GOT UCSF PRIDE?
Celebrate and support UCSF as we take on the hardest problems in health. Order a campaign t-shirt like those worn by UCSF student leaders (left to right) Sumitra Tatapudy, Loreen Atallah, Jessica Baisley, Janella Leano, Aaron Snyder, and Joanna Diel.
CAMPAIGN.UCSF.EDU/SHIRT.
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Treating babies born without immune systems in a new genomic era.

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We are tackling three Grand Challenges

Decoding Life to Improve Health
First we learn how biological systems work. Then we rewire, repair, and reprogram them to prevent and cure disease.

Leveraging Discovery to Revolutionize Care
We translate new knowledge into care and cures in real time – and reimagine health care in the process.

Partnering to Achieve Health Equity
Driven by our public mission, we ensure access to life-sustaining care and cures for everyone.

UCSF: THE CAMPAIGN
Humankind is at a historic inflection point in its ability to understand the mysteries of health and life.

At this singular moment, there is nowhere I would rather be working in the health sciences than here in San Francisco. This is a destination for diverse ideas and people, a home to unparalleled innovation and entrepreneurship, and a hub for unprecedented knowledge creation—a place where the life sciences and technology collide.

It is clear to me that this is UCSF’s moment. Every day, innovators and mavericks band together across departments and disciplines to relentlessly attack problems and answer questions. We at UC San Francisco are not afraid of unconventional ideas or unorthodox approaches. We embrace them, questioning assumptions and shattering barriers to arrive at radical solutions.

That’s why in October, I announced the launch of UCSF: The Campaign. This transformative undertaking seeks to raise $5 billion to solve the hardest problems in human health: decoding life, revolutionizing care, and achieving equitable access for all to the benefits of these advances. At UCSF, pursuing these grand challenges is the culmination of everything we do.

In this issue, I invite you to discover, join, and support the brilliant minds of UCSF—from the pioneers who are mapping the circuitry of the human brain, to the unconventional thinkers who are using poetry and music to combat children’s diabetes in vulnerable communities. See our Campaign portrait gallery beginning on page 24 to meet the visionaries, the advocates, the mavericks, the compassionate, and the inspired at UCSF—all of whom are transforming human health as we know it.

Sam Hawgood, MBBS
Chancellor
Arthur and Toni Rembe Rock
Distinguished Professor
What’s Stopping Us from Putting an Astronaut on Mars?

People assume it’s flight technology. Not so. “Human physiology is the limiting factor,” says Thomas Lang, PhD, the Presidential Professor of Craniofacial Sciences and a fellowship alumnus. The low-gravity and radiation associated with spaceflight affect our musculoskeletal, cardiovascular, and immune systems in ways that look a lot like the effects of aging here on Earth.

Bone loss, back pain, dried plums
After just eight days in orbit, the Apollo astronauts of the 1960s and ‘70s were so weak that they had to be pulled from their landing capsules. In the following decades, astronauts began to exercise in space to keep their muscles conditioned. Still, many astronauts suffer back pain for years after returning to Earth.

To figure out why, Jeffrey Lotz, PhD, the David Bradford Professor of Orthopaedic Surgery, studied the spines of astronauts after their time in space. He discovered the source of the back pain was deconditioning of the multifidus muscles, small muscles that connect and support the vertebrae. Lotz is working with NASA to devise an in-space exercise program for astronauts to prevent the condition.

Exercise is key for bone health as well, and Lang has been studying the effect of space travel on bones for decades. Bones grow and repair themselves in response to supporting loads against gravity. A lack of gravity interrupts the natural cycle of bone function, which operates like this: Bone cells called osteocytes detect regions of damage to bone tissue, triggering other cells, called osteoclasts, to resorb bone that has been damaged by repetitive strain. The work of osteoclasts triggers yet other cells, osteoblasts, to move in and rebuild the bone where it is needed.

Yet in the absence of gravity, osteoclasts continue to resorb bone, but osteoblasts don’t replenish it. The breakdown in the repair function might put astronauts at increased risk for injury. This may be the same process involved in osteoporosis, according to Daniel Bikle, MD, PhD, a professor of medicine and of dermatology.

Radiation exposure during spaceflight can also cause bone loss for astronauts, though one study points to a surprising prescription for this. Bernard Halloran, PhD, a professor of medicine, found that mice subjected to radiation and fed a diet containing plum powder lost significantly less bone. His next steps are to discern what compounds in prunes are responsible and put them in a pill.

Heart of the matter
The radiation and low gravity of space also have an impact on the body’s vascular system, causing circulatory problems for astronauts when they return to Earth and an increased risk of heart attack later in life, says vascular surgeon Marlene Grenon, MD. Grenon has a diploma in space sciences from the International Space University and developed UCSF’s first course on the effects of spaceflight on the body. She has found that lack of gravity can thin vascular walls and create changes in the cells that conduct electricity in the heart, which may put astronauts at risk of cardiac arrhythmias.

Sonja Schrepfer, MD, PhD, an associate professor of surgery, and Tobias Deuse, MD, the Hoffman Professor of Cardiac Surgery, are studying changes in the function of vascular cells after space flight. “When astronauts return to Earth’s gravity, muscle weakness is only part of the reason they can’t stand up,” Schrepfer says. “They also don’t get enough blood to their brains, because their vessel function is impaired.” Schrepfer and her team have identified a small molecule that prevents vascular walls from thinning in mice and plan to do safety trials of that molecule on humans in the near future.

Immune response
Schrepfer has also received an award to study the effects of microgravity on the immune system as a model of aging, both in space and after returning to Earth. She is looking at gene expression and the role of microRNA (miRNA) – tiny molecules that can switch genes on or off. Her research revealed that five miRNAs which control genes that activate T cells weren’t working properly.

These are the same changes seen over the course of decades in aging, leaving the elderly with less robust immune systems. In space, though, the changes begin to occur after 30 minutes. The research by Schrepfer could help people who travel in space but is also an opportunity to study changes on Earth – but at a far quicker pace.
Baldness Exposed

UCSF researchers recently discovered that a type of immune cell generally associated with controlling inflammation might have a hair-raising side job: controlling baldness.

In experiments with mice, the researchers found that regulatory T cells, or Tregs (“tee-regs”), trigger stem cells in the skin to promote healthy hair growth. Without these immune cells as partners, the stem cells cannot regenerate hair follicles, leading to baldness.

The study suggests that defective Tregs could cause alopecia areata, a common autoimmune disorder characterized by hair loss. They could potentially play a role in other forms of baldness, too, including male pattern baldness, says Michael Rosenblum, MD, PhD, an assistant professor of dermatology at UCSF and senior author of the new paper.

The research adds to scientists’ growing sense that immune cells play a much broader role in tissue biology than had previously been appreciated, says Rosenblum. He plans now to explore whether Tregs in the skin may also affect wound healing, since the same follicle stem cells are involved in regenerating skin following an injury.

In this microscopic image of mouse hair follicles, the Tregs show up as red dots.

Gut Microbes May Influence MS Progression

Researchers at UCSF identified certain gut microbes in patients with multiple sclerosis (MS) and then showed that these microbes help regulate immune responses in mice with the disease. The finding suggests that gut microbes may play a role in MS’s neurodegenerative symptoms. That could help scientists understand the origins of MS and potentially lead to improved treatments, such as dietary changes or drugs based on microbial byproducts.

Top Reasons for Avoidable Emergency Room Visits

1. Alcohol Abuse
2. Dental Issues
3. Depression

According to a new UC San Francisco study. The researchers stressed that emergency departments are often ill prepared to handle such conditions. They also noted their findings suggest a lack of access to health care rather than intentionally inappropriate use.
One Step Closer to a Bionic Kidney

The long-held dream of an implantable artificial kidney is nearing human trials.

Kidney failure is a debilitating and ultimately deadly illness — and a health policy crisis. Although 468,000 people are on dialysis in the U.S., at a cost to the government of $31 billion a year, very little money is spent on researching alternatives to current treatments.

_Wired_ magazine’s Megan Molteni recently visited Shuvo Roy, PhD, to check in on the development of an implantable artificial kidney, which has been in the works for more than 20 years. Roy, a professor of bioengineering and therapeutic sciences, directs the Kidney Project, the multi-institution collaboration behind the project.

The implantable artificial kidney employs silicon filters and will encapsulate living cells that will help recreate most of the essential functions of the kidneys.

