UCSF
MAGAZINE
Fall 2013

THE PROMISE EMERGES

Harnessing data to personalize care

PRECISION MEDICINE SPECIAL ISSUE

UCSF MAGAZINE
FALL 2013

Postdoc Pranidhi Sood, PhD (left), and graduate student Mark Slabodnick (right) conduct research in the lab of Wallace Marshall, PhD. Read about Marshall's work on page 20.

FEATURES

DEPARTMENTS

COVER ILLUSTRATION: MARTIN KRZYWINSKI; THIS SPREAD: STEVE BABULJAK

Early in my career, when I was in clinical practice, a 28-year-old mother came to see me with a very aggressive form of breast cancer. She was a new mom, with a wonderful baby, a loving family, and what should have been a long life ahead. But despite my best effort, I could not save her.

Millions of people like that young mom suffer and die because we are not more rapidly creating the right medicines. A pioneering new field – precision medicine – promises to change that. Precision medicine aims to integrate a wealth of data arising from both the human genome and studies on the molecular basis of disease with information on environmental factors and patients' electronic medical records. Already well under way, the integration of this data is informing lab research and clinical care across the spectrum – and is leading to better diagnostics and treatments customized for individual patients.

In this issue of *UCSF Magazine,* you will learn more about how our faculty are tapping the unprecedented potential of precision medicine, and how their efforts are helping to define the future of this extraordinary field. From hosting the first global OME Precision Medicine Summit, to building the platform that will give shape to the field, to educating future leaders in precision medicine, UCSF is guiding the world toward a day when all patients receive medical treatments tailored specifically for them – increasing markedly their chance of living a long and healthy life.

Susan Desmond-Hellmann, MD, MPH
Chancellor
Arthur and Toni Rembe Rock Distinguished Professor

UCSF MAGAZINE

FOR ALUMNI AND FRIENDS

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PHOTO: THOMAS BROENING

DIALOGUE

TWEETS AND POSTS FROM THE UCSF UNIVERSE

Buzz from the OME Precision Medicine Summit

@genentech: Hal Barron: "Over 90% of drugs fail to make it through the development pipeline – we need to do better as an industry"

@sharonfterry: We must change our language from THEY to WE. It is about US. Precision medicine will be transformed through our shift.

@DrKhouryCDC: Success of #precisionmedicine requires medicine-public health collaboration #OME2013

@atulbutte: Steven Burd CEO Safeway: healthcare is like Safeway with no price tags! And it becomes free when you hit out of pocket max! Crazy #ome2013

@lelandkim: Goal: collect 1 million data sets to launch precision medicine for better health and lower cost.

@Duncande: An amazing assemblage of thinkers, innovators, leaders at #ome2013 at UCSF, my brain is tired with all the ideas swirling.

See the related story on page 12.

More Buzz

@latimeshealth: Videogame created @UCSF teaches senior citizens to multitask as well as folks in their 20s. Result: Better memory.

@AtulGroverMD: Listen up if boarding a plane w @SamuelLJackson MT @UCSF: How to survive a snakebite, with a nasal-spray http://bit.ly/16JHNZ5

@SFGiants: Pablo Sandoval visits with children at UCSF Benioff Children's Hospital this morning. pic.twitter.com/tRhxekeFuY

@scifri: "One size doesn't fit all when you're diagnosed with cancer. Cancer is not an emergency." – Laura Esserman of @UCSF

David Vlahov is the Dumbledore of nursing school deans. I have boundless respect for that man!

– Steven T. Johnson via School of Nursing Alumni Facebook page

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Genetics may contribute to pain following breast surgery, according to a first-of-its-kind study.

PAINFUL PREDISPOSITION

After breast cancer surgery, many women experience lingering, persistent pain that surgeons can't explain and that some even deem irrelevant. Yet according to a recent study by Christine Miaskowski, RN, PhD, a professor in the UCSF School of Nursing, postsurgical pain syndrome is not only quite real, it is common – and possibly genetic.

Miaskowski's research shows that after surgery, some 25 percent of women experience persistent pain in their breast and 35 percent in their arm or shoulder. Though the sensation is thought to arise from nerve damage, her work shows that the most widely prescribed medications are antidepressants. "Why these women were not on pain medicine, we do not know," says Miaskowski, a postdoctoral alumna who holds the Sharon A. Lamb Endowed Chair in Symptom Management Research.

Digging deeper into the origins of such pain, Miaskowski and Bradley Aouizerat, PhD, a molecular geneticist, uncovered two sets of genetic markers – one for breast pain, the other for shoulder and arm pain. It was the first formal study anywhere of the potential contribution of genetics to pain following breast surgery.

"The story is still unfolding, but it does look like there may be certain genetic characteristics that define risk for some pain complications," says UCSF neurologist Gary Abrams, MD, a co-investigator on the project. "Knowing these associations may be important in terms of who will develop pain, who will need to avoid certain types of treatment, and what the best pharmacological treatments should be."

Read more about this research at scienceofcaring.ucsf.edu.

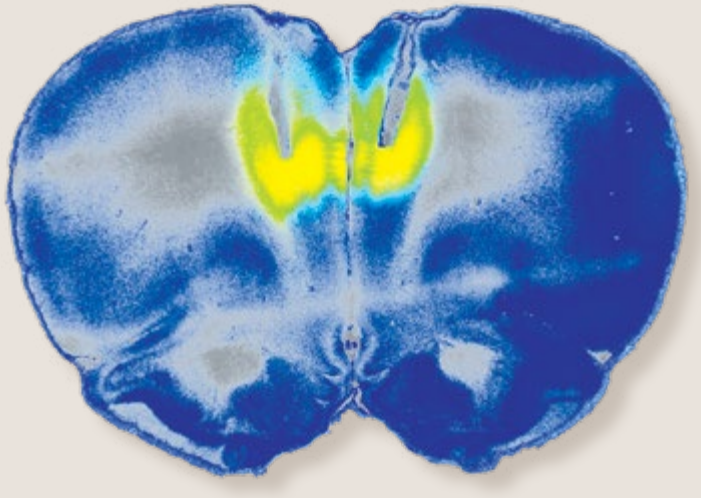
AN ADDICTION OFF-SWITCH

A recent study sheds new and potentially life-saving light on addiction — quite literally. With the shot of a laser to a specific part of the brain (see scan at right), researchers have successfully erased cocaine dependence in mice.

Scientists from UC San Francisco and the National Institutes of Health (NIH) reported in the journal *Nature* that they found very little electromagnetic activity in the prefrontal cortexes of cocaine-addicted mice. But "when we turn on a laser light in the prelimbic region of the prefrontal cortex of the mice, the compulsive cocaine seeking is gone," says Antonello Bonci, MD, an adjunct professor at UCSF and the scientific director of the intramural research program at the NIH's National Institute on Drug Abuse, where the work was done. When the researchers deactivated the nerve cells, the cocaine-seeking behavior resumed.

The research suggests that a modified form of the new therapy could be tested immediately in cocaine-addicted humans, who have been shown to exhibit the same lack of electromagnetic activity in the prefrontal cortex. Called transcranial magnetic stimulation (TMS), the treatment involves electromagnetic stimulation outside the scalp. It is a modality that has already been successfully used in the treatment of depression.

Clinical trials are currently being designed to see if the same effect applies to humans. The research has the potential to radically change the societal and personal toll of cocaine in this country. Approximately 1.4 million Americans are addicted to the drug. It was the cause of nearly half a million emergency room visits in 2008 alone and is a top cause of heart attack and stroke in people under age 35. And beyond its detrimental effects on health, cocaine use is also a source of crime, incarceration, and lost wages.



PHOTOS: TOP, KHENG HO TOH; BOTTOM, BILLY T. CHEN

PINSTRIPED LAB COATS

Industry veterans teach UCSF students how to commercialize their ideas.

Students in UC San Francisco's Idea to IPO course are thrown headfirst into entrepreneurship. The reward for their hard work goes beyond a grade, with a substantial cash prize going to the team that creates the most commercially viable business model.

Seasoned entrepreneurs, industry experts, and mentors dispense straight-from-the-trenches expertise to help students learn how to commercialize an invention or practice. The 70 or so students in this year's course were a mix of postdocs, PhD students, residents, and faculty. They formed teams to focus on an idea, assess its market potential, and create a business model. Students also learned about such critical parts of the process as clinical trials, regulations, intellectual property law, and operational basics.

First place went to a team that created a new sensor-based approach to brain mapping called Spiria, which appears to be safer and faster than current methods. "This class was a great introduction to business," says Anuradha Madhavan, PhD, a member of the Spiria team and a postdoc in neuroscience. "You learn from people in the industry and listen to them firsthand. It helps to have that exposure."

The prize money came from G. Steven Burrill, chief executive officer of Burrill & Company, a global life sciences investment firm based in San Francisco. "Most scientists, by and large, wouldn't know what a business is," he says. "We brought people with $10 billion or $15 billion in venture capital into the room."

The course is offered through UCSF's Entrepreneurship Center, which is run by Stephanie Marrus. An industry veteran, she joined UCSF a year ago with the goal of starting companies and raising the level of understanding within the institution about commercialization.

The six new life-sciences companies generated each year by the course are proof positive that students don't have to choose between science and entrepreneurship – they can do both.

PHOTOS, FROM LEFT: SUSAN MERRELL, GIUSEPPE COSTANTINO

"I had thought it was going to be a gimmick, but after [trying it] I became a zealot."

Cardiothoracic surgeon Pierre Theodore, MD, on using Google Glass in the operating room, quoted in a ***Wall Street Journal*** blog

STAYING POWER

Palav Babaria, MD, was working her first shift in a rural Haitian hospital when she was informed of a man in the ICU with end-stage kidney failure. In-country for only 12 hours, Palav learned the hard way that there was no formal referral process to hospitals in Port-au-Prince, three hours away. There were no Haitian doctors available right then, and the local ambulance was on another call. "We finally got an ambulance from another town. I scribbled down some notes and sent him on his way," recalls Babaria, a UC San Francisco Global Health-Hospital Medicine Fellow. "I have no idea whether he even made it."

Several months later, Babaria had to refer an HIV-positive woman to another hospital. This time, her colleague Pierre Jacquelin Auguste, MD, a physician trained in Haiti, called up a friend at a hospital with many HIV specialists. He explained the case, made sure the patient had a bed, and arranged transport. "Everything happened at the snap of his fingers because he knew the local resources," says Babaria. "In global health, there is just no substitute for local knowledge."

> "Everything happened at the snap of his fingers because he knew what the local resources were. In global health, there is just no substitute for local knowledge."

The experiential wisdom garnered from working in the developing world is critical for physicians like Babaria, who intends to devote her career to enhancing care in resource-poor areas. "In a setting where there are few formal processes in place, the ties between local professionals are lifesaving," she says. "Partnering with in-country colleagues to develop systems out of their informal relationships is a great solution going forward."

Leaving systems in place, as well as educating local providers to carry them out, represents both the goal of the Global Health-Hospital Medicine Fellowship (GHHMF) – the first fellowship of its kind in the world – and a paradigm shift in global health. "Over the years, global health and tropical disease eradication movements have had some great successes, including the smallpox vaccination program and the headway we've made with HIV," says Sriram Shamasunder, MD, who co-founded the GHHMF with Phuoc Le, MD, MPH. "But they left little infrastructure."

GHHMF fellows, by contrast, work in public hospitals and are actively engaged with the ministries of health and nongovernmental organizations in their host countries of Haiti, Liberia, and India. "Our fellows work with the public sector on long-term quality improvement projects driven by local people and organizations," says Shamasunder.

The fellowship also seeks to train the next generation of global health leaders. As the burden of chronic disease continues to rise worldwide, those leaders must bring hospital-based tools to the field to manage the complexity of care. Babaria estimates that nearly half her patients suffer from chronic diseases, with heart failure being the most common diagnosis. "Ideally we would like to see our patients with heart failure, hypertension, or diabetes once a month to track their progress," she says. But asking patients to make frequent treks to the hospital poses too big a burden. Typically, a patient would have to walk for hours to reach a main road, then spend a month's salary to hire a motorcycle for the last leg of the trip. Only the sickest made the journey. "I knew if my patient was a mother that there were children home, unattended," says Babaria. "And if my patient was a father, no one was earning a wage that day."

Global Health-Hospital Medicine Fellow Palav Babaria (at center, in scrubs) worked closely with colleagues at a Haitian hospital to develop lasting health care solutions.

By the year's end, Babaria and her in-country colleagues had developed a chronic hypertension clinic – run by Auguste – to address the enormous toll of chronic disease.

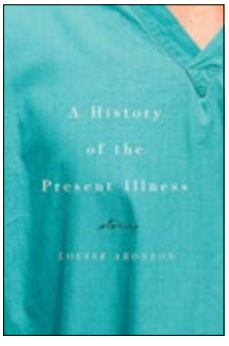
Shamasunder hopes the fellowship will be a new prototype for global health. "We want to create a longitudinal model, where we mentor the local population, learn from them, and create reliable and predictable protocols that improve the lives of the poorest," he says.

UCSF FACULTY ON THEIR SET-IN-SAN FRANCISCO BOOKS

Louise Aronson, MD, resident alumna

A History of the Present Illness

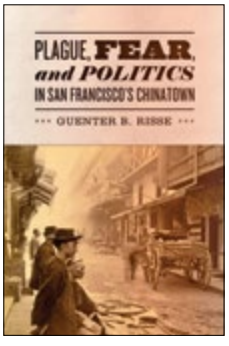
"I wanted to write a medical book that made reading about doctors, patients, and medicine as pleasurable as reading a good novel, and on the exact same pages I wanted to write a literary book that was brutally honest about the challenges, pleasures, and ambiguities of life, illness, and doctoring [in San Francisco]."



Guenter Risse, MD, PhD

Plague, Fear, and Politics in San Francisco's Chinatown

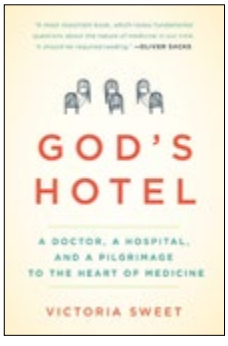
"History often repeats itself. I wanted to contribute to our understanding of AIDS in San Francisco by presenting a somewhat similar episode involving another deadly infectious disease and a stigmatized local population: the Chinese."



Victoria Sweet, MD, PhD '03

God's Hotel: A Doctor, a Hospital, and a Pilgrimage to the Heart of Medicine

"I was walking across Spain and thinking about the three books I wanted to write – the one about my patients [at San Francisco's Laguna Honda Hospital] and slow medicine, the one about health care politics and the 'efficiency of inefficiency,' and the one about Hildegard of Bingen and the 'greening power of nature.' Suddenly I realized: it was just one book."



STICKER SHOCK

The next time you're looking for affordable emergency room care, you might want to shop around. A team of researchers led by a member of the UCSF faculty identified giant discrepancies in patient charges for the 10 most common outpatient conditions seen in emergency rooms across the country.

Out-of-pocket patient charges ranged from $4 to $24,110 for sprains and strains; from $15 to $17,797 for headache treatment; from $128 to $39,408 for kidney stone treatment; from $29 to $29,551 for intestinal infections; and from $50 to $73,002 for urinary tract infections.

While the study was not designed to evaluate specific reasons behind these discrepancies, the investigators noted that previous research had attributed cost differences to variations in geographic location and provider reimbursement levels. What patients end up paying depends on whether they have insurance and what kind, says the study's senior author, Renee Hsia, MD, a UCSF associate professor and an attending physician in the San Francisco General Hospital and Trauma Center emergency department.

"Uninsured patients are stuck with the [full] bill. For privately insured patients, if they accidentally end up in an out-of-network hospital, or their annual limit has been reached, then they, too, may be faced with the entire bill," she says.

These wide and unpredictable variations in charges demonstrate the flaws in our health care system, Hsia notes. Information on medical pricing "is far too difficult to obtain," she says. "We need . . . more transparency, to better inform consumers," as well as "a more rational system of costs and charges."

"When she first saw the beating cardiomyocytes, she did a little dance."

Molecular pathologist Thea Tlsty, PhD, on the reaction of her postdoctoral fellow Somdutta Roy, PhD, upon learning that breast stem cells successfully created heart cells, quoted in *Smithsonian* magazine

PHOTO: DELIORMANLI

HEADS UP

Carlin Senter, MD, an assistant clinical professor of sports medicine, was recruited to UCSF four years ago to lead the concussion program. One year ago, she helped launch the Bay Area Concussion and Brain Injury Program in collaboration with UCSF Medical Center, UCSF Benioff Children's Hospital, and San Francisco General Hospital and Trauma Center.

Football, soccer, and biking injuries are the most common cause of concussions seen at UCSF.

What is a concussion?

Senter: An injury to the brain caused by a blow to the head, neck, or body. It's followed by an onset of symptoms – usually immediately, but sometimes delayed for up to 48 hours – including headache, confusion, difficulty concentrating or remembering, dizziness, problems with balance or coordination, fatigue, nausea, and depression or anxiety. Physicians diagnose concussion based on this classic history; there's no MRI or blood test that can diagnose concussion.

Who is most likely to experience concussion?

Senter: High school athletes – among boys, football players, and girls, soccer players. We also see a fair number of adults who were in bicycle accidents. There are 3.8 million sports- or recreation-related concussions in the US every year.

What's the best treatment?

Senter: Rest – both cognitive and physical. Take time off from work or from school, if necessary. Do not return to play on the same day as the injury and take at least a week or two off from physical activity. We recommend staying away from loud, crowded environments and video games because they're too stimulating, and we sometimes recommend taking a break from using a computer because that kind of eye movement promotes dizziness. And don't drink alcohol. The risk of repeat concussion is highest in the first seven to 11 days postconcussion, so it makes sense to wait and let your brain recover.

