DISCOVERIES

INNOVATIONS IN RESEARCH, HEALTH CARE AND EDUCATION

VOLUME 5 / 2014

UC San Diego
HEALTH SCIENCES

DISCOVERIES

INNOVATIONS IN RESEARCH, HEALTH CARE AND EDUCATION
VOLUME 5 / 2014

Contents

On the cover:

Fibrous neural connections are depicted in this tractograph of a human brain. The technique maps the flow of water molecules inside and outside of neurons using multiple imaging technologies and computer analyses, producing a three-dimensional rendering for use in diagnoses and treatment.

Image courtesy of Nemtics (Leipzig, Germany) and Sebastian Eichelbaum, Mario Hlawitschka and Gerik Scheuermann, University of Leipzig (IEEE Transactions on Visualization and Computer Graphics, Vol. 19, 2013)

discoveries.ucsd.edu

"Our goal is to not just ease the human condition, but improve it through new discoveries and therapies across the spectrum of medical science."

David A. Brenner, MD

THE 19TH-CENTURY ENGLISH NOVELIST GEORGE ELIOT ONCE ASKED, "WHAT DO WE LIVE FOR, IF IT IS NOT TO MAKE LIFE LESS DIFFICULT FOR EACH OTHER?"

I'm reminded of those words by the efforts of the thousands of men and women who work within UC San Diego Health Sciences to not just ease the human condition, but improve it through new discoveries and therapies across the spectrum of medical science.

I'm reminded too by those who make ideas happen, the men and women, foundations and corporations, who have been extraordinarily generous in their support of this institution and its mission to deliver outstanding patient care, groundbreaking research and inspired teaching to create a healthy world one life at a time. This year's issue of *Discoveries* offers tribute to all.

We lead with the future: the potential of stem cells to cure many of our ills. UC San Diego is at the forefront of this endeavor, in no small part due to the support of T. Denny Sanford, whose $100 million gift will create the new Sanford Clinical Stem Cell Center, dedicated to putting basic research into clinical practice. The Sanford Center is scheduled to open in 2016.

We recall a pair of enduring efforts to overcome the modern-day scourges of Alzheimer's disease and HIV/AIDS. In both cases, UC San Diego scientists and doctors were among the first to sound the alarm and take up the fight at places like the Shiley-Marcos Alzheimer's Disease Research Center, the Alzheimer's Disease Cooperative Study, the Owen Clinic and the Center for AIDS Research, efforts vitally sustained by benefactors like Darlene Shiley and her late husband, Donald.

We celebrate the naming of The Pauline and Stanley Foster Hospital for Cancer Care, which will occupy three floors of UC San Diego Jacobs Medical Center, slated to open in 2016. This will be San Diego's first facility entirely devoted to treating every form of malignancy and fully integrated with nearby UC San Diego Moores Cancer Center, the only National Cancer Institute-designated comprehensive cancer center in the region.

Jacobs Medical Center will also house the new Hospital for Advanced Surgery and the new Hospital for Women and Infants. These hospitals represent the future of care in the region, which burns brightly thanks to Joan and Irwin Jacobs. Their $75 million gift in 2010 launched the facility's construction, and they remain among our staunchest advocates, along with many supporters who continue to contribute as part of an ongoing anonymous challenge in which any Jacobs Medical Center gift is matched, dollar for dollar, up to $25 million.

Rising beside Jacobs Medical Center is the Altman Clinical and Translational Research Institute, linking UC San Diego's clinical and research enterprises. It opens in 2016 as well, thanks to the generosity of Lisa and Steve Altman.

In this issue, we recognize and honor many grand gifts, all furthering a shared and grander vision of a better, healthier and less difficult life for all of us.