“Silicon is the most perfected man-made material on Earth,” Roy told _Wired_.

Thanks to an outpouring of public interest and donations, initial clinical trials are planned for early 2018.

“Government funding is critical to encourage our scientists to pursue not just the challenges that are relatively easy, or obviously profitable, but the ones that are fiendishly hard — yet crucial.”

**Alexander Marston, MD, PhD,** a UCSF microbiologist and clinical fellow alumnus, in _Vox_, on the need to continue federal funding for basic research.

“Around here it’s not PTSD [post-traumatic stress disorder]. There’s nothing ‘post’ about it.”

**Alicia Boccellari, PhD,** a UCSF psychiatrist and founder of the Trauma Recovery Center at Zuckerberg San Francisco General Hospital, in the _New York Times_. The center has become a national model for hospital-based care for victims of gun violence, sexual assault, hate crimes, and other violent offenses.

“Many people need gluten-free foods because of disease. But if you don’t, [a gluten-free diet] may be undermining your own health attempts.”

**Andrea Garber, PhD,** chief nutritionist for the Eating Disorders Program and Childhood Obesity (WATCH) Program at UCSF, to _Healthline_, on how eating gluten-free products because of their perceived health benefits could pose serious health risks, especially for children.
New Insight into Parkinson’s

Abnormal protein clumps in the brain feature prominently in Parkinson’s and other neurodegenerative diseases, but the role these proteins play in the normal brain is unknown.

Now, research by UC San Francisco neuroscientist Robert Edwards, MD, has uncovered the role of a protein – alpha-synuclein – long implicated in Parkinson’s. Edwards believes understanding alpha-synuclein’s normal function can lead to better insight into what happens when it fails. And that, in turn, may help with prevention and management of Parkinson’s.

In healthy nerve cells, alpha-synuclein is present at nerve synapses, where bubble-like vesicles fuse with neurons to release the neurotransmitter dopamine, which is depleted in individuals with Parkinson’s. Any disturbance in this fusing process disrupts the neuronal communication that’s required for nearly all brain activity.

Edwards’ team found that in abnormally high amounts, alpha-synuclein blocks this fusing process and thus the release of dopamine. But in normal amounts, it has a very different effect, helping speed dopamine’s release.

How can one protein have both negative and positive roles in neurotransmitter release? And how might the former contribute to Parkinson’s?

Most people with Parkinson’s don’t inherit the disease through mutations, Edwards explains, instead, acquiring it by unknown mechanisms. His research has convinced him that the disease’s common form arises from a defect in alpha-synuclein’s natural ability to promote dopamine’s release.

Breast Density Tops List of Breast Cancer Risk Factors

The density of women’s breasts may explain a greater proportion of breast cancers than any other known factor, according to a recent study headed by UCSF researchers. Breasts that appear denser on a mammogram contain more glandular tissue (that is, the lobules that produce milk) and fibrous tissue, while breasts that appear less dense contain more fatty tissue.

In what is believed to be the first large-scale study quantifying the proportion of breast cancer cases attributable to breast density, the researchers evaluated risk factors in more than 200,000 women over age 40. About 18,000 of the women had varying stages of breast cancer, while about 184,000 did not.

Women with denser breasts were found to have a greater risk of breast cancer, and breast density was found to be the most prevalent risk factor – even more prevalent than family history of the disease.

Natalie Engmann, a PhD candidate in epidemiology and translational science and the paper’s first author, says dense breasts are more common in younger women and in women who weigh less (as measured by body mass index). Treatment with tamoxifen, which blocks the hormone estrogen, is the only current intervention shown to reduce breast density. But, Engmann adds, the drug can have serious side effects, so it’s recommended only for women at high risk of breast cancer.

“Our study highlights the need for new interventions to reduce breast density for women at average risk,” Engmann says.
Go Easy on the Avocado Toast: ‘Good’ Fat Can Still Be Bad

Avocados and olive oil are loaded with monounsaturated “good” fat, but a recent UC San Francisco study indicates that too much of a good thing can still be bad for you.

Researchers in the lab of Jacquelyn Maher, MD, the William and Mary Rice Professor and director of the UCSF Liver Center, studied the role of different nutrients in the development of fatty liver disease – a risk factor for metabolic disorders like type 2 diabetes and hypertension.

They created four distinct high-calorie diets from different pairings of either saturated or monounsaturated fat with either sucrose- or starch-based carbohydrates. All the diets contained about the same number of calories, as well as roughly 40 percent carbohydrates, 40 percent fats, and 20 percent protein, a ratio similar to the average American diet. Four groups of 10 mice were fed the experimental diets for six months.

The researchers expected saturated fat – the “bad” kind – to cause more fat buildup in the livers of the mice, but instead they found that the most severe fatty liver disease resulted from the diet combining “good” monounsaturated fat and starch. For now, it’s unclear why this pairing seems to exacerbate fatty liver, but the finding emphasizes that simply counting calories does not guarantee a healthy diet.

Caroline Duwaerts, PhD, an associate research biologist at the UCSF Liver Center and first author of the findings, says it’s all a matter of proportion. A drizzle of olive oil on your salad is fine, but a daily habit of pasta drenched in olive oil could be cause for concern.

“I always think back to what I was told as a child,” she says. “Everything in moderation.”
Anatomy – the foundation of much of what a medical student needs to know – is often a dreaded memorization ordeal. But for first-year medical students at UCSF, virtual reality is bringing the subject to life in totally new ways. The technology, combined with hands-on cadaver training and textbook learning, is giving students a better grasp of the relationships between the body’s bones, muscles, nerves, and organs. “It’s a learning experience almost like putting a puzzle together,” says Derek Harmon, PhD, an assistant professor of anatomy, who – with Kimberly Topp, PhD, PT, a professor of physical therapy and of anatomy – is leading a pilot test of the technology’s use as a teaching aid.
Hundreds of Interlaced Fingers: A Kidney Doctor’s Search for the Perfect Match

UCSF nephrologist and resident alumna Vanessa Grubbs, MD, traces her journey from kidney donor – her boyfriend desperately needed one – to kidney doctor. Along the way, she shares her discoveries about racial disparities in the way donated kidneys are allocated and how patients, families, and clinicians alike struggle with decisions about dialysis.

Read: bit.ly/ucsf-read-w18

TED Talk: “What Really Matters at the End of Life”

UCSF palliative care specialist B.J. Miller, MD ’01, asks big questions regarding how we think about death and honor life. Miller lost three limbs in an accident in college and drew upon his experiences to pioneer a new model of palliative care. His talk, viewed more than 6 million times, prompted so many responses that TED hosted a Q&A on Facebook for the many people eager to learn more about dying with dignity.

Watch: bit.ly/ucsf-watch-w18

Carry the One Radio podcast: “The Hidden Addiction”

Sugar scientist and professor of health policy Laura Schmidt, PhD, MSW, MPH, explores the tactics corporations use to get people hooked on sugary products – and how she and her colleagues are fighting back. Carry the One Radio is produced by a dedicated band of young UCSF scientists, graduate students, and postdocs.

Listen: bit.ly/ucsf-listen-w18

Can Green Tea Block Lung Fibrosis?

The health benefits of green tea – used for thousands of years in traditional Chinese medicine – are widely known. UCSF researcher Harold Chapman, MD, has added one more benefit to the list.

Epigallocatechin gallate, or EGCG, the active component in green tea, has long been considered an antioxidant. Chapman’s team has found that in animal models, it also effectively blocks pulmonary fibrosis, or scarring of the lung tissue. Furthermore, it appears that only a small amount of EGCG is effective against pulmonary fibrosis. By contrast, although components of green tea have been shown to be effective against other diseases (and the consumption of green tea has been shown to be safe), in many cases humans could never drink enough for it to be truly effective.

Chapman is now seeking funding for a proof-of-principle study that he hopes will lead to a phase II clinical trial.
National Leader, Alumna Named Nursing Dean

Catherine Gilliss, RN, PhD ’83, a national leader in nursing and former UCSF faculty member, has been appointed dean of the UCSF School of Nursing. Gilliss, who will also serve as associate vice chancellor for nursing affairs, returns to UCSF from Duke University. After 10 years there as dean of the School of Nursing and vice chancellor for nursing affairs, she stepped down in August 2014 and was on leave for the 2014-15 academic year as a fellow in the Stanford University Distinguished Careers Institute. Gilliss previously served as dean of Yale University School of Nursing and as chair of UCSF’s Department of Family Health Nursing.