Are there patients who don't recover in the typical one to three weeks?

Senter: About 10 percent of people recover more gradually or didn't receive the right treatment off the bat. For patients with postconcussive syndrome, we run a monthly multidisciplinary clinic where we bring together a variety of experts in sports medicine, neurosurgery, physical medicine and rehabilitation, neurology, neuropsychology, physical therapy, and neuroradiology. We see patients as a team and come up with a comprehensive treatment plan.

What about long-term consequences, such as chronic traumatic encephalopathy (CTE)?

Senter: CTE is a progressive degenerative disease that can only be diagnosed on autopsy. It was found in former NFL player Junior Seau, for example. While concussion and CTE are associated, it has not been proven that concussion causes CTE. We need more research in this area. UCSF is part of a multicenter study looking at longitudinal risk in college football players compared to professional players. This fall we're kicking off a research project examining postconcussive syndrome patients to develop some objective tools for diagnosis. We're interested in correlating brain changes on MRI with how a patient is functioning.

Wouldn't it be safer to keep children from playing sports?

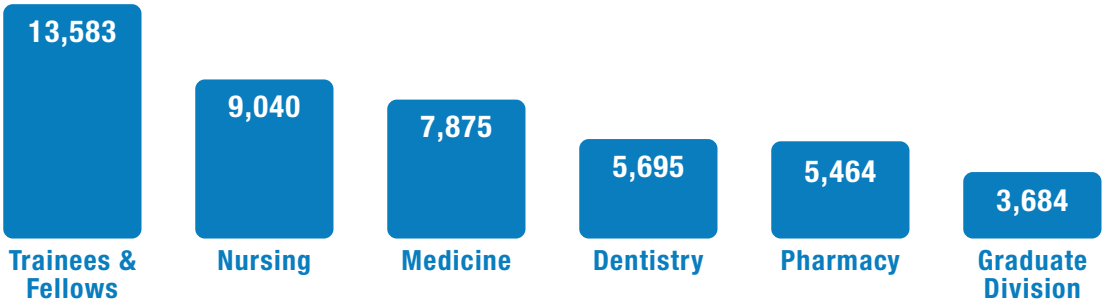
Senter: There are so many great benefits from playing sports. That's why I'm a sports medicine doctor. My main goal in being a physician is to help people be physically active, so if they're experiencing a pattern of head injuries, I help them to choose a sport that's lower risk. Rather than football, what about basketball? Rather than soccer, what about softball? You can still be an athlete.

Watch Carlin Senter discuss concussions on NBC News: bit.ly/ucsf-senter

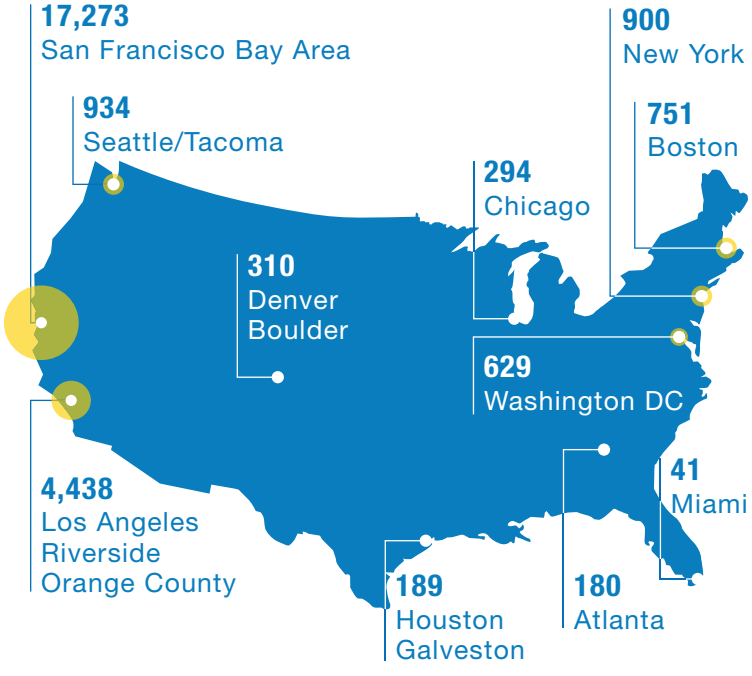
PHOTO: YOBRO10

UC SAN FRANCISCO ALUMNI: BY THE NUMBERS

45,341
TOTAL ACTIVE ALUMNI



ALUMNI IN SELECT US METROPOLITAN AREAS



2,640
Alumni married or partnered to other alumni

4,926
Alumni with more than one degree or training from UCSF

TOP EMPLOYERS

HEALTH
- UCSF Medical Center
- Kaiser Permanente
- San Francisco Department of Public Health
- Stanford University Medical Center
- Palo Alto Medical Foundation

RESEARCH
- Genentech
- Gilead
- Novartis
- Amgen
- Pfizer

ACADEMIA
- UCSF
- Stanford
- UC Berkeley
- UCLA
- Harvard
- University of Washington

INFOGRAPHIC: JOSE FERNANDEZ

"We as a profession have our corpus of knowledge, and we owe it as a profession to educate the lay public."

Amin Azzam, MD, MA, a resident alumnus and associate clinical professor who will teach UCSF medical students to edit Wikipedia articles about diseases, quoted in the *New York Times*

REACHING OVER THE COUNTER

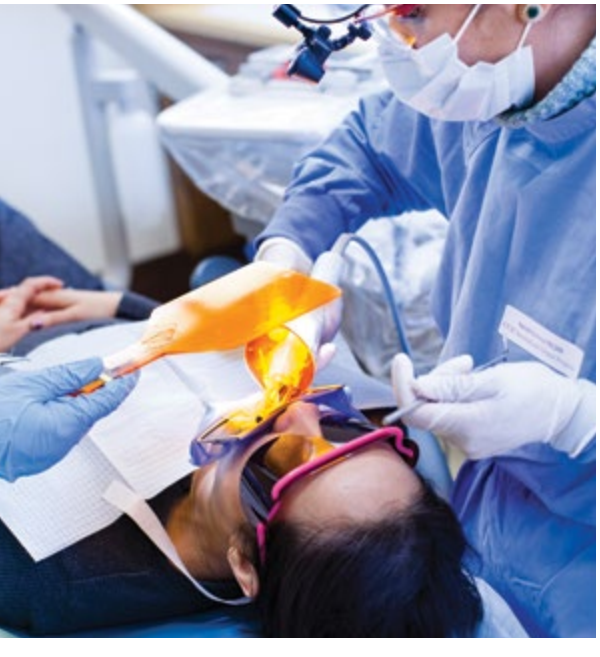
The UCSF School of Pharmacy, where the practice of clinical pharmacy was born, is once again expanding the role of pharmacists by partnering with Safeway Inc. to help the chain's customers quit smoking.

At 20 California Safeway locations, pharmacists were trained in UCSF's proven smoking-cessation techniques. The stores now locate nonprescription nicotine-replacement therapies near store pharmacy areas, giving customers convenient access to the pharmacist so he or she can answer questions. This is the first time ever that a smoking cessation intervention has been applied systematically across a network of pharmacies.

"Pharmacists are often the most accessible health care provider for patients within their communities, but we haven't maximized their expertise in that setting," says B. Joseph Guglielmo, PharmD, resident alumnus and dean of the School of Pharmacy. "This project offers Safeway customers the full patient care skill set of pharmacists, with a goal of helping customers prevent and manage their chronic conditions."

As part of the program, pharmacy teams use the "Ask, Advise, Refer" model, in which pharmacy technicians, clerks, and pharmacists routinely ask patients whether they smoke and, if they do, advise them to quit. For those who are ready to quit, pharmacists offer them information on medication options and refer them to the California Smokers' Helpline (1-800-NO-BUTTS).

The Safeway project included a three-month UCSF study led by Lisa Kroon, PharmD, resident alumna, and Robin Corelli, PharmD '89, to evaluate the program's impact. At the conclusion of the study, over 15,000 patients had been asked about their tobacco use. Approximately 1,300 patients were identified as current smokers, with almost 1,200 of those receiving smoking cessation materials and over 200 receiving advice from the pharmacist about smoking cessation medications.



FLOSS YET?

UC San Francisco researchers may have come up with yet another good reason to brush and floss regularly – to protect kidney health.

According to Vanessa Grubbs, MD, MPH, an assistant professor and kidney specialist at UCSF, preliminary studies suggest a connection between kidney disease and periodontal disease, which is an inflammation of the gums due to persistent infection. Research has shown that bacteria from diseased gums can affect the heart, and Grubbs suspects that gum disease can also put the kidneys at risk, possibly from bacteria traveling through the blood stream.

She is teaming up with two professors in the School of Dentistry – George Taylor, DMD, MPH, DrPH, and Mark Ryder, DMD – to create a first-of-its-kind yearlong study to track the progression of kidney disease in patients who are receiving treatment for periodontal disease.

"If we at least start to show that treating periodontal disease can slow the progression of kidney disease, the long-term ramifications for dental policy and how we manage patients with chronic kidney disease are huge," says Grubbs, a fellowship alumna who is based at San Francisco General Hospital and Trauma Center. Funding routine dental care for people at all income levels could potentially become a priority as a way to prevent kidney disease. "It's certainly cheaper to pay for preventative dental care than dialysis," points out Grubbs.

PHOTOS, CLOCKWISE: WIKIMEDIA COMMONS, TEIN, ELENA ZHUKOVA

FACULTY ACCOLADES

Adam Abate, PhD, received a prestigious National Science Foundation CAREER award, which will provide $750,000 in funding over five years. Abate, an assistant professor in the Department of Bioengineering and Therapeutic Sciences, a joint department of the Schools of Pharmacy and Medicine, is developing a new technology to allow scientists to determine in just a few days the genetic makeup and activity of each individual cell in samples as large as a million cells.

Three UCSF scientists were elected to the American Academy of Arts and Sciences, one of the nation's most prestigious honorary societies for top scholars, scientists, writers, artists, and civic, corporate, and philanthropic leaders. The new members include School of Medicine Professors **Arturo Alvarez-Buylla**, PhD, Department of Neurological Surgery, who holds the Heather and Melanie Muss Endowed Chair, and **Donna Ferriero**, MD '79, resident alumna, chair of the Department of Pediatrics, and the W.H. Marie Wattis Distinguished Professor; and **Regis Kelly**, PhD, director of the California Institute for Quantitative Biosciences.

Leslie Benet, PhD '65, won the 2013 Ebert Prize, the oldest US pharmacy award. The prize, administered by the American Pharmacists Association Academy of Pharmaceutical Research and Science, recognizes the best original investigation of a medicinal substance published in the *Journal of Pharmaceutical Sciences* during the prior year. The winning paper was co-authored by Maribel Reyes, PhD '10, who earned her doctorate in Benet's lab. Benet is a professor in the Department of Bioengineering and Therapeutic Sciences, a joint department of the Schools of Pharmacy and Medicine.

Two School of Medicine professors – **Michael Brainard**, PhD, Departments of Physiology and Psychiatry, and **Dyche Mullins**, PhD, Department of Cellular and Molecular Pharmacology – were selected to be Howard Hughes Medical Institute (HHMI) investigators. They were among 27 new investigators chosen from among 1,155 applicants and will receive financial support to pursue new, creative ideas.

John D.B. Featherstone, PhD, dean of the School of Dentistry, was selected as an honorary fellow of the Pierre Fauchard Academy, an international honorary dental organization. The academy, which "seeks to consistently focus on professionalism, integrity, and ethics worldwide," lauded Featherstone for his many contributions to scientific research and dental education.

B. Joseph Guglielmo, PharmD, resident alumnus, an honored School of Pharmacy professor and mentor, as well as a leading pharmacist and clinical scientist specializing in antimicrobial therapies, was named the school's new dean. Guglielmo, who joined the faculty in 1979, had served as interim dean since July 2012 and was previously chair of the school's Department of Clinical Pharmacy.

David Julius, PhD, chair of the Department of Physiology and the Morris Herzstein Professor in Molecular Biology and Medicine, was named the winner of the 2013 Dr. Paul Janssen Award for Biomedical Research. Julius won the award, which carries a $100,000 prize, for his discoveries of the molecular mechanism that controls the sensory perception of temperature and of its role in the sensation of acute and inflammatory pain.

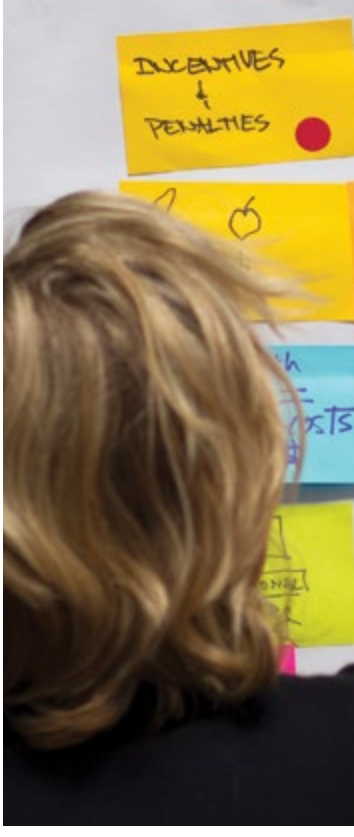
Thuan Le, DDS, PhD '07, received the 2013 Academic Senate Distinction in Teaching Award for faculty who have been at UCSF for five years or fewer. Le is an assistant professor in the School of Dentistry's Department of Orofacial Sciences and director of the postgraduate pediatric dentistry residency program.

Kathryn Lee, RN, PhD, associate dean for research in the School of Nursing, was inducted into the International Nurse Researcher Hall of Fame of Sigma Theta Tau International, a nursing honor society. Lee holds the James and Marjorie Livingston Endowed Chair in Nursing and is also a professor in the Department of Family Health Care Nursing. Her research focuses on women's health, with an emphasis on sleep patterns.

Sally Marshall, DDS, PhD, professor emerita in the School of Dentistry's Department of Preventive and Restorative Dental Sciences, received the 2013 Irwin D. Mandel Distinguished Mentoring Award from the American Association for Dental Research. The award recognizes outstanding efforts to foster and promote research training and career development of students, trainees, and junior faculty.

Dorothy Rice, BA, ScD (Hon), was selected as the 2013 winner of the William B. Graham Prize for Health Services Research (formerly the Baxter Prize), the highest distinction in that field. Rice, a professor emerita in the School of Nursing's Institute for Health and Aging, was recognized for her career-long emphasis on applying health economics and statistics to improve public health worldwide.

Alice Wong, MS '04, was appointed to the National Council on Disability by President Barack Obama. Wong is a research associate for the School of Nursing's National Center for Personal Assistance Services, which conducts research and training about personal care services that help people with disabilities live in the community.



SUMMITING the Precision Medicine MOUNTAIN

By Anne Kavanagh

The name OME is not an acronym but comes from the suffix -ome, which in biology is used to denote a totality of precise elements and their interrelationships. Thus the entirety of a person's genes forms a genome, proteins form the proteome, microbes form the microbiome.

ome

A call goes around your office for donations. But the volunteers leading this drive aren't seeking toys, books, or even canned goods – they want your genetic data.

You just might receive such a request soon if the ideas generated at the first global OME Precision Medicine Summit, convened by UC San Francisco, morph into reality. The concepts and plans that emerged from the summit this past spring – as unusual as some might sound today – could help make medicine more predictive, preventive, and precise.

PHOTOS: © 2013 DEANNE FITZMAURICE

From the left: UCSF Chancellor Susan Desmond-Hellmann addressing the participants; ideas posted on sticky notes; guide for the two action-packed days; Ann Wojcicki, CEO and co-founder of 23andMe, concentrating on a teammate's explanation; a facilitator from IDEO leading a brainstorming roundtable.

UCSF is pursuing this ambitious goal – which entails harnessing technological prowess, scientific acumen, and medical records – to better understand the roots of disease and develop targeted therapies. But the road to precision medicine is filled with challenges: How do we collect and analyze the vast amounts of genetic and biological data stored in different places and formats throughout the world? How do we encourage people to share their personal health details? How do we address regulatory barriers? How do we pay for it all?

Even individually, much less cumulatively, this is no small charge – which is why 170 top scientists, entrepreneurs, technology gurus, business executives, and government leaders found themselves at UCSF Mission Bay for two days in May.

Developed with the global design and innovation firm IDEO and staged inside the gym at the William J. Rutter Center, the summit was far from a talking-heads conference.

Surrounding a raised platform that served as a stage stood whiteboards covered with zigzagging charts and doodles. Comfy couches, and tables stacked with fluorescent Post-it notes, encircled the room. Coffee flowed freely.

In the midst of it all, luminous minds were hard at work.

"Today people are diagnosed with diseases – diabetes, breast cancer, lung cancer – and precision medicine is about connecting the dots in a new, data-driven way so we can understand the underlying biology," OME leader and UCSF Chancellor Susan Desmond-Hellmann, MD, MPH, told the participants in her opening remarks. "It could completely transform the way pharmaceutical companies and biotech approach development. It could turn a multi-decade process into a rapid process."

Fired by that vision, participants were split into teams to

Clockwise from the top: UCSF Foundation board members Leigh Matthes and Lynne Benioff (both seated) sharing a laugh with UCSF Chancellor Susan Desmond-Hellmann and (on the far right) Executive Vice Chancellor and Provost Jeffrey Bluestone; UCSF Vice Chancellor for Research Keith Yamamoto (right), and Rémi Brouard, a vice president of the global pharmaceutical company Sanofi-aventis, delivering their pitch; Steven Burd, former CEO of Safeway; participant commitment pledge sheet; NIH Director Francis Collins listening to Lloyd Minor, dean of Stanford University School of Medicine.

encourage a flow of ideas across industries and disciplines. Each team was charged with tackling one thorny obstacle to implementing precision medicine.

