic disease or turn cells into living drugs. Since 2003, regulatory agencies in China, Europe, and the U.S. have approved fewer than a dozen gene-therapy products, including those for certain cancers and disorders of the blood, eye, and neuromuscular system. But the technology holds promise for countless cures.

"Within 30 years, it will probably be possible to make essentially any kind of change to any kind of genome," says Jennifer Doudna, PhD, a professor of chemistry and of biochemistry and molecular biology at UC Berkeley. She became world renowned in 2012 for her work on a genome-editing tool called CRISPR-Cas9 and now co-directs the Innovative Genomics Institute (IGI), a partnership between UCSF and UC Berkeley that explores potential uses of genome-editing and its societal implications. "You could imagine that, in the future, we're not subject to the DNA we inherit from our parents," she says, "but we can actually change our genes in a targeted way."

Such on-demand editing could be done, as it is today, in diseased tissues like retinas, nerves, or, one day, even brains. But it could also apply, controversially, to reproductive cells and embryos. This latter approach, called germline engineering, would enable genetic changes, therapeutic or otherwise, to be passed on to future generations. "Does that mean directing our own genetic destiny?" Doudna asks. "I say it does."

Given the enormity of this power, many experts, including Doudna in 2015, have called for a moratorium on germline engineering in humans. The latest outcry came this past fall, after a scientist in China claimed to have created twin girls from embryos edited to prevent HIV infection. Although the IGI takes an official stance against the current use of the practice, Doudna thinks it can't – and perhaps shouldn't – be stopped indefinitely. Families of children with heritable diseases awaiting cures have changed her mind, she says. "So many parents have emailed me saying, 'Please help.' I feel a responsibility to at least explore what it would it take for the science and ethics to be at a place where this kind of editing is safe and responsible."

The further we explore gene therapies and brain implants, however, the more we will confront the question of what it means, as Doudna puts it, "to control the very essence of who we are."

*B*eyond *T*herapy

Ethicists ask whether these technologies could turn someone into a different person. The concern is not unfounded. Scores of studies show it's possible to genetically engineer mice to dial up or down just about any behavioral or cognitive trait: aggression, compulsion, sociability, learning, memory, etcetera. Likewise, certain changes to the human brain – traumatic injury or neurodegeneration, for instance – can induce dramatic changes in character, such as emergent criminality or creativity. Even antidepressants go "beyond treating illness to changing personality," making the shy bold or the solemn cheerful, as psychiatrist Peter Kramer observed in his 1993 bestseller *Listening to Prozac*.

It's unlikely that today's gene therapies would have serious psychological or metaphysical side effects. They typically act on only one gene out of a possible 20,000 in a fraction of a patient's cells, such as retinal cells or immune cells. But genome editing might one day treat or prevent disorders that involve up to hundreds of genes, including obesity, heart disease, and psychiatric illness.

If and when we use this technology to control such complex health conditions, Doudna speculates, we may inadvertently influence complex personal traits. Genes, after all, don't work alone but in networks; they often serve multiple functions, which scientists are still uncovering. "In the future, if people are able to edit their children's genomes," she asks "to what extent does that alter the nature of the child?"

As for brain implants, ethicists debate the extent of their psychic risks. A minority of patients who have received such implants have said they identify with their device ("It became me") or feel controlled by it ("You just wonder how much is you anymore"). Do these impressions reflect a distorted sense of self? The answer is murky, says neuroethicist Winston Chiong, MD '06, PhD, an associate professor of neurology who studies the ethical and policy implications of brain diseases and therapies. "Sometimes these quotes are questionably interpreted," he explains. In a recent paper, for example, Australian ethicist Frederic Gilbert, PhD, points to a case in which a patient receiving deep brain stimulation for Parkinson's disease reportedly told her interviewers, "I feel like an electric doll"; some ethicists misquoted the comment as "I am an electric doll." "While the latter quote may involve a psychotic (delusional) episode," Gilbert writes, "the former could simply represent a playful and moody remark."

In other rare instances, patients with implants have become hypersexual, impulsive, or depressed. However, the cause may not necessarily be their device, says Simon Outram, PhD, a research specialist in UCSF's Program in Bioethics. As part of a two-year study being run in partnership with Baylor College of Medicine and the University of Florida, Outram is helping conduct patient interviews and surveys to examine how brain implants impact autonomy, personal identity, and risk-taking. "It's very difficult to separate the progress of the illness from the effects of the treatment itself," he says.

The fear that a brain implant may threaten one's personhood "maybe isn't bearing out as we collect more data," Chiong says. Nevertheless, he adds, "it's an issue we should keep checking in about," particularly as researchers pursue technology able to treat mood disorders and other psychiatric conditions.

> "*D*oes that mean directing our own genetic destiny? *I* say it does."
>
> —*Jennifer Doudna*

Meanwhile, implants are getting smarter, with artificial intelligence playing an ever-greater role, Chiong notes. "We're talking about devices being developed now that can monitor someone's brain function and make adjustments on the fly," he says. Such AI-controlled implants may present ethical quandaries that previous interventions, such as pharmaceutical drugs, do not.

Chiong offers an example: "We're all familiar with alterations in our brain function from things that we ingest, whether it's a pill or a cup of coffee," he explains. "We might feel a little strange or act a certain way, but then we might think, 'Well, I wouldn't have acted that way normally – maybe it's the medication or the caffeine.'" People may lack this intuition if an intelligent machine controls the dosage, he says. "Oftentimes, a patient may not even be aware of what the device is doing and when it's active." Such scenarios, Chiong says, raise questions about human agency and who – or what – is responsible if things go awry.

Ultimately, the rise of gene therapies and brain implants suggests the possibility of recasting parts of ourselves we once accepted as elemental or fixed. Given this new biological liberation, Chiong says, "we'll face a choice we didn't face before: Do we want to remain the way we are, or do we want to change?"

WINSTON CHIONG

neuroethicist and member of the UCSF Weill Institute for Neurosciences

BARBARA KOENIG

founding director of the UCSF Program in Bioethics

PHOTOS: TOM SEAWELL; STEVE BABULJAK

ILLUSTRATION: MIKE MCQUADE

Great Power, Great Responsibility

The answer will impact not only the human self but also our societies. The genomic tweaks and neural tunings we choose to value, for instance, could shift social norms, ethicists say. Most Americans today would feel remiss if they did not correct poor vision, straighten their teeth, or vaccinate their kids. Will tomorrow's citizens feel obligated to get cognition-boosting implants and edit their children's genes to protect against asthma, cancer, or learning deficits?

We might very well enjoy such gains. But the more we strive toward ideals of health or ability, ethicists warn, the less we may tolerate people who don't meet them, whether by circumstance or choice. Some people with diagnoses of disability or disease, including dwarfism, deafness, autism, and even hemophilia, consider their conditions part of their identities and aren't interested in cures, points out Jodi Halpern, MD, PhD, a professor of bioethics and of medical humanities in the UC Berkeley-UCSF Joint Medical Program. "We don't want to be Luddites about humans changing what's possible for themselves," she says, "but we do want to appreciate the threats to human dignity and human diversity that can come from too much perfectionism."

The specter of eugenics looms, as does the danger of exacerbating disparities in health and wealth. "All of these technologies are landing right now in a society with horrible problems of increasing income inequality," says Barbara Koenig, PhD '88, the founding director of the UCSF Program in Bioethics. "Who's going to be able to enhance their children? It's going to be the people who already are sending their children to private school and paying thousands of dollars for SAT tutors." Similarly, if a future therapy lowers one's risk of diabetes or susceptibility to smog, "who gets access to that?" asks Sara Ackerman, PhD, MPH, a medical anthropologist in Koenig's program. "It may be the people who already live in neighborhoods with healthy food and clean air."

Of course, those are big ifs. Gene therapies and brain implants are still new frontiers; we can't know for sure where they will lead. But ethicists and researchers alike agree: We don't want to wait until the implications are upon us before we start grappling with them. As Doudna says, "We should be encouraging an open discussion: What are the pros and cons? What types of applications would be considered responsible? How do we regulate them? How do we pay for them? Who decides who gets to use them and when?"

Increasingly, social scientists like those in UCSF's Program in Bioethics work alongside clinical investigators to help begin addressing such concerns – a practice Koenig refers to as embedded ethics. She and collaborators are also exploring ways to encourage and make use of public discourse. "There's no road map for thinking about how you ethically translate these very foundational discoveries into the clinic," she says. "You're building the road map as you're going."

The question, then, is not whether we should go down the road toward genetic and neural self-augmentation. We already are. Rather, the decision we now face is how far we want to go and how we'll get there.

This story is *our* story – of the future that awaits us and generations to come. It's up to us to learn what we can about these emerging technologies – how they work, what they may be able to do, and the visions researchers have for them. We must consider their profound potential for good and ponder their possible dangers. We must think long and hard about the human qualities we value and what we would change if we could. And we must ask ourselves: Who do we want to be?

Who will benefit from precision medicine?

By Lindsey Konkel

One morning, as you're getting out of bed, an intense pain grips your feet. Your toe joints are swollen again. It's been happening for months now. You decide it's time to get the problem checked out, so you pay a visit to your doctor, who tells you that you have rheumatoid arthritis.

What happens next depends on who you are. If you're white, for instance, with good health insurance and access to state-of-the-art care, your doctor probably doesn't think twice before ordering a biopsy of your joint tissue and then sending the sample off for genetic testing. As luck would have it, according to the results, you're a perfect match for a powerful new therapy. It's woefully expensive, but luckily again, your insurance covers it. Within days, your pain and swelling are gone.

But what if you're poor and uninsured? Even if you manage to cobble together enough money to pay for a genetic test out of pocket, there's no way you can afford the recommended treatment. Or say you're a person of color. Because researchers haven't studied many people like you, no special therapy exists that targets your disease's particular genetic profile. So your doctor prescribes the standard regimen of steroids and painkillers, which causes weight gain and puts you at risk for stomach ulcers. Plus, your feet still hurt.

This future scenario is, of course, hypothetical. But it reveals both the promise and the potential pitfalls of what's known as precision medicine.

A revolutionary approach to patient care, precision medicine uses advanced biomedical tools, including genetic and molecular testing and big-data analytics, to help clinicians better predict which treatment and prevention strategies will work best for which patients. It aims to replace the current one-size-fits-all model – in which therapies and interventions are developed for the "average" person – with one that tailors care to each patient's unique biology and life circumstances, including their race, finances, and living environment.

Ideally, this customization will bring faster, more effective care to more people. "In the next 30 years, for example, someone with type 2 diabetes will be immediately placed on the medicine that is best suited for their genetic predisposition, their ethnicity, their age, their sex, and the duration of time they've had the disease," says Suneil Koliwad, MD, PhD, the Gerold Grodsky Professor at UC San Francisco's Diabetes Center. "They're not going to have to try one therapy, and if that doesn't work, try another, and another."

Yet, as Koliwad and other UCSF experts point out, a future in which precision medicine benefits everyone is not guaranteed. For that to happen, they argue, the health care industry must first tackle today's health disparities, including differences in disease outcomes and access to care based on race, gender, and socioeconomic status. "The worst-case scenario is that certain populations will miss out" – either because some precision therapies won't work for those populations or because they'll be unaffordable – "and the gap between the 'haves' and 'have-nots' will widen," says Hala Borno, MD, an oncologist and assistant professor of medicine at the UCSF Helen Diller Family Comprehensive Cancer Center.

ILLUSTRATION: MIKE MCQUADE

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Koliwad puts it this way: "If we don't get ahead of health disparities at the same time we're developing these amazing precision technologies, we won't have accomplished what we set out to do."