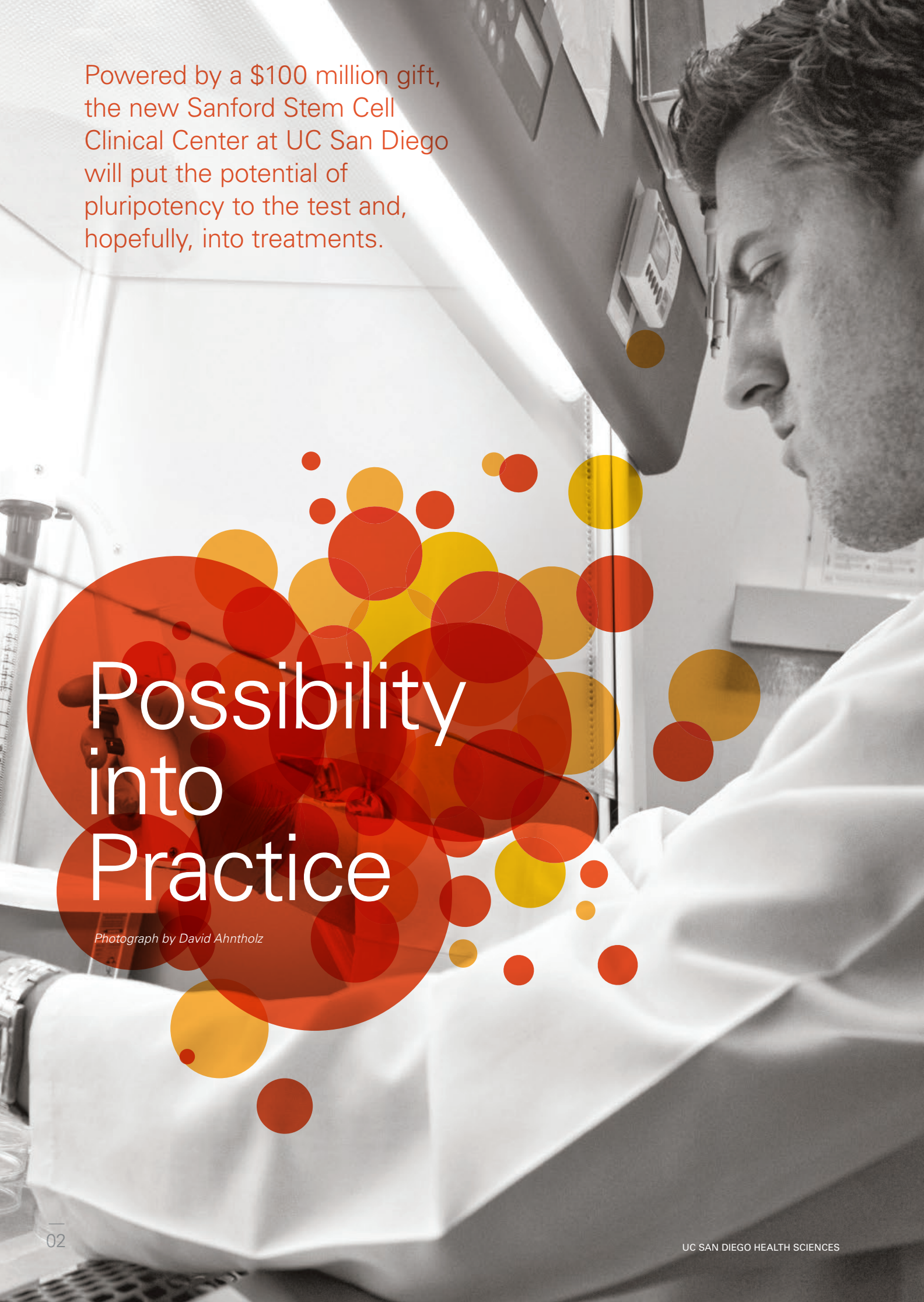
Sincerely,
David A. Brenner

Vice Chancellor, Health Sciences and
Dean, UC San Diego School of Medicine

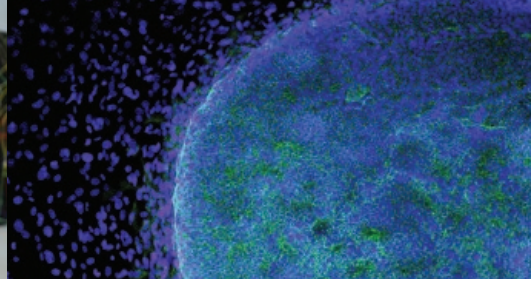
Powered by a $100 million gift, the new Sanford Stem Cell Clinical Center at UC San Diego will put the potential of pluripotency to the test and, hopefully, into treatments.

Possibility into Practice

Photograph by David Ahntholz

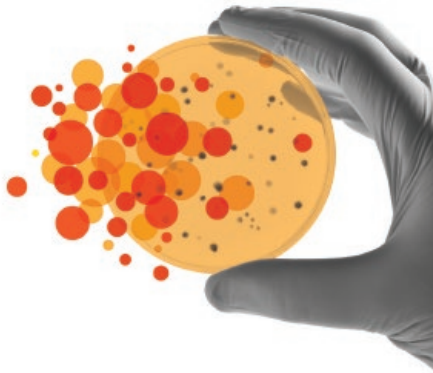






Stem cells have been touted as the basis for possible treatments of everything from cancer and Alzheimer's disease to literally mending a broken heart. Their therapeutic potential is almost limitless.

But can they deliver?



Above, left to right: Sanford Consortium, T. Denny Sanford and a cultured stem cell colony.

IN A BOLD AND SINGULAR STEP TOWARD ANSWERING THAT QUESTION, businessman and philanthropist T. Denny Sanford has committed $100 million to the creation of the Sanford Stem Cell Clinical Center at UC San Diego Health System.

The Sanford Center will accelerate development of drugs and therapies inspired by and derived from current human stem cell research by establishing, promoting and disseminating clinical trials and patient treatments that will more quickly transform promise into reality.

The center will integrate operations at four locations: UC San Diego Jacobs Medical Center and a nearby proposed clinical space, both slated to open in 2016; UC San Diego Center for Advanced Laboratory Medicine; and the Sanford Consortium for Regenerative Medicine.