Vale Wins “Nobel of the East”

Ronald Vale, PhD, vice chair of cellular and molecular pharmacology, won the 2017 Shaw Prize in Life Science and Medicine for his seminal research on motor proteins, which perform functions crucial to life. He shared the $1.2-million prize, often called the “Nobel of the East,” with UC Berkeley’s Ian Gibbons, PhD.

Best Hospital in California!

UCSF Medical Center was ranked the fifth-best hospital in the country and the top-ranked hospital in California in U.S. News & World Report’s 2017-18 “Best Hospitals” survey. In a separate set of pediatric rankings, UCSF Benioff Children’s Hospitals placed among the nation’s premier children’s hospitals in nine pediatric specialties.

Cancer Screening Idea Wins Big

An idea for improving how skin cancer is detected won the 2017 Cancer Center Impact Grant, a Shark Tank-style competition at UC San Francisco that champions high-risk, high-reward projects unlikely to be funded by conventional sources. The winning team aims to develop an artificial intelligence–based screening tool for melanoma. Currently, clinicians must visually inspect patients’ skin, which can be a challenge, especially in patients with hundreds of moles. The team – (above, from left) Michael Keiser, PhD ’09; Maria Wei, MD, PhD, a resident alumna; and Robert Judson-Torres, PhD ’12 – has high hopes. If detected early, melanoma has a 100-percent survival rate.
Traumatic brain injury patients— and the researchers studying them— face a steep ascent

A DEVASTATING FALL,
A CLIMB BACK TO HEALTH

By Dresden Joswig

On a clear night in February 2017, Steve McConnell stepped onto a friend’s San Francisco rooftop to admire the city skyline. From his Nob Hill perch, the gregarious 31-year-old attorney might have seen the glimmering lights of the Golden Gate Bridge or the sharp angles of the Transamerica Pyramid. He might have reveled in the sense of perspective bestowed by his bird’s-eye view.

He likely felt content: He was on track to make partner at a law firm; he’d just bought his first home, a condo outside of Los Angeles; and he was spending time with friends in a city he loved, a favorite pastime for the travel buff.

But Steve can’t tell us what he felt that day. Because in a setting that should have inspired awe, something tragic happened. A step into an unprotected rooftop shaft sent him plummeting down a narrow opening, stripping him of his memories and— for a time— of any ability to walk, speak, and engage with the world.

The 40-foot fall left Steve trapped in a 3-foot-square space with fractures of his hips, ribs, and neck; damage to his kidneys, spleen, and lungs; and a severe traumatic brain injury (TBI). “No one knew where the shaft went,” his father, Tim McConnell, remembers. “The urban search and rescue team finally got to him through a tiny hole in his friend’s first-floor apartment. That gave him a shot at survival.”

Nevertheless, the McConnells feel fortunate Steve landed at ZSFG that day. The hospital, the only Level I trauma center in the Bay Area, is home to UCSF neurosurgeon Geoffrey Manley, MD, PhD, a leader in the study of TBI and head of the most robust TBI research initiative in the world, TRACK-TBI. “We wouldn’t be having this conversation if not for ZSFG and Dr. Manley,” Tim says.

The McConnell family met Manley a few days into Steve’s ICU stay. At the time, Steve was in an induced coma and on life support. “We pressed for specific answers about Steve’s potential for recovery, and there just weren’t answers,” Tim remembers. “But we were so grateful for Dr. Manley, who held our hands, stayed with us for close to an hour, and encouraged us to keep trying to communicate with our son.”

While Steve was wheeled, unconscious, into the Zuckerberg San Francisco General (ZSFG) emergency room, his parents and his sister were asleep in Southern California. They didn’t yet know that Steve had become a devastating statistic— one of an estimated 2.8 million people treated in the U.S. each year for traumatic brain injury, a class of diseases about which frustratingly little is known.

2.8 million: Number of TBI-related ER visits, hospitalizations, and deaths in 2013

The force of the fall had badly injured Steve’s brain, rupturing blood vessels and causing extensive bruising. Damage to his nerve fibers had left Steve in a state of
minimal consciousness, and his brain had begun to swell, putting potentially deadly pressure on his brain tissue. Doctors alleviated the swelling by draining excess cerebrospinal fluid, but the injury “was just terrible,” Tim says.

The extent of the damage Steve had suffered was unusually severe, but its scope – broken vessels, torn nerve fibers, and bruised tissue – was textbook, insofar as any TBI can claim that designation. That’s because no patient experiences a traumatic brain injury in exactly the same way. It’s a category of diseases even more complex, some TBI scientists say, than cancer.

Just a decade ago, Manley, a member of the UCSF Weill Institute for Neurosciences, and his team would have been unable to see, with such precision, how the fall had impacted Steve’s brain. But eight years of TRACK-TBI work involving more than 3,000 patients across the injury spectrum has taught them what tools give the most complete picture of traumatic brain injury. That is crucial information for patients like Steve when it’s time to make decisions about treatments and when questions arise about long-term outcomes.

With a combination of imaging techniques, including structural MRI, diffusion tensor imaging (DTI), and functional MRI, Manley could see in microscopic detail the damage to Steve’s brain tissue, blood vessels, and neural highways. He could also make some predictions about how Steve might fare long-term, based on patterns emerging from the TRACK-TBI patient database. Even 10 years ago, this would have been impossible.

40%: Percentage of people who visit an ER after a TBI but are never seen by a doctor

Today, the CT scan is still the only FDA-approved diagnostic for TBI, but it’s a tool that was unable to uncover the injury at the root of Steve’s inability to wake up. His structural and functional MRIs held those answers, revealing multiple tiny hemorrhages associated with Steve’s nerve damage and demonstrating disruptions in his normal brain connectivity.

Together, these data points would have hinted at challenges ahead, even if Steve’s injury had been far milder. Regardless of how a TBI is categorized – mild, moderate, or severe – patients who exhibit these markers tend to struggle cognitively, experience disability, and/or suffer from other significant post-injury symptoms.

But even with the dynamic picture generated by these results, Manley couldn’t answer many of the McConnells’ early questions. That’s because, Manley says, “we still
For years, the archetypal TBI patient was like Steve – active, young, and male. But demographic shifts mean that today, more than half of TBI patients are over 65.

“Heart, cancer, and joint replacement doctors have done an incredible job keeping [people] highly active into their 80s and 90s,” Manley says. “What that means is that older folks have falls, and they hit their heads.”

But most TBI research is conducted on younger cohorts. “Many studies use age cut-offs and exclude patients with pre-existing medical conditions,” explains UCSF neurologist Raquel Gardner, MD, a resident alumna. “As a result, older adults are severely underenrolled in TBI research.” When they are studied, she adds, they’re “very different than younger people with TBI.”

Gardner is tackling the problem by developing statistical models to track recovery patterns in older adults. By examining everyday function, life satisfaction, cognition, and mood, she hopes to identify predictors of good versus poor recovery. “We want to reinvent how we classify individual patients’ injuries and measure recovery over time,” she says.

Gardner is also interested in understanding if a single TBI can lead to dementia. She studied data from 20,000 retired individuals to see if a history of TBI increased the likelihood of later-life cognitive, mobility, or functional problems. She found no evidence of cognitive impairment following TBI, “which was very reassuring,” Gardner says. She did, however, find a link between TBI and functional impairments in later life.

UCSF researchers are examining other aspects of TBI among older individuals. Caroline Tanner, MD, PhD, has determined that those who’ve experienced a TBI are 1.5 times more likely to develop Parkinson’s disease. And Kristine Yaffe, MD, the Scola Professor of Psychiatry and a resident alumna, found that older veterans who’ve suffered any brain injury, even a concussion, exhibit “a lot more depression, anxiety, PTSD, and issues with ... executive function.” She’s currently combing 2 million veterans’ medical records to see if there’s a link between TBI and dementia, Parkinson’s, and other conditions.

**2%:** Percentage of the U.S. population living with long-term physical, cognitive, and psychological TBI-related disabilities

**0:** Number of successful clinical trials or treatments for TBI

Manley has been racing to bring the discipline up to speed since the beginning of his career. “When I started as a neurosurgery resident in 1995, I saw that this was an area that affects millions of people every year, and no one really knew much of anything,” he explains. “I’m not exaggerating when I say we were treating patients with techniques developed a hundred years ago.” Change, he realized, was long overdue. Manley decided to shift his focus from brain tumors – where research was far more advanced – to TBI.