Huddled in one corner might have been the president of the Institute of Medicine, a leading cancer researcher at Pfizer, a prominent Silicon Valley venture capitalist, and a cutting-edge scientific illustrator. Hashing out details at a whiteboard, one might have seen the director of Lawrence Berkeley National Lab, the dean of Hong Kong's top medical school, and a space technology expert. And conversing here and there, one might have spied the FDA commissioner, a partner at TEDMED, a seasoned political strategist, and the head of Rockefeller University.

At one point, even Facebook founder Mark Zuckerberg stopped in to listen to the deliberations, as did California Governor Jerry Brown.

"It's pretty amazing to be in the room with so many leaders in the whole area of precision medicine from inside and outside the country," said Francis Collins, MD, PhD, director of the National Institutes of Health and an OME participant. "We're working on projects that could be initiated, that could bring us closer to dramatic developments for prevention and treatment of disease."

The summit culminated in a quick-pitch session, during which teams presented pilot projects designed to surmount barriers and make precision medicine a reality.

Desmond-Hellmann gave the final presentation, stressing that the keys to making precision medicine work are raising public awareness, getting support for new legislation to change patient privacy laws, and enlisting people to donate their data in the interest of helping their loved ones – and humanity.

"We will leave this summit not only with an action plan," she said, "but with 170 incredible human beings who will take the messages we've shared and honed back to their day jobs – and that has enormous value."

Watch innovators at OME speak about precision medicine: bit.ly/ucsf-ome

SMART TOILET

Create a "smart toilet" that could analyze stool samples, which are a key health indicator. The toilet would use the data in a real-time health dashboard that could be accessed by the patient's family members and doctors, and it could also send anonymous data to researchers interested in looking at patterns on a larger scale.

LESSONS LEARNED FROM FAILED CLINICAL TRIALS

Make public data from the vast majority of failed clinical trials for drug treatments. That data is valuable to other researchers tackling the same problems, yet the Food and Drug Administration isn't allowed by law to release it, and pharmaceutical companies don't have any incentive to share it. Making the data public would require a change in legislation, or an agreement among major biopharma companies and research universities like UCSF.

GLOBAL BIOLOGICAL DATA CONSORTIUM

Form a global consortium that would establish standards for collecting and analyzing biological data. Currently, research data doesn't have any such standards, a situation the team likened to "Betamax versus VHS." The consortium would ensure that researchers begin working in the same data language, starting with a couple of pilot disease areas.

PRECISION MEDICINE TECHNOLOGY FOUNDATION

Create a nonprofit foundation that would certify precision medicine technology for early reimbursements. Typically, there's a six-year cycle to bring ideas to market, but often money begins to run out after the first couple of years. The foundation, which could be funded by major health care providers, would help promising projects get on an accelerated track and reduce risk for innovators.

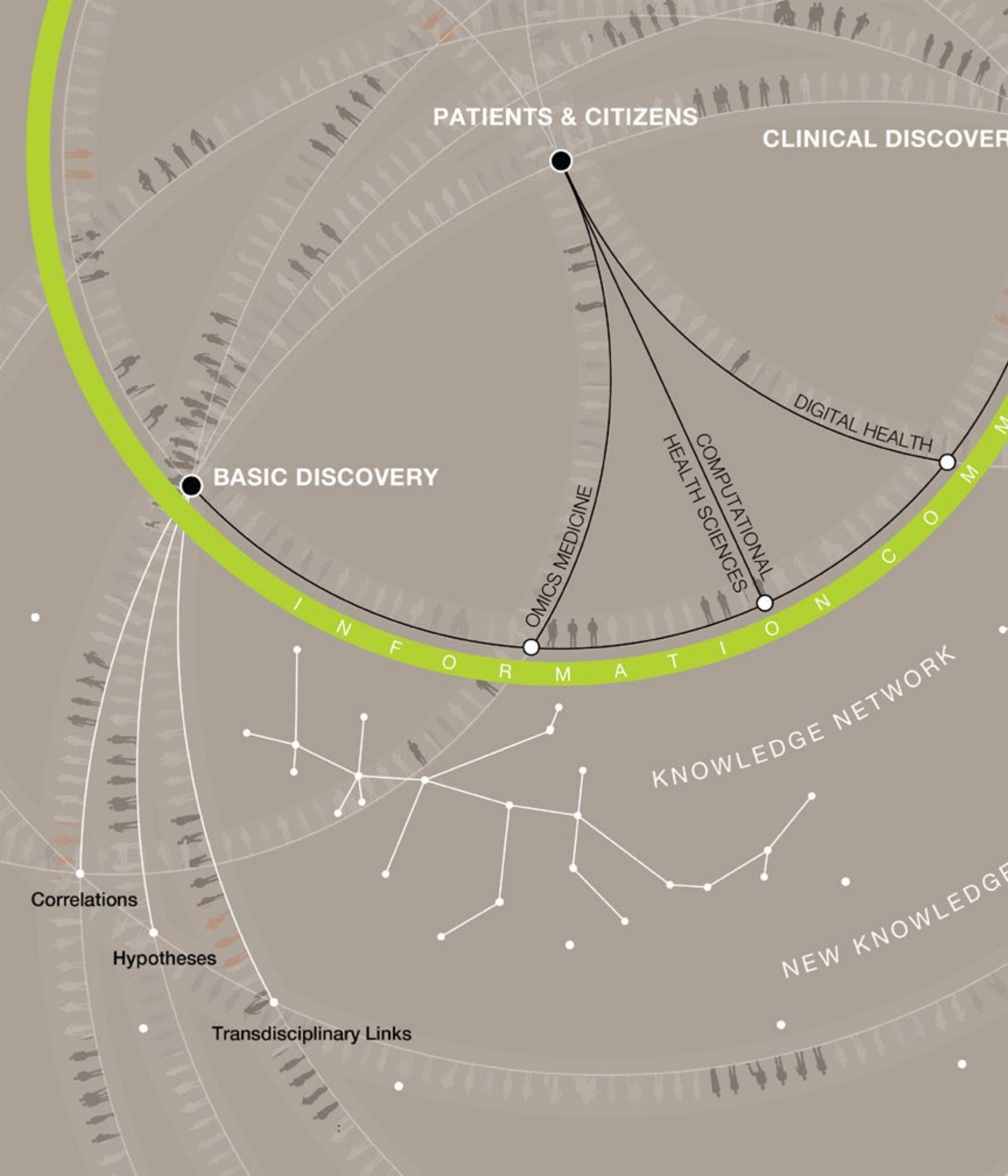
IMMERSIVE DATA VISUALIZATION DATABASE

Develop a computational database with a unique user interface able to manipulate complex data sets. The system would be a way to visualize data that could accelerate the pace of scientific discovery for neurodegenerative diseases. UCSF neuroscientist William Seeley, MD '99, has partnered with Lawrence Berkeley National Laboratory and Oblong Industries to create a pilot project using 10 years' worth of research data collected by Seeley, but financial resources are needed to expand the project.

DATA DONOR DRIVE

Approach gathering genetic data the same as running a blood drive, by tapping into people's sense of volunteerism and philanthropy. Start a grassroots campaign that seeks to collect one million data sets.

By Louise Chu and Juliana Bunim


PATIENTS & CITIZENS
CLINICAL DISCOVER
DIGITAL HEALTH
COMPUTATIONAL HEALTH SCIENCES
OMICS MEDICINE
BASIC DISCOVERY
INFORMATION COM
KNOWLEDGE NETWORK
NEW KNOWLEDGE
Correlations
Hypotheses
Transdisciplinary Links

Harnessing the POWER of Precision Medicine

Twenty years ago, if only one person out of hundreds went into remission during a clinical trial for a cancer drug, that patient would have been considered just plain lucky and the therapy deemed a failure. But today, with a host of tools garnered from precision medicine, one person's "good luck" can be leveraged into a precise and effective therapy for countless others whose tumors have a similar genetic profile.

Precision medicine explores the interplay of all aspects of human health, including not just genetics, but also environment, behavior, and lifestyle. Multiple layers of population information are entered into technological tools that have the unprecedented power to distill worldwide data down to a solution for just one person.

In late 2011, a National Academy of Sciences committee passionately endorsed precision medicine as the best means to explore the cause, development, cure, and prevention of the world's most daunting illnesses. Its co-chair was UC San Francisco Chancellor Susan Desmond-Hellmann, MD, MPH, a resident alumna.

UCSF stands among the global leaders working to move this nascent field forward. The institution's six-pillar platform of methods, tools, and resources will support precision medicine efforts everywhere. Our experts across all disciplines are giving new hope to billions of patients, one by one, around the world. Read on to find out how.

Watch Jeffrey Bluestone, PhD, executive vice chancellor and provost, discuss how UCSF is driving the field of precision medicine: bit.ly/ucsf-precision

ILLUSTRATION: MARTIN KRZYWINSKI

IT'S ALL ABOUT NETWORKING

Which would you choose if you were diagnosed with early-stage breast cancer? You could receive a standard chemo regimen, followed three months later by an MRI scan to determine the treatment's success. Or, instead, a genomic analysis of your biopsied breast tissue could help determine a drug regimen tailored to your own genetic makeup.

An MRI scan would assess your progress just three weeks later so, if need be, your oncologist could quickly switch to a different chemo protocol to attack the cancer.

The second approach adds several additional layers of information: your unique genetic profile, the early follow-up MRI, an ongoing assessment of your treatment's effectiveness, and the chance to respond quickly to new information.

Now envision a truly global extension of this multilayered tactic. Beyond improving treatment protocols, this approach also offers a path to further discovery.

A scientist studying how a misfolded protein triggers a degenerative disease might see another lab's recent results online, for example, and learn that the same protein causes a different disorder. Such a link suggests a common molecular mechanism for both conditions – a precious clue that could yield cures.

Or picture experts in disparate fields, using vastly different routes to discovery – molecular analysis, genomics, epidemiology – but each studying resistance to viral attack. With more ready access to each other's results and to novel analytic tools that tap reservoirs of related findings, they transcend their specialties and boost the chance to see the pieces of the puzzle come together.

Such researchers are immersed in a kind of information commons, awash in a virtual library of interconnected laboratory notebooks and volumes of new analytic tools and data. With an increased ability to harvest information automatically and far more powerfully, they can more easily find the connections among discoveries that would otherwise go unrecognized.

Think of it as highly sophisticated scientific crowdsourcing. The shared information and insights create a rich "knowledge network."

"The knowledge network is the 'integrating center' for precision medicine," says Keith Yamamoto, PhD, vice chancellor for research, a professor of cellular and molecular pharmacology, and a leader of the precision medicine effort under way at UC San Francisco. "For the clinician-researcher, each added level of insight – say, finding the link between a specific genetic signature and an aggressive type of cancer – can lead to new ways to diagnose and treat the disease."

The oncologist treating early-stage breast cancer, for example, might learn of a new online tool to refine analysis of MRI scans. Or a colleague seeing her preliminary progress may suggest a potent new strategy to screen for the best drug. Either way, the search for better treatments just got a little smarter.

"And in fundamental research," says Yamamoto, "the network will be a 'discovery generator,' revealing new correlations testable in the lab or new clues to mechanisms that drive disease. The pace of research is extraordinary at many levels, but the real payoff lies where insights intersect."

MAKING CONNECTIONS VISIBLE

"Ten years ago, the accumulation of new data was a warehousing problem. Now it's a networking problem," says Joe Hesse, a computational expert and technology strategist at UCSF's Memory and Aging Center.

"Almost all areas of biomedical research are inundated with new information, but what we don't have are good ways to link up the data to see the connections," points out Kate Rankin, PhD, a postdoctoral alumna who is now an associate professor in the Memory and Aging Center and one of the prime movers in advancing the idea and reality of a knowledge network.

Rankin and a cadre of colleagues at UCSF and a few other institutions envision analytic pipelines that connect different types of data, yielding unsuspected correlations between, say, the progression of diseases and the pace of cell-cell interactions.

The new online analytic tools will be a crucial component of the knowledge network. In Rankin's field of clinical neuroscience, scientists commonly use a visualization strategy that allows users to stack a number of MRI brain scans on top of each other and compare the same part of the brain in different patients.

She and colleagues have developed pattern-matching algorithms to identify specific diseases based on an individual's pattern of neurologic damage. One of her goals is to link these two tools to create easy-access pipelines for both researchers and clinicians to use.

ILLUSTRATION: MARTIN KRZYWINSKI

Another promising pipeline being developed mines publicly available libraries of gene functions to identify sets of genes statistically associated with specific metabolic functions. It has already been used to streamline identification of genes that are particularly active in inflammation – a condition now under increasing focus as a driver of a range of diseases, including atherosclerosis, diabetes, and cancer. Essentially, the analytic tool winnows down the candidates to an "inflammation gene set." Researchers or clinicians can upload genomic data from a patient to learn if the telltale inflammation genes are active. If so, the patient might need treatment for inflammation even if the condition is not yet obvious.

UCSF's Laura van 't Veer, PhD, who focuses on cancer diagnostics, is a leader in clinical trials to develop drug regimens tailored to discrete genetic profiles in different tumors. She fully endorses the multilevel approach to help develop new cancer treatments. She also wonders if other health complications – other levels – might affect the course of a disease.

"Yesterday I talked with a diabetes researcher. The knowledge network should help collaborators in different fields ask, 'Does diabetes influence how normal cells get derailed in cancer?'" says van 't Veer, who holds the Angela and Shu Kai Chan Endowed Chair in Cancer Research.

With an increased ability to harvest information automatically and far more powerfully, scientists can more easily find the connections among discoveries.

She also questions inflammation's role in so many diseases. "What are the connections? What can we learn from the fact that inflammation is expressed in what we think of as very different disorders?

"The knowledge network keeps evolving," she says. As novel tools and richer, ongoing exchanges lead to fresh insights, she explains, "we can apply new knowledge more quickly and more easily to develop the next type of treatment."

EXPANDING THE KNOWLEDGE NETWORK

The goal of a fully functioning knowledge network will not be easy to reach. It will function well only with wide participation, new analytic tools, and powerful computational capacity.

Hesse cites pioneering work at the Lawrence Berkeley National Lab by Adam Arkin, PhD, who is developing a software platform called KBase that offers a template for developing a knowledge network in any field.

Arkin proposes assigning "values" to similar kinds of data from different sources, ranking the reliability of the findings based, for example, on the size of the sample, the metrics used to assess it, and the statistical power of the reported results.

Neuroscientist Kate Rankin and technology expert Joe Hesse are collaborating to advance the knowledge network.

"With this type of information available, one can decide the likely importance of an outlier result when compared with several others," Hesse explains. "If the value is low because, say, the sample is small, the finding may be skewing interpretations. But if its value ranking is high, the result may warrant serious follow-up."

Both the brain scan analytic strategy and the genetic profiler in Rankin's neuroscience field are being programmed with the promising KBase platform as a template.

Providing ways to increase research networking would seem to be a natural for scientists. "We share our new findings at meetings and in journal articles that often get published many months after the research is complete," Rankin says. "A true knowledge network would keep up with the pace of discovery."

At the same time, not all researchers will want to share their data. Scientists can be very competitive, and some would certainly resist offering early access to their research. Respecting and protecting researchers' privacy within the network poses a huge challenge.

Still, given the pace of discovery today, those who don't share might risk being left out.

"Clinical researchers often find they don't have large enough samples to carry out a new investigation of interest to all of them," says Rankin. "Now it's becoming more common for them to decide to pool their data: 'I've got 34 patients, you have 47; let's collaborate.'"

Hesse also sees the knowledge network as a natural extension of today's online culture. "Sharing our information, experiences, and pictures online with our various personal networks has become second nature, so we're primed to share research this way," he says.

"We need to develop a rich online communications network that can at the same time protect privacy when it's needed. But we will. It's critical – and it's inevitable."

By Wallace Ravven

PHOTO: STEVE BABULJAK

DIGGING DEEPER INTO CANCER

What a pathologist looks for in a Pap test sample, but hopes not to find, are oddly shaped cells with abnormally large nuclei. The same is true for prostate and lung cancer biopsies. In fact, most cancer cells display distorted structures.

"If you just open a text on the pathology of cells, you see hundreds of strange-looking cells – this one with a gigantic nucleus, that one with vacuoles that push the nucleus aside," says Wallace Marshall, PhD '97, an associate professor of biochemistry and biophysics. "It's like an atlas of freakish cells."

Marshall wondered if this lineup of distorted cells might hold a clue to a new way to fight cancer. Because cancer cells divide so quickly, they're on a fast track to mutate and develop resistance to chemo drugs. So new drugs are continually added to the mix, often triggering an arms race between the chemo drugs and the cancer – a race that the cancer sometimes wins.

Marshall thought of a different strategy: what if the enlarged nuclei, and specialized cellular structures called organelles, actually drive cancer metabolism? If so, then developing ways to reverse organelle growth could rob cancer cells of the proteins and other resources they need to grow and proliferate.

The hypothesis exemplifies one of UC San Francisco's precision medicine pillars: basic discovery. The long path to developing potent new treatments often starts with an observation in the lab that then leads to a question about a fundamental life process. This in turn prompts a "testable" hypothesis. Science is full of hypotheses that don't pan out because experiments fail to support them. But those that survive the rigors of investigation can change minds – and save lives.