It will provide resources to further leverage stem cell research currently conducted at the consortium – an innovative "collaboratory" of San Diego scientists from UC San Diego, the Sanford-Burnham Medical Research Institute, the Salk Institute for Biological Studies, The Scripps Research Institute and the La Jolla Institute for Allergy & Immunology – and other institutions on the Torrey Pines mesa, such as the J. Craig Venter Institute.

"Every day, scientists learn more about the regenerative powers of stem cells, which tantalize with their potential to treat, cure, even prevent myriad afflictions," said Sanford. "I see it in the amazing collaborative advances at the consortium and across the mesa. We're on the cusp of turning years of hard-earned knowledge into actual treatments for real people in need. I want this gift to push that reality faster and further."

Sanford's $100 million donation is core to a larger, ongoing $275 million effort by UC San Diego to develop and promote stem cell-based clinical trials and therapies. UC San Diego scientists are currently working on stem cell treatments for, among other things, leukemia, dementia and spinal cord injuries.

PUTTING KNOWLEDGE TO THE TEST

Since 2006, the California Institute for Regenerative Medicine (CIRM), the state's stem cell agency, has awarded UC San Diego scientists more than 70 grants totaling almost $148 million, with millions more given to other area institutions. In addition, CIRM awarded the consortium $43 million in 2008 to help build its unique space; Denny Sanford gave an additional $30 million. Lawrence Goldstein, PhD, director of the UC San Diego Stem Cell Program and new Sanford Center, said funding from CIRM and elsewhere has already helped push some stem cell-based projects into early clinical trials, with more nearing readiness.