He chipped away at the problem for close to 15 years, recruiting patients into small-scale studies at ZSFG and bringing on outstanding physicians and scientists dedicated to the subject. A grant to apply at three additional centers the imaging techniques his team was already using at ZSFG planted the seeds of what is now known as TRACK-TBI.

“We think of it as an essential, foundational study for traumatic brain injury, just as the Framingham study was for heart disease,” says Manley’s close colleague Pratik Mukherjee, MD, PHD, a neuro-radiologist and a co-leader of TRACK-TBI.

“It’s not enough to evaluate a treatment for TBI on a group of young, college-educated people without other medical issues,” Mukherjee explains. “That’s a small fraction of TBI patients; you have to show that any treatment strategy works in the whole population.” That’s why the initiative has centers in cities like Pittsburgh, Miami, and Houston and enrolls patients of all ages, ethnicities, and socio-economic backgrounds.

With his parents’ consent, Steve became part of the landmark study soon after he was admitted to ZSFG. “We knew it was a decision he would support,” Tim says. Every TBI patient in the 18 participating hospitals is offered the same opportunity.

According to Manley and Mukherjee, the absence of a foundational study is partly responsible for the fact that there’s still no drug effective against TBI. “There have been close to a hundred TBI clinical trials of drugs and other interventions,” Mukherjee says. “They’ve all failed because the hypotheses were not based on good enough data.” (See the sidebar on page 17 for a preview of one promising therapeutic.)

For Steve, that meant there was no way doctors could treat his primary traumatic brain injury. They could only draw excess cerebrospinal fluid from his brain to help prevent further injury. And at Manley’s suggestion, the family supplied constant stimulation. “We played music from his phone,” Tim says. “We talked to him and we held his hand, engaging him in that sweet spot just below agitation.”

As Steve gradually grew more alert in the weeks following his injury, he began intensive physical therapy, speech therapy, and occupational therapy. “He would eat soup with a fork. He couldn’t tell us who the president was,” Tim remembers. “And if you asked him where he was, the answer was everything from Santa Cruz to Israel.”
After six weeks, Steve was finally able to leave ZSFG, but he was far from ready to return to normal life. “Dr. Manley was traveling, but he was on the phone with me and lobbying with providers to get Steve into the best inpatient rehab,” Tim says. “He said, ‘I want you to be closer to your home so you can sleep in your bed at night.’ But we wanted to stay close to Dr. Manley and ZSFG.”

After an exhaustive search, the family secured an inpatient spot at a San Francisco-based rehab facility. When Tim and his wife weren’t sleeping in a rented apartment, they were at the center with Steve. “After five weeks, the insurance ran out and they told us we had to leave,” Tim says. “It wasn’t nearly enough time.”

Steve moved on to a rehab facility closer to home, where he received outpatient treatment just three days a week, for less than three hours a day. It was all that Steve’s insurance would cover. On the off days, “we did yoga with him, we’d go to the gym, we’d try to make it fun,” Tim says.

Despite their best efforts, the makeshift regimen was inadequate. Four months after his injury, Steve’s progress stalled. “He became somewhat apathetic,” Tim says. “He just wasn’t challenged.”

Yet initially, Steve’s naturally sunny disposition remained intact. That was a surprise to the McConnells, who knew that those who experience TBI – even a concussion or other “mild injury – often suffer depression, anxiety, and/or irritability. It was only later that Steve exhibited these symptoms.

The McConnells knew Steve needed more intensive therapy and more tailored support. With Manley’s encouragement, they found him a spot at a top-tier rehab center in Southern California. They sacrificed to provide the additional therapy, which even Steve’s comparatively “good” insurance would not cover. (Manley has lobbied for better TBI rehab options. “TRACK-TBI is collecting crucial health economic data to support the need for more services for TBI patients and reduce disability from TBI,” he says, noting that the economic burden of the disease is an estimated $76 billion per year.)

There, with all-day regimens of speech therapy, physical therapy, and occupational therapy, Steve made progress. By August 2017, he began testing the professional waters with some basic legal work from home one day a week. It was part therapy, part work. “A partner at the firm would delegate work for him, then he’d review it and give feedback to Steve’s speech therapist,” Tim explains.

Eight months after his fall, Steve moved back into the condo he had purchased just before the accident. Quickly, it became apparent that the move was premature. Today, “he rarely spends the night alone, and we help him with grocery shopping, bills, and transportation,” Tim says. It’s likely that Steve will soon move back home.

His work at the law firm might also be ending. Even Steve, who has lacked self-awareness since the injury, sees the writing on the wall. He can no longer recite legal statutes or think quickly on his feet. The McConnell family is now helping Steve to reimagine his future outside the law. “What you do becomes your identity,” Tim says. “We need to help him find a new purpose in life.”

Tim hopes that, with renewed motivation and the support of a psychologist, the family can help Steve stave off the depression and sadness that he has begun. “We thought we’d gotten past the worst part, but now we’re as afraid as we’ve ever been,” he says. “Depression could destroy all the progress we’ve made.”

Despite the ambiguity and upheaval, Tim says, “we have nothing but gratitude for where we are today and for the support we’ve received.” Manley, he says, deserves a huge amount of credit for Steve’s progress thus far. “His miracles are just as valuable outside the operating room,” Tim reflects, referring to the emotional support Manley provided his family.

Soon, the McConnells and millions of other families impacted by TBI might gain more clarity about what lies ahead and more support for their journey after an injury. “We now have the statistical tools, the imaging tools, and the blood biospecimen tools to understand traumatic brain injury so much better,” Manley says. “We’re sitting on the world’s largest collection of advanced imaging data for TBI patients – and we might have the largest clinical neuroscience data set that has ever been amassed.”

In the coming years, Manley and his team will work to mine that data to answer fundamental questions about TBI and to ensure that every patient gets the best possible care. With objective biomarkers and the ability to predict how a patient will do after injury, they should be able to diagnose traumatic brain injury more quickly and precisely, make smart recommendations about short- and long-term care, conduct better drug trials, and push for adequate insurance money to be allocated for rehabilitation.

“I think we’re on the threshold of changing the way this disease is addressed at every level,” Manley says. “We can and will create a new normal for patients after a traumatic brain injury.”

76 billion: Estimated annual direct and indirect costs from TBI

Find more news about TBI at medium.com/ucsf-magazine
In July 2017, UCSF scientists reported that an experimental drug had completely reversed severe learning and memory impairments caused by TBI in mice. The drug, known as ISRIB, fully restored the ability of the brain-injured mice to learn and remember, even when the animals’ first treatment was as much as a month after the injury.

Most research on brain injury has suggested that treatments must be initiated as quickly as possible to preserve normal function, making the latter aspect of the results particularly striking.

The study offers a promising new avenue for treating TBI in humans. “We need to do much more research,” says Susanna Rosi, PhD, whose team led the study. “But I have high hopes that this drug can bring back lost memory capacity to our patients who have suffered brain injuries.”

ISRIB was discovered in 2013 in the lab of Peter Walter, PhD, a UCSF professor of biochemistry and biophysics and winner of the 2018 Breakthrough Prize in Life Sciences. “These results are extraordinarily exciting,” says Walter. “We think that ISRIB may uncover an untapped reservoir in the brain that allows damaged memory circuits to be repaired.”

The drug was licensed in 2015 to Calico, a company working to understand the biology that controls human life span.

Scientists in Rosi’s lab tested ISRIB – which had previously been shown by Walter’s team to enhance memory in normal mice – in mice with two different types of brain injury, both of them known to degrade learning and memory in humans. The goal was to see if the drug could also improve the mice’s ability to learn and form memories. “In general, animals with these injuries never learn well again,” says Rosi, who is director of neurocognitive research in UCSF’s Brain and Spinal Injury Center. “So it’s remarkable that ISRIB could restore the ability to form new memories even when we delayed giving the drug for four weeks after the injury. This has not been considered possible.”

PHOTO: STEVE BABULJAK

EXPERIMENTAL DRUG REVERSES MEMORY FAILURE CAUSED BY TBI

By Pete Farley
Q&A WITH ATUL BUTTE, MD, PHD. Butte wears many hats at UCSF: professor of pediatrics, director of the Institute for Computational Health Sciences (ICHS), and the Priscilla Chan and Mark Zuckerberg Distinguished Professor. He is also executive director of clinical informatics for UC Health, the infrastructure uniting all six UC medical centers: UCSF, UC Davis, UC Irvine, UCLA, UC Riverside, and UC San Diego. Butte and his team are harnessing the collective power of UC’s systemwide biomedical data – which he sees as a first step in building a massive global database that will someday enable precise, targeted, accountable care in California and around the world.