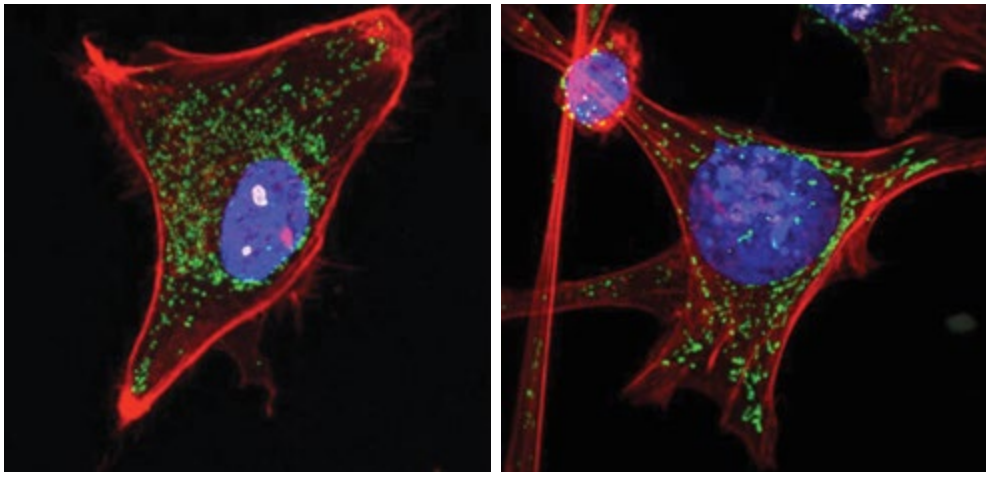
Marshall's lab has begun to study the processes by which organelles enlarge. Once armed with that understanding, his team plans to test drug candidates to "deprogram" them and counter their growth.

Such a treatment approach could circumvent the key vulnerability of chemotherapy, Marshall says. It would not aim directly at the biochemical pathway that allows cancer cells to multiply rapidly – the very capacity that also allows them to mutate and develop resistance to drugs.

Instead, it would attack the cascade of chemical signals that regulates organelle growth. Marshall reasons that these signals are not likely to be the same ones that cancer cells use to mutate and evade the drugs.

Even if cancer cells did develop resistance to drugs targeting their organelle growth, Marshall says, they would have double the work to evade both these drugs and the more conventional ones countering cellular proliferation.

Marshall likens organelles to "reaction vessels" – akin to tanks in a chemical plant, churning out products through chemical reactions. The size and design of the reaction vessels, he says, are just as important as the chemistry going on inside them. Shrink the vessels, and you cut their productivity.



These micrographs show two cells from mouse connective tissue. The nucleus is stained blue in both cells. The first cell (left) is normal. In the second image, the same kind of cell has become cancerous, and the nucleus has become so large that it nearly fills the entire cell.

ILLUSTRATION: MARTIN KRZYWINSKI; CELLS: MARK CHAN

Biochemist Wallace Marshall is researching cellular structures called organelles to see how closely they are related to cancer metabolism.

PHOTO: STEVE BABULJAK

"We have the trajectory of how they change as they become cancer cells. If we can move them back along the same trajectory, we'll see if that can arrest the cancer growth."

He actually has two hypotheses about the link between organelle size and cancer. One postulates that gargantuan nuclei and organelles derive from the cancer cell's need to ramp up its metabolism. If the "reaction vessels" could be made to return to their earlier, smaller configuration, the cancer cell might starve.

In his second scenario, the cancer cell's hypermetabolism is a result of organelle growth, not its cause. But, again, by driving the organelles back to a more normal size range, the cell would revert to a less malignant state.

Marshall stresses that neither scenario has been tested. That's his long-range goal. To get there, he must first understand the natural mechanisms that regulate organelle growth. His lab is now at the stage of finding out what specific steps control organelle growth – how a cell knows the size of its nuclei and mitochondria, for example, or knows if it's well fed.

If he can identify the genetic controls or enzymes and other molecules that underlie these processes, he would have targets for potential drugs to reprogram the abnormal growth.

In collaboration with UCSF's Small Molecule Discovery Center, his lab is carrying out automated, "high-throughput" tests, like those used in commercial drug development, to screen for drug candidates that impede specific genes or molecules. Such screening efforts often search through tens of thousands to hundreds of thousands of compounds to find the few able to block the target enzyme.

His colleague Davide Ruggero, PhD, who holds UCSF's Helen Diller Family Endowed Chair of Basic Science in Urological Cancer, has developed a technique to inject/introduce oncogenes into progenitors of connective tissue known as fibroblast cells. This induces tumor formation. By then using special stains to reveal the organelles in the resulting tumor cells, Marshall's team can scrutinize cells at various stages of cancer growth.

"We have the trajectory of how they change as they become cancer cells. If we can move them back along the same trajectory, we'll see if that can arrest the cancer growth."

It's a long way from a fundamental insight to an approved therapy, and Marshall is the first to admit it. But he says UCSF's precision medicine mindset will likely play a key role in making that journey more quickly.

"I think the standard drug therapy approach is often a 'fire and forget' strategy – like a ballistic missile. You pick the drug, you give it to the patient, and cross your fingers that it will work. But precision medicine entails following up with more research to measure how the individual patient is responding – through physiological indicators or gene expression patterns or, if our organelle-based approaches pan out, measuring at the level of cellular structure."

Precision medicine, then, extends the process into an ongoing, evidence-based approach to find not only whether a patient got better, but how and why and at what rate.

"This will allow us to steer patients back to a more healthy state instead of only hammering them with drugs," Marshall says.

By Wallace Ravven

BIG DATA, TAILORED CARE

What looks like an old-school phone book is gripped by UCSF neuroscientist Pierre-Antoine Gourraud, PhD, MPH. But he soon sets the record straight: the thick packet he is holding is actually the medical file of a single patient with multiple sclerosis (MS), a complex, chronic, and incurable disease that can ravage the nervous system over decades.

"Keeping a big paper file is hardly a 21st-century approach to managing massive amounts of data," says Gourraud as he tosses aside the file and picks up an iPad. One swipe of his finger reveals a single screen showing a highly detailed, well-organized overview of the same patient's long medical history, along with how that history compares to the disease trajectories of thousands more MS patients.

This "MS Bioscreen" application – a team effort led by Gourraud and UC San Francisco Department of Neurology Chair Stephen Hauser, MD, an international MS expert – is a prime example of clinical discovery, one of UCSF's precision medicine pillars. In clinical discovery, researchers and clinicians are taking vast amounts of patient data, often collected through first-ever clinical studies, and putting it into tools like MS Bioscreen that have a direct impact on patient care.

"The new revolution of 'big data' in medicine," says Gourraud, "will use information technology to transform how we handle and decipher the complexities of diseases like MS."

The Bioscreen enables clinicians to compare a particular patient to others with the same disease based on similarities in their clinical symptoms, brain imaging, and biomarker data. By viewing the outcomes of similar cases, each patient has a better idea of how he or she will eventually fare – and what can be done now to bring about the best possible outcomes later.

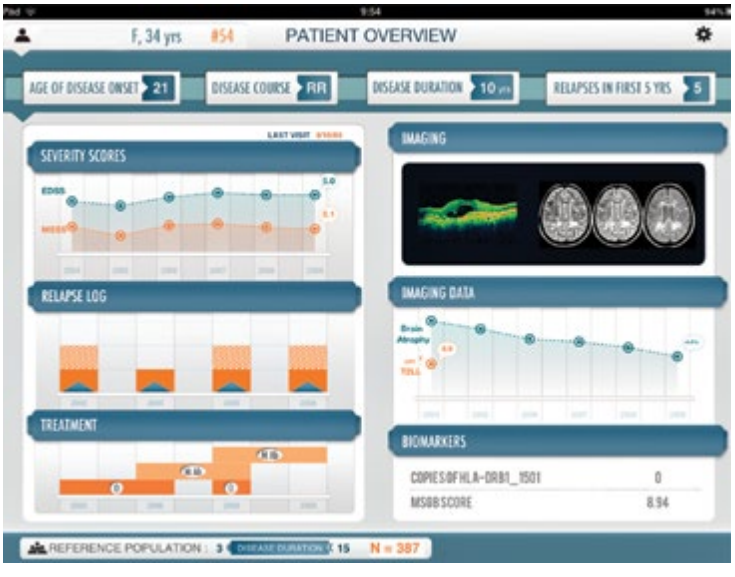
"MS is one of the great mysteries in medicine; it can be a benign disease with occasional problems, or an unrelenting condition that puts people into wheelchairs at a very young age," says Hauser. "I want to be able to tell a 16-year-old with MS whether she can forgo risky treatment because her disease will be little more than a nuisance during her life, or we should treat it aggressively now in an effort to avoid extreme disability down the road."

FUELING PRECISE TREATMENT DECISIONS

The majority of current Bioscreen data came from MS-EPIC, a trailblazing MS study begun at UCSF nine years ago. Short for "expression, proteomics, imaging, clinical," the study involves intensive observation of 800 MS patients – the largest MS population ever tracked with such exactitude.

Hauser and his team maintain a 360-degree perspective on every EPIC patient. They scan the entire genome of each patient and family member to determine which genes may have played a part in the patient's susceptibility to MS (a process that led to the identification of more than 110 new genes implicated in the disease). They meticulously monitor disease progression through sophisticated MRIs of the eye, brain, and spinal cord, and they look for biomarkers, like malfunctioning B cells, that can hasten its progress. Finally, they record the results of every therapy administered over the course of a patient's disease.

All of this data has gone into MS Bioscreen, where it can be instantly called down from secure cloud storage and synthesized in a seemingly infinite number of ways. For example, a clinician can go to the "Reference Population Settings" section of the app and filter



The MS Bioscreen captures a patient's medical information in a single screen.

TOP ILLUSTRATION: MARTIN KRZYWINSKI

the entire data set according to demographic factors or dozens of other clinical, imaging, and biomarker characteristics. Tap the "Set" button, and the app's comparative and predictive algorithms crank out graphs, charts, and even 3D MRIs that clearly put into context the details of the patient in question against those of the filtered dataset.

"Our decisions are based on evidence rather than art, and personalized to an individual patient's particular characteristics."

"We have many different kinds of details that we can compare very easily," notes Gourraud. "For instance, we can look at how a specific patient's EDSS score – which stands for 'expanded disability status scale' and serves as a method for quantifying functional disabilities – stacks up against the EDSS scores of other patients with similar characteristics. We can then pinpoint the particular severity of the patient's disease according to the percentile range in which he or she falls. It's like a growth curve for kids."

From there, guided by the tool and its algorithms, clinicians can make treatment recommendations based on what has (or hasn't) worked for others with similar underlying characteristics. "We can consider who in that group had success with a highly active but potentially risky drug, such as one of the monoclonal antibody treatments for MS; who is likely to do well with a safer but less powerful treatment, such as one of the injectable drugs; and who might require no treatment at all. We can use the knowledge to determine which drug has a high probability of success for the patient in question," Hauser says. "Our decisions are based on evidence rather than art, and personalized to an individual patient's particular characteristics."

MILLIONS MORE MS PATIENTS TO BENEFIT

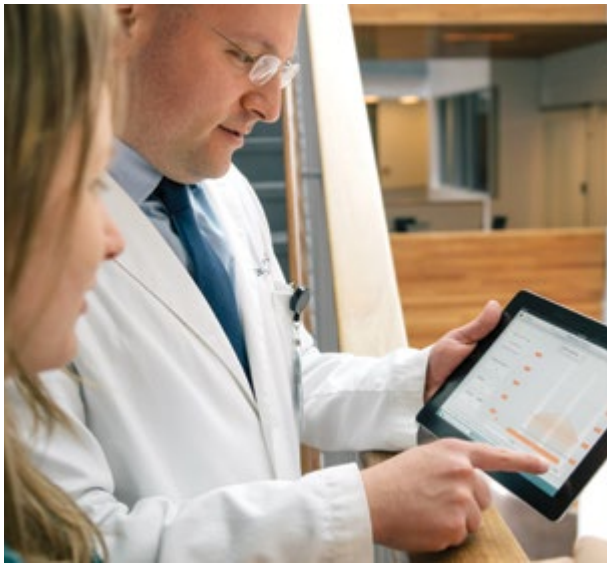
Hauser is now working with several venture firms to make the Bioscreen available to the 2.5 million MS patients around the world. In addition, the Bioscreen application can be used to monitor people with other chronic, complex diseases. Giving patients direct access to the app is a primary goal of the Bioscreen project and, in a broader sense, a critical component of precision medicine's clinical discovery area, which seeks revolutionary improvements in the way patients themselves interface with the health care system.

"In our clinic right now, we have research stations with iPads where patients can access and discuss their information on the Bioscreen with the appropriate support of investigators," says Gourraud. "This ability to see their personal stats compared to others has made our patients feel more engaged and empowered. They understand more vividly why we're proposing one treatment versus another – and that understanding is why they're more willing to stick with their treatment plan."

"With a potentially life-altering disease like MS, there are very personal treatment decisions that must be made by patients," Hauser observes. "They think to themselves, 'How do I feel about the unlikely, yet not impossible, event of a life-threatening side effect of this medicine?'

"When making these decisions, we want to be able to give both patients and clinicians an evidence base. The more patients we add to the Bioscreen, the more this evidence base will grow – and the more accurate will be our predictions of the future for every patient."

By Stephanie Bruzzese



PHOTOS, FROM LEFT: ANDREW BARNECUT; CINDY CHEW

Left: Patients are able to view their information on the Bioscreen app and discuss it with their doctor. Right: Renowned MS expert Stephen Hauser, the Robert A. Fishman Distinguished Professor (left), and neuroscientist Pierre-Antoine Gourraud (right) are leading the MS Bioscreen project.

PRECISION MEDICINE: COMPUTATIONAL HEALTH SCIENCES

THE FABRIC OF DISEASE

If biology is destiny, then the slightest change in a gene's DNA can become an agent of destiny. About 99.9 percent of the DNA "letters," or chemical bases, that make up genes are identical in everyone. But the remaining sliver of variability can change a life.

A tweak in just one base out of thousands may make the difference between a healthy old age and an early decline into Alzheimer's disease.

More often, researchers find that a number of diseases and traits – such as prostate cancer, type 2 diabetes, and high body mass index – arise from combinations of DNA variants scattered within and between our genes. In some cases, hundreds of these individual DNA units apparently work in concert with environmental factors to influence the onset and progression of disease.

Identifying the links between slight genetic aberrations and complex diseases is one of modern biology's great challenges.

A team of scientists from UC San Francisco and Kaiser Permanente Northern California is now four years into an ambitious effort to trace the genetic and environmental roots of a range of disorders, from diabetes to cancer. They are doing so by tapping into one of the world's largest and most thorough collections of patient health records.

They are drawing on the heath histories of more than 100,000 Kaiser member volunteers, each of whom spits for science – providing a saliva sample for genetic analysis.

Kaiser's electronic medical records track up to 25 years of patients' prescriptions, cholesterol levels, mammograms, MRI scans, and disease diagnoses. UCSF and Kaiser researchers have collaborated to create genetic profiles of the Kaiser volunteers and are working together to analyze this rich source of genetic, environmental, and health data.

The analysis and cross-analysis of this mother lode of Kaiser members' health data and their genetic profiles is expected to speed early prediction of many disorders, aid development of treatments and cures, and personalize medicine by allowing physicians to tailor drugs and other therapies to each patient's unique genetic makeup.

"The sheer size and ethnic diversity of the Kaiser population we are studying greatly increase the likelihood that our research will lead to new understanding of the genetic underpinnings of complex diseases," says Neil Risch, PhD, the Lamond Family Foundation Distinguished Professor in Human Genetics, the director of UCSF's Institute for Human Genetics, and co-leader of the collaborative research.

The Kaiser Permanente Research Division's Cathy Schaefer, PhD, is co-leader of the research and executive director of Kaiser's Research Program on Genes, Environment, and Health, which oversees the collaboration.

The research project is a pioneering example of computational health sciences, a central component of UCSF's precision medicine platform. The discipline relies on computationally intensive – and sensitive – approaches, from mathematical and statistical strategies to genotyping and bioinformatics. These methodologies are used to analyze and cross-analyze large but discrete collections of data, such as the Kaiser members' health histories and genetic makeup.

ANALYZING GENETIC VARIATIONS

Single DNA variants are called SNPs, or single nucleotide polymorphisms. The research effort detects and analyzes SNPs throughout the entire genome of each of 110,266 Kaiser members.

UCSF genetic analysis experts look for SNPs at up to 900,000 sites in each person's chromosomes – a kind of census of genetic variation. The analysis is known as a genome-wide association study, and this is one of the largest ever undertaken.

Armed with patients' electronic medical records, Kaiser researchers zero in on changes over time in key health measures such as blood pressure and cholesterol level, as well as on the progress of any diseases, and then correlate this information with the genetic data.

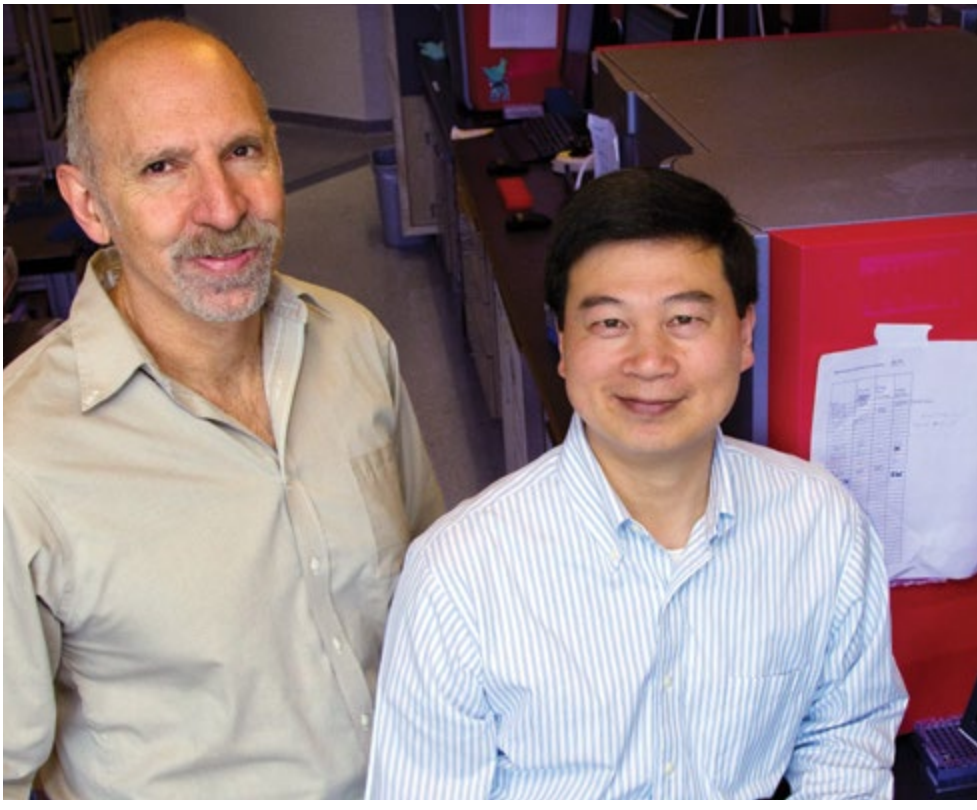
From this extraordinarily large collection of clinical and genetic data, computational scientists apply sensitive and powerful statistical tools to determine the likelihood that specific genetic variations or combinations of variations might contribute to a specific disease.