"Clinical trials are not the finish line, but they are essential to advancing the science and ultimately creating much-needed drugs and therapies," Goldstein said. "We have made profound progress in understanding the basic nature and abilities of stem cells. We know a great deal about how they work and differentiate and, in a number of cases, how to make them become the kinds of cells we think we need. Now we have to put that knowledge to the test in people, for people."

To learn more about innovative stem cell research at UC San Diego and to watch a video about how you can help redefine the future of health care, visit health.ucsd.edu/clinicaltrials/Sanford.

Recalling Forward

Alzheimer's disease is an old nemesis, but a familiar one to scores of UC San Diego scientists and doctors who have been battling it for decades – lately with encouraging results.

IT'S EASY TO FORGET, BUT NOT SO LONG AGO, ALZHEIMER'S DISEASE (AD) WAS CONSIDERED TO BE RARE. That changed when the late Robert Katzman, MD, a UC San Diego School of Medicine neurologist and founding director of the Shiley-Marcos Alzheimer's Disease Research Center (ADRC), published a 1976 editorial in *Archives of Neurology* in which he declared AD to be "a major killer."

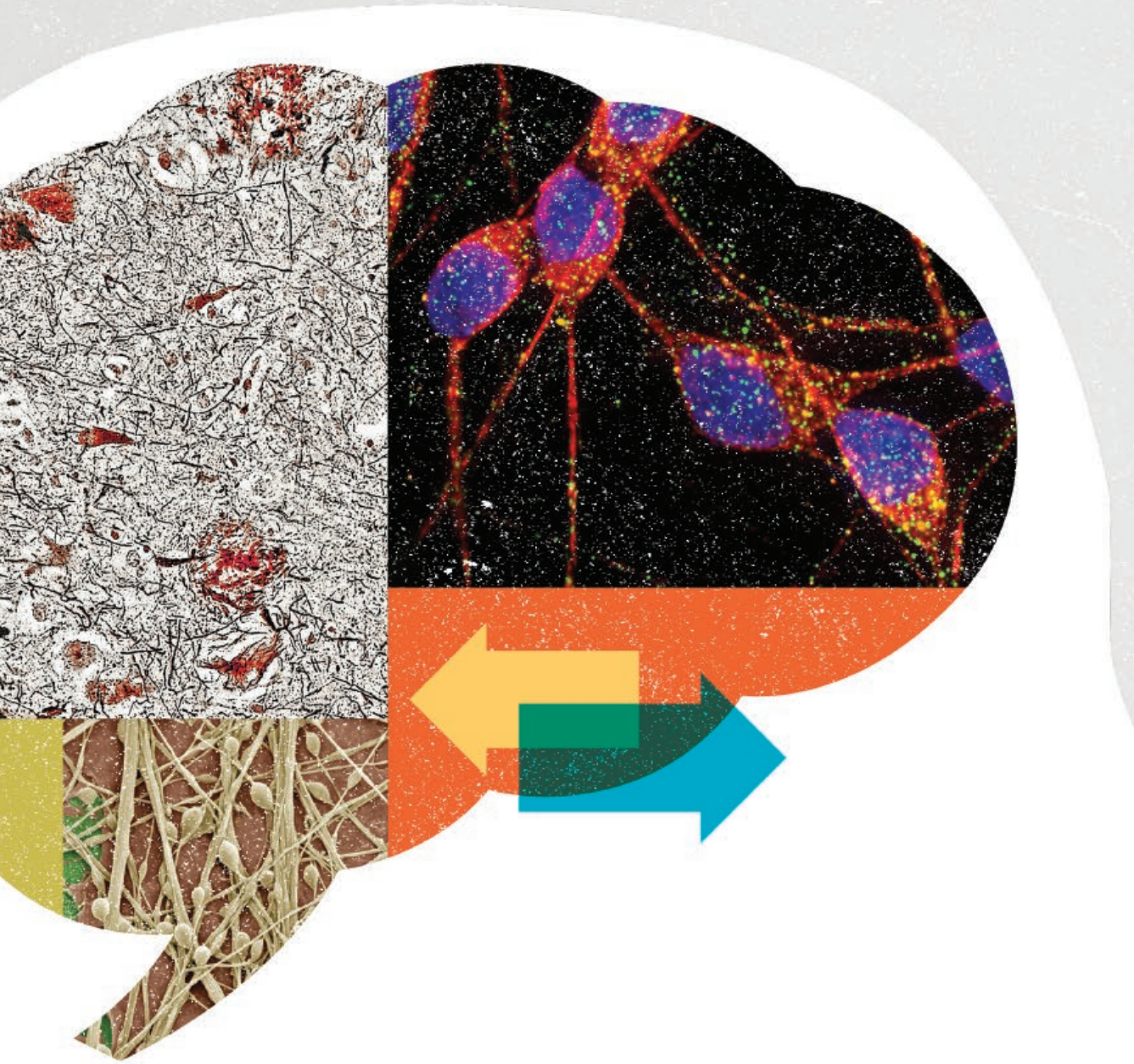
"He and Bob Terry (a neuropathologist and professor emeritus at UC San Diego) demonstrated to the world that Alzheimer's is an aging epidemic," said Paul Aisen, MD, professor in the Department of Neurosciences in the School of Medicine and director of the Alzheimer's Disease Cooperative Study (ADCS), a 23-year-old, ongoing collaboration between the National Institute on Aging and UC San Diego.