WHAT KIND OF DATA ARE WE TALKING ABOUT?
Some data is easy to get at – like electronic medical records [EMRs], lab results, admissions notes. Some is more scattered – like DNA samples, gene expression data, clinical trial records. We’ve invested millions of dollars in EMR systems and cool gizmos like wearable medical devices to generate more and more data. Much of it is accessible with the right governance and permissions, and it’s more than enough to make a difference. But we’re really not doing much with it at this point. Data by itself does nothing. We have to turn it into knowledge to effect changes in policy and behavior. All this data is just sitting there, waiting for us to ask the right questions.

HOW DO WE MAKE SENSE OF IT?
We need to train people to ask, “What can I do with it?” Biomedical big data is, by definition, big, raw, and messy. The more we have, the more amazing it is. But the hard part is figuring out what to do with it. The solution is to educate – and inspire – more data scientists, people trained in biomedical and computer sciences and statistics. Companies offer high salaries to snap up these folks, so it takes dedication for them to stay in academia. We might need to start training and recruiting even earlier, in high school.

WHAT KINDS OF PROBLEMS CAN YOU SOLVE WITH BIG DATA?
Say you’re researching a treatment for liver cancer. You could start with millions of chemicals and petri dishes full of cells and eventually get a drug into a clinical trial, which costs a billion dollars and takes 15 years. But start with the data instead, and a dedicated researcher can launch a data-driven experiment for just $50,000. In fact, ICHS researcher Bin Chen did exactly that for hepatocellular carcinoma. [See sidebar.] It’s known as drug repositioning: We take data on tens of thousands of drugs – some already approved for human use – and match them with gene expression data on a given disease, looking for drugs made for another purpose that can affect this disease. It’s like Match.com for drugs. Data can also lead us to other solutions, like designing a more specific blood test, or eliminating unnecessary blood transfusions, or creating maps of disease and death that show us how a disease will behave over time.

WHERE IS ALL THIS LEADING US?
If we want to change the world, we need to do something with our data and discoveries; we can’t just keep writing papers. For example, the ICHS is working with all six UC medical centers to aggregate 15 million patient records – strictly regulated to safeguard privacy – into one safe, secure, reliable repository. There’s no other set of academic medical systems in the U.S. with as much patient data and as much computing power to analyze it as UC has. This is where we need to start if we are going to get all our data in one place. Not just UCSF’s data, not just UC’s data, but everyone’s data – what care we provided, what worked, what didn’t work. We can then predict what will happen with any given patient or any given disease in any environment over the next 90 days or year or 10 years. We’ve got to get there so we can provide truly customized, precise, and accountable medical care for everyone.

As told to Patricia Meagher
Here are three of the projects that researchers at the Institute for Computational Health Sciences are working on:

**Passion can make a curious researcher even more curious.**

**BIN CHEN, PHD,** is a native of China, where there’s a high incidence of hepatocellular carcinoma (HCC), a leading cause of cancer deaths. Searching through publicly available gene expression data, he found 274 genes that regulate cancerous liver tissue. Then, among drugs known to target those genes, he discovered a deworming pill that, in combination with standard HCC therapeutics, was highly effective at killing cancerous tissue. The approach could help turn HCC from a lethal disease into a chronic condition.

**Could the ubiquitous smartphone serve as a tool for managing health? Absolutely, says IDA SIM, MD, PHD, who studies mobile apps and sensors designed to track patient data. Users get real-time feedback to help them manage chronic conditions and maintain better health; they can also share the data with their physicians. Sim cofounded Open mHealth, a nonprofit that supports mobile app and data integration through an open software architecture. She is also developing data-sharing methods that could speed up clinical trials and bring down their cost.**

**Each year, 15 million babies worldwide are born prematurely, putting them at risk for serious, lifelong complications. MARINA SIROTA, PHD, is part of a multidisciplinary team that’s investigating immunity – specifically, the tolerance mechanisms that prevent maternal and fetal immune systems from rejecting each other in healthy pregnancies. Sirota’s lab is also building an integrated data repository for collaborative studies on adverse pregnancy outcomes and advancing management and prevention strategies by studying genetic, environmental, and clinical factors that may contribute to preterm birth.**
Time for Joy

Stopping a rare disease in a new genomic era

By Claire Conway

Joy Littlesunday hams it up with her parents, Jarvion and Christina, on a visit back to UCSF Benioff Children’s Hospital San Francisco, where she received a life-saving bone marrow transplant at age 2 months.
Joy Littlesunday is an irresistible kid with a gravitational pull that triggers a hug from every person who crosses her path. She has boundless energy and an insatiable desire to connect. Though only 4 years old, Joy is making up for lost time. She was born with a genetic disorder that left her without an immune system – which meant that merely brushing against someone with a cold could have been life-threatening for her. A bone marrow transplant performed at UC San Francisco when she was 2 months old saved her life. Her condition, severe combined immunodeficiency (SCID), if undetected can be lethal by the time a child turns 1 year old. It’s a disease that haunts Navajo families like Joy’s, who are at a far higher risk of SCID than the rest of the population. But now all babies born in the Navajo Nation are screened for SCID using a test that the tribe played a crucial role in making possible.

Babies born with SCID, a group of rare disorders, lack the capacity to produce functional forms of the immune system’s big guns – B and T cells. B cells and T cells collaborate to detect and attack invaders and to identify and kill infected cells. Together, they insulate us from life’s daily insult of infection and disease. But havoc can be wrought in this precisely calibrated process by a mutation in a single gene. Joy’s mutation was in the DCLRE1C gene, giving her an unusual form of SCID, known as SCIDA, which occurs with greater frequency among Athabascan speakers, in particular Navajo and Apache Indians. Joy was 2 weeks old when she screened positive for SCID.

The results initially seemed inconclusive, however, and the reservation doctor, an expert on SCID, was out of town when the test results came in. So the clinic staff instructed Joy’s mother, Christina, to head home and keep her baby isolated until they could verify the results. Home was on the reservation, in a house with no electricity or running water (though with a view of the sacred San Francisco Mountains, which are part of the Navajo story of origin). The Littlesundays – whose surname derives from the fact that Joy’s great-grandfather picked up goods at a trading post on Saturdays, a day referred to in Navajo as “little Sunday” – had to haul in water from eight miles away. The water was fine for washing and showers, but not for drinking. “I took her home and bathed her in this water,” Christina recalls. “When I think about it now...”

Her guilt is as visceral as it is undeserved for a woman who, soon thereafter, tore herself away from all she knew to get her daughter the bone marrow transplant that would spawn her a new immune system. “I was not ready for San Francisco or for anything medical,” says Christina, recalling her first trip to UCSF. “I just remember looking out the airplane window, thinking, ‘Wow, that’s a lot of water and a lot of lights,’” as she gazed down at the city she would call home for the next two and a half years – a city a thousand miles from the reservation. On that day some four years ago, Christina carried Joy tightly swaddled to a papoose board – a sacred crisscross of wood and ornaments – like a care package from a different place in time.

Mort Cowan, MD, performed Joy’s bone marrow transplant in a sterile hospital room just three miles from the Pacific Ocean. Cowan, a resident alumnus and the founder of UCSF’s bone marrow transplant program, had been working with Navajo families for decades by the time he did Joy’s transplant, as a drawer full of patient family photos attests. His UCSF colleague Jennifer Puck, MD, a pediatric immunologist, created the screening test that triggered Joy’s transplant. Through the decades, Puck has met countless families from all over the country who have lost a first child to SCID but caught the illness in a second child before it was too late. “Grandmothers talk about how a baby was sick all the time, or about how a pediatrician questioned whether they sterilized their bottles,” recalls Puck. “Why should you have to have a tragedy with the loss of one affected baby to save the life of a second baby?” That agonizing question compelled her to create a screening test for SCID. She and Cowan worked with the Navajo Nation to test the validity of the screen.
Then, in 2009, they started screening infants born in two Navajo hospitals. By the end of 2017, 48 states will be screening all infants for SCID, accounting for over 90 percent of all births nationwide. In a 2014 study involving data from 11 newborn screening programs that had tested over 3 million babies, Puck and Cowan showed that SCID has an incidence of 1 in 58,000 births, nearly double what was previously thought. And SCID is more frequent still among the Navajo people, at 1 in 2,000 births.