GENOMICS' DIVERSITY PROBLEM

The first step will be overcoming the lack of diversity in genetic research. Today, people of color make up nearly 40% of the U.S. population and are expected to become the majority by mid-century. Historically, however, genetic studies – which inform precision therapies and knowledge of disease risk – have almost exclusively enrolled whites.

In a world moving toward precision medicine, this racial bias is "a glaring problem," says Esteban Burchard, MD, PhD, the Hind Distinguished Professor of Pharmaceutical Sciences and co-director of the UCSF Center for Genes, Environment, and Health. That's because discoveries made about cohorts of mostly white participants may not apply to underrepresented groups, he explains. "There are important biological differences that are being missed."

For instance, an estimated 86% of Asian Americans have genes that make them hypersensitive to warfarin, a common anticoagulant drug, meaning they could experience uncontrolled bleeding as a side effect of the drug at lower dosages than would most white Americans. Meanwhile, up to 75% of Pacific Islanders respond poorly to the drug clopidogrel, a blood thinner, which leaves them at higher risk of heart attack and stroke. And albuterol, the most-prescribed asthma medicine in the world, is least effective in African Americans and Puerto Ricans, Burchard and his colleagues have determined, even though the prevalence of childhood asthma is highest in these groups.

"The problem is even worse when you start talking about older adults," says geriatrician John Newman, MD, PhD, a UCSF assistant professor of medicine. "There is very little clinical data on people over 75. They're just not studied."

> "In 30 years, health care [could] look really good for some people and really bad for others."
>
> —*Esteban Burchard*

"We have a lot of catch-up to do," Burchard admits. Diversifying clinical data should be a top priority of health institutions and companies, he says. Otherwise, he warns, "in 30 years, health care will look really good for some people and really bad for others, simply because modern scientific advances have not been applied to all populations equally."

That's beginning to change, thanks to efforts at UCSF and elsewhere. For example, the All of Us program, created in 2015 by the National Institutes of Health, aims to enroll at least 1 million people who reflect the diversity of the U.S. population. That includes people who historically have been left out of health research – not only seniors and racial and ethnic minorities but also rural Americans, people with disabilities, and those who identify as LGBTQ. The program will collect genetic and other medical and lifestyle information on the enrollees to create the largest health database of its kind.

"All of Us is an opportunity to understand how therapeutics, prevention, and screening can be done more effectively in different subpopulations of the U.S.," says Robert Hiatt, MD, PhD, a professor of epidemiology and biostatistics who leads the program for UCSF, one of six recruitment centers in California. So far, Hiatt and his counterparts across the country have signed up over 350,000 participants, 80% of whom come from underrepresented populations.

The program achieves this degree of diversity through community engagement, Hiatt says. People can sometimes be hesitant to enroll in research studies due to language barriers, financial constraints, or other worries. So All of Us recruiters hand out information and talk with folks at community events and other venues, such as Cinco de Mayo celebrations or the Bay Area Aloha Festival.

CELLS TO SOCIETY

The importance of diversity to precision medicine's success is hard to overstate. "If you look at obesity, or even cancer," Hiatt explains, "these are big, hairy, complex societal problems. We need to understand the origins of differences that go beyond inherited biology – to the environmental, cultural, and social factors that shape disease."

Scarlett Gomez, PhD, MPH, a UCSF professor of epidemiology and biostatistics, refers to such multidisciplinary scholarship as "cells to society." She studies how social stressors affect outcomes for men with prostate cancer, a disease that disproportionately kills African Americans. "This is one of the biggest, longest-standing health disparities, and we don't know why," Gomez says. She suspects that biases in mortgage lending, redlining (refusing to issue loans for houses in certain neighborhoods), exposure to high levels of neighborhood crime, and other examples of what's known as structural racism may play a role in increasing African Americans' risk of developing more aggressive forms of the disease.

Greater awareness of such factors, she hopes, will allow clinicians and health policymakers to identify the best ways of reducing risk in these men. This kind of population-based approach to disease management is often called "precision public health" because it applies the principles of precision medicine – finding the right care for the right patient – to groups of people. It also differs from precision medicine in that it focuses more heavily on prevention than treatment.

The strategy may be particularly effective for controlling infectious diseases, which can be more virulent in some populations than others. Take valley fever, a lung infection caused by the fungus *Coccidioides*, which flourishes in the hot, dry soils of the American Southwest, including California's Central Valley. Cases are on the rise, and symptoms range from benign to life-threatening. "We know that African Americans and Filipinos are much more likely [than white Americans] to have severe complications," says Anita Sil, MD '98, PhD '96, a UCSF professor of microbiology and immunology. "But," she adds, echoing Gomez, "we don't know why."

In the lab, Sil and her colleagues study the fungus's life cycle, and its interactions with human immune cells, in the hope of solving this mystery. The researchers' discoveries could help clinicians identify which communities are most susceptible to valley fever and then develop interventions designed specifically for them. This targeted approach, Sil says, "could help us combat a number of pathogens, not just the valley-fever fungus."

The advantages of precision public health extend to chronic diseases, too. Type 2 diabetes, a common sugar-processing disorder, is just one example. Because studies show a link between diabetes risk and obesity, people who are overweight are often advised to slim down. But that may not be the best advice for everyone, says Koliwad, the diabetes expert. "The fact is, obesity doesn't impact disease risk in all people equally," he says. For example, in Southeast Asian, Native American, and some Latinx populations, people tend to develop diabetes at a lower BMI (body mass index) than the average white American, suggesting that weight has less effect on their risk of disease. Consequently, weight loss might *not* be the most effective risk-reduction strategy for these populations.

Ultimately, Koliwad and his colleagues aim to discover biological markers "at the molecular, cellular, and tissue level that will help us better understand a person's lifetime risk in a very personalized and precise way," he says. "Once we learn that information, we can customize nutrition, exercise regimens, and medications for each patient." But until then, he says, establishing more precise prevention strategies based on broader categories, such as ethnicity, could go a long way toward improving standards of care.

> "[*P*atients] are not going to have to try one therapy, and if that doesn't work, try another, and another."
>
> —*Suneil Koliwad*

THE COST CONUNDRUM

Even if precision medicine solves its diversity problem, however, there's still a big elephant in the (exam) room: cost.

Oncology is one field where precision medicine has begun to take off. Physicians now can scrutinize a tumor's DNA for mutations that might predict a good – or bad – response to available drugs. It's called genomic sequencing, and that alone can cost upward of $5,000. The precision therapies that a patient may subsequently be prescribed, based on the results of genomic sequencing, can carry staggering price tags, too – often more than $10,000 a month. Private insurance plans may not cover these tests or therapies, leaving many Americans unable to afford this cutting-edge cancer care.

Increasingly, the health industry will face hard questions about who will get access to precision-medicine advances, who will pay for them, and which therapies are worth the price. "As with any health-care intervention, we need to assess the cost-benefit tradeoffs," says Kathryn Phillips, PhD, a professor of clinical pharmacy and the founding director of UCSF's Center for Translational and Policy Research on Personalized Medicine. "We have to figure out where to use these precision technologies most effectively, efficiently, and equitably."

Many UCSF experts are optimistic that this can be done, given enough investment in addressing financial and health disparities. By personalizing the prevention and treatment of disease, they agree, precision medicine promises to not only improve but also save a great many lives. The real measure of its success, however, is whether it will fulfill that promise for all.

IS THE FUTURE (ON MARS) FEMALE?

Will the first "manned" mission to Mars be led by an all-female crew?

That's a question prompted by NASA-funded research from the lab of UCSF neuroscientist Susanna Rosi, PhD. Her findings suggest that female space travelers might fare better in the face of galactic cosmic radiation (GCR), one of the foremost dangers of deep space exploration.

While male mice show significant behavioral impact, cognitive decline, and brain structure changes when exposed to simulated cosmic radiation, female mice remain surprisingly unaffected at the behavioral, cellular, and molecular levels.

What makes the female brain resistant to space radiation? Rosi's data shows that the brain's immune system, made up of so-called microglial cells, might be aberrantly activated in males but remains perfectly normal in females. While the active state often triggers inflammation in surrounding brain tissue, the resting state appears to have crucial neuroprotective effects.

As humankind prepares for a 2024 launch into deep space, it's essential that scientists understand the effects on astronauts' health of space stressors like GCR. These rays can whiz straight through the hull of a spaceship – and any humans housed inside – causing serious health problems.

Rosi's earlier work suggested it might be possible to level the playing field for space travelers of both sexes: In 2018, her team successfully reset microglia in the brains of male mice exposed to GCR, preventing any loss of cognitive function.

She was recently awarded a new grant to probe the synergistic effects of radiation, altered gravity, and stress on astronauts' cognitive, behavioral, and motor function. Rosi, who is a member of the UCSF Weill Institute for Neurosciences, has also been named a leader of NASA's Moon to Mars mission.

Regardless of what comes next from this promising research, women might indeed rule Mars: The latest class of astronauts is 40% female.