Much has happened since Katzman's editorial. AD was once terrifyingly mysterious. It's still terrifying, but less mysterious. There are now established, if not yet complete or completely embraced, theories to explain the genesis and progression of AD.

"We've made big leaps, from understanding the very basic pathology of plaques and tangles to the elemental molecules involved," said Douglas R. Galasko, MD, current director of the Shiley-Marcos ADRC, which is celebrating its 30th anniversary this year.

Thousands of researchers and doctors now study and treat AD; billions of dollars are spent. UC San Diego has become an international hub for AD research. Local scientists and physicians have launched or helped coordinate scores of clinical trials to explore new drugs and therapies designed to slow, if not cure, AD. Many of these efforts have failed or fallen short of expectations, but some have produced symptomatic benefit or remain promising.

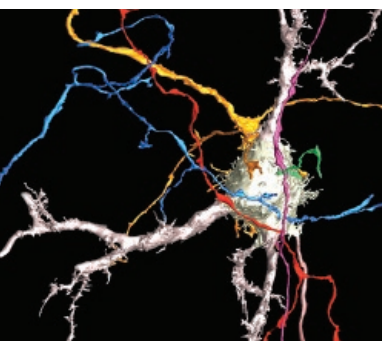
"Certainly the last decade has been discouraging in some ways, with no new drugs, for example," said Aisen. "But I think we needed to better understand the disease first before we could really, effectively, find ways to treat it or prevent it. That's happened. We've made significant advances. The field is really moving."



Clockwise from upper left: Alzheimer's disease plaques and tangles (Thomas Deerinck, National Center for Microscopy and Imaging Research at UC San Diego); stem cell-derived neurons from Alzheimer's disease patients (Lawrence Goldstein, UC San Diego); cultured hippocampal neurons (Mark Ellisman, National Center for Microscopy and Imaging Research at UC San Diego).

"Making highly purified and functional human Alzheimer's neurons in a dish – that's never been done before."

Lawrence Goldstein, PhD, Director of the UC San Diego Stem Cell Program



Digital reconstruction of neuron depicts axons (colors) competing to form synaptic inputs on the white soma or cell body. Image courtesy of George Spirou and Brian Hoffpauir, West Virginia University and Thomas Deerinck and Mark Ellisman, National Center for Microscopy and Imaging Research at UC San Diego.