"Why should you have to have a tragedy with the loss of one affected baby to save the life of a second baby?"
—Jennifer Puck

A power tool
SCID's path out of obscurity tells a captivating story about the ascent of genetics and technology in medicine over the last few decades. Cells from patients with several forms of SCID will soon be used as a platform for an extraordinary technology – CRISPR. Discovered by Jennifer Doudna, PhD, a professor of chemistry and of molecular cell biology at UC Berkeley, CRISPR is a tool that enables scientists to edit the genome. While many bioethicists and scientists are wringing their hands with worry about potential rogue uses of the tool to edit human embryos, many of those same scientists, as well as clinicians and patients, are excited and hopeful about possible applications of CRISPR for correcting genetic defects within somatic cells, such as the cells that form the immune system.

Doudna and Puck, for example, use CRISPR to edit DNA sequences in blood-forming stem cells so that they can correct immune defects. "Jennifer Puck was my first clinical partnership," says Doudna. "She and I bring to the table very different expertise – I am a basic scientist, and she is a clinician. But together, we will do something potentially transformative for diseases with single mutations."

Studying diseases with single mutations, like SCID or sickle cell anemia, is particularly compelling because the target and the potential cause and effect of manipulating it are so clear. Yet SCID does pose a unique problem: People with SCID don’t have any T lymphocytes to begin with. “How do you study or treat a type of cell that isn’t there in the first place?” asks Puck. So the researchers must start with the stem cells that give rise to the mature T cells that are missing in SCID patients – bone marrow stem cells.

Puck and Doudna isolate blood-forming stem cells and, using CRISPR, edit the genes that encode the mutations that they find in affected patients. They grow the stem cells in cultures in a lab setting. “Even if you only have a few cells,” explains Puck, “you can make edits and recreate in a cell system the genetic problem that we seek to correct in a human. Then we can watch those cells and make them differentiate in tissue culture to see where they get stuck.” If some cells don’t get beyond a certain point, then that shows the researchers which gene is malfunctioning and needs to be corrected.

Old school
Mutations in any of at least 16 different genes can lead to SCID. Puck identified the gene for X-linked SCID, the most common form of the condition, back in 1993. Soon after that, Cowan identified the mutation in SCIDA. In the 1990s, the genome had not even been sequenced yet (that came a decade later, in 2003, and Puck was part of that effort, too, during a stint at the National Institutes of Health). “Back then, to identify mutations, we would gather many families to do what we called linkage analyses,” Puck explains. Cowan did that on the Navajo Nation. The process involved contacting members of families with multiple affected individuals and studying which portions of their DNA were co-inherited with the trait leading to SCID. It took 20 years from the time they started SCIDA studies to when they identified the gene and sequenced the Navajo mutation. “If we were starting today, it would probably take six months, because now we have the human genome sequenced and whole exome sequencing,” says Cowan, a professor emeritus and former chief of the Allergy, Immunology and Blood and Marrow Transplant Division at UCSF Benioff Children’s Hospital San Francisco. The exome refers to the 1.5 percent of the genome that encodes the proteins that form the building blocks of all of our cells, including cells of the immune system. So if there’s a functional flaw
in a baby’s immune system, it will often show up there. “If we’d had whole exome sequencing, we could have found it just like that,” says Cowan, snapping his fingers.

**The promise of gene therapy**

Cowan and Puck are now ramping up for a new clinical trial of gene therapy for SCIDA, the form of the disease that most affects the Navajo people. They will take blood-forming stem cells out of patients with SCIDA and will use what’s known as a lentivirus to insert a correct copy of the gene into the DNA of these cells. When the cells divide and differentiate into blood cells, the correct gene copy will persist, allowing maturation of functional T and B cells that will last throughout the life of the patient. Prior to receiving the gene-corrected cells back, patients will receive a very low dose of chemotherapy to clear out spaces in their bone marrow, giving the corrected stem cells a place to land and populate after being injected back into the patients. “The gene-corrected, blood-forming stem cells will become rooted in the bone marrow and grow an immune system for the patient,” says Puck.

SCIDA is the most difficult type of SCID to cure with standard bone marrow transplant therapy. Cowan and Puck will enroll both newborns and older patients with SCIDA in whom an initial bone marrow transplant was not fully successful. Many patients with SCIDA, including Joy, recover only T cell immunity after a standard transplant, making regular intravenous infusions of gamma globulin necessary. These infusions make up for the missing B cells that typically don’t recover in SCIDA patients even after a transplant. “The immune system is composed of single cells, unlike a solid organ,” explains Puck. And the immune system is portable, making it ideal for the planned gene-addition therapy. The stem cells that give rise to the immune system can be removed, modified, and replaced. “And the immune system remakes itself every day,” she adds. Hopefully the new gene therapy will give patients a second chance at a fully functioning immune system, allowing them to be free of gamma globulin infusions.

While Puck and Cowan are optimistic about the SCIDA trial – the use of a lentivirus to carry a correct copy of the gene into blood-forming stem cells – there are likely to be still more improvements in the future. The next step for SCID may be gene editing – taking out blood-forming stem cells from the marrow, correcting their mutation with CRISPR, and returning the corrected cells to the patient. But that still leaves the issue of having to create space for the corrected marrow. “The ultimate goal,” says Cowan, “would be to correct the defect by gene editing directly in the patient’s stem cells, without having to first remove them. This would eliminate the need to give any space-creating chemotherapy beforehand.” With only one gene to correct, SCID is an ideal target for such a treatment. Puck and Doudna’s professional partnership may make that come to pass as the technology is further refined.

**Grounding**

But as heady as the science is, it’s the people who are preeminent. Puck and Cowan never fail to board a plane for Arizona to hold an annual clinic on the Navajo Nation for their previously treated patients. They have known some of these patients for decades. After the clinic, all the patients and families and doctors get together for a barbecue to check in with one another.

“I remember my first patient get-together with Joy,” recalls Christina. Joy was just shy of 3 years old and was finally home, though not yet on the reservation. Joy and her family now live in a little house with running water and electricity on a street serendipitously named San Francisco. All the SCID families at the gathering, in a dusty garden outside the Navajo Indian Health Service Hospital, took turns telling their stories. “This one young lady stood up and introduced herself,” Christina says. “She was 20-something with twin baby girls. She had SCID. That’s when I realized that Joy has a whole life ahead of her.”

“**That’s when I realized that Joy has a whole life ahead of her.**”

—Christina Littlesunday, Joy’s mother
UCSF: The Campaign is taking on the world's most complex health challenges, powered by an exceptional community of mavericks, innovators, and advocates. Together we will make the Bay Area and our world healthier for all. Join us as we decode life to improve health, leverage discovery to revolutionize care, and partner to achieve health equity.

Learn more in the pages that follow and at CAMPAIGN.UCSF.EDU
ENGINEERED CELLS CAN MIMIC THE IMMUNE SYSTEM – HEALING ORGANS AND KILLING DISEASED CELLS PREVIOUSLY THOUGHT OUT OF REACH.

UCSF scientist Wendell Lim, PhD, programs cells to fight disease and is ushering in a new era of therapeutics. Right now, he and other UCSF researchers are programming immune cells to recognize, hunt, and kill diseased cells in cancers that were deemed universally lethal just five years ago. They’re offering not just short extensions of life, but in some cases cures. Yet the promise of cell engineering extends far beyond cancer. Engineered cells could someday halt dementia or repair damaged spinal tissue.
Asthma hits poor and minority communities especially hard and may be the best-known example of a health disparity. But what does it really mean to challenge such inequity?

Pediatrician Dayna Long, MD (left), pioneered a program that connects families to resources for issues like homelessness and food insecurity, which can have more impact on a child’s health than medical care.

Pediatrician Nooshin Razani, MD ’01, MPH (right), brings her young patients into the woods for a big dose of awe – and the better health outcomes her research has demonstrated.

Esteban Burchard, MD, MPH (facing page), recently discovered that most respiratory studies have included far too few minorities to be meaningful; he is undertaking the nation’s most comprehensive gene-environment study of asthma in minority children.