"The research has already led us to discover more than 100 different genes underlying HDL and LDL cholesterol and triglyceride levels with more certainty than any previous effort," Risch says.

Perhaps the most tantalizing early finding comes from a study of

ILLUSTRATION: MARTIN KRZYWINSKI

"The sheer size and ethnic diversity of the Kaiser population we are studying greatly increase the likelihood that our research will lead to new understanding of the genetic underpinnings of complex diseases."



Neil Risch (left) and Pui-Yan Kwok (right) are tracing the genetic and environmental roots of a range of diseases by tapping into one of the world's largest collections of patient health records.

DNA segments called telomeres that were also measured in the 100,000-plus Kaiser participants. Telomeres seal off the ends of chromosomes and protect them from damage. Among the participants, who have an average age of 65, those with the shortest telomeres were statistically likely to have a 24 percent increased mortality risk over three years, the researchers found.

This increased health risk is roughly equivalent to the effect of smoking cigarettes for 20 to 30 years, says Kaiser's Schaefer.

The association between telomere length and health has become an area of great interest over the last decade. The UCSF-Kaiser telomere study was undertaken as a collaboration with UCSF's Elizabeth Blackburn, PhD, who holds the Morris Herzstein Endowed Chair in Biology and Physiology and won the Nobel Prize in 2009 for her pioneering studies of telomeres and the enzyme that maintains them.

Because of the ethnic diversity of the Kaiser population, the research project can also investigate how slight genetic variations associated with ethnicity might lead to increased risk for diseases such as hypertension or diabetes.

The scientists can also pinpoint how lifestyle choices – such as smoking or drinking histories, diet, and exercise – as well as demographic information interact with genetic factors and lead to disease. The data for this additional layer of correlations comes from surveys filled out by Kaiser member volunteers.

"So many studies have uncovered tantalizing connections between genetics and disease risk, but often with small numbers of patients and health records spanning just a short time – or even assessments of patient health at just one point in time," Schaefer says. "But longitudinal data on such a large and fairly representative cohort allows us to look for common molecular origins of diverse diseases – a key concept in precision medicine."

The tool used to detect SNPs is called a gene array, but to look for gene-disease links in an ethnically diverse population this large, UCSF genetic analysts needed to be able to customize the arrays. They turned to a company called Affymetrix that had recently built a highly automated genotyping instrument capable of handling customized arrays.

Using the new arrays, the Institute for Human Genetics was able to complete genotyping of the 110,000 samples in just 14 months, says Pui-Yan Kwok, MD, PhD, an expert in genomics at the UCSF Institute for Human Genetics and leader of this critical component of the project. Kwok holds the Henry Bachrach Distinguished Professorship at UCSF.

As far-reaching as the UCSF and Kaiser research ambitions are, Risch seems simply grateful for the distinct talents being brought to bear on the study of genetics and health.

"The truth is that this project would have been impossible at any other time or place. No single institution could have combined this level of genetic science and computational skill with such deep health records and epidemiologic expertise on this large and diverse patient population. It is an intellectual pleasure with great potential for human health."

By Wallace Ravven

PHOTO: SUSAN MERRELL

THE GENE MACHINE

Scientists have discovered that the human body contains more than 25,000 genes, but what they do remains mostly a mystery. "We don't know the function of the vast majority of genes," says Nevan Krogan, PhD, director of the UC San Francisco branch of the California Institute for Quantitative Biosciences.

He and his team are seeking to crack this conundrum by examining genes and the proteins they encode through a superwide lens, as well as by creating large-scale physical and genetic interaction maps.

This approach turns traditional biological research on its head and is integral to precision medicine. In years past, most researchers studied genes or proteins one at a time, Krogan explains. That bottom-up pursuit usually began with a hypothesis and very little understanding of the enormously intricate structure housing the gene.

But once scientists had identified and mapped all the genes in the human genome, this extensive knowledge, along with sophisticated new tools, led to a top-down hunt. Investigators like Krogan now look globally at biological systems to better grasp the inner workings of cells. He's particularly focused on the interactions between genes and the proteins they make, which perform a vast array of functions in the body.

"If you understand the machine in which the protein operates, then studying that protein, and the corresponding gene, becomes so much easier," says Krogan, who is also an investigator at the UCSF-affiliated J. David Gladstone Institutes. Researchers gain this bird's-eye view by analyzing a copious amount of data using complex computer algorithms.

This unbiased strategy forgoes hypotheses and lets the data do the talking. "The cells are smarter than we are. If we can develop the tools to let the cells tell us their secrets without interjecting what we think we know, the data become so much more powerful," he explains.

Molecular biologist Nevan Krogan is mapping how genes and proteins interact, knowledge that may lead to new drug targets.

Krogan's systems work is not only illuminating how genes and proteins function, it's also shedding light on the underlying biology of disease for each person – a central goal of "omics" medicine, one of the pillars on which UCSF's precision medicine platform rests.

VEXING VIRUSES

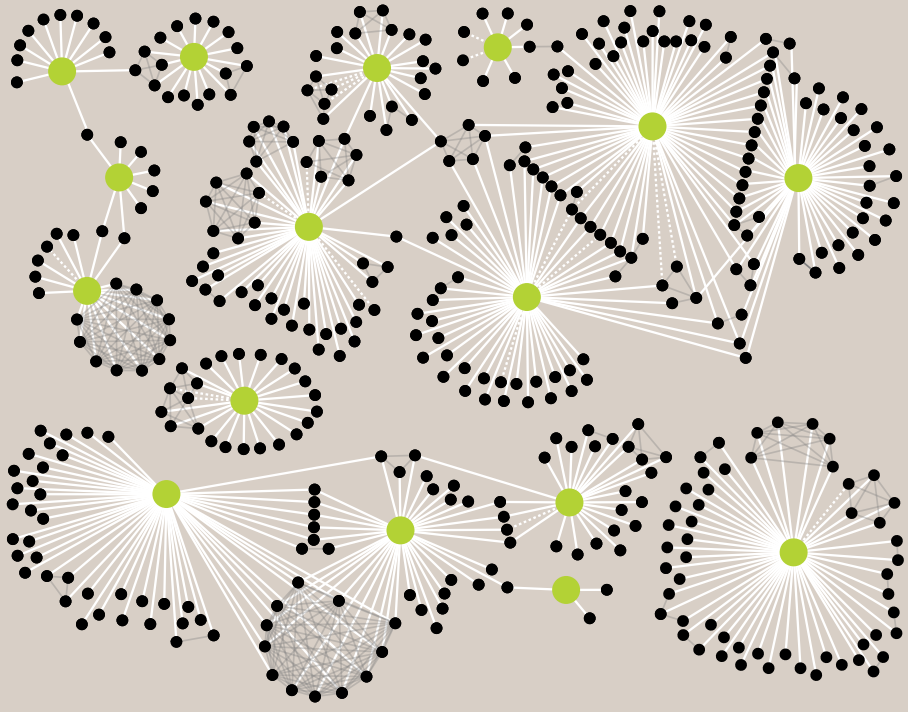
Infectious diseases caused by viruses are in Krogan's crosshairs. Many viruses have fewer than two dozen genes but are a "fantastic tool for understanding molecular biology," he says. "They basically hijack and rewire every major biological process in the cell they infect."

To learn how viruses complete this assault, Krogan and his team tag viral proteins, inject them into a human cell, then pull them out. Next, using a tool called mass spectrometry, they identify which human (or host) proteins the viral proteins attack. "Essentially, we are taking a step back to look at the global landscape of what the virus needs during the course of infection," he says.

They started with HIV, injecting the 18 HIV proteins into a human cell. The team uncovered 400 human proteins hijacked by the pathogens. They subsequently analyzed a dozen other viruses, including polio, flu, herpes, hepatitis C, and dengue and discovered that the viral proteins commandeered a common set of host proteins.

These host proteins could serve as targets for new drugs, says Krogan. "If you can prevent these interactions, the cell has more of a fighting chance." Directing drugs at protein interactions rather than at viruses could also avoid drug resistance, he notes, since viruses are able to mutate quickly and become resistant to drugs.

ILLUSTRATION: MARTIN KRZYWINSKI; PHOTO: SUSAN MERRELL



A protein-protein interaction network involving HIV and human proteins.

HIV proteins (green nodes) and human proteins (black nodes) were found to physically interact (white lines). Interactions among human proteins (gray lines) reveal the molecular machines hijacked by the HIV proteins during the course of infection. Interrupting the connections among HIV and human proteins could provide future therapeutic strategies for the fight against AIDS.

"Are these proteins ultimately going to serve as better therapeutic targets for future studies? I believe the answer is yes. We are trying for the silver bullet."

CREATING A MEGA-MAP TO MASTER MUTATIONS

Krogan is delving deeper into his examination of HIV by collaborating with Steven Wolinsky, MD, an infectious disease expert at Northwestern University. Wolinsky and several others have spent three decades monitoring a cohort of about 7,000 HIV-resistant men, trying to discover what makes them resistant. Krogan gave Wolinsky the list of 400 genes identified by his team as viral targets. Wolinsky is now sequencing these genes to determine if any mutations exist. If so, Krogan plans to apply his approach to study how these genes work to foster resistance.

While he's currently focusing on viruses, Krogan believes the same methodology can be used to reveal the underlying biology of other diseases. "Just like the genes in viruses conspire to produce infection, mutated genes work together in a devious fashion to create a disease state," he says.

Science has made great strides in identifying sets of mutated genes that lead to certain diseases. "But if we don't know what those genes do, how can we figure out how to fight them?" asks Krogan.

He wants to create large-scale maps of protein-protein and genetic interactions to provide a window into how all genes and proteins in a cell talk to one another – how they connect and interact both physically and functionally. It would be similar to a diagram of a machine showing how all the parts work together when the machine is running smoothly.

This comprehensive picture of cellular connectivity promises to help researchers pinpoint how unmutated genes function. Knowing that a protein is part of a four-protein complex, for example, would make studying that protein much simpler. Then a mutation could be introduced to see what unfolds. Are certain connections interrupted or pathways broken?

"If we can develop the tools to let the cells tell us their secrets without interjecting what we think we know, the data become so much more powerful."

"Precision medicine could become more powerful because we would have a foundation with which to compare when genes go awry," Krogan prophesies.

By Anne Kavanagh

ILLUSTRATION: MIKE SHALES

A DIGITAL PATH TO HEALTH

Ask Aenor Sawyer, MD, about the promise of digital health, and she'll tell you about a pitch for a health-related app that she critiqued not long ago. The app purported to improve spinal health – something that Sawyer, an orthopedist and a former physical therapist, knows a thing or two about.

"I raised my hand and asked, 'Does it work?'" recalls Sawyer, who is an assistant clinical professor at UC San Francisco. "The developer's answer was, 'It has 1,500 downloads and is fully funded.'"

His metrics for success were understandably different from a clinician's, but his answer indicated to Sawyer an obvious need to have experts from multiple disciplines – including health care *and* technology – at the table when designing digital innovations. Digital health inventions can come in the form of software or devices that sense, collect, integrate, and analyze health data. "Some of the earliest digital health apps were developed with minimal clinical input and had early-adopter appeal, but little or no demonstrated effectiveness," says Sawyer, who is also the associate director of strategic relations at the new UCSF Center for Digital Health Innovation (CDHI). "Thankfully, that is changing as we create partnerships across sectors."

Led by UCSF's associate vice chancellor for informatics, Michael Blum, MD, the CDHI is vital to the success of the institution's precision medicine initiatives. The CDHI not only shepherds the development of digital health innovations created at UCSF, but also validates the effectiveness of digital health devices developed both within and without the institution. A key focus of CDHI is facilitating the flow of data from disparate sources into the clinical care process so that optimal treatment can be offered to each individual patient.

UCSF faculty, staff, and students who are developing new digital health systems and devices benefit from the vantage point of being integral to the processes and practices they seek to enhance. "I call them frontline innovators because they can target problems that people from the outside may not appreciate," Sawyer points out. "They also bring in the evaluation component to ensure that the technologies being developed are not only used, but are effective."

"The CDHI's partnerships help UCSF innovators cross the arc from 'idea to impact.' Ongoing efforts are under way to build these valuable industry-academic relationships. Our diverse partners span technology, design, business, and even policy," says Sawyer. "They advise our innovators on every aspect of making a commercially viable product."

The CDHI has begun to serve as a coordinating center for other UCSF organizations – such as the Office of Innovation, Technology, and Alliances; Information Technology Services; and the Clinical and Translational Science Institute's Catalyst program – all of which help digital health innovators to develop, validate, and scale their work beyond the University. "Catalyst alone has more than 100 industry and academic leaders in fields such as engineering, design, legal, and finance who serve as advisers to help innovations evolve and move out of UCSF," she says.

The CDHI has a broad portfolio of pipeline projects, of which Trinity is but one example. Developed by Sawyer and Pierre Theodore, MD, a cardiothoracic surgeon, Trinity is a web-based tool that enables a multidisciplinary

"I call [UCSF faculty, staff, and students] frontline innovators because they can target problems that people from the outside may not appreciate."

ILLUSTRATION: MARTIN KRZYWINSKI; PHOTO: STEVE BABULJAK

Aenor Sawyer (right) of UCSF's new Center for Digital Health Innovation advises students, faculty, and staff on the development of digital devices and systems.

team of physicians to confer virtually about complex cases. In cancer care, such teams, known as tumor boards, are made up of 20 or more physicians who leave their clinical duties to meet for an hour or two each week to review their patients' clinical, radiology, laboratory, and pathology data. Tumor boards engage in crucial discussions about the most challenging cases, but it may take four weeks to schedule a face-to-face meeting and another two weeks to initiate the resulting treatment plan. With Trinity, team members can access all the relevant data online and comment and confer with colleagues virtually – at their own convenience, in a way that safeguards patient privacy – and then treatment plans can be implemented in 48 hours.

"Technology enables us to deliver better care at lower cost," says Sawyer. "We have also demonstrated the ability to gain input from specialists outside UCSF – and even the country – on unusual cases." Trinity is fully operational at UCSF. Plans for building it into a commercialized product are under way.

Other technologies in development at the CDHI use mobile devices and social media to collect dizzying amounts of health information from people, as they go about their lives, and make use of it to serve individual patients. Social analytics, which measure, analyze, and interpret our social interactions and patterns, are also a key part of the data used in digital health innovations. "We now have the ability to peer beyond our clinical settings and integrate real-life data with the physiologic data collected by the health care system to better understand their contributions to health and disease," says Sawyer. "The challenge will be managing and analyzing the data in a way that is clinically useful."

Fundamental to that challenge will be integrating systems and data into compatible languages so that the new technologies work together, while maintaining patients' privacy. The CDHI will also guide developers in an array of evolving legal and regulatory matters, such as the Health Insurance Portability and Accountability Act (HIPAA), a federal law that safeguards patient privacy.

"We are living in an exceedingly complex world involving technologies that will allow associations not previously possible," says Sawyer. "With digital health as the great communicator, we will see the integration of genomic, physiologic, behavioral, social, and environmental data to achieve not just descriptive, but ultimately predictive and perhaps prescriptive information for patients and providers." As that evolution takes place, the CDHI will be poised to ensure that all these new sensors, apps, and databases interface efficiently with the clinical care process, in order to realize precision medicine's promise of timely, individualized, data-driven care.

By Claire Conway

PHOTO: STEVE BABULJAK

Pamela Munster, MD, is program leader of Developmental Therapeutics at UCSF's Helen Diller Family Comprehensive Cancer Center. She shares a breast cancer story here – her own.

You know how you can just tell when something is wrong? Well, I was skiing in Montana with some friends when we started to plan a 50th birthday trip to Alaska, two years later. I suddenly thought, "How do I know I'll still be alive in two years?" The next Monday I walked straight into clinic and told my nurse practitioner I needed a mammogram. A few days later I got the call saying they wanted me to come back for more tests. Do you know how many times I have made that phone call to my own patients?

I had a very early form of cancer in one breast. While some might have had just one breast removed, I chose to have a double mastectomy because I was young for the diagnosis. Yet, even after the operation, I still felt there was something amiss. So I took a blood test to see if I had a mutation in my BRCA1 or BRCA2 genes. These are genes that, if abnormal, increase the risk for breast and ovarian cancer in women and for prostate cancer in men – and put both genders at increased risk for melanoma and pancreatic cancer. My probability of having this mutation was less than 1 percent because I have no family history of these diseases. I took the test anyway because I was under 50. My suspicions were confirmed: I have the BRCA2 mutation. It gives me an 85 percent chance of developing breast cancer and a 40 percent chance of developing ovarian cancer.