CLINICAL TRIALS

An obvious and urgent goal of AD research has been the development of drugs and therapies to treat patients diagnosed with the disease – patients who already manifest distinct symptoms and behaviors. While scientists say that goal remains vital, a growing number also argue that the long-term better bet is resolving the disease at its earliest stage, known as "prodromal AD."

People with prodromal AD have traditionally not been considered to have AD, said Michael Rafii, MD, PhD, director of UC San Diego Health System's Memory Disorders Clinic. They do not exhibit telltale signs, according to Rafii, "but we recognize prodromal AD as a condition where we may be able to intervene and possibly prevent it from progressing to full-blown AD."

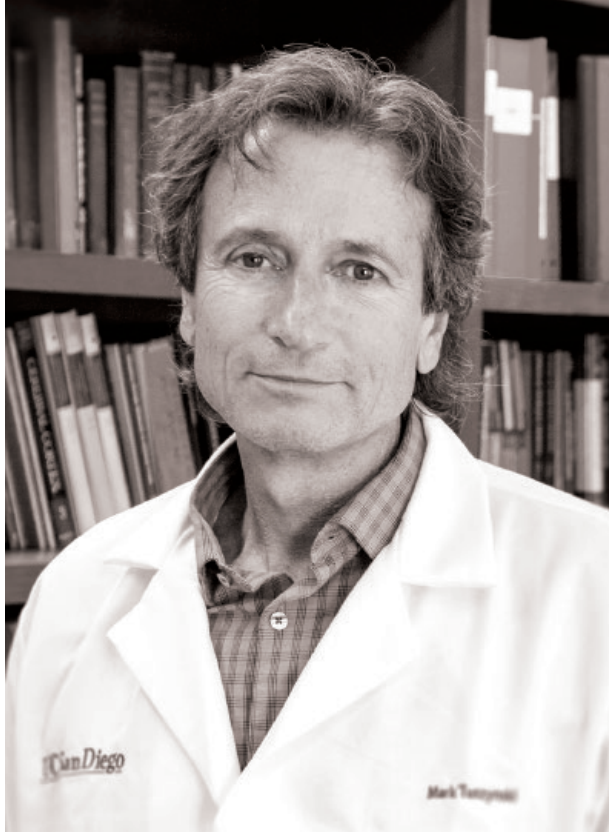
Such talk is buttressed by efforts like the global Alzheimer's Disease Neuroimaging Initiative, which has produced major advances in neuroimaging and helped identify biomarkers of AD. With technologies like positron emission tomography scans able to accurately measure amyloid deposits in the brain, it's now possible to project who's most likely to develop AD a decade or more before symptoms emerge.

That kind of progress has fueled clinical trials targeting amyloid plaques and other indicators of AD. UC San Diego is a participating site in many of them. For example, Rafii is principal investigator at UC San Diego for Scarlet Road, a multi-year, multi-institution study to assess the effects of gantenerumab, an antibody-based drug shown to attack and remove beta-amyloid plaques in animal models.

Rafii also oversees interventional clinical trials testing the beneficial effects of resveratrol – a compound found in red grapes, chocolate and tomatoes – in patients with mild to moderate dementia due to AD.

Perhaps most notable is Anti-Amyloid Treatment in Asymptomatic Alzheimer's, nicknamed A4. It's among the most ambitious and anticipated clinical trials in AD research history. It will involve 1,000 qualified participants (out of more than 5,000 recruited and screened) at sites across the country and world, including UC San Diego. Aisen is co-leader of the study.

Qualified A4 participants won't have clear symptoms of AD, but will have amyloid deposits building up in their brains. They will receive an experimental drug designed to clear amyloid protein out of the brain before it becomes toxic. The $100 million trial will last three years and is the biggest test yet of the idea that AD can be prevented.