Esteban Burchard is the Harry Wm. and Diana V. Hind Distinguished Professor of Pharmaceutical Sciences II.
This country is plagued by racial and ethnic disparities in some of the deadliest diseases. Righting that wrong requires more inclusive research and more comprehensive models of care.
Patient-monitoring technology is alarmingly imperfect. With a false-positive rate of 89 percent, current equipment can cause “alarm-fatigued” nurses to ignore or switch off alerts and risk missing an emergency. At UCSF, David Mortara, PhD (center), a monitoring-equipment expert and philanthropist, is taking aim at the problem with a generous gift to the School of Nursing that will establish the Center for Physiologic Research. Working with Mortara, nurse-scientist Michele Pelter, MS ’95, PhD ’01 (left), and biomedical engineer Xiao Hu, PhD (right), are developing a next-generation technology that will not only provide a more complete picture of each patient, but also sound the alarm only when a nurse’s attention is truly required.
THE VISIONARIES WHO ARE LOOKING BEYOND MEDICINE TO TACKLE CHILDREN’S BIGGEST HEALTH RISKS
To prevent type 2 diabetes in low-income communities, physicians at UCSF are inspiring kids and teens to serve as agents of broader change.

Led by Kirsten Bibbins-Domingo, PhD ’94, MD ’99, MAS ’04, UCSF’s Center for Vulnerable Populations collaborates with Bay Area youth groups to get kids to create poetry, music, and videos about obesity and diabetes. The award-winning project has reached millions on YouTube.

Kirsten Bibbins-Domingo is the Lee Goldman, MD, Professor of Medicine.

Prematurity is the leading cause of death worldwide among children under age 5, and socioeconomics are the strongest determinant of an infant’s risk of prematurity. Larry Rand, MD, sparked the creation of the Preterm Birth Initiative at UCSF and leads the program in California. His team looks not only at genetics but also at social, economic, and environmental issues to develop a precise understanding of this epidemic – and how to stop it. (Another arm of the program, based in East Africa, focuses on interventions tailored for that region.)

Larry Rand is the Lynne and Marc Benioff Professor of Maternal and Fetal Medicine.
Who Are Impeding the World’s Deadliest Diseases

For Christine Sheridan, a doctoral candidate in biomedical sciences (right), working in the lab of acclaimed virus hunter Joseph DeRisi, PhD (left), is an opportunity to pursue unorthodox ideas.

DeRisi invented the Virochip, a virus detector not much bigger than a stick of gum. He used it to identify the SARS virus, then later adapted it to combat malaria. Malaria kills hundreds of thousands of children under age 5 every year, 95 percent of them in Africa. Those figures mean Sheridan’s own work, on blocking placental malaria, is potentially transformative. DeRisi’s work has also inspired Jayant Rajan, MD, PhD (rear), who studies tuberculosis.

Sheridan’s research is supported by the Discovery Fellows Program, UC’s largest PhD endowment, which funds nearly 700 PhD students in the basic sciences.

A $30-million gift from Sir Michael Moritz and Harriet Heyman launched the Discovery Fellows program in 2013.

Joseph DeRisi is the Gordon M. Tomkins Professor.
“JOE IS WILLING TO TRY ANYTHING ... AND CAN COME UP WITH WHAT SEEM LIKE CRAZY, OUT-THERE IDEAS THAT TURN OUT TO BE RIGHT.”

– Christine Sheridan
ANCERS ARE INHERITED CANCERS

THE RESOLUTE WHO ARE JOINING FORCES TO ERADICATE INHERITED CANCERS
The BRCA1 and BRCA2 genes significantly elevate a person’s chance of being diagnosed with multiple cancers – including breast, ovarian, skin, and prostate. Alan Ashworth, PhD, president of the UCSF Helen Diller Family Comprehensive Cancer Center, was part of the team that first identified the BRCA2 gene. Ten years later, he discovered a revolutionary way to kill off BRCA cancers by administering a drug that exploits a flaw in cells with the mutation. Physician-scientist Pamela Munster, MD, works at the intersection of research and care – translating laboratory discoveries in real time into treatments for her patients, who are in the most advanced stages of disease.

A carrier of the BRCA2 mutation herself, Munster knows firsthand the challenges of navigating multiple cancer risks for herself and her children. Together, she and Ashworth founded the UCSF Center for BRCA Research, which brings together the defining work of both their careers.

Alan Ashworth is the E. Dixon Heise Distinguished Professor of Oncology.

“We have an audacious goal: to end BRCA-related cancers in our children’s lifetimes.”
Who Are Mapping the Brain to Understand What Makes Us Human

Neurosurgeon Edward Chang, MD '04 (right), implants intricate networks of electrodes on the surface of patients’ brains to map regions that trigger epilepsy, control anxiety and depression, and enable speech. The goal: Pinpoint networks in the brain that go awry and try to remodel them to restore healthy functioning. His work bridges psychiatry, neurology, and engineering, and will ultimately answer questions about what makes us human. His team’s efforts could one day lead to an implanted device that emits a minute impulse to shift brain circuitry from unhealthy to healthy. Such a device could enable paralyzed patients to speak and move and help the brain “unlearn” depression and anxiety.

The work of Chang’s team is likely to radically change the way depression is diagnosed and treated.
Who Are Restoring Smiles and Hope

“They aren’t just fixing holes in people’s teeth…they are fixing holes in people’s lives!” says Jeff Eaton, DDS ’83 (left), faculty director of the UCSF Community Dental Clinic (CDC), about the student volunteers who run the clinic.

The clinic provides comprehensive no-cost dental services to displaced refugees, undocumented immigrants, and the uninsured homeless. Arvin Pal (below, right), a third-year student and the clinic director, says the people treated at the CDC see their lives change. “For the first time, they get to see a different, better version of themselves.”

Facing page (left to right): CDC student volunteers Julianna Ko, Victoria Nguyen, Michael Nguyen, and Avigael Lerman
“Doing this work changes our patients. It changes us. It’s what UCSF is all about.”

– Irene Cheng, DDS ’17
Who Are Stemming Diabetes in Vulnerable Communities

Mary Massella's journey to UCSF started in poverty. She left Guatemala, determined to get an education, and earned an MS in nursing at UCSF in 2017, thanks to a fellowship. Massella (left) is now not only thriving but also giving back to those facing similar challenges. Her faculty mentor, Maureen McGrath, RN, MS '95 (right), encouraged her to pursue the School of Nursing's pioneering diabetes minor program, which McGrath directs. Massella gained the tools she needed to care for the many families in her community impacted by the disease.
“MY OWN JOURNEY HAS BEEN NOTHING SHORT OF A MIRACLE, AND IT’S AN HONOR TO GIVE BACK.”

– Mary Massella
Who Are Helping Sick Kids Carry On – and Keep Learning

The Marie Wattis School at UCSF Benioff Children’s Hospital San Francisco is in session every weekday, with 10 teachers serving more than 60 students a day. Pictured here, teacher and schoolroom coordinator Erika Shue (second from right) leads students and volunteers in an interactive game called Hedbanz. She and her fellow teachers coordinate with the kids’ regular schools to provide academic continuity during hospitalizations as well as a place to have fun, stay positive, and, for a little while, feel normal.
Who Is Blasting through Boundaries to Cure Brain Cancer

Over the last 20 years, neurosurgeon Mitchel Berger, MD, has tripled the post-diagnosis life span of his patients with glioblastoma, an especially aggressive brain tumor. He’s achieved that with better-targeted drug delivery and radiation and advanced imaging that enables more aggressive but safer surgery. His research has also uncovered biomarkers in brain tumors that allow Berger, who is beloved by his patients, to offer them highly personalized therapies from the outset.

*Mitchel Berger is the Berthold and Belle N. Guggenheim Professor.*
ALUMNI HUB

We invite you to get involved!

Join UCSF Connect, our networking platform for alumni, students, residents, fellows, and postdocs. With more than 1,200 followers, it’s a great place to connect with colleagues and keep growing in your profession. Don’t miss Alumni Weekend, our flagship event taking place June 1–2, 2018, at the Hyatt Regency San Francisco, where you might run into UCSF alumni like those profiled in these pages. Look for your invitation in early 2018 or register now online. And learn more about UCSF: The Campaign, our $5-billion fundraising effort and the nation’s largest university campaign focused exclusively on driving innovation in science and medicine.