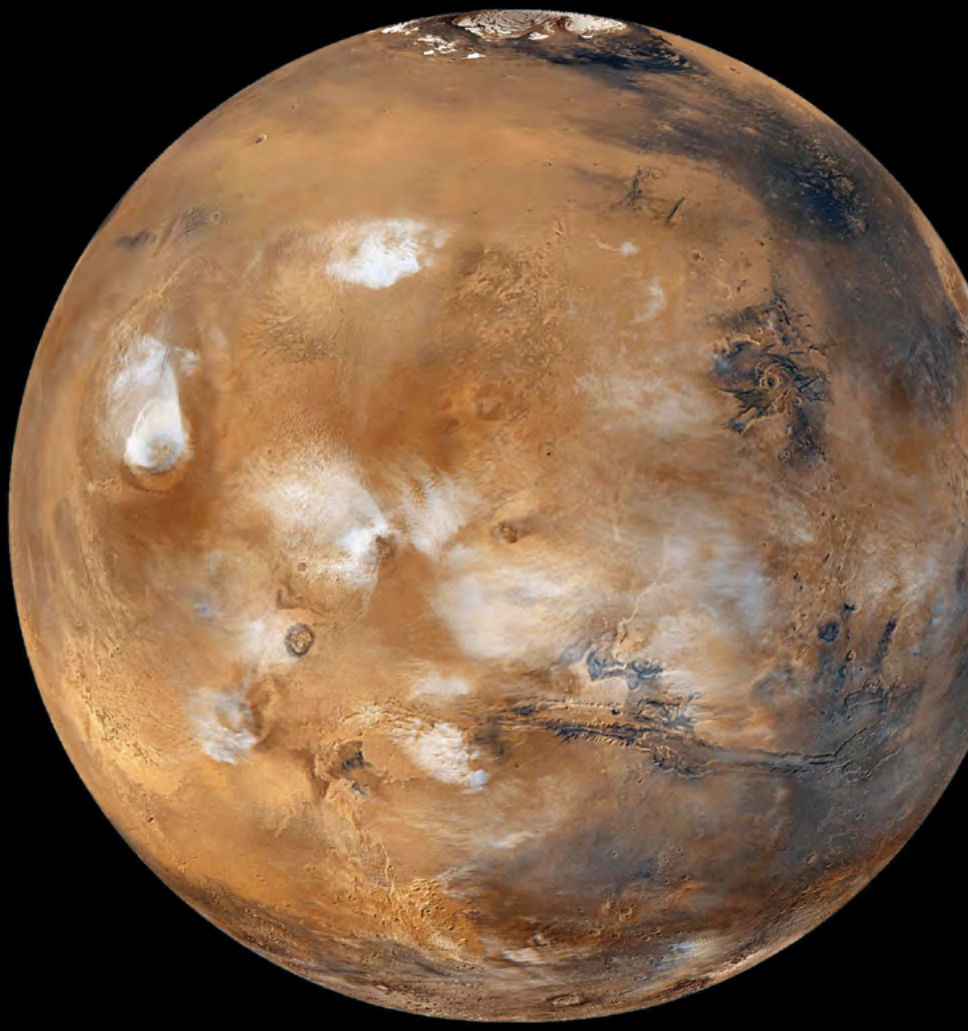


PHOTO: NASA/JPL/MSSS

BETTER EYES

CUSTOMIZING VISION

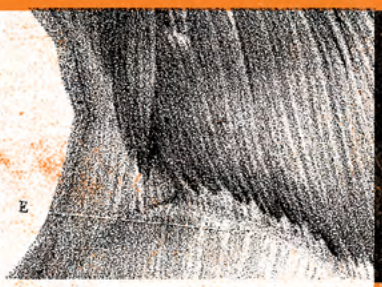
Our eyes often take a long, slow slide to a very blurry place: cataracts. Surgeons can replace clouded lenses with artificial ones, but about half the time, people still need glasses to achieve 20/20 vision. Not anymore. Ophthalmologist Daniel Schwartz, MD '84, partnered with Robert Grubbs, PhD, a Nobel Prize-winning chemist at Caltech, to develop a first-of-its-kind lens that is adjustable with light. Postsurgery, after the eye has healed, doctors beam light into the lens, precisely reshaping it to optimize vision without the need for spectacles. "No one has ever done this before," says Schwartz, who worked for 20 years on the innovation, which the FDA approved in 2017. "It's been a challenging technology to develop, but it is very gratifying to see how patients appreciate customization of their lens implant using only light."

BETTER EARS

COMPOSING PERFECT HEARING

The human auditory system is an intricate orchestra of tiny bones, canals, tubes, hair cells, and nerves, among other elements. "It's so sophisticated, it's hard to believe it works at all," says neurotologist Charles Limb, MD. Replicating its function artificially has proven remarkably challenging. Even cochlear implants, the best option today for treating severe to profound sensorineural hearing loss, are "badly out of tune," says Limb. Why? Like hearing aids, they have been designed around a simple goal: perceiving speech. But Limb is turning to music to radically improve the technology. Perceiving music – given its melodies, harmonies, pitches, and tones – is a much more complex goal. "If you can hear music well, you should be able to hear anything well," the avid jazz lover explains. An evolutionary leap in technology could finally lead to a long-sought dream: perfect hearing restoration.

ILLUSTRATION: MIKE MCQUADE



BETTER MOUTHS

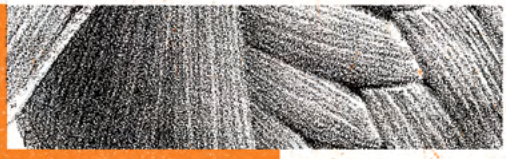
IMPROVING THE BODY'S GATEWAY

Move over, toothbrush. The microbiome just may become dentistry's most potent weapon. "The oral cavity seeds many parts of our body," says orofacial scientist Yvonne Kapila, DDS, PhD. Every time we brush our teeth, we dislodge bacteria that can then travel to distant places – our brain, arteries, intestines – where they can set up shop and wreak havoc in those who are susceptible. Studies have linked oral bacteria to Alzheimer's disease, colon cancer, diabetes, and other health issues. And many of us suffer from oral bacteria's home-turf shenanigans: cavities and gum disease. Kapila wants to tame the bad actors (but keep the good ones) in our mouth's microbiome. She's found a way to thwart those that cause periodontal disease in mice: probiotics. "We don't want to wipe out all bacteria," she explains, "just change the members of the party." Probiotics, she says, "could alter the landscape of how we treat and prevent oral diseases."

BETTER MUSCLES

MAINTAINING MUSCLE MIGHT

Popeye had his spinach; someday we may have a pill to keep us strong to the finish. Today, though, the sad reality is that our muscles decline as we age. This wasting occurs mostly because the stem cells that maintain and repair our muscle fibers dwindle and lose their function. Molecular biologist Andrew Brack, PhD, is aiming to prevent this from happening – or even reverse it. He and other scientists have shown that exposing aged human muscle cells to young blood boosts their function. Brack's lab is seeking to identify the factors that rejuvenate the muscle stem cells and those that inhibit their repair mechanisms. These naturally occurring molecules can be made into a nontoxic drug that would stop or even turn back muscle weakening. "My dream is that in 2050, most 70-year-olds can run a marathon if they want to," he says.



BETTER JOINTS

TAPPING BONE SECRETS

Skeletons, rise up! We're going to learn that the skeleton is as "essential to our health as our nervous system is," predicts cell biologist Tamara Alliston, PhD. Why? Deep in our bones are cells called osteocytes that make up a vast network, stretching from our head to our toes, just like nerves. Alliston has discovered that these cells influence the health of our joints – specifically, that their function is suppressed in human arthritis. Finding how to turn that function back on could lead to a much-needed new treatment for the disease, or even to drugs that could prevent arthritis from developing. But this finding may reveal only a trace of our skeleton's power. "We've mostly thought of our bones as this mechanical tissue that helps get us around," Alliston says. "I think we're going to have a much deeper appreciation of what they can do to support our systemic health."

BETTER ORGANS

CREATING ORGANS ON DEMAND

Forget agonizing waits for donor organs, which may be too big, too small, or not compatible. In the future, scientists will be able to grow or print organs customized for each patient's genetics, age, and size. They may also be able to integrate the organs with nanotechnology and wireless communication to monitor their function and transmit performance data to the patient's health care team. So envisions Shuvo Roy, PhD, a scientist who works at the convergence of biology and engineering. Roy and his team are paving the way to this future by creating the world's first bionic kidney. The coffee-cup-size device includes a silicon nanotechnology-based filter to cleanse the blood, while living kidney cells grown in a bioreactor perform the other functions of a natural kidney. Patients with these bioartificial kidneys, which screen the body's immune cells, won't need immunosuppressant drugs, and such transplants will cost far less than hemodialysis in a dedicated dialysis center. Roy is striving to have the device ready for the first patients in just five years.

124.3

BETTER LIMBS

BLASTING BEYOND BIONIC LIMBS

Imagine having prosthetic legs but still being able to feel the grass beneath your feet. Or telling your artificial knee to bend using your thoughts alone. Welcome to a cybernetic future, where biomechatronic limbs will communicate with the human brain. "It's space-age, futuristic thinking," says Richard O'Donnell, MD, an orthopaedic surgeon who is leading UCSF's Musculoskeletal Research Consortium. "We are using titanium, bone-anchored, percutaneous implants and advanced plastic surgery techniques to amplify nerve signals," explains O'Donnell. Those signals "are then decoded with sophisticated algorithms to control prosthetic movement and transmit sensory feedback from the external environment. We're asking," he continues, "'Can we help otherwise "disabled" amputee patients become not only able-bodied but even *supra*-able? Can we leverage what we learn with this brain-computer interface technology to cure paralysis? Can we engineer limbs that are stronger and smarter, capable of withstanding the rigors of aging and even long-term deep space travel?' That's our 30-year vision."

Better Parts

AGELESS MUSCLES. OFF-THE-SHELF ORGANS. BIONIC SUPER LIMBS. AND MORE. **SCIENCE THAT SOUNDS LIKE SCI-FI IS UNDERWAY ACROSS UCSF TO IMPROVE OUR BODIES, NOW AND IN THE FUTURE.**

By Anne Kavanagh

Emerging Threats

WHAT WILL IT TAKE TO STOP THESE SCOURGES?

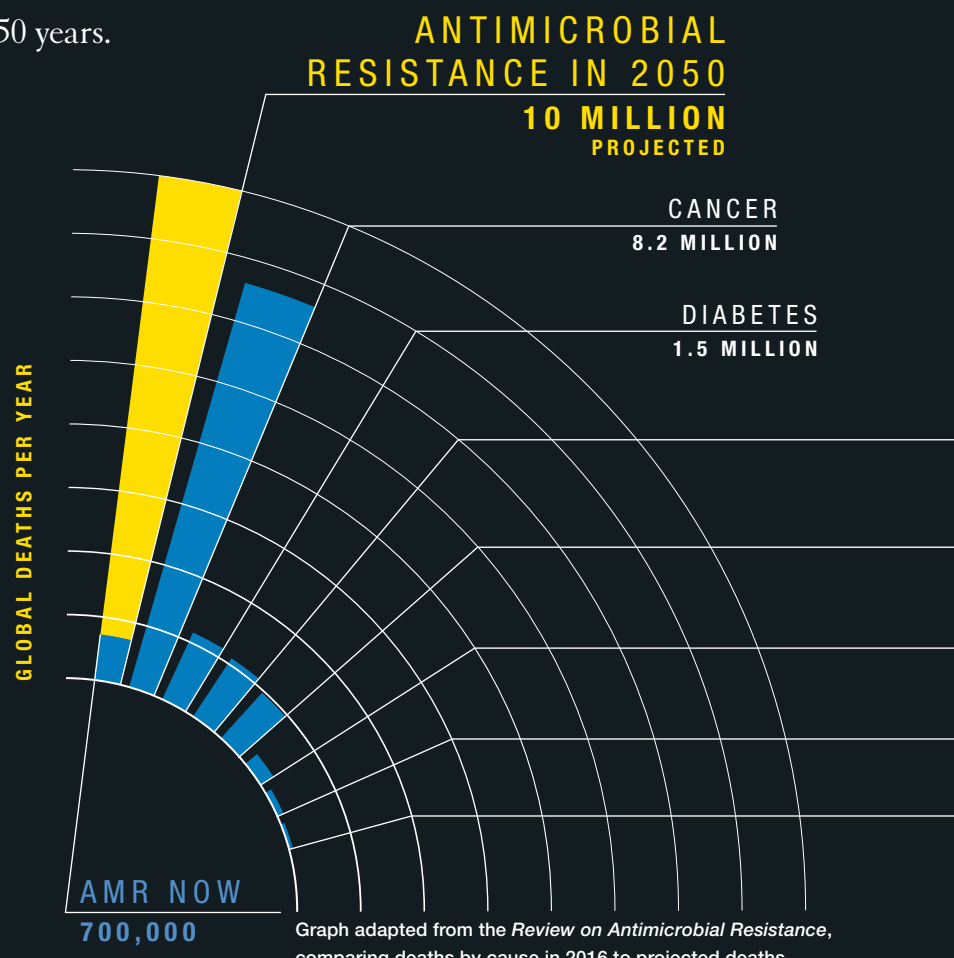
SUPERBUGS

*B*efore the advent of antibiotics in the early 20th century, you could die from an infected scrape – if smallpox, cholera, pneumonia, or any other rampant infectious disease didn't kill you first. *I*t's no wonder that the average life expectancy back then was less than 50 years.

Today, so many routine medical procedures depend on antibiotics that it is impossible to envision the modern world without them. And yet a global crisis of antimicrobial resistance (AMR) is forcing us to imagine just that. It's an arms race between deadly pathogens and the drugs that fight them. "And if you had to pick whether the bugs or the drugs are winning, a lot of people would say it's the bugs," says Lisa Winston, MD, a professor of medicine at UCSF and an epidemiologist at Zuckerberg San Francisco General Hospital.

According to the World Health Organization, these so-called superbugs are "one of the biggest threats to global health, food security, and development today." Without urgent global action, experts warn, superbugs could kill 10 million people a year by 2050 – more than the current toll from cancer and diabetes combined.