NERVE GROWTH FACTORS

In 2001, Mark Tuszynski, MD, PhD, director of the Center for Neural Repair at UC San Diego, and colleagues began an audacious experiment. They injected nerve growth factor (NGF), a small secreted protein that helps neurons grow and stay healthy, into specific regions of the brains of patients with diagnosed AD.

The idea was that NGF might stimulate neuronal function and prevent cell death. In animal studies, NGF had improved memory and prevented degeneration of cells from injury, overproduction of amyloid or aging.

The research is now in Phase II clinical trials with 49 patients, with half receiving the NGF gene therapy procedure and the other half undergoing a control-sham surgery. The trial is double-blind, with neither patient nor evaluating physician knowing who is receiving which treatment. The first measurable results are expected in about a year.

Tuszynski and colleagues are also advancing another effort that "will use new technology to do the gene therapy procedure in a magnetic resonance imaging (MRI) scanner so we can very accurately identify the precise location for gene delivery in the brain and monitor its spread." They hope to move from encouraging animal tests to human clinical trials in one or two years.

UC San Diego has become an international hub for AD research, with local doctors and scientists helping lead the way.

30 YEARS

Clockwise from left: Mark Tuszynski, MD, PhD, the late Robert Katzman, MD, Michael Rafii, MD, PhD, Lawrence Goldstein, PhD, Paul Aisen, MD, and Douglas R. Galasko, MD

Alzheimer's by the Numbers

More than 5 million Americans have AD. It's the sixth leading cause of death, and the future is daunting. By 2025, the estimated number of people age 65 and older with AD will reach 7.1 million; by 2050, it will be 13.8 million, or one American developing the disease every 33 seconds.

STEM CELLS

Imbued with the ability to become any cell type, pluripotent stem cells offer the promise of an ultimate treatment or cure for AD: Just grow new neurons to replace those damaged by disease.

That reality is a long way off, but in 2012 a team of UC San Diego School of Medicine scientists and others – led by Lawrence Goldstein, PhD, director of the UC San Diego Stem Cell Program – achieved something remarkable. They created the first stem cell-derived, *in vitro* models of sporadic and hereditary AD using induced pluripotent stem cells from patients with the disease.

"Making highly purified and functional human Alzheimer's neurons in a dish – that's never been done before," said Goldstein, who will head the Sanford Stem Cell Clinical Center when it opens at UC San Diego in 2016.

The accomplishment has significant ramifications. For one thing, it means that scientists can now more directly study the biology of AD. "You can't just do a biopsy on living patients," Goldstein said, "so researchers have had to work around this, mimicking some aspects of the disease in non-neuronal human cells or using limited animal models. Neither approach is really satisfactory."

Goldstein has already employed stem cell-derived neurons to good effect, reporting in 2013 that they had used genome editing technology in stem cells to resolve a controversy about the role of a key mutated protein called presenilin, which can cause familial early-onset AD.

They have also begun using the Alzheimer's neurons in drug screening, "looking for compounds that change the cells' phenotypic (observed) response," said Goldstein. Such work is an essential first step toward ultimately finding or developing new AD treatments. The neurons promise to make the effort easier and faster.

The Milk Man

Ask Lars Bode why "breast is best," and his answer will be short and sweet. Well, sweet at least. It's all about those human milk oligosaccharides.

Photograph by David Ahntholz

Lars Bode, PhD

LARS BODE WAS A DEDICATED COLLEGE ATHLETE, DEVOTING MUCH OF HIS TIME to special diets intended to improve his strength and endurance. So much so, in fact, that his brother began teasing him about his "strange" performance-improving concoctions and suggested he ought to pursue a career in nutrition.

Bode agreed, changed his academic focus, got an internship at a baby formula company and, in time, became one of the few researchers in the world to study the science behind the saying "breast is best."

"Between my fascination with nutrition and my internship at the baby formula company, I started to study the composition of breast milk," said Bode, now a PhD associate professor in the Department of Pediatrics at the UC San Diego School of Medicine. "I became really interested in how human milk molecules impact the health of infants and how this might be applicable on a larger scale."