I can't tell you how many times patients have asked, "What would you do?" So I have reflected on this question countless times. I have never once had doubts about the double mastectomy, even before I knew about the mutation. I had my ovaries removed as well. I am settling slowly into the knowledge that I have a higher risk of developing pancreatic cancer and melanoma. My father was just diagnosed with pancreatic cancer last week. Honestly, when you have a known cancer mutation, you're never out of the woods.

I have three children – two sons, 12 and 13, and a 9-year-old daughter. Of course I am very curious about their genetic status, but we are a very empowered and independent family and I want them to eventually make that decision themselves. Typically, when BRCA2 is present in a family, aggressive screening is done at age 35.

For me, the difficult decisions early on were whom do I tell and how do I deal with the fact that I have what I treat? I was a little worried about how my patients would feel if they knew that all of a sudden I'd become one of them. For my patients who know, it has been a positive. Once, I was talking with a patient who had had a bilateral mastectomy and was feeling really depressed. I asked her what was wrong. She said that I just didn't get it. I told her that I knew exactly how it is – that I had been sitting in the very same exam room just one year before. "But you look so beautiful and upbeat," she said to me. I told her, "So will you in a few months, I promise." It was powerful, knowing exactly what this patient was experiencing and being able to coach her through it.

My diagnosis and the operations I have had have given me a visceral understanding of how vulnerable cancer leaves you. It was hard for me to surrender control to someone else. But perhaps even more difficult was the nature of the surgeries. I identify not just as a doctor and a scientist, but also as a mother and a woman, and I had had the very organs that define me as a woman removed. A skilled plastic surgeon made me feel whole again. The care and love my team lavished on me left me with minimal scars. Of course my experience made me think about Angelina Jolie and how potent her voice has been for young women facing cancer. Angelina personifies beauty and femininity the world over. Cancer can't change that.

I am sharing my story because, as a scientist, I want people to know that you can live with cancer. As a doctor, I know how unpredictable cancer is. As a patient, I have faced my mortality.

But I'm lucky. Every day, I get to work in a lab and with patients to develop and apply new cancer therapies. It's not just my job, it's my passion. I am often up at 2 a.m., searching for a pencil to write down all the ideas rushing through my head. It's why I was back at work two days after surgery; even my plastic surgeon made fun of me. Of course, now I am motivated in part by my disease and by the possibility of my children having the same mutation. But my own universe is not everything. I am also driven by every patient I have ever seen whom I felt I couldn't help.

I have always been blessed with the ability to see some good in anything bad, and there has been plenty of good along the way. Professionally, I have never been more energized. The recent Supreme Court ruling banning the patenting of genes could unleash mountains of critical information about BRCA mutations if patients' rights activists win their fight to access it. That data would be put to good use in my lab. We have plenty to work with, though, while we wait. We are already well aware of the specific pathway that BRCA tumors follow, so we know where to set up the roadblocks. I am not just hopeful; I'm confident.

Personally, I now realize that saying each day is precious is far different than knowing it. I have gone from being a woman who needs no one to being someone who can ask for support. People came out of the woodwork to help me, and my family stood strong. The other day my daughter asked me, "Are you done with that cancer now, Mommy?" I got to say, "I'm working on it, honey."

What could be more powerful than that?

As told to Claire Conway

PHOTO: STEVE BABULJAK

BRAVE NEW WORLD

By Kate Volkman Oakes

WHEN JULIA CHOI'S GRANDMOTHER SUFFERED HER THIRD STROKE, A DOCTOR IN THE EMERGENCY ROOM GAVE HER BLOOD THINNER MEDICATION TO PREVENT ANOTHER STROKE. NOT LONG AFTER, CHOI'S GRANDMOTHER EXPERIENCED GASTROINTESTINAL BLEEDING – A COMMON SIDE EFFECT OF BLOOD THINNERS. SHE LATER PASSED AWAY. CHOI NEVER FOUND OUT IF THE BLEEDING WAS INDEED CAUSED BY THE DRUG OR BY SOMETHING ELSE.

The memories of her grandmother's struggle came flooding back to Choi last spring when she took a course in genetics and drug response as a first-year pharmacy student at UC San Francisco. Not only did she learn that some people carry variants in their genes that cause adverse reactions to clopidogrel, the drug her grandmother had been given, but Choi also had the opportunity to have her own genes tested for such mutations.

The UCSF School of Pharmacy is one of the first pharmacy schools in the nation to offer its students genetic testing for drug response. It's just one way UCSF is educating students about precision medicine – an emerging approach that collects and integrates vast amounts of data and new technologies to develop individualized treatments. As the health care providers of the future, today's students will be diagnosing and treating patients based on a barrage of information not just about the person in front of them, but also about millions of other patients around the world.

Genetic codes; environmental and nutritional data; reports from patients' electronic health care monitors; and input from epidemiologists, informaticians, and scientists studying the molecular underpinnings of disease – all these factors must be considered in the world of precision medicine. The upside is that "we will be able to find the right treatment for our patients, without going through all the trial and error we do today," says Catherine Lucey, MD, a resident alumna and the vice dean for education at UCSF School of Medicine.

"What's so great about being at UCSF is that we're fortunate enough to have people who strive to practice tomorrow's medicine today," she continues. The University has been educating its students regarding precision medicine for years by teaching them about genetics, population-based clinical research, and the nature and importance of working in multidisciplinary teams.

TAPPING THE POWER OF GENES

As Choi learned firsthand in the School of Pharmacy's Genetics and Pharmacogenetics course, a single gene can influence drug response – knowledge that is shaping more precise approaches to therapeutics.

She was one of 22 out of 122 students in her class to opt in for the genetic testing, which evaluated the CYP2C19 enzyme. People who have variants of this enzyme can over- or under-metabolize clopidogrel (also known by the brand name Plavix), which means they are 3.6 times more likely to suffer a heart attack, stroke, or even death. These outcomes can be easily avoided, however, by first testing a patient for the genetic mutations and then prescribing a higher or lower dose of the drug or another drug entirely.

"How much do you learn when you have a touchstone to the material?" asks Kathleen Giacomini, PhD, professor and co-chair of the Department of Bioengineering and Therapeutic Sciences. "If it's in your genes, you're going to learn it."

Choi certainly did. She was relieved to discover that the CYP2C19 variant is not present in her own genes. The experience was intensely personal for her but, she says, "even for the students who didn't participate in the testing, it became personal. We're such a small class and we know each other well, so everyone was invested in the results."

By educating students about how a single gene can affect drug response, the testing illuminated how helpful such information can be

ILLUSTRATION: STEPHANIE DALTON COWAN

for their future patients, says course co-director Esteban Burchard, MD, MPH, the Harry W. and Diana V. Hind Distinguished Professor in Pharmaceutical Sciences II. Choi echoes his sentiment, adding, "As we become the next generation of pharmacists – and doctors and nurses could implement this, too – it will be important for us to use genetic testing to provide more effective medications, as well as cost savings."

Practicing this kind of precision medicine will not only save money, it will save lives, says Nadav Ahituv, PhD, an associate professor of bioengineering and therapeutic sciences. According to the Food and Drug Administration, adverse drug reactions are the fourth leading cause of death in the United States, outranking pulmonary diseases, diabetes, AIDS, pneumonia, and accidents.

As medications are metabolized in the body, they interact with more than just one gene. Multiple genes end up influencing how an individual responds to a drug, says Ahituv. "Because patients are getting their genomes sequenced, we can now look beyond just one gene and its response to a specific drug to a multitude of genes and their responses to many drugs."

In his course Principles of Pharmacogenomics, Ahituv teaches both PharmD and PhD students how a drug interacts with many genes during its metabolism, and how those interactions determine the correct dosage of the drug. He also demonstrates how to use genomic websites, such as PharmGKB, to get a fuller picture of this process.

"I think we should be much smarter about what drugs we prescribe based on a patient's genetics," says Ahituv. "And for PhD students doing pharmacogenomic research, they will walk away from this course knowing that when a new drug comes on the market, it's important to discover which genes it interacts with and how."

Such knowledge can be sharpened even further by analyzing genetics at a population-wide level. "You need large numbers of people, typically, to research and understand and prove that one drug will do better in one type of person than another," says Jeffrey Martin, MD, MPH, a resident alumnus and a professor of epidemiology and biostatistics. In his course Epidemiological Methods, he teaches students how to design a study to generate that data, and then how to interpret it.

For example, 1,000 cancer patients might have gene A and 50 might have gene B. In examining people with gene A, you find that a new drug didn't make any difference. But among the gene B group, it had a whopping effect. "Now you know to use this particular chemotherapy in people with gene B, but you stay away from it in gene A," says Martin.

EXPANDING TEAMWORK

As more and more data become available to help diagnose and treat patients, UCSF leaders like Lucey say health care providers and basic scientists will need to interact more closely. Basic scientists can help clinicians interpret their molecular data, and clinicians can help basic scientists understand how their research is applied at the bedside. UCSF already offers a crash course for each set of students, designed to teach them about their colleagues on the other side of the bedside/lab bench divide.

Medical students can dive deeply into basic science for a period as short as a summer or as long as a year through the Molecular Medicine Pathway – one of five pathways medical students use to guide their education at UCSF. By putting would-be doctors to work in a lab, the program helps them to better comprehend genetic mutations and drug design, says its co-director, Ben Cheyette, MD, PhD, an associate professor of psychiatry.

"FOR PHD STUDENTS DOING PHARMACOGENOMIC RESEARCH, THEY WILL WALK AWAY FROM THIS COURSE KNOWING THAT WHEN A NEW DRUG COMES ON THE MARKET, IT'S IMPORTANT TO DISCOVER WHICH GENES IT INTERACTS WITH AND HOW." – NADAV AHITUV

While medical students are getting behind the microscope, PhD students are getting in front of physicians and their patients in the course Introduction to Human Biology and Medicine.

Of all that course's lectures – about everything from leukemia to kidney disease – one of the most popular is on epilepsy. Daniel Lowenstein, MD, a resident alumnus who holds the Dr. Robert and Mrs. Elinor Aird Endowed Chair in Neurology, begins with the basics: he defines a seizure, lists possible forms of treatment, and explains how many patients suffer from the condition. Then he brings the facts to life by introducing a patient whose uncontrolled seizure activity was grooming her hair. Multiple drugs had failed her, so she opted for surgery. While she's sitting in front of the students, Lowenstein shows a movie of her operation, with her skull open and her brain visible. In the movie, the surgeon interacts with her to determine which part of her brain to remove to eliminate the seizure focus, while still preserving critical brain function.

"The students are just awestruck," remarks course director Andrew Leavitt, MD, a fellowship alumnus and a professor of labora-

tory medicine. “Listening to patients talk about their experiences empowers the students to think big. It’s really neat for them to see – ‘if I develop a drug, this is the person who is going to take it.’”

DATA, DATA EVERYWHERE

With their eyes set on precision medicine, UCSF leaders are considering how to evolve these existing courses to best educate future physicians, pharmacists, nurses, and dentists. What they consistently find is that data, massive amounts of data, will transform every discipline.

“We are asking, ‘What resources are available to access and interpret this data, and how do we use them?’ We all will need to be at least partial experts in informatics,” says Clay Johnston, MD, PhD, a resident alumnus, the associate vice chancellor of research, and the director of UCSF’s Clinical and Translational Science Institute.

Two UCSF professors are leading the charge to increase the computational literacy not just of the University’s students, but also of its residents, fellows, and faculty. Launching the Institute for Computational Health Sciences are Neil Risch, PhD, director of the Institute for Human Genetics and the Lamond Family Foundation Distinguished Professor in Human Genetics, and Michael Fischbach, PhD, a resident alumnus and an assistant professor of bioengineering and therapeutic sciences. UCSF also plans to develop a systems pharmacology program with support from the Li Ka Shing Foundation, a key partner in helping advance precision medicine.

Another evangelist, Robert Nussbaum, MD, a professor of genetics, is striving to spread knowledge of the emerging field more widely within the UCSF community. He is the force behind an introduction to genomics course that will be offered in January 2014 through the online learning company Coursera, another UCSF partner. He’s also spearheading two patient-focused genetic conferences that will help educate students, residents, and clinical faculty in a conversational format much like that of weekly rounds. One conference will infer targeted therapies for tumors based on genomic analysis. The other will attempt to diagnose otherwise nearly impossible to diagnose disorders or diseases – an effort that “will take a tremendous amount of bioinformatics and computer analysis,” says Nussbaum, who is also the Holly Smith Distinguished Professor in Science and Medicine.

Mastering such data will mean far more for patients if the providers of the future – and those who teach them – experience precision medicine personally, say UCSF leaders. As Burchard and his team prepare to offer genetic testing to another class of first-year pharmacy students next spring, and add even more enzymes that affect drug response, he and his fellow faculty in the Department of Bioengineering and Therapeutic Sciences had the chance this summer to participate in a similar effort. They learned about how they respond to well-known drugs and how their genetic ancestry can influence drug response. In the School of Medicine, Lucey and Johnston are crafting an opportunity for whole genome sequencing – first for faculty and then for students.

“We’re working together to prepare for the day when it’s no longer going to be an individual doctor with her black bag, but a doctor with a big computer,” Lucey says. “But the best part is that our patients will get better care. If we can design systems that help us do our work more efficiently, so we can spend more time giving more personalized care to patients, I think everyone will be happier.”

PHOTO: STEVE BABULJAK

Pharmacy student Julia Choi received genetic testing in one of her courses, an experience that she says was intensely personal – and important training for her future as a pharmacist.

Paying Tribute to Mission Bay's Big Dreamers and Doers

UC San Francisco Marks 10 Years at Mission Bay, Thanks to Group of Dedicated Donors and Friends

As UCSF celebrates a decade since opening its first research building at Mission Bay, it's hard to imagine what San Francisco – or the University – would be like if UCSF had moved out of the city 10 years ago.

In the late '80s and '90s, UCSF was running out of space on Parnassus but was looking to expand. The University might have been forced to build its next campus outside of San Francisco, if it hadn't been for the strategic acumen of the Bay Area Life Sciences Alliance, or BALSA.

A team of committed UCSF donors and friends, BALSA convinced the city of San Francisco and the Catellus Development Corp. to donate 43 acres of land at Mission Bay to UCSF. The group partnered with many leaders from UCSF, government, business, and the community.

Together, they planned a campus that would generate new bioscience discoveries and revolutionize the quest for better ways to deliver health care. They also believed it would fuel the economy and create jobs.

Ground broke in 1999, and Genentech Hall, the first building completed on the new UCSF Mission Bay campus, opened its doors in October 2003. A decade later, the planners' ambitious vision has been more than realized and UCSF benefits from a campus that is an epicenter for science, health, and hope. Nearly 4,000 students, faculty, staff – including three Nobel laureates – learn, work, and teach there. It has attracted a growing ecosystem of more than 50 bioscience start-ups, nine established pharmaceutical and biotech companies, 10 venture-capital firms, and several top scientific institutions.

Now occupying 57 acres, the Mission Bay campus continues to change the city landscape. UCSF Medical Center at Mission Bay will open in 2015, furthering the vision of the pioneering members of BALSA. It will include the Bakar Cancer Hospital, named in honor of Gerson and Barbara Bass Bakar in recognition of their long-standing commitment to cancer programs. As one of the most advanced cancer care facilities in the country, Bakar Cancer Hospital will help guide the future of cancer treatment, research, and education.

Hear more about Mission Bay's success: bit.ly/ucsf-mb

BALSA Board of Directors (1999)

- Gerson Bakar, chairman, Gerson Bakar & Associates
- T. Robert Burke, chairman, AMB Property Corporation
- Donald Fisher, chairman, The Gap Inc.
- Clifford Graves, president, BALSA
- John Larson, Esq., senior partner, Brobeck, Phelger & Harrison
- Rudolph Nothenberg, chief administrative officer (retired), City of San Francisco
- Sanford Robertson, president, S.R. Robertson & Co.
- William Rutter, PhD, chairman, Chiron Corp.
- Lloyd Smith, Jr., MD, associate dean, UCSF School of Medicine
- Thomas Swift, executive vice president, BALSA

PHOTO: AUDREY FEELY

Alumni Hub

GRADUATES FLOCK TO ALUMNI WEEKEND FUN

UC San Francisco hosted its second campus-wide alumni reunion April 25-27, 2013. The event, which united all four professional schools and the Graduate Division, boasted 2,200 attendees, a 20 percent increase over the inaugural weekend in 2012. Alumni, faculty, students, staff, and friends from 24 states and five countries enjoyed more than 88 events, including a zero-year reunion for 2013 graduates, a mini-medical school on integrative medicine, and a kickoff reception with legendary percussionist Pete Escovedo.

Save the date for Alumni Weekend 2014: May 29-31!

PHOTOS: NOAH BERGER; DONALD CHAN; ELISABETH FALL

AAUCSF President's Message

UCSF has played an integral role in my life for more than a decade. It was here that I earned my advanced nursing degree, formed lifelong friendships, met my husband (Mike Thomas, DDS '72), and staked out my career. As the 2013-2015 president of the Alumni Association of UCSF (AAUCSF) Board of Directors, I have the great privilege of serving as an ambassador for our alma mater – a global educational powerhouse in the diverse, innovative Bay Area – and giving back to the university and alumni communities that have given me so much.

This is a unique time in the history of UCSF. Innovation and creativity thrive on both the Parnassus and Mission Bay campuses, which have been transformed by the addition of beautiful new buildings and facilities. I invite you to come and see the changes for yourself!

One thing has remained constant: we continue to train tomorrow's health care leaders. The future of UCSF is bright and exciting, and I encourage all members of the UCSF community to get involved with AAUCSF. Across the country and around the globe, we offer many opportunities to connect with alumni and friends through our regional chapters, local events, mentorship and travel programs, and our signature event, UCSF Alumni Weekend. Last spring drew more than 2,000 guests from 24 states and five nations to almost 90 events! (Save the date for May 29-31, 2014!)