The impact will be felt most acutely in health care settings. "It's going to start in hospitals because that's where all of the nastiest bugs are and where there is the most evolutionary pressure" for microbes to develop drug resistance, says pharmaceutical chemist Ian Seiple, PhD, an assistant professor at UCSF's Cardiovascular Research Institute. "All of the signs are there that this is going to be a really, really big problem."



Graph adapted from the *Review on Antimicrobial Resistance*, comparing deaths by cause in 2016 to projected deaths from AMR in 2050.

700,000 DEATHS CAUSED BY ANTIMICROBIAL RESISTANCE (AMR)

2016

2019

Antibiotic overuse in medicine and agriculture is responsible for the AMR crisis.

30 Percentage of oral antibiotics prescribed in U.S. that are **unnecessary**.

60 Percentage of sore throat cases for which U.S. doctors prescribe antibiotics. (Antibiotics are **necessary in only 10%** of these cases.)

"*If* you had to pick whether the bugs or the drugs are winning, a lot of people would say it's the bugs."

—Lisa Winston

Three Strategies for Squashing Superbugs

REDUCING ANTIBIOTIC OVERUSE

UCSF is one of many hospitals nationwide that have established antimicrobial stewardship programs to reduce unnecessary antibiotic use. As of September 2019, federal regulations require all U.S. hospitals to institute such programs.

EMPLOYING NOVEL TECHNOLOGIES

The UCSF Center for Next-Gen Precision Diagnostics, led by Charles Chiu, MD, PhD, is among the first labs in the world to utilize advanced genetic-sequencing techniques to quickly identify new infectious threats. Another technology, cryo-electron microscopy, allows researchers to see the precise mechanisms by which resistant organisms evade their attackers. With these tools, scientists could conceivably engineer new antimicrobial drugs fast enough to stay ahead of microbial resistance.

INVESTING IN DRUG DISCOVERY

Historically, the world has relied on pharmaceutical companies to capitalize on research breakthroughs in order to bring new antimicrobial drugs to market, but the industry has almost entirely abandoned this effort. Antimicrobial drugs, which cost a fortune to develop but are relatively low-cost and prescribed only in short courses, just aren't profitable. Ultimately, acquiring a drug arsenal capable of defeating superbugs will require political will and public investment.

DIARRHEAL DISEASES
1.4 MILLION

TRAFFIC ACCIDENTS
1.2 MILLION

MEASLES
130,000

CHOLERA
100,000–120,000

TETANUS
60,000

10 MILLION DEATHS PROJECTED

2050

80 Percentage of all U.S. antibiotics sold for use in **animal agriculture**. Resistant bacteria bred in such settings can be transmitted to humans through our food.

PHOTOS: SCHARVIK; NICHOLAS WEILER; KOSTSOV

PANDEMIC FLU

"Just like people in California await the next big earthquake, we in the infectious disease field are waiting for the next influenza outbreak," says UCSF professor of medicine and infectious disease specialist Peter Chin-Hong, MD.

Influenza, commonly known as the flu, is a viral infection of the human respiratory tract. Seasonal virus strains spread around the world annually, doing minimal harm to the average healthy adult. But a few times a century, a new strain jumps to humans from another animal species, such as chickens or pigs, and can trigger a pandemic.

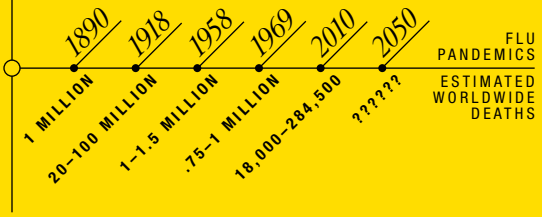
Such cross-species outbreaks are especially contagious and deadly because they can introduce traits against which humans have no defense. Previous flu pandemics have resulted in millions of deaths worldwide. But there's reason to think we may be able to thwart the next one, says Charles Chiu, MD, PhD, director of the UCSF Center for Next-Gen Precision Diagnostics. Here are a couple of promising approaches:

IMPROVING SURVEILLANCE

Vigilant, real-time surveillance and reporting are today's best hope for stopping an influenza outbreak, Chiu says. His team uses rapid DNA sequencing to identify and diagnose cross-species diseases in remote regions of the world in order to understand, track, and – hopefully – prevent another pandemic.

PURSUING A UNIVERSAL VACCINE

Seasonal flu vaccines are ineffective against an influenza pandemic. But a vaccine that can fight off any flu – even novel, cross-species strains – might be within reach, Chiu says. "If a universal vaccine becomes available," he says, "mass global vaccination efforts could nearly or completely control influenza by 2050, just as was done for poliovirus more than 50 years ago."



*F*alling *F*oes

CAN WE ERADICATE THESE GLOBAL KILLERS BY 2050?

MALARIA

*M*alaria has ravaged humanity for tens of thousands of years. *C*alled the "king of diseases" in ancient texts from *I*ndia, this wily foe long stymied scientists. *E*ven its name is a misnomer: *T*he *R*omans thought swamp fumes caused the illness, so they dubbed it *mal aria*, or "bad air."

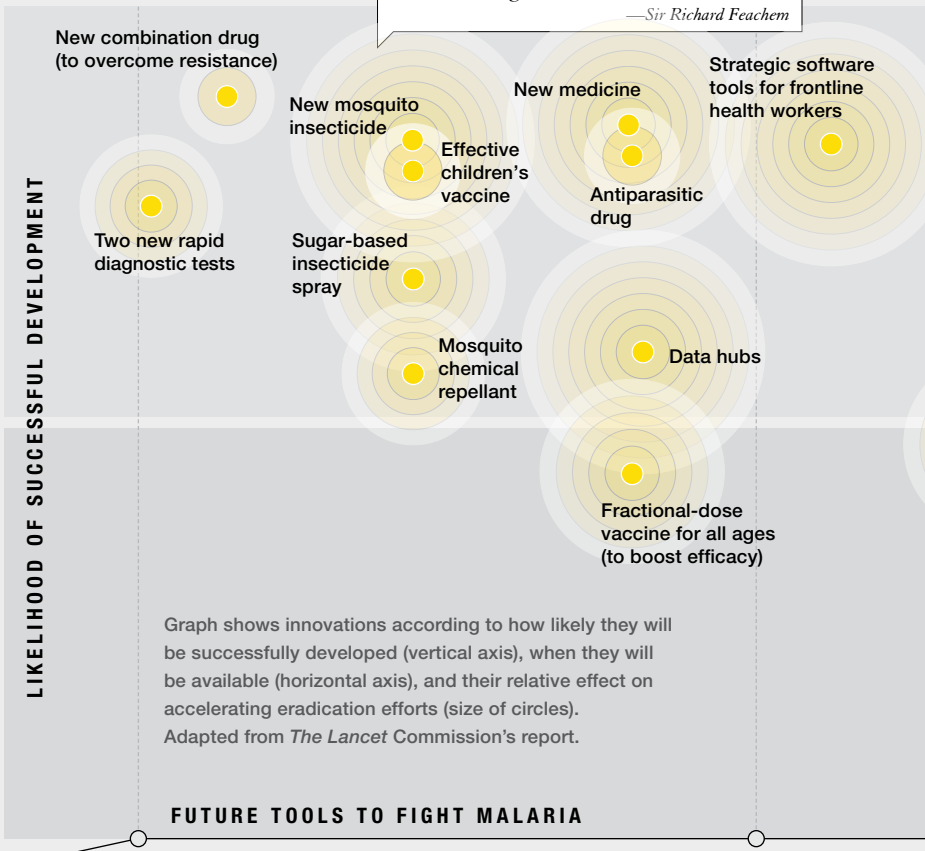
In the 19th century, researchers finally discovered the real culprit: a microscopic parasite called *Plasmodium*, which is spread by female mosquitoes who inhabit wet, marshy places. Attempts to eradicate malaria gained steam after World War II but then waned in the 1970s and '80s in the face of enormous challenges, according to Sir Richard Feachem, DSc(Med), PhD, director of the Global Health Group at UCSF. But today the tide is turning again. In the past 20 years, cases of malaria and deaths from the disease have been roughly halved worldwide. Now experts are once again asking: Can we rid the planet of it for good?

The answer is a resounding yes. Given the right tools, strategies, and sufficient funding, the world could be malaria-free by 2050, according to a report published by *The Lancet* Commission on Malaria Eradication in September 2019. (The commission, co-chaired by Feachem, is a joint endeavor between *The Lancet* and UCSF.)

But there's a catch. "To achieve this common vision, we simply cannot continue with a business-as-usual approach," Feachem says. "We must instead challenge ourselves with ambitious targets and the bold action needed to meet them."

"*W*ith longer-lasting insecticides, bed nets would need to be replaced less frequently. *T*he chemical used to spray houses would last one or two years instead of six months. *T*hose are huge benefits."

—*Sir Richard Feachem*



Graph shows innovations according to how likely they will be successfully developed (vertical axis), when they will be available (horizontal axis), and their relative effect on accelerating eradication efforts (size of circles). Adapted from *The Lancet* Commission's report.

219 MILLION CASES OF MALARIA

2017

2019

The Lancet Commission says **eradication by 2050 is possible.** Success hinges on these steps:

1 Strengthening malaria **control** programs by improving management and engaging communities and the private sector.

2 Developing and rolling out new **innovations** for disease treatment and prevention.

"*It's* hard to overestimate what a huge achievement it would be for humankind to eradicate malaria, once and for all."

—Sir Richard Feachem

HIV/AIDS

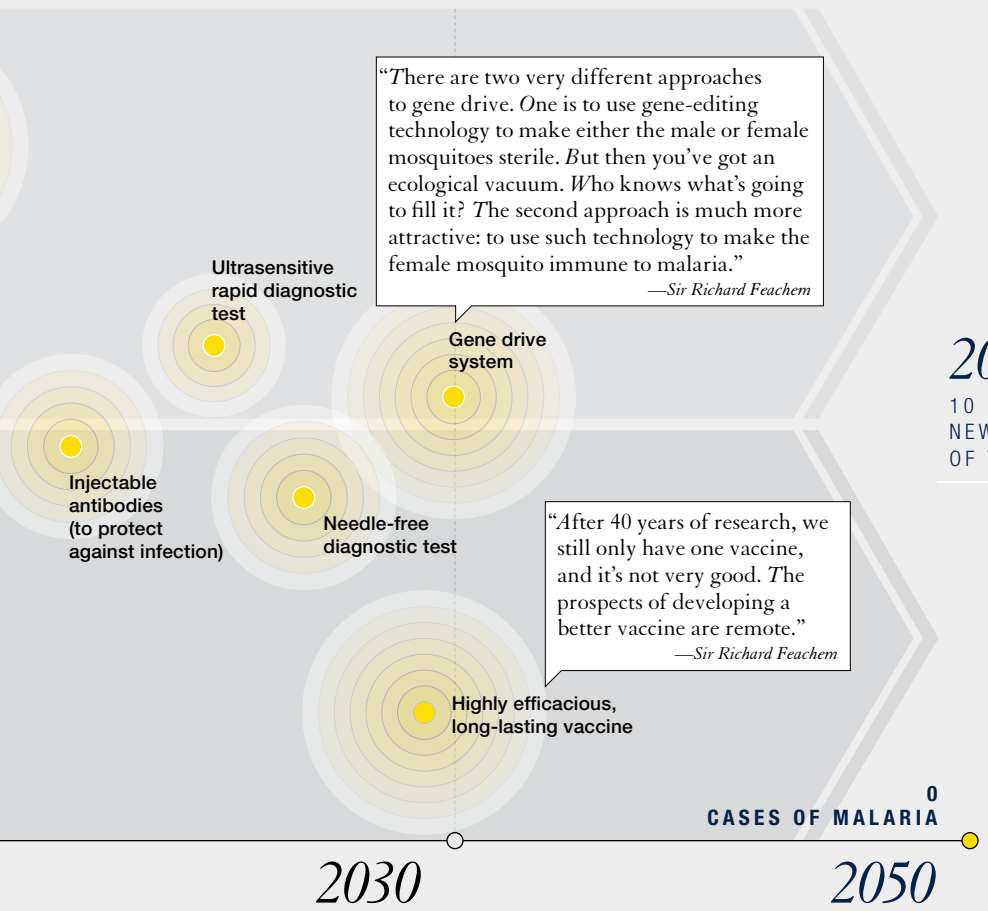
An HIV diagnosis in the 1980s was effectively a death sentence. The virus had hit San Francisco hard, and UCSF clinicians endeavored to care for its many victims. But their drive to overcome HIV/AIDS helped transform the disease from fatal to merely chronic. Research at UCSF spurred the development of antiretroviral therapies, and later, PrEP (pre-exposure prophylaxis), a preventive pill.