Breast milk is a complex blend of proteins, carbohydrates, fats, minerals, vitamins and sugar molecules called human milk oligosaccharides or HMOs. There are about 150 types of HMO, and like thumbprints, their combination and concentrations are unique to each nursing mother.

These sugar compounds, which are nearly invisible, don't actually feed the infant. Rather, they congregate in the newborn's gastrointestinal tract, where they act as a prebiotic, promoting the growth of beneficial microorganisms that boost the immune system and protect the infant from infection.

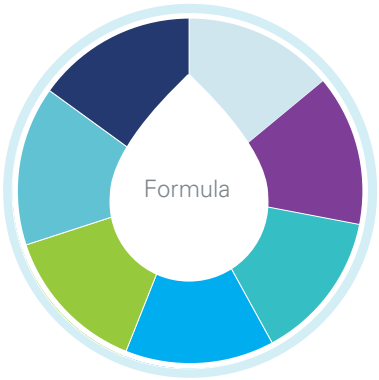
Complex sugars also act as a kind of protective anti-adhesive. When a pathogenic virus, bacteria, parasite or fungus enters the infant's tract, it's more likely to latch onto tasty sugar molecules than healthy gut cells.

PREVENTS ILLNESS

"We've gone to great lengths and ocean depths to discover new compounds for medicine," said Bode, "but natural compounds in human milk could be a key to unlock future, alternative approaches and make a difference worldwide."

For example, sugars linked together in human milk are associated with preventing certain illnesses like diarrhea and have been found to reduce the risk of HIV transmission. In a recent study, Bode and colleagues discovered that HMOs might be responsible for why just 10–15 percent of breast-fed infants in developing countries are infected by their HIV-positive mothers.

Ingredients Found in Formula



Water
Protein
Carbohydrates
Fats
Vitamins
Minerals
Lipids: Synthetic DHA/ARA

Ingredients Found in Breast Milk

Water
Protein
Carbohydrates
Fats
Vitamins
Minerals
Lipids: Natural DHA/ARA
Enzymes
Growth Factors
Hormones
Antibacterial Factors
Antiviral Factors
Antiparasitic Factors
Antiallergenic Properties

48+

"Scientists have been unable to reproduce more than 48 ingredients in formula that occur naturally in human breast milk."

Christy Jo Hendricks, *Birthing, Bonding & Breastfeeding*

DONOR MILK

Other studies have found that breast milk cuts an infant's risk of getting necrotizing enterocolitis (NEC) by half. The deadly gastrointestinal disease primarily affects premature babies, causing inflammation that destroys part of the bowel. Although it strikes just one in 2,000 to 4,000 births, Bode said NEC represents one of the most common and serious intestinal disorders among hospitalized preterm infants.

Not surprisingly, the sugar structures of baby formulas and cow's milk are different from human breast milk. Bode suggests that mothers use donor breast milk if they cannot breastfeed. He said frozen, pasteurized donor breast milk is far more beneficial than formula, provided that processing of the milk leaves the oligosaccharides intact.

"Breast milk really is the liquid gold of nutrition for newborns and infants, but we are trying to find a way to reproduce compounds in laboratories that could be added to formula and possibly produce the same health benefits as HMOs," Bode said. "We may never be able to recreate Mother Nature in a laboratory, but since formula is not going away, we can at least try to improve it."

Bode hopes his research will help mothers understand the power of molecules in breast milk and encourage them to breastfeed. But he sees other potential health benefits as well. He believes HMOs might eventually be used to treat some illnesses in adults.

"As a scientist, I have a passion for studying areas not yet explored. Like a little kid learning how to ride a bike for the first time, I get excited when my team uncovers a new discovery. Whether from a nursing mother, chemistry lab or donor's milk, I hope HMO research has a profound impact on how our world values the health benefits of human milk."

GO WITH THE FLOW