SCHOOL OF DENTISTRY

Yan Kalika: Master of beautiful smiles for children

When Yan Kalika, DMD, MS ’01, resident alumnus, arrived in San Francisco in 1989 from the former Soviet republic of Moldova, he didn’t speak English. But he was a professional chess master, had strong math and science skills, and was motivated to be successful. At that time, the Bay Area was still recovering from the Loma Prieta earthquake, so Kalika quickly found a construction job reinforcing damaged building foundations. He also started taking English classes at City College and planning for his future.

Soon he was attending UC Berkeley, where he was a member of Phi Beta Kappa, and then Harvard, where he earned a DMD. Hoping to practice orthodontics in San Francisco, he headed back west to UCSF for orthodontic specialty training and a master’s degree in oral biology.

Now, after travels and training around the world, he practices at Image Orthodontics, which he founded in 2002.

“I love putting beautiful smiles on kids’ faces,” he says. Helping others has always been a priority for Kalika. For his UCSF master’s thesis, he studied how to improve access to orthodontic care for California’s underserved communities.

Today, he serves on the UCSF School of Dentistry’s Advisory Council and Dean’s Council, as well as on the boards of several medical-dental device companies, striving to improve the patient experience and patients’ overall health.

In his practice, he keeps orthodontics fun by playing music in the office and celebrating the accomplishments of both patients and staff. He also finds that his chess skills come in handy.

“Orthodontics is almost like a chess game for me. I look at the beginning and end of the game, count the moves, and figure it all out in my head — so I can achieve the ideal facial balance and make the teeth perfect.”
SCHOOL OF MEDICINE

Bonnie Gutierrez: Caring for kids, inside and out

After completing her MD at UCSF, Yvonne “Bonnie” Gutierrez, MD ’92, headed south to Children’s Hospital Los Angeles for her pediatric internship, then her residency, then a fellowship. Twenty-five years later, she’s still there.

“I love that we care for a lot of underserved patients,” she says. “Children are especially interesting little puzzles, because they often can’t tell you what’s wrong.” Also a clinical professor of pediatrics at the University of Southern California’s Keck School of Medicine, she teaches students from high school through medical residency, often modeling the great teachers she remembers from UCSF.

“All of my professors were so approachable and so smart,” Gutierrez says. She recalls that, on the first day of her first-year anatomy lab, her professor, Sexton Sutherland, PhD, had memorized the name of every student in the class. And she credits Lawrence Tierney, MD – longtime associate chief of the medical service at the San Francisco VA Medical Center and a resident alumnus – with inspiring her to pursue primary care.

“I truly believe UCSF was the best place to go to medical school,” Gutierrez adds. Another bonus: That’s where she met her husband, Steven Lerman, MD ’92, a pediatric urologist at UCLA Medical Center. With their son and daughter now in college, they hope to have time to travel and renovate their home.

But at work, her focus is on helping others. Gutierrez is part of a multidisciplinary team that cares for children with craniofacial conditions, patients she finds especially rewarding.

SCHOOL OF NURSING

Deborah Yano-Ino: Once a nurse, always a nurse

A “wonderful adventure” is how Deborah Yano-Ino, RN, MS ’87, describes her career. “Nursing is an incredible profession,” she says. “It offers so many possibilities.”

Yano-Ino (formerly Yano-Fong) received her nursing training at UCSF, where she learned to think creatively, communicate clearly, and take on leadership roles. She joined UCSF’s nursing staff and within two years moved from bedside care into nursing management. She proceeded to take on other roles, including patient relations and clinical research.

“UCSF always provided new opportunities, so I never got bored,” she says. In 1988, when her son Andrew was born, she and another new mother, Susan Alves-Rankin, RN, MS ’87 (now manager of service excellence), proposed UCSF’s very first job share, becoming co-directors of patient relations. They set an expert example of balancing their professional and personal lives.

When the Health Insurance Portability and Accountability Act (HIPAA) passed in 1996, it ushered in a new era of patient protections. A few years later, then-Chancellor J. Michael Bishop, MD, tapped Yano-Ino’s experience and wisdom, appointing her UCSF’s inaugural chief privacy officer. Her role was to translate complex regulations into simple yet meaningful rules for staff, work she found engaging for more than 16 years, until her retirement last July.

That same month, she married John Ino, DDS, a volunteer UCSF faculty member who also teaches bioethics in Japan part-time, so the two fly back and forth frequently. She also enjoys volunteering at health fairs and, although she no longer has a formal role in health care, she says, “Once a nurse, always a nurse.”
SCHOOL OF PHARMACY

Glen Stimmel: Chiseling a place for psychiatric pharmacy

When he isn’t working at the University of Southern California (USC) School of Pharmacy, you might find Glen Stimmel, PharmD ’72, in his backyard, transforming heavy blocks of soapstone and alabaster into delicate carvings of faces and figures.

“I received a piece of soapstone and file as a birthday gift, and then I was hooked,” he says. “I’d been all science, all the time, and suddenly I’m creating sculptures. It’s pure fun.”

A man with many interests, Stimmel majored in Mandarin Chinese as an undergraduate at San Francisco State. He arrived at UCSF School of Pharmacy in the late ’60s, when everyone was challenging the status quo – pharmacists included.

“Pharmacy students were questioning traditional practice, trying to get more directly involved with patient care,” he says.

Stimmel forged his own unique path, becoming the first pharmacy student to pursue a clinical clerkship in a psychiatric facility. He developed an inpatient psychiatric pharmacy elective, as well as the nation’s first psychiatric pharmacy residency program.

Realizing that this new specialty could make a real difference for patients, he arrived at USC in 1974 and launched its School of Pharmacy’s first clinical psychiatric program. Now a professor of clinical pharmacy, psychiatry, and behavioral sciences and the associate dean of academic affairs, Stimmel focuses his clinical work on depression. He also served as interim dean of the school in 2015-16.

“About every dozen years,” he says, “I have to change what I’m doing to keep myself entertained.”

GRADUATE DIVISION

Karen Ring: Sharing her knowledge of stem-cell science

After years studying stem cells, Karen Ring, PhD (Biomedical Sciences) ’12, made a sudden career change when she felt drawn to writing about science rather than doing it.

“I appreciated my time in the lab, but I focused on just one disease and one model,” she says. “I was interested in science education and communicating about other diseases.”

Inspired by her parents, who were both scientists, Ring spent many weekends in her father’s lab, where he developed drugs for treating metabolic disorders. “I had so much fun, and he was a good teacher,” she says. “He instilled in me a passion for scientific questions.”

Later, her father’s diagnosis with Parkinson’s motivated her to pursue the biological sciences all the way to a PhD. While a graduate student at UCSF, she developed a method of reprogramming mouse and human skin cells into neural stem cells. The goal of her study, published in Cell Stem Cell in 2012, was to develop patient-specific models of Parkinson’s, Alzheimer’s, and other neurodegenerative diseases – in the hope of uncovering biomarkers for new diagnostics and therapeutics.

Now, as website and social media manager for the California Institute for Regenerative Medicine, she’s helping laypeople understand stem cell research. She also oversees an internship program for underserved high school students and is president of the UCSF Graduate Division Alumni Association and vice chair of San Francisco’s Women in Bio chapter.

“My advice to current doctoral students is to think a few steps ahead and start networking right away. Science PhDs have a wide range of career possibilities, and you can’t predict your journey.”

For 40 years, I largely avoided any administrative role, but now I really enjoy it. I’ve had a wealth of experience, and I think that helps me make the big decisions.”

HOMETOWN: Lancaster, Calif.
NOW: Pasadena, Calif.

HOMETOWN: Redwood City, Calif.
NOW: San Francisco
Brainy Bridge

When she’s not engrossed in engineering proteins, neuroscientist Ashley Smart, PhD ’17, spends her time painting and drawing. One day, she noticed that the beams and supports of the Bay Bridge look astonishingly like neurons. Her vision came to life in this illustration, with the bridge transformed into a neuronal network and neurons also filling the city’s buildings. “Science and art both let me explore the world and share the wonder of how life works,” Smart says. See more of her illustrations at questioninglines.com.
For 40 years, Stephen Hauser, MD, fought scientific convention to pursue an idea that has revolutionized our understanding of multiple sclerosis (MS) and laid the foundation for a remarkable new drug that halts the disease in its tracks. This is the kind of breakthrough science that you support when you give to UCSF. Thank you for being one of the visionaries who make this work possible.

After demonstrating that B cells (above) play an active role in MS, Hauser helped create the first MS drug to target them.

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