"We have the tools to stop the epidemic," says Paul Volberding, MD, director of UCSF's AIDS Research Institute and the Weiss Memorial Professor. But eradication by mid-century is unlikely, he predicts. Besides the sheer magnitude of the problem (about 40 million people currently live with HIV), stigma presents a formidable hurdle. "We will make a lot of progress," he says, "but we still have much work to do on the societal and behavioral issues that perpetuate HIV."

TUBERCULOSIS

For a curable disease, tuberculosis (TB) still cuts an astonishing swath of destruction across the globe. The U.S. and most other developed countries have wrestled TB mostly into submission through concerted treatment, education, and prevention measures. But countries plagued with overcrowding, poor hygiene, lack of fresh water, and inadequate public health care systems have struggled to contain the pandemic.

A TB vaccine has been available since 1921, but it is not very effective. "We've known for a long time that a better vaccine that can prevent infection *and* progression to disease in those already infected will have the biggest epidemiologic impact," says Payam Nahid, MD, MPH, a TB expert and professor of medicine. A recent candidate has shown unprecedented promise, stirring excitement among TB scientists. Meanwhile, researchers are working to improve treatments and diagnostic tests. With this confluence of advances, "the sky's the limit for improving TB outcomes by 2050," he says, except for one major stumbling block: "The funding is nowhere near where it needs to be."



3 Increasing **financing** by galvanizing new donors and encouraging greater support from individual countries.

4 Establishing strong global **leadership** and **accountability** mechanisms.

Contributors: Ariel Bleicher, Anne Kavanagh, Cyril Manning, Mika Rivera

Keeping cancer under wraps

By Susan Godstone

New treatments like immunotherapy are producing astonishing outcomes for some cancer patients. *Five*-year survival rates have increased dramatically since the early 1960s. *And* novel therapies that target specific genetic mutations are prolonging and saving lives while causing fewer side effects than radiation and chemotherapy.

But cancer is not a single disease, which is why finding a single cure is so elusive. *Basic* scientist *Zena Werb, PhD*, has been studying cancer cells in *UCSF* labs for more than four decades. *Here*, she shares her take on the future of cancer medicine.

Where do you think cancer research is headed?

We've mostly studied the nasty things about cancer – oncogenes and suppressor genes that propel cancers forward. What we haven't looked at adequately is what keeps a cell in a non-cancer state. By 2050, I believe scientists will be addressing the neighborhood, or microenvironment, around a tumor and better understanding its role in keeping cancer cells under wraps.

How does that fit in with new treatments like immunotherapy?

Recent breakthroughs in immunotherapy and precision medicine have the potential to drive increased interest in the tumor microenvironment. People don't realize the immune system is broader than just T cells and CAR T cells. The whole neighborhood, or matrix, around a tumor – not just the tumor itself – is important, and specifically how genes, microbes, organisms, and proteins all interconnect. Understanding this process, known as "biological cross-talk," could uncover a great deal about the mechanisms that lead to cancer metastasis. Research directed at how the many disparate pieces of this complex biological system work together and influence health will become increasingly important.

Why have we seen so many breakthroughs recently?

New technologies have allowed us to image and sequence the genomes of tumors and cancers in ways that were never possible before. Targeting specific tumor pathology and genetic mutations with personalized therapies has produced incredible results for some patients. It's really remarkable. But at the same time, we have to continue developing models of care and therapies that impact populations and not just individuals. Big-data analytics will play a huge role in that effort.

How might treatment decisions change?

I anticipate the next generation of clinicians and patients will place a greater emphasis on quality of life when making treatment recommendations and decisions. Also, because of long-term clinical studies with large cohorts of patients, like the WISDOM study (a five-year trial testing two different approaches to breast cancer screening), we'll know more about which cancers need to be dealt with aggressively and which we can and should leave be.

What other kinds of therapies do you expect to surface?

We'll have evidence-based information on the impact of noninvasive treatments. For example, as proof emerges about the contribution of the microbiome to our overall health, I believe we'll see even more diet- and lifestyle-related choices for the prevention, prevention of recurrence, and treatment of cancer.

What is your greatest hope for 2050?

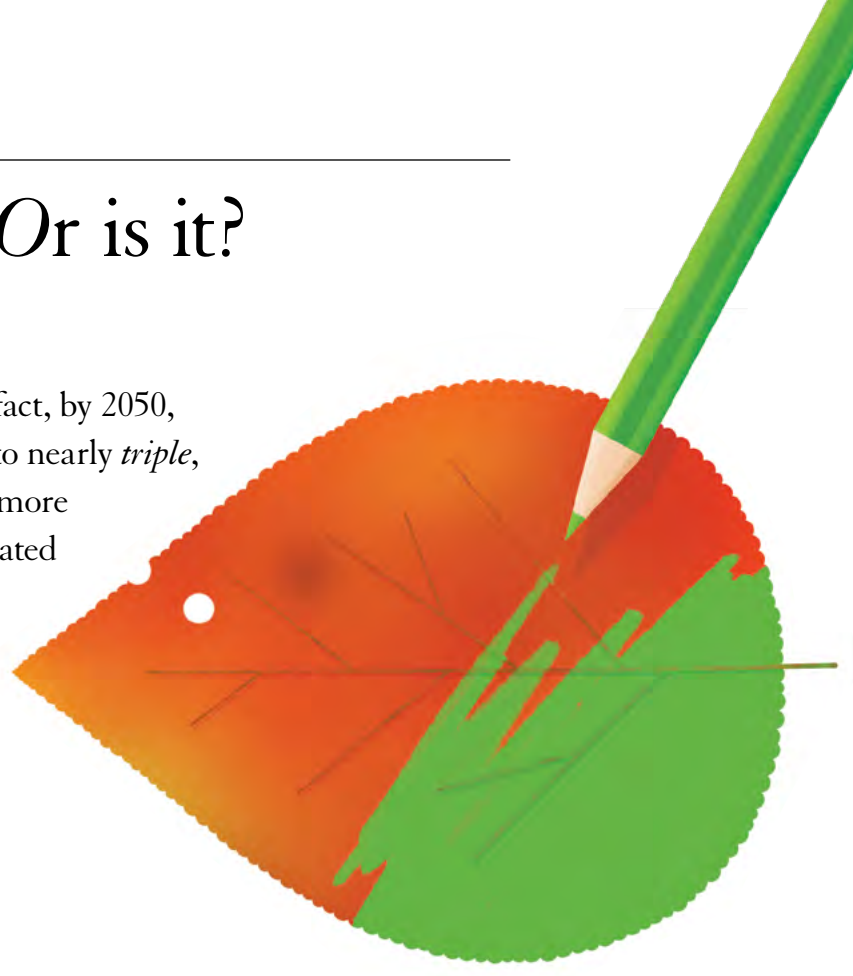
That our treatment goals for many more cancers will have shifted from eradication to managing these diseases as long-term conditions, like arthritis. In other words, we'll die with it, not from it.

Zena Werb is a professor in the UCSF Department of Anatomy and associate director for basic science at UCSF's Helen Diller Family Comprehensive Cancer Center.

ILLUSTRATION: ABIGAIL GOH

Aging is not optional. Or is it?

By Silver Lumsdaine



It's not your imagination – the world is graying. In fact, by 2050, the global population age 65 and older is projected to nearly *triple*, to 1.5 billion. With this aging population, it will be more important than ever to reduce the burden of age-related disease. In the future, science will allow us to intervene in the aging process to make this a reality, according to geriatrician John Newman, *MD*, PhD. He explains what that means below.

What does an aging population mean for society?

It's imperative to keep our older population healthy and independent as long as possible. As this population grows, we'll need to provide help to increasing numbers of older people who are no longer independent. It will be a huge challenge for us as a society in the next 20 or 30 years.

What is aging? Why study it?

Aging is a biological and physiological process like any other. We can learn how it works – how cells and molecules create what we see as "aging" in a person. Aging can be beautiful, but it is also the number-one risk factor or driver of most of the medical problems that we treat in adults: cancer, diabetes, dementia, Alzheimer's disease, cardiovascular disease, strokes, and heart attacks. The crazy thing is we can manipulate the aging process. We can adjust it. We can treat it.

That sounds like science fiction.

None of this is science fiction anymore. It's all science fact, right up to the part where people are doing clinical trials of drugs that treat complex health problems through targeting molecular aging mechanisms. In geroscience, we seek to understand the relationship between aging, disease, and quality of life. The promise of this field is that by intervening in the process of aging, we could slow, prevent, delay, or reduce the risk of all sorts of diseases – all at the same time.

What interventions are being tested right now?

Metformin, a commonly used diabetes drug, also acts on mechanisms of aging. Clinical trials are looking at whether giving older people metformin will slow the rate of not only diabetes but also several other chronic diseases simultaneously. Also of interest are TOR inhibitors, which are drugs that can help cells better repair their proteins. In early clinical trials, it looks like treating older adults with TOR inhibitors can greatly reduce the rate of serious age-related respiratory infections like pneumonia and flu.

How will a visit to your primary care doctor look different in 2050?

You'll have your aging mechanism risk factors checked, and you'll probably have preventive treatments. For example, we'll treat your senescent (old, inactive) cells or your autophagy (the process by which your body removes old, damaged proteins). If something is amiss in your risk factors, then we'll make adjustments. It'll just become part of regular preventive medicine.

Will these interventions benefit everyone?

You can't ignore disparities when you talk about aging and older adults. We need to figure out how to apply geroscience interventions through our health care system in a way that lets everyone access them. Wealth is one of the strongest predictors of life expectancy, overall health, overall function, and independence. There's a biology to how wealth disparities affect aging and health. We don't know what that is yet, but we aim to find out.