Thank you for representing UCSF so well through your loyalty and success. Please contact us if you'd like to get involved or learn more, or visit our website (www.ucsfalumni.org) for news and events. I look forward to seeing you in May, if not before!

Susan Walczak, MS '02
President, Alumni Association of UCSF

School of Dentistry

ALUMNI PROFILES

Medal of Honor recipient Harvey Brody, DDS '63, surrounded by some of the students whose lives he transformed.

AWARD WINNER: HARVEY BRODY

If you really want to know Harvey Brody, DDS '63, a winner of this year's Medal of Honor, just ask one of the students whose lives he transformed to describe him.

The program he co-founded, UC San Francisco's Post-Baccalaureate Reapplication Program, gives underserved applicants who are on the cusp of acceptance a second chance at applying to dental school. The first of its kind for prospective dental students, the 18-month program involves an academic boot camp, an internship, and life coaching to help students reapply from a stronger position.

"Their personal narratives are just amazing; I still get chills thinking about them," says Brody. Many came as immigrants to the United States at 11 or 12 years old without knowing English. They grew up in the poorest of neighborhoods, often around violence and drug abuse and with parents who were absent either physically or emotionally. "For some magical reason, these kids had the perseverance to get through all that and come out the other end very positive and compassionate," says Brody.

Some 95 percent of his students have been successfully accepted to dental schools, and 83 percent of them have gone on to work in underserved communities. Yet the best proof of concept is this: one of his former students now codirects, with Brody, the San Francisco State University Dental Post-Bac Program.

Brody's early career aspirations were also driven by access to care and equality. He started the UCSF Mount Zion Upward Bound Clinic, which provides free dental care to underprivileged teens. At that point Brody was living a double life between his Upward Bound patients and his private practice in the Marina. So he moved his private practice to Mount Zion. "I would treat presidents of corporations and foundations alongside my impoverished patients," Brody recalls. "It was sort of a living laboratory. My private patients saw the work being done and then made donations that subsidized the clinic."

He went on to chair Mount Zion's Department of Dentistry and created a residency program for treatment of the underserved during his tenure.

What drove Brody to a career of service? He thinks it all "crystallized" when he was at UC Berkeley as an undergraduate during the civil rights movement. "I took a class that covered the Supreme Court case that resulted in the Japanese being interned," recalls Brody. "All of the sudden it just resonated with me – there were gaps between what the government said and what our society and culture does. So I've essentially tried to address my personal life and professional life to that gap."

AWARD WINNER: PO-PING WONG

Po-Ping Wong, DDS '65, comes from a line of high achievers. Wong's grandfather was a chief county administrator during the Qing Dynasty in China, and his father was a revolutionary with Sun Yat-sen, eventually becoming a lieutenant general in Chiang Kai-shek's army. It's no surprise, then, that Wong was named a winner of the 2013 UCSF School of Dentistry Medal of Honor.

Wong immigrated to the United States in 1949 to pursue higher education. He had planned to return to China until the Communists swept into power. Wong's father advised him to stay in the US and transfer his "allegiance and love of country to the United States," he remembers.

Taking his father's words to heart, Wong decided to change occupations from agriculture, with which he had intended to fight famine in China, to "something more service oriented, to help the community in the US," he notes. That's how he arrived at the UCSF School of Dentistry. He was doubly proud when he took the oath of US citizenship during his junior year.

Shortly after graduating, he established a solo practice in Garden Grove, Calif., continuing to serve patients for 39 years until he retired in 2004. Wong has been an active member of the Lions Club since 1966, earned his real estate broker's license in 1978, and was the founding chairman of the first Chinese bank in Orange County, Calif., in 1982.

In his self-described "benevolent-dictator" style, Wong channeled two of his sons into following his footsteps to the UCSF School of Dentistry: Ted, DDS '84, and Andre, DDS '01. Wong is especially proud that he and Ted hold the record for the shortest period of time between graduation for father and son – just 19 years.

While his classmates have long applauded Wong's numerous talents and achievements, there was one overwhelming theme evident in their Medal of Honor nomination letters: They all recounted fond memories of Wong leading them in singing the alma mater at the conclusion of the annual Dental Alumni Association (DAA) Scientific Session. Marsha Mayer, RDH '65, summed it up when she wrote, "I knew it would be no effort to sing the praises of Po-Ping Wong."

ALUMNI PROFILE: DAA INSPIRES PRESIDENT-ELECT

When Chris Hayashi, DDS '93, MS '96, attended her first DAA board meeting she got a big surprise. The members weren't just faculty and staff of the UCSF School of Dentistry, as she had assumed, but busy dental professionals volunteering their time. "I was pretty impressed by that," Hayashi remembers. "I felt a sense of duty to help out."

As president-elect, Chris Hayashi will lead the planning for next year's DAA Scientific Session at Alumni Weekend, which she describes as "a great way to get your CE units and reconnect with the school."

Over the years, Hayashi has served not only as a member of the board, but also as chair of the membership committee, secretary, and now president-elect. Duty aside, she discovered that being involved on the DAA board "is fun. It's a great group of people who want to give back to the school that has given them an excellent training and livelihood," she says.

What Hayashi appreciates most, however, is the board's emphasis on providing support to students. "In the past five years, there's been a strong drive to increase the camaraderie and feel-good environment at the school," she says.

The DAA welcomes new students with a UCSF sweatshirt designed especially for their class and at the end of Introduction to Dentistry Week presents students with white lab coats that signal their official entry into the profession. Hayashi also values the fact that the DAA makes it a priority to contribute to student scholarships. And on a purely social level, she says the DAA has a blast hosting the annual Bear Bash party for students and alumni. "The DAA is always looking for ways to help students feel like UCSF isn't just a place to get a great education, but also a place where they are proud to belong."

It's a feeling Hayashi knows well. "Dental school was tough at times, but I am very proud to be an alum of UCSF. As a periodontist, I have the opportunity to see a lot of dentistry, and I am proud of the excellent clinicians and high-caliber dentists who are graduates of the UCSF School of Dentistry."

Family flew in from across the country to celebrate with Po-Ping Wong, DDS '65, as he received the 2013 Medal of Honor.

PHOTOS, THIS SPREAD: MILES GUYTON; DAVID HAND

SAVE THE DATE
Alumni Weekend

2014

May 29-31
Palace Hotel and UCSF

DAA President's Message

The UCSF Dental Alumni Association (DAA) is a vibrant organization of dentists and dental hygienists. Established in 1882 to meet the desire of alumni for a continuing relationship with the school, the DAA supports fellowship through student outreach and a host of other alumni activities.

This year we proudly celebrated our 117th annual DAA Scientific Session at Alumni Weekend – it's an outstanding multiday event filled with CE courses and networking events. As part of the session, class reunions are organized.

We also host student and alumni panels throughout the year, provide scholarships to students, and sponsor many alumni social events to promote camaraderie among alumni, students, and the dental school – such as our Bear Bash and Thirsty Bear Alumni Reception.

As president, I am honored to serve you. My goal is to increase membership and continue to provide a strong network for new graduates and alumni, and to use the DAA as a resource for communication among dentists, dental hygienists, and all other dental professionals.

Carmen Hipona, DDS '96
President, Dental Alumni Association

School of Medicine

ALUMNI PROFILES

Glenn Braunstein, MD '68, accepts the Alumnus of the Year Award at Alumni Weekend 2013.

AWARD WINNER: GLENN BRAUNSTEIN

In a classic 7-year-old-boy move, Glenn Braunstein attempted to lift a car. One excruciating groin sprain later, he was captivated by medicine.

"Our family physician paid a house call, gave me a shot, and the pain disappeared," recalls Braunstein, MD '68. "I thought, 'Wow! He's very powerful.' From that point on, I decided I was going to be a doctor."

And what a doctor this year's Alumnus of the Year would become: a renowned endocrinologist whose pioneering research on the human chorionic gonadotropin (hCG) hormone led to the development of the home pregnancy test.

Braunstein's UCSF classmates and professors recognized his promise early on, selecting him at graduation as one of the three student members of the Gold-Headed Cane Society, for best exemplifying the qualities of a "true physician."

He took that promise and ran with it, heading to Harvard for his residency. But the budding endocrinologist truly ramped it up at the National Institutes of Health, where he helped conduct pathbreaking studies on hCG while fulfilling his Public Health Service commitment.

The extensively cited work was the first of many influential studies in the field of reproductive endocrinology that would unfold over his impressive career.

After launching and heading Cedars-Sinai's first endocrinology division, Braunstein chaired the Department of Medicine for 26 years. The department flourished under his tenure, with many of its divisions consistently ranked in the top 50 by *U.S. News & World Report.* He also educated generations of medical students at UCLA, where he served as a professor.

The energetic father of two and

Second Annual UCSF Alumni Weekend Captures Smiles

Clockwise from top left: J. Renee Navarro, PharmD, MD '86, resident alumna, and Ken Bermudez, MD '92, resident alumnus; Julia Walsh, MD '74, resident alumna; Lon McCanne, MD '63, Don McCanne, MD '63, Richard Sherins, MD '63, and Robert Sherins, MD '63; Erin Sullivan, MS4, and Glenn Nakadate, MD '63; Class of '63 Medaling Ceremony toast; Andrew Baldwin, MD '03, and Chancellor Susan Desmond-Hellmann, MD, MPH, resident alumna.

grandfather of six has shared his expertise widely, advising the US Food and Drug Administration, serving on prestigious editorial boards, and even blogging for the *Huffington Post.* His peers and patients alike have lauded his contributions, from the *Los Angeles Business Journal,* which named him a Master of Medicine, to the Endocrine Society, which awarded him one of its highest honors.

"Besides being a superlative academician, Glenn is one of the finest human beings I have been privileged to know," his longtime Cedars-Sinai colleague Zab Mosenifar, MD, wrote in his nomination letter.

In a career packed with accomplishments, Braunstein says his favorite part has been caring for patients. "It reminds me why I went into medicine," he explains. Another reminder appeared when the son of his family doctor from all those years ago arrived at Cedars-Sinai for his medical training. "It really came full circle," Braunstein laughs.

Q&A: GENES AND PRECISION MEDICINE

Lindsey Criswell, MD '86, MPH, DSc, is a genetic epidemiologist, rheumatologist, and lupus expert at UCSF.

How would you define the burgeoning field of precision medicine?

Precision medicine is a process. The first phase is understanding how specific genes influence the development of disease. Some diseases are determined almost exclusively by genes; others are influenced by genes, but in a much more complicated way. Once we identify genes, then we can learn what biological pathways are relevant. Together with my collaborators within and outside the US, we have identified more than 30 genes that contribute to rheumatoid arthritis and lupus. We are now working to understand more specifically how these gene variants influence disease risk and outcome.

Lindsey Criswell is the Jean S. Engleman Distinguished Professor of Rheumatology at UCSF and chief of the division.

The second phase of precision medicine is developing drugs that target the pathways that are affected in individual patients.

What does precision medicine mean for your lupus patients?

Lupus can be difficult to diagnose because initially there may not be many signs of the disease. Plus there is no single test that can tell us who does and does not have lupus. We have to look for specific clinical features and consider specific blood test results, and then put the whole picture together. We have few clues that tell us at the outset if a patient will develop a severe form of the disease. Also, we don't have perfect drugs. Many have negative consequences for patients, such as increased susceptibility to infection.

With the final phase of precision medicine – maybe five years from now – ideally we'll be able to perform a blood test that is a panel of genetic variance relevant to lupus. Based on that information, we could say, for example, "You absolutely have lupus, and it's this type of lupus. That means you're more likely to have kidney disease, you're less likely to have blood clotting, and your disease is likely to become quite severe." Knowing how these genes influence disease outcomes and response to treatment will tell us more precisely how aggressively to intervene and with what specific therapies.

What do you think precision medicine means for the practice of medicine?

It represents a much more efficient way of practicing medicine than we have right now, because we would get a precise diagnosis, a precise management strategy, and a precise treatment. So we won't waste money. We won't waste health in terms of side effects from ineffective treatments. And we won't waste time with delays in diagnosis.

PHOTOS, THIS SPREAD: NOAH BERGER; UCSF

MAA President's Message

This past year, as I welcomed our first-year students at the annual Medical Alumni Association (MAA) New Student Barbeque, I was reminded of my own first weeks at UCSF. I remember wondering how I had been lucky enough to be attending this amazing school. As I met my classmates, I realized that each possessed skills, qualities, and backgrounds that were different from my own. All of us were there for a reason and would travel our own paths to graduation and on into our careers. Even so, we had two things in common: we could say we were part of the UCSF community, and we were all going off to change, and in some cases save, the lives of people we had yet to meet.

This year, the 150th anniversary of the founding of this great school, it is my honor to assume the office of president of the MAA. I can't help but think about all of the medical professionals who came before me and the countless numbers of patients they each helped, as well as the significant advancements accomplished because they followed this special path. It is my honor to carry on their legacy.

Kenneth Bermudez, MD '92
President, Medical Alumni Association

School of Nursing

ALUMNI PROFILES

Catherine Gilliss, RN, PhD '83, FAAN

AWARD WINNER: CATHERINE GILLISS

Listing Catherine Gilliss' career highlights is like lettering a Hollywood marquee: Chair, UC San Francisco Family Health Care; Dean, Yale School of Nursing; Dean and Vice Chancellor, Duke School of Nursing; Jane Norbeck Distinguished Alumna.

Gilliss, RN, PhD '83, FAAN, has played a leading role in every nursing production she has joined. She was among the first nurse practitioners in the country and went on to serve as president of the National Organization of Nurse Practitioner Faculties, an organization credited with providing major guidance for faculty who teach primary care nationwide. Her contributions to the field of family nursing are just as remarkable. She is internationally renowned for broadening the scope of the field beyond the focus on childbearing. Her research encompasses the influence of the family system on chronically ill patients and their illness.

Given her propensity to rise to the top, Gilliss has some well-informed and unique perspectives on leadership. She characterizes herself as a "servant leader," one who leads by serving others. "I think a lot of people are not successful as leaders because they are imposing an agenda, as opposed to developing the group they are leading," she says. "A good leader guides people toward a strong match of capability with opportunity."

According to Gilliss, she "cut her teeth" in leadership at UCSF with people she characterizes as some of the greatest minds in the field. "Not only did I earn my degree there, but I had the opportunity to take on some small, entry-level leadership responsibilities that ultimately led me to head Family Health Care."

Her son, Brian Gilliss, who was born at Moffitt Hospital, is now a fourth-year chief resident in anesthesiology. And his daughter is a legacy at the child care center across the street. "Yes, the generations continue at UCSF!" Gilliss says.

She is stepping down from the deanship at Duke later this year, having hired 75 percent of the faculty and more than tripled the size of the student body. "It's time for another to lead," she says. Her next move? "I would like to share the lessons I have learned about leadership in academic settings."

STUDENTS AWARDED ALUMNI SCHOLARSHIPS

Through the generosity of alumni, the NAA helps the school attract the best students, regardless of financial background, through its endowed scholarship fund. Congratulations to Holly Carpenter, Sharon Smith, Ryan Anson, and Danielle Hasting, who were each selected and awarded $4,000 at the Nursing Alumni Annual Luncheon. Additional congratulations to Jonathan Van Nuys, who received the 2013 Graduation Meritorious Community Service Award.

CELEBRATING HELEN MARTIN

This spring the School of Nursing celebrated the power of preceptors by honoring the legacy of the late Helen Martin, RN, MS '91, who was a preceptor, leader in faculty practice, and volunteer faculty member. Her husband, Seth Ammerman, and friends organized a Faculty Practice Award reception as a tribute to Martin and named Steve Leiner, MS, and Laurie Galaty, MS '92, as the award's first recipients.

The late Helen Martin, RN, MS '91, with her husband, Seth Ammerman.

Alumni Accoladesss

The Association of Women's Health, Obstetric, and Neonatal Nurses presented its highest honor, the Distinguished Professional Service Award, to Audrey Lyndon, RN, MS '04, PhD '07, FAAN, for her contributions to the field of women's and newborn care at UCSF School of Nursing. Lyndon is an associate professor in the Department of Family Health Care Nursing.

Congratulations, Audrey!

UCSF Alumni Weekend 2012
Good Times with Fellow Graduates

Members of the Class of 1953 celebrate their 60th reunion at Alumni Weekend.

The NAA is ably governed by a board consisting of graduates from 1975 to 2013, as well as student and faculty representatives. Get to know their names and introduce yourself at one of the alumni events throughout the year. Left to right: Julie Rossie, MS '05; Arielle Bivas, MS '14; Austin Nation, PhD '14; Elaine Lanier-Bohan, MS '02; Melissa Meighan, MS '03; Debra Vails-Qualters, BS '75, MS '84; Candace Miller, MS '77; Mark Wandro, BS '77; Zina Mirsky, RN, EdD; Catherine Camenga, MS '03; Susan Walczak, MS '02; Laurel Friesen, MS '75; Emily Rodda, MS '13; Dean David Vlahov, RN, PhD. Not pictured: Pauline Chin, BS '78, MS '92; Rebecca Conroy, MS '14; Alphoncina Kaihura, PhD '14; Elda Kong, NP '14; Judy Martin-Holland, MS '88, PhD '05; Marilyn Sargent Morgan, MS '06; Linda Ottoboni, PhD '15; Jensine Russell, MS '10; Sharon McCole Wicher, MS '82.

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NAA President's Message

As a graduate of UCSF School of Nursing, you are conferred membership in the Nursing Alumni Association (NAA). Our network of more than 9,000 alumni worldwide provides mutual support and friendship. We develop events and programs to foster an engaged community and to support the school in preparing the finest advanced-practice nurses and researchers.

The NAA is governed by a board comprising graduates from 1975 to 2013. Get to know our names and introduce yourself at one of our alumni events (see photo and caption at left).