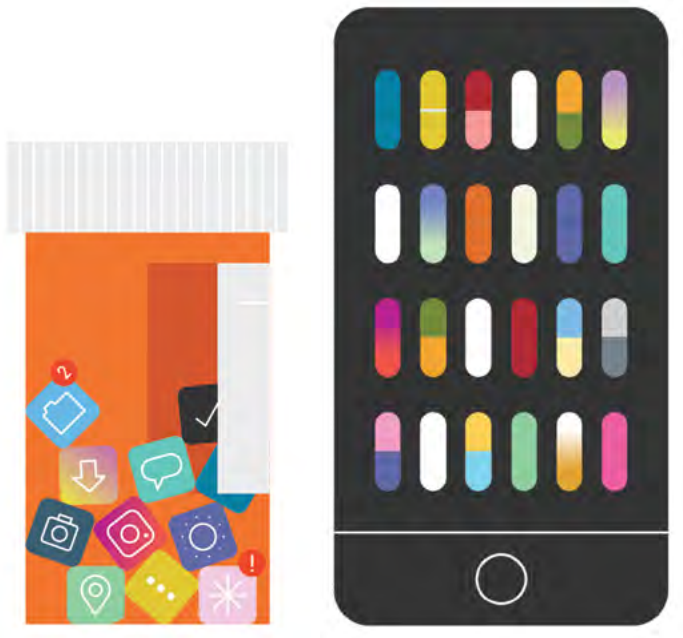
John Newman, a resident alumnus, is an assistant professor in UCSF's Division of Geriatrics and a researcher at the Buck Institute for Research on Aging.

ILLUSTRATION: ABIGAIL GOH

How to mend our broken minds

Technology is a cause – and a solution.

By Adam Gazzaley, MD, PhD



Anxiety. Depression. ADHD. Dementia. The human brain is in trouble. More than half a billion people worldwide suffer from debilitating impairments in cognition. While there are many sources fracturing our cognition, we must face the reality that our brains simply have not kept pace with the rapid changes in our environment – specifically, the introduction and ubiquity of information technology.

This new environment challenges our brains and behaviors at a fundamental level. Scientists have documented the influence of information overload on attention, perception, memory, decision-making, and emotional regulation. We also see strong associations between the use of technology and rising rates of depression, anxiety, suicide, and attention deficits, especially in children.

But the same technologies contributing to the cognition crisis could help solve it.

By leveraging sophisticated sensors to collect and interpret data about us, mobile technologies could one day help us to better and more deeply understand ourselves in the real world and in real time.

These tech-based assessments could be optimized to yield a much more nuanced perspective of our abilities, allowing us to explore the eddies and tides in cognition from childhood to our senior years, in response to life's unpredictable joys and traumas. They could become the next generation of cognitive assessments.

Of course, this approach will need to advance carefully, protecting sensitive data and preempting its abuse. It will require that we overcome deeply rooted biases around our inclination to think of cognition as a reflection of "who we are." (Consider how we refer to someone as *being* inattentive, but as *having* high blood pressure.)

Once we better understand our cognition, we can work to enhance it, creating powerful technological experiences that maximally harness our brain's plasticity to boost our cognition, refine our behavior, and ultimately elevate our minds.

A technology-based, closed-loop approach could generate experiences that selectively activate brain networks and then apply constant pressure to those networks with interactive challenges. Over time, such an approach would drive the brain's plasticity to optimize its function.

Imagine playing a video game in which your data is collected with sensor technology – performance metrics, emotional responses, body movements, brain activity – and used in real time to guide the environment you are experiencing, personalizing challenges and rewards to improve your cognition. Many laboratories and companies, including my own, are actively pursuing this vision right now.

Take all of this one step further, and think of the role that artificial intelligence (AI) and virtual reality might play. Picture yourself deeply immersed in a multisensory virtual environment in which your full-body interactivity is coordinated by an AI that knows you more deeply than any human being could, including yourself. It would pick up on subtle shifts in perception, mood, aggression, attention, and memory to strengthen your brain's function by driving its natural plasticity. It wouldn't control you; it would give you control over your own mind, helping prevent a slippery slide into major depression, anxiety, ADHD, or dementia.

What better use is there for AI than in enhancing HI – human intelligence? If we are creative and forward-thinking, we can achieve what may be technology's ultimate promise: the establishment of an environment that fosters the next phase in the evolution of the human mind.

Advances in medicine have elevated the overall health of humanity to a level that far exceeds past gains. But for our species to continue to thrive in this increasingly complex world, we must turn our lens inward and look for cracks in the mirror.

When it comes to the functioning of our brains and minds, we are at a crisis point. Now is the time to take stock of what we truly value about being human, embrace it, and mend our broken minds.

Adam Gazzaley is a professor of neurology, physiology, and psychiatry and the founder and executive director of Neuroscape at UCSF. He holds UCSF's David Dolby Distinguished Professorship.

This piece was adapted from an essay by Gazzaley titled "The Cognition Crisis," which originally appeared in *OneZero*, a *Medium* publication.

ILLUSTRATION: ABIGAIL GOH

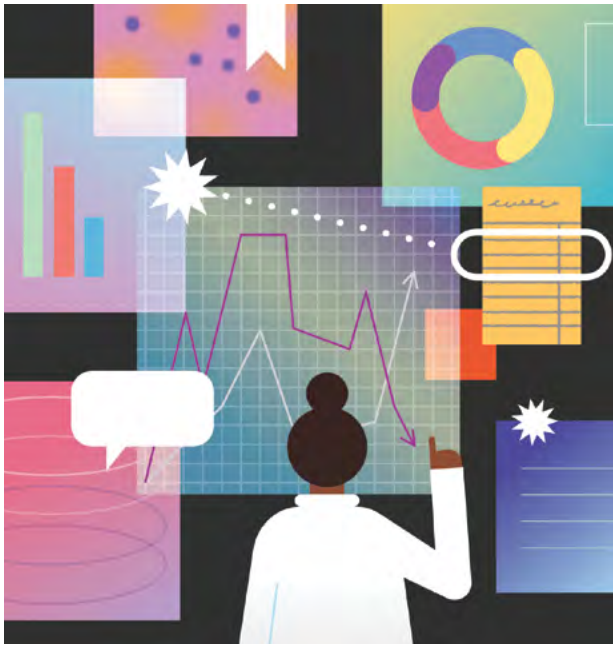
AI will give your doctor superpowers

By Ariel Bleicher

*A*rtificial intelligence (*AI*) permeates our lives. *I*t manages our phones and homes, helps us navigate, and advises us what to watch, read, listen to, and buy. *S*oon it will transform our health, says trauma surgeon and data-science expert *R*achael *C*allcut, *MD*, *MSPH*. *S*he answers some questions about the *AI* future:

What is the advantage of AI in medicine?

There is a certain amount of bias that we, as humans, bring to any clinical scenario: Without even realizing it, we may look past critical pieces of information that could help our patients get better. AI, which is essentially a computer algorithm that learns from data, can uncover patterns that we can't see – either because of those biases or because the human brain simply can't assimilate the vast quantity of medical data that is now available from hospital sensors and other digital health devices. Ultimately, AI promises to reduce human error and make our care more efficient, which will improve outcomes for our patients.



How is AI used in clinics today?

Its footprint is still relatively small. Only about 20 to 25 AI applications for health care have been cleared by the U.S. Food and Drug Administration. Most of these applications are marketed directly to consumers and are used for low-risk conditions – they do things like screen for eye disease or use your Apple Watch to detect certain heart-rhythm problems. Very few AI applications are actually used in hospitals for patient care, but this is beginning to change. For instance, my team at UCSF recently led the development of a new AI algorithm that works with portable X-ray machines. When a patient comes into an emergency room and gets a chest X-ray, the AI algorithm can review the image and detect certain life-threatening conditions, such as a collapsed lung. It can then alert the bedside clinician, which could lead to a faster diagnosis.

Imagine your wildest AI dreams have come true. A patient comes into the trauma bay. What happens next?

Data about the patient's condition would already be streaming to us from emergency responders' equipment. Then, as soon as the patient arrives at the hospital, we'd attach them to monitors. And as their vital signs are being tracked – and as physicians, surgeons, respiratory technicians, anesthesiologists, and everyone else is providing care and calling things out – an AI is recording all this information and integrating it into some kind of easy-to-navigate visualization on a screen.

Like in the film *Minority Report*?

Sure – we're dreaming, right? You can imagine that very quickly we begin to see a story about the patient that could help us understand more rapidly what to do next.

What else is coming down the pike?

Within probably a decade, AI will be ubiquitous in the clinical environment. It will likely be embedded in ways that you, as a patient, may not even be aware of. As you are talking with your physician, for example, an AI application might be listening and crafting notes for your file. AI will certainly be an integral part of how we, as clinicians, take and read medical images. It will help us assimilate this information and other medical data to make informed recommendations, such as next steps or treatments that are optimal for your condition.

Will robots ever replace human doctors?

Never. If I told you, "You're going to fly on a plane with no human pilot," you're not going to board that plane. It will be the same in medicine. AI is very powerful; it enhances what clinicians do and makes our jobs better. But we will always need to be there to guide it, inform it, and interpret what it's doing.

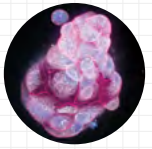
Rachel Callcut is an associate professor of surgery and the director of data science for the SmarterHealth Artificial Intelligence Program at UCSF's Center for Digital Health Innovation.

ILLUSTRATION: ABIGAIL GOH

What will health and medicine look like in 2050?

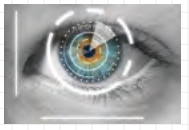
NO ONE CAN SEE THE FUTURE, BUT THAT WON'T STOP US FROM TRYING. WE ASKED UCSF FACULTY MEMBERS AND ALUMNI TO SCORE THESE PREDICTIONS FOR LIKELIHOOD AND IMPACT.

GAME-CHANGING



The end of cancer

"The idea that cancer is one disease and we are going to cure it has slowly turned into 'Cancer is many diseases, and we'll cure some of them and keep working to make the others manageable.'"
—*Zena Werb, PhD*
Werb has studied cancer for 40 years.
See our Q&A with her on pg. 42.



Bionic eyes banish blindness

Mental health drugs are as precise and effective as antibiotics

"I hope we collectively decide *not* to use this technology to alter future generations but instead use this opportunity to create cell medicines to treat disease while preserving our sense of humanity."
—*Alex Marson, MD, PhD*

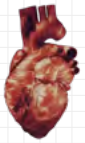
Gene editing creates a new category of human

Mental illness without stigma

Universal health coverage in the U.S.

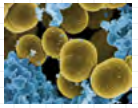
AIDS eradicated

Global pandemic wipes out millions



Lab-grown organs make human donors obsolete

E-health records interoperability solved



Superbugs proliferate

Cell and gene therapies made affordable

A pill to effectively treat obesity

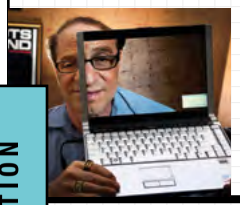
"We are getting closer and closer to being able to engineer a solution. I'm not sure it'll be a pill, though. It might be a biologic or maybe even cell therapy. Whatever the therapy, I bet there will still be a role for good old exercise."
—*Joanna Balcerek, MD, PhD*

Fully cybernetic limbs

FICTION

PREDICTION

THE FAR OUTLIER



Humans and AI merge (aka "the singularity")

Cure for the common cold

Dentistry integrated into primary care

Ability to regrow lost teeth

The U.S. is the healthiest nation

Medical residents work 40-hour weeks

AI "doctors" deliver primary care

Instant disease diagnosis via your smartwatch

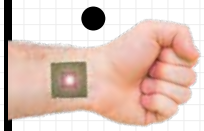
"This will just add to the stigma in our death-phobic culture, where the wish to live forever is often a transmuted wish to simply live better." —*Alex Trope, MD '15*

The rich stay forever young with antiaging therapies

Male contraceptives go mainstream

California's nurse shortage solved

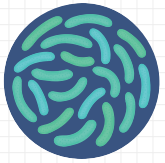
Injectable "nanobots" deliver targeted therapies



Implanted electronic health records

"This idea was in vogue a decade ago. Given the advances in cloud and mobile technology, it's far more likely that the future of the patient-controlled medical record will be one in which patients will carry their medical records on their smartphones, or they will be stored in the cloud, rather than being implanted."
—*Robert Wachter, MD*

Amazon runs the world's largest HMO



Microbiome therapies make billions

Microbiome research at UCSF is moving at breakneck speed. Whether today's science translates into blockbuster corporate profits remains to be seen, but the potential to expand our knowledge and create game-changing therapeutics is undisputed. Visit microbiome.ucsf.edu.

OVERHYPED

Did we nail it? Get it horribly wrong? Share your predictions for the future of health at **Future2050@ucsf.edu** or tag **#UCSF2050 @UCSF**.

PHOTOS: UC REGENTS (CANCER); MARTA ORTIZ (BIONIC EYES); MOLLY ADAMS (UNIVERSAL HEALTH COVERAGE); D-KEINE (PANDEMIC); AKBAR95 (AIDS); TOLOKONOV (LAB ORGANS); METAMORWORKS (E-HEALTH RECORDS INTEROPERABILITY); NIAID (SUPERBUGS); KENISHIROTIE (MENTAL HEALTH DRUGS); GETTY IMAGES (GENE EDITED HUMAN); DRAFTER123 (MENTAL ILLNESS STIGMA); YINYANG (CELL AND GENE THERAPIES); APOMARES (OBESITY PILL); THE JOHNS HOPKINS UNIVERSITY APPLIED PHYSICS LABORATORY (CYBERNETIC LIMBS); RYANJLANE (MALE CONTRACEPTIVES); IRINA_STRELNIKOVA (DENTISTRY); TREVOR COLLENS (SINGULARITY); TRAVELER1116 (COMMON COLD); CAMILA CARLOW (REGROW TEETH); ELISABETH FALL (NURSING SHORTAGE); DOOMU (NANOBOTS); ANDRIANO_CZ (IMPLANTED EHRS); IPGGUTENBERGUKLTD (U.S. HEALTHIEST NATION); BOB D'AMICO (40-HOUR WEEK); ENTERTAINMENT PICTURES (AI DOCTORS); DAVID RYDER (AMAZON HMO); LEILA_DIVINE (MICROBIOME THERAPIES); INEWSISTOCK (SMARTWATCH); GEDEON MAHEUX / 20TH TELEVISION (RICH ANTIAGING)

THE GAME CHANGER

Who Is Inventing New Drugs to Reduce Cognitive Decline

Ask Peter Walter, PhD, about his wonder molecule known as ISRIB, and he'll place in your palm a wee plastic model. It's long and knobby, like a grub, and spray-painted gold. "Our gold mine," he says, beaming.

Indeed, ISRIB's impact on human health could be huge: In experiments with mice, ISRIB – short for "integrated stress response inhibitor" – completely reversed severe cognitive impairments caused by traumatic brain injuries. Even in healthy mice, the molecule significantly improved learning and memory.

"It's just amazing," says Walter, a professor of biochemistry and biophysics whose work is being supported by a new gift from longtime UCSF donors George and Judy Marcus. "We think that ISRIB may uncover an untapped reservoir in the brain that allows damaged memory circuits to be repaired," says Walter. Beyond healing injured brains, he hopes that ISRIB, or molecules like it, can one day be used to treat neurodegenerative disorders like Alzheimer's and Parkinson's. "There are so many people suffering," he says. "If ISRIB works as well in people as it works in animals, that would be revolutionary!"

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PHOTO: STEVE BABULJAK

ALUMNI HUB

The Remarkable

Visionaries, boundary-breakers, extraordinary healers and leaders. We honor the 2019 **UCSF: The Campaign** Alumni Award winners:

The Audacious

Stella Dao, MD '92
Jennie Chin Hansen, MSN '71
Michelle Tam, PharmD '00

The Innovators

Zubin Damania, MD '99
Bryan Irving, PhD '93
Kenneth Wells, MD '74, MPH

The Compassionate

Ernest Goodson, DDS, MPA, Resident Alum '84
Orlando Rodriguez, MD '83
Ramona Tascoe, MD '79

The Dedicated

Jennifer Frazier, PhD '99
Donald Kishi, PharmD '68
Maribelle Leavitt, RN, PhD '88

The Pathfinders

Kjeld Aamodt, MS '15, DDS '12
Erin Green, MS '08, DPT '09
Nicolás Barceló, MD '15

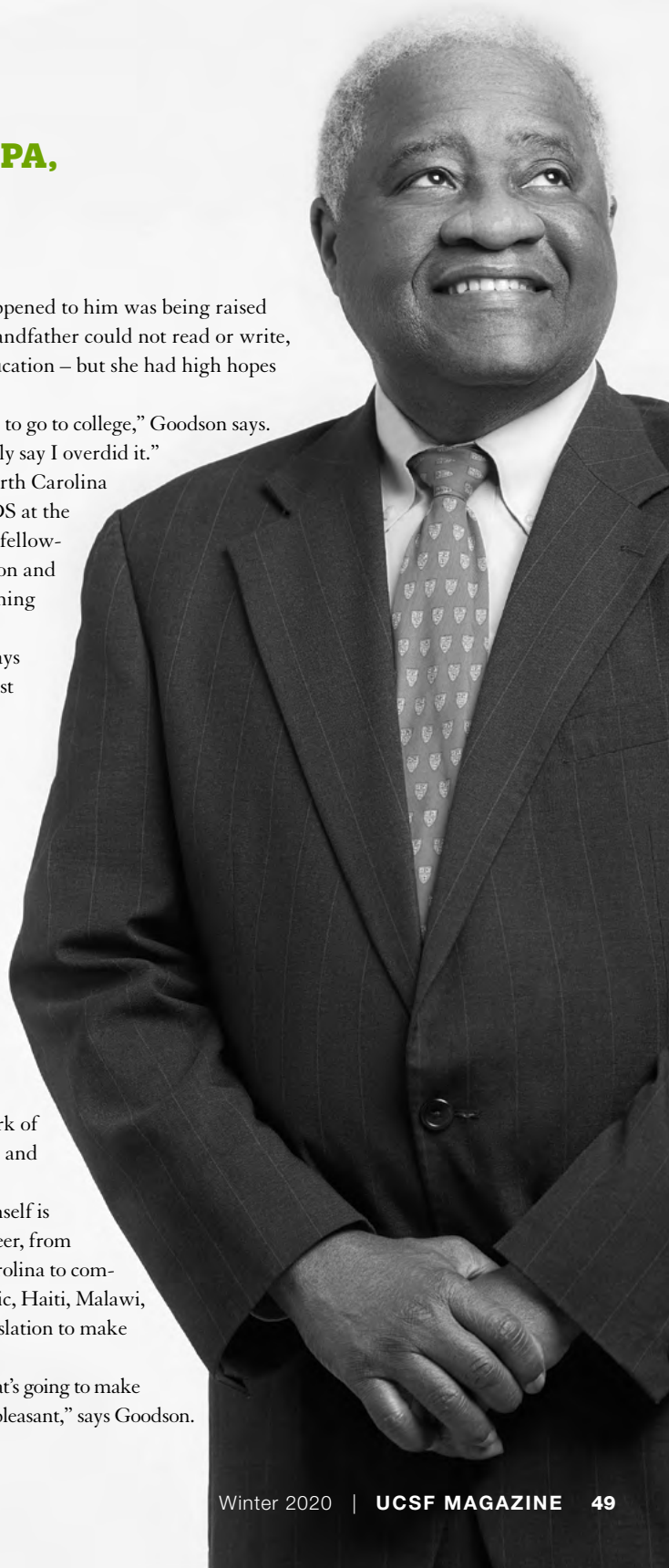
Meet them all:
alumni.ucsf.edu

Save the Date:
Alumni Weekend
June 5–6, 2020

SCHOOL OF DENTISTRY

Ernest Goodson, DDS, MPA, Resident Alum '84

Shining a light on dentists



Ernest Goodson says the best thing that ever happened to him was being raised by his grandparents in Kannapolis, N.C. His grandfather could not read or write, and his grandmother had only a sixth-grade education – but she had high hopes for Goodson.

"My grandmother always said she wanted me to go to college," Goodson says. "But if she was around today, I think she'd probably say I overdid it."

After graduating from the University of North Carolina at Chapel Hill, Goodson went on to earn his DDS at the UNC School of Dentistry. He later completed a fellowship in dental surgery at the University of London and a residency in orthodontics at UCSF, before opening an orthodontics practice in Fayetteville, N.C.

"I had never met a black dentist in my life," says Goodson. "I didn't know if I wanted to be a dentist for sure, but I decided to give it a shot. I worked hard and did the best I could."

After more than two decades in dentistry, Goodson earned a master's degree in public administration from Harvard University's Kennedy School of Government in 2002. He is currently researching the role African American dentists have played in civil rights and orthodontics. He has an interview scheduled in Atlanta with former U.S. Representative and United Nations Ambassador Andrew Young and his brother, Walter, a dentist. (The Young brothers' father also practiced dentistry in New Orleans.) Goodson has also been working with libraries around the country to illuminate the work of early African American dental leaders in his state and community.

Taking care of people less fortunate than himself is something Goodson has done throughout his career, from volunteering at free clinics throughout North Carolina to completing dental missions in the Dominican Republic, Haiti, Malawi, and Liberia. He also lobbies Congress to pass legislation to make dental care more affordable.

"I get real pleasure knowing I did something that's going to make someone's life a little more comfortable and more pleasant," says Goodson.

PHOTO: STEVE BABULJAK

SCHOOL OF PHARMACY

Michelle Tam, PharmD '00

Sharing food, family, and fun as a blogger

Michelle Tam didn't set out to become CEO of the food juggernaut known as Nom Nom Paleo. In fact, she was intent on enjoying the flexibility and work-life balance afforded by her position as a night pharmacist. But as her family grew, Tam found her energy flagging, her waistline expanding, and her food cravings off the charts.

After seeing her husband thrive on a paleo diet, Tam committed to the same regimen, and the Nom Nom Paleo food blog was born. She soon won both a Webby and an award from *Saveur* magazine and authored two *New York Times* bestselling cookbooks with her husband, co-creator of Nom Nom Paleo. Still, Tam is modest about her accomplishments. "Our main focus is always food, family, and fun," she says, "I only share things that I hope are helpful and delightful to people – and useful."

Tam credits her time at UCSF as a valuable springboard to her current career. "I think being detail-oriented in pharmacy school helps me a lot in recipe creation," she says. "Also, just learning to question things, and not just taking things at face value, is something that I learned after going to UCSF."

When asked what impact she wants to create with Nom Nom Paleo, she replies, "My big hope is that people will start cooking again and make it a regular routine, just like brushing their teeth and paying their taxes." She continues, "I'm not trying to convince people to be paleo. I just want them to be mindful of how they feel when they eat certain foods and to focus on the foods that make them feel better."

Despite pivoting from full-time pharmacist to full-time "farmacist," Tam remains resolute in her focus on healing and well-being. Her proudest accomplishment: "I've helped people take charge of their health by teaching them how to cook at home with real food ingredients."

PHOTO: STEVE BABULJAK

SCHOOL OF NURSING

Maribelle Leavitt, RN, PhD '88

Advocating for healthier families

As a UCSF doctoral student, Maribelle Leavitt saw how loved ones and their families often went into a tailspin when a medical blow struck a household. Husbands, wives, and children frequently were poorly equipped to cope when a close relative was diagnosed with a life-threatening illness or was discharged after a prolonged hospitalization – and everyone suffered.