You can enrich the NAA with your active participation. Attend an event, precept a student, connect with your peers, mentor a recent grad – there are many ways you can contribute to our vibrant alumni community! It has been an honor to serve as president, and I look forward to connecting with you. I hope that you will let me know how we can better serve you.

Catherine Camenga, MS '03
President, Nursing Alumni Association

PHOTOS, THIS SPREAD: ANGEL CHEN AND LISA FINKELSTEIN; BUTCH KARNASH; UCSF

School of Pharmacy

ALUMNI PROFILES

UCSF School of Pharmacy Dean B. Joseph Guglielmo, PharmD, resident alumnus (left), with Lloyd Young, PharmD '69 (right).

AWARD WINNER: LLOYD YOUNG

"I've been lucky. I've been in the right place at the right time," says Lloyd Young, PharmD '69, of his outstanding 44-year pharmacy career. But his fellow alumni believe that more than luck led to his remarkable contributions – and they recently made that clear by naming Young the 2013 Distinguished Alumnus of the Year.

It all began when he fortuitously chose pharmacy for an occupation and UCSF for his education. Close to graduating with a degree in public health from UC Berkeley, Young was simply seeking a way to support himself. "I knew that meant health care," he recalls. Of all the highlights from his career, Young says, "I'm most proud of being a UCSF graduate" – an honorable but humble remark considering all Young has accomplished.

His class was among the first to receive training in clinical pharmacy, in which pharmacists team up with nurses and physicians at the patient bedside to administer drugs and make treatment decisions. Captivated by this fresh approach to patient care, Young worked with the pioneers of the UCSF Medical Center Ninth Floor Project – a 24/7 satellite pharmaceutical service situated on the ninth floor of Moffitt Hospital, the first in the United States to bring the clinical pharmacy concept to life.

Young's early commitment to clinical pharmacy extended beyond patient care: along with his Medical Center colleague Mary Anne Koda-Kimble, PharmD '69, now dean emerita of the UCSF School of Pharmacy, he worked to further train pharmacy students in the field. The two also combined their expertise in a seminal textbook – Koda-Kimble and Young's *Applied Therapeutics* – that helped transform clinical pharmacy education nationally and internationally.

His reputation caught the attention of Washington State University's College of Pharmacy, which wooed the rising young faculty member to develop experiential training opportunities into a clinical pharmacy program. The next stop in Young's trailblazing path was the University of Texas, El Paso, where he founded a cooperative pharmacy program with the University of Texas, Austin, to draw more underrepresented students to the profession.

In 2000, Young seized an opportunity to chair the Department of Clinical Pharmacy at his alma mater. "He did some very hard things that were not particularly popular but paid off," reflects Koda-Kimble. "He began to focus the faculty on the importance of research, because he knew funding was down and they would need to generate their own salaries through research grants," she explains. "Today, that department brings in as many research dollars as the basic science departments."

Young retired in 2006, feeling that he had reached the pinnacle of his career in clinical pharmacy. But he was lured back into service as dean of the Eugene Applebaum College of Pharmacy and Health Sciences at Detroit's Wayne State University, where he currently oversees 12 health care programs ranging from pharmacy to physical therapy to mortuary science.

"Lloyd's career reflects his personality," says Koda-Kimble. "He's understated, but highly influential; his impact on the practice and education of pharmacists has been huge."

Befitting his unpretentious nature, Young concludes, "I keep using the word lucky to describe my career. I read recently the definition of luck is the intersection of opportunity and preparedness. I'm not sure I was prepared, but there were opportunities, and I took them."

The extraordinary career of Lloyd Young, PharmD '69, Distinguished Alumnus of the Year, was celebrated during Alumni Weekend.

PAA President's Message

Since joining the Pharmacy Alumni Association (PAA) board three years ago, I've seen it flourish in both activity and impact, and much of this growth can be attributed to our fantastic outgoing president, Wilma Wong, PharmD '73. Thank you, Wilma. I also want to thank Larry Pinson, PharmD '73, for his hard work as the immediate past president, as well as Nancy Ichuiji, PharmD '83, and Lily Lee, PharmD '77, who will continue to serve as secretary and treasurer, respectively. I am also pleased to announce that Brian Komoto, PharmD '81, has assumed the role of present-elect.

John Young, BS '54; Cooky Quandt, PharmD '72; and Joanne Yasuda, PharmD '94, recently stepped off the board. The contributions they made to UCSF are immeasurable. Their seats have been filled by Stewart Akahoshi, PharmD '83; Wendy Sui, PharmD '10; and Glenn Yokoyama, PharmD (who will add a unique and valuable perspective as a non-alumnus member of the faculty).

I look forward to seeing and interacting with many of you during my time as PAA president – especially during Alumni Weekend 2014 (my 50th reunion)!

Robert Levin, PharmD '64
President, Pharmacy Alumni Association

Regional Alumni Events

Hundreds of alumni – a few dozen of whom are pictured here – enjoyed themselves at recent events in Irvine, Las Vegas, Sacramento, San Diego, and the San Francisco Bay Area.

Second Annual UCSF Alumni Weekend

Left: The Class of 1983 celebrates 30 years. Right: Dean Emerita Mary Anne Koda-Kimble, PharmD '69, poses with two current students.

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PHOTOS, THIS SPREAD: MELANIE DERYNCK, NOAH BERGER

Graduate Division PHD AND POSTDOCTORAL ALUMNI

ALUMNI PROFILES

Pablo Valenzuela, PhD, a postdoctoral alumnus, makes his way to the podium to accept the Graduate Division's first-ever Distinguished Alumnus of the Year Award at Alumni Weekend 2013.

AWARD WINNER: PABLO VALENZUELA

UC San Francisco's Graduate Division bestowed its first-ever Distinguished Alumnus of the Year Award on a scientist who sets a high bar for the award: Pablo Valenzuela, PhD. The former UCSF faculty member and postdoctoral alumnus has saved countless lives with his inventions and propelled science forward with his transformative discoveries.

The Chilean national was recruited to UCSF by William Rutter, PhD, then head of the Department of Biochemistry and Biophysics. Valenzuela's groundbreaking work on hepatic viruses in Rutter's lab pulled him out of academia and into applied sciences. In 1981, he and Rutter partnered with Edward Penhoet, PhD, to start Chiron Corporation, which by 1997 was the second-largest biotechnology company in the world. Within four years of Chiron's founding, Valenzuela had invented a vaccine for hepatitis B and a test that could be used to screen donated blood for the virus. His work in this area also led to his discovery of hepatitis C and a blood screening test for its detection. Perhaps more momentous still, Valenzuela invented the first test to detect HIV.

"Our work made the world's blood supply safe," says Valenzuela. "It's very gratifying knowing that we saved lives."

In fact, Valenzuela holds more than 50 patents – to date. And his hepatitis B vaccine is the highest producer of royalties for the University of California system.

Valenzuela left Chiron after 20 years to form Chile's first biotech company, GrupoBios SA, and the Fundación Ciencia & Vida. The Fundación is a nonprofit organization that acts as an interface between academia, government, and industry to improve economic and societal development through the advancement of the biological sciences.

The ties between the Fundación and UCSF are quite strong. Valenzuela has created a Science and Friendship society, which enables UCSF faculty and graduate students to visit the Fundación for one week each year to connect with their Chilean counterparts. "For science to flourish, we have to have international interaction among scientists," says Valenzuela. "We need to get together to talk about science and our lives."

When the program started, it was difficult to recruit graduate students. "Now we are in our 10th year, and we have 60 applications for 18 spots," says Valenzuela. Some 30 UCSF professors have participated, including Chancellor Susan Desmond-Hellmann, MD, MPH. Many UCSF graduate students also do pre-postdoctoral training at the Fundación in the intervening months between their graduation and the start of their formal US postdoc programs.

Valenzuela still actively collaborates with UCSF faculty on research ventures. "I love UCSF. I chose to study and work there because it was where the greatest science was being done by the best teachers," he says. "Without UCSF, I wouldn't be where I am today."

Graduate Division Gala Dinner at UCSF Alumni Weekend

Bioengineering grads and alumni at start-ups connect during the Graduate Division Gala.

Alumni from UCSF Professor Peter Walter's lab celebrate with Walter, PhD, and his wife, Patricia Caldera-Muñoz, PhD (second and third from left).

UCSF alumni now at Genentech enjoy the Graduate Division reception.

ALUMNI PROFILE: FROM SECRETARY TO SCIENTIFIC STANDARD-BEARER

Vicki Chandler, PhD '83, never thought she would make a significant mark in science. She never even thought she would get a college degree.

By the time she was 20, Chandler had married, become the mother of two children, and divorced. She was working as a secretary when she met several other young single moms who were going back to school. "It became clear to me that this was something I could do," she remembers. "When I got married, I assumed I was giving up that career path."

Chandler enrolled at Foothill College and, as an avid scuba diver and ocean lover, planned to study marine biology. But an introduction to biology sparked her enthusiasm for genetics, and she never looked back. Two years later, she transferred to UC Berkeley, where she majored in biochemistry and studied yeast cell division.

When it came time to select a graduate program, she found herself caught up by the energy of innovative young scientists at UCSF, especially Keith Yamamoto, PhD, now vice chancellor for research. Chandler joined his lab and continued to study gene regulation, this time in animal systems. "What characterized Vicki at the time still characterizes her today – smart, enormous passion, drive, and hard work," says Yamamoto.

While looking for postdoc opportunities, Chandler stumbled upon some plant literature that shaped the rest of her career. It described maize (corn) as an ideal system for studying gene expression – in particular, a phenomenon in gene silencing called paramutation.

Until Chandler started her postdoc at Stanford University, paramutation was "this huge black-box mystery: it suggested there was a lot we didn't understand about how genes change each other's expression," she explains. Over the course of her career, first at the University of Oregon, then at the University of Arizona, her lab uncovered some of the underlying mechanisms of the phenomenon, bringing clarity to that black box. Her team's results have implications for animals and humans, too.

In 2009, the Gordon and Betty Moore Foundation beckoned Chandler with a new challenge – serving as director of the organization's science program. In that role, she is responsible for leading a team charged with identifying and funding early-stage research across the life and physical sciences.

"Vicki understood from early on that there are many ways to use PhD-level training in the biological sciences," says Yamamoto. "From yeast to mammals to maize into science policy and support, she has applied rigorous problem-solving to rise to leadership across the field. Her career is a standard-bearer for that very point and for UCSF training. It's really impressive."

Vicki Chandler, PhD '83, trained in Keith Yamamoto's lab and later served with him on the Board on Life Sciences – the committee that recommended the National Academy of Sciences' seminal report on precision medicine.

PHOTOS, THIS SPREAD: MARK SANCHEZ; UCSF

SAVE THE DATE
Alumni Weekend

2014

May 29-31
Palace Hotel and UCSF

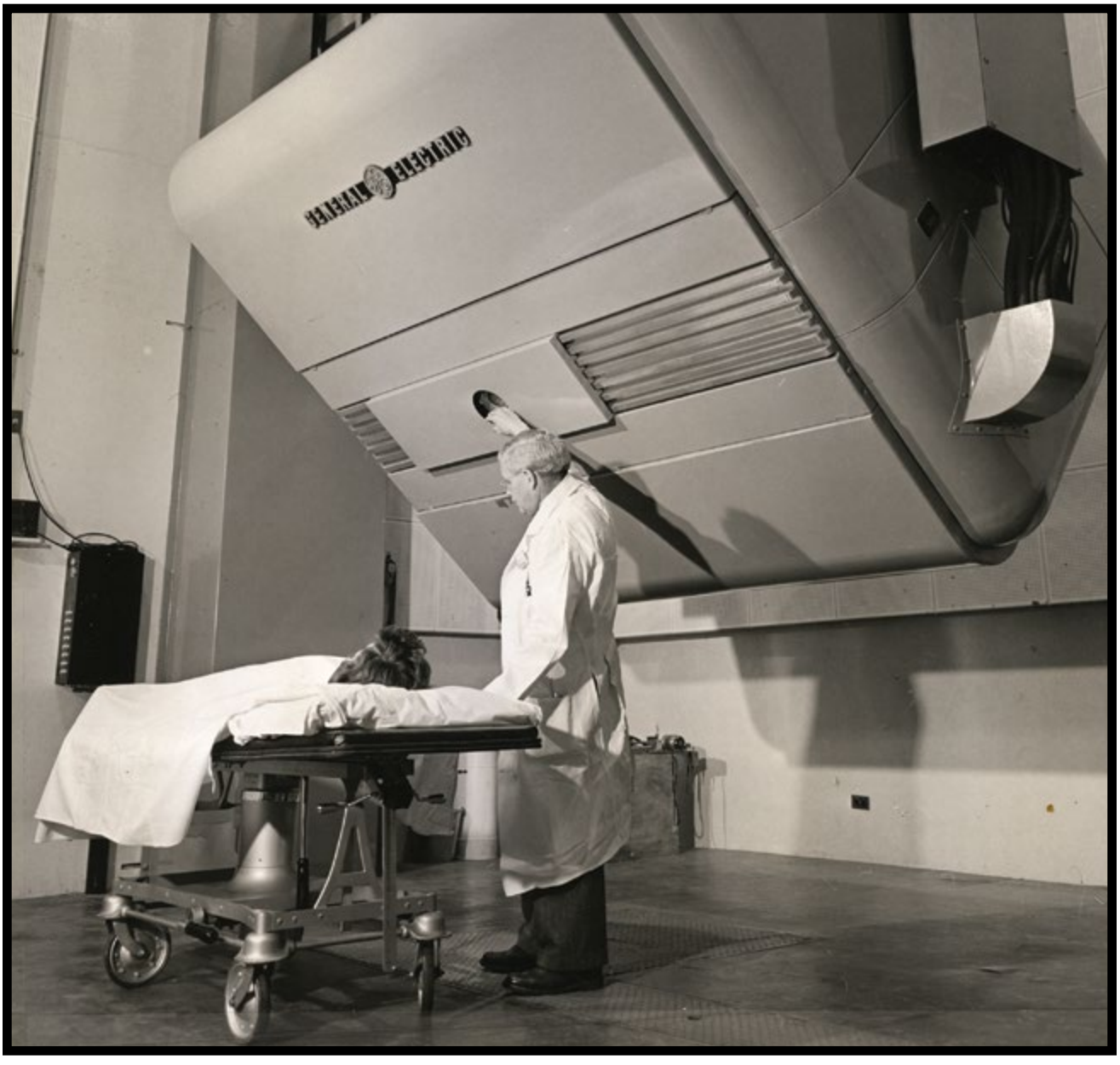
GDAA President's Message

As a doctoral, master's, or postdoc alumnus, you belong to the Graduate Division Alumni Association (GDAA): a network of thousands who trained in the world-class research environment at UCSF. I am proud and excited to serve as your GDAA board president this year.

In the past year, we've seen the GDAA grow through events and programs designed for UCSF's research community – from lab reunions at the second annual Graduate Division Gala during Alumni Weekend to regional receptions at professional meetings to student and postdoc mentoring events on campus. I hope you have also enjoyed the research highlights and UCSF updates featured in the Graduate Division eNews. Stay tuned to learn more about the GDAA, what's planned for the coming year, and how to get involved.

I look forward to connecting with many of you, and I hope you will email me at gradalumni@support.ucsf.edu with your ideas for the GDAA!

Adam Mendelsohn, PhD '11 (Bioengineering)
President, Graduate Division Alumni Association



Robert Stone and the Synchrotron | Circa 1956

UCSF Library Archives and Special Collections

Recruited in 1935 to head the new Division of Radiology at what was then called UC Medical School, Robert Stone, MD, worked with Nobel Laureate Ernest Lawrence, PhD, and other physicists at Crocker Lab at UC Berkeley to pioneer X-ray technology and radiation therapy. He stands here with his 70MeV electron synchrotron, which he built with General Electric, under contract from the Atomic Energy Commission. Cancer patients were treated with the massive radiation device from 1956 to 1964.

The work Stone did with the machine laid the foundation for safe clinical use of radiation in the fight against cancer. Stone's work in safeguarding scientists against the dangers of radiation during WWII had earned him what was at the time the nation's highest civilian honor. Called the Medal for Merit, the award was bestowed upon him in 1946 by President Harry Truman.

Listen to a 1964 recording of Stone: bit.ly/ucsf-stone

PHOTO: COURTESY OF ARCHIVES AND SPECIAL COLLECTIONS, LIBRARY AND CENTER FOR KNOWLEDGE MANAGEMENT, UCSF

Kids at Our Core

We need private philanthropy to help us fight for the health, hope, and happiness of the critically ill children we treat. For more information on how to support children's health at UCSF, please contact Tammy Nicastro at 415/502-8304 or tnicastro@support.ucsf.edu.

ucsfbenioffchildrens.org

UC San Francisco's physician-scientists are driven by the urgency of treating the most vulnerable young patients who have run out of options elsewhere. Combining basic science research with innovative clinical care, UCSF is world renowned for delivering breakthrough therapies that have saved the lives of countless children.

In 2015, the Benioff Children's Hospital at UCSF's Mission Bay campus will open its doors, offering pacesetting pediatric facilities. The state-of-the-art hospital will adjoin two additional new hospitals – for women and for cancer patients – ensuring a seamless transition for children who encounter a range of challenges, from complications of birth to a diagnosis of cancer.

PHOTO: ERIC DESCH PHOTOGRAPHY

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READ HOW **PRECISION MEDICINE** AT UC SAN FRANCISCO IS:

Gaining steam with help from some of the world's foremost thought leaders.
PAGE 12

Using big data to personalize care for multiple sclerosis patients.
PAGE 22

Enlightening students as they opt to have their own genes tested.
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AND DON'T MISS:

The story of an oncologist who discovers she has the BRCA2 mutation.
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