"A very sick patient can suck up a lot of energy in the family, and people get left behind," says Leavitt. She went on to become an assistant clinical professor at UCSF's School of Nursing and a champion of the evolving field of family health care nursing.

Instead of concentrating solely on the patient's health, Leavitt's teaching and research focus on the wellness of the family as a unit. To improve the chances of a loved one's recovery and to keep the family emotionally sound, relatives have "to be taught practical skills to take care of a very ill patient," she says.

Her work has helped illuminate the needs of families in crisis and has showed generations of UCSF nursing students how to empower families to successfully care for a sick relative while keeping their household intact.

"The more involved the family was in a positive way, the less the patient and the family suffered," says Leavitt, who wrote an early textbook on the subject, titled *Families at Risk*.

While the family-focused approach hasn't caught on to the degree Leavitt hoped, nurses have become thought leaders and advocates for family health care, says her UCSF classmate and colleague, Catherine Chesla, RN, PhD '88, a professor emerita of family health care nursing. "Maribelle, for as long as I've known her, has appreciated the fact that families are essentially important to health," says Chesla.

PHOTO: STEVE BABULJAK

GRADUATE DIVISION

Bryan Irving, PhD '93

Pursuing novelty to make a difference

Bryan Irving loves the excitement of new experiences.

He once posed as his identical twin brother, Brad, a former member of the San Francisco Symphony Chorus, for a single performance. His proclivity for excitement also led Irving to a career exploring new approaches to autoimmunity and tumor immunotherapy.

"Discovering something novel is far more rewarding than making incremental advances," he says. "In research, it is important to take risks. I learned to respect, but not accept, dogma. I challenge it."

This penchant for pushing boundaries was nurtured in the lab of Arthur Weiss, MD, PhD, UCSF's Ephraim Engleman Distinguished Professor, who emphasized the value of collaborative research. Irving also benefited from the lab's supportive environment, which fostered his pioneering work with Weiss on single-chain chimeric antigen receptor (CAR) technology, which is now used to treat hematologic malignancies.

"It's one of those instances where the basic research experiment can now translate into a new paradigm for clinical treatment," says Irving, who today is chief scientific officer of Five Prime Therapeutics, which identifies and innovates new immune therapies.

Irving pivoted to cancer immunotherapy early in his career while working at Genentech. Despite facing skepticism, he and his lab began working on the PD-L1 protein. In collaboration with many of his Genentech colleagues, Irving eventually developed an antibody that became the drug atezolizumab (Tecentriq), which is now used to treat cancers of the lung, breast, and bladder, among others.

The drug's introduction to patients was a defining moment for Irving. He remembers receiving a letter from the physician of the first patient who responded in the clinical trial – a critically ill father of two young children who had failed all prior treatment options. Within months of starting the new treatment, the patient was able to play with his kids and resume his normal activities. He wanted to meet the people who had developed the drug that had saved his life.

"To have such a positive impact even on one person's life was more gratifying to me than any of my research papers," says Irving.

PHOTO: STEVE BABULJAK

SCHOOL OF MEDICINE

Stella Dao, MD '92

Solving a serious problem for new mothers

The American College of Obstetricians and Gynecologists recommends breastfeeding for the first year of a baby's life. As a medical doctor, Stella Dao was well aware of this advice. But when she went back to work after giving birth to twins, she found herself without the time to pump.

"In an emergency-room environment," says Dao, "you can't schedule when you eat or even when you go to the bathroom, and you definitely can't schedule when to pump milk." And yet Dao knew that if she didn't pump every few hours, she might end up with a low milk supply. And her babies, especially because they were born prematurely, needed her breast milk.

Instead of giving up and feeding her twins formula, Dao decided to look for a way to help herself and other women. "I knew many women must be in the same boat," she says. She wanted to create an attachment for existing breast pumps that would allow her to move around while she pumped. And with the help of her husband, Dan Garbez, who already had a career in business and manufacturing, that is what she did.

The husband-and-wife team put their heads together and came up with several designs. They were aiming for a device that was versatile enough to fit different types of pumps and that was comfortable for any woman to wear under her clothing. Since 2009, they have been honing their invention based on customer feedback and research. A few years ago, they also designed a quieter pump to work with the attachment.

Over the past three years, the product, known as Freemie, has won three major awards: the 2016 Best of Baby Tech, the 2017 Edison Award Gold Medal in Health and Wellness, and the 2018 *USA Today* Innovation Award. Today, Dao's husband runs the operations side of their company, while she is chief of occupational health at Kaiser Permanente in Sacramento.

"I hoped to give women more freedom, mobility, and flexibility," says Dao. "I was outraged there was no solution, so my husband and I created one."

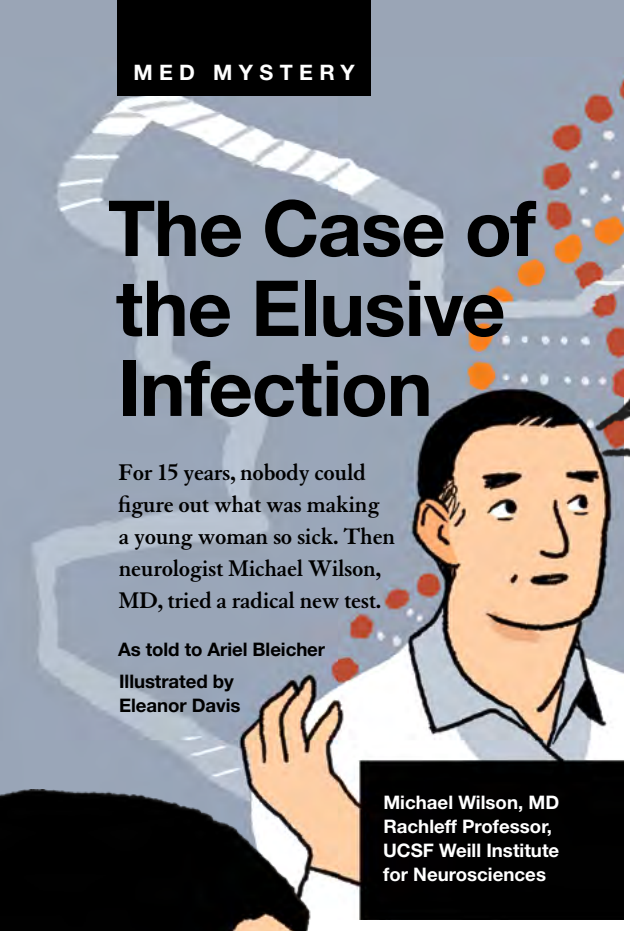
PHOTO: STEVE BABULJAK

The Case of the Elusive Infection

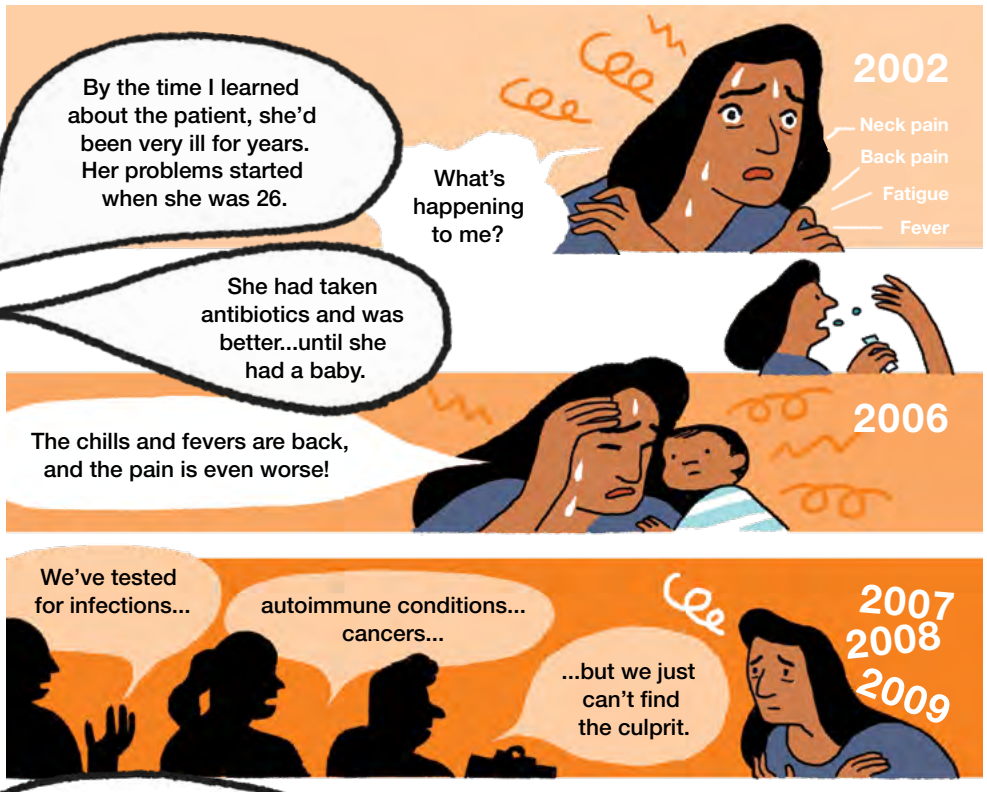
For 15 years, nobody could figure out what was making a young woman so sick. Then neurologist Michael Wilson, MD, tried a radical new test.

As told to Ariel Bleicher

Illustrated by Eleanor Davis



Michael Wilson, MD
Rachleff Professor,
UCSF Weill Institute
for Neurosciences



UCSF The Campaign

A SCIENTIST'S AUDACIOUS IDEA
A PATIENT'S REMARKABLE RECOVERY

Linda McCulloch is alive today thanks to UCSF and the visionary support of donors like you. In 2008, she was diagnosed with **stage 4 melanoma and an inoperable brain tumor.** Chemotherapy offered little promise, but a clinical trial led by Adil Daud, MD, used Linda's own immune system to target her particular cancer. Today, Linda remains cancer-free. Her response to this treatment – which was not typical for patients with her diagnosis – offers hope that one day we will be able to crack the code of precision cancer therapy and predict exactly which patients will benefit from these lifesaving medicines.

PHOTOS: NOAH BERGER

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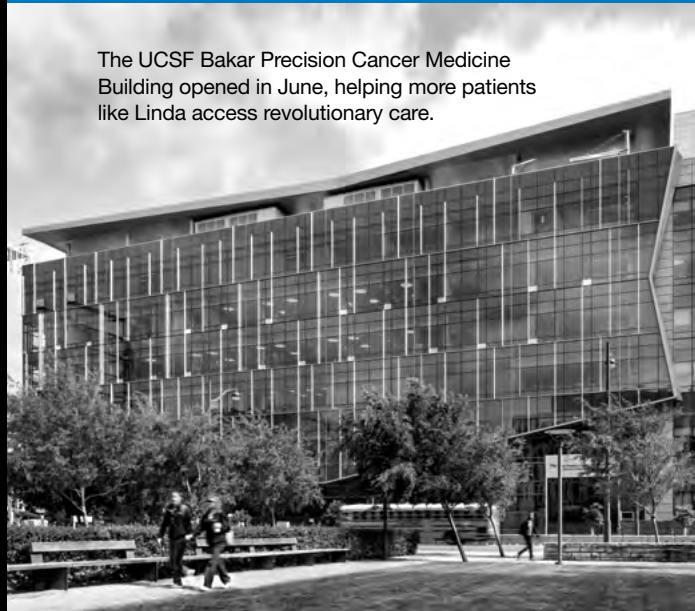

The UCSF Bakar Precision Cancer Medicine Building opened in June, helping more patients like Linda access revolutionary care.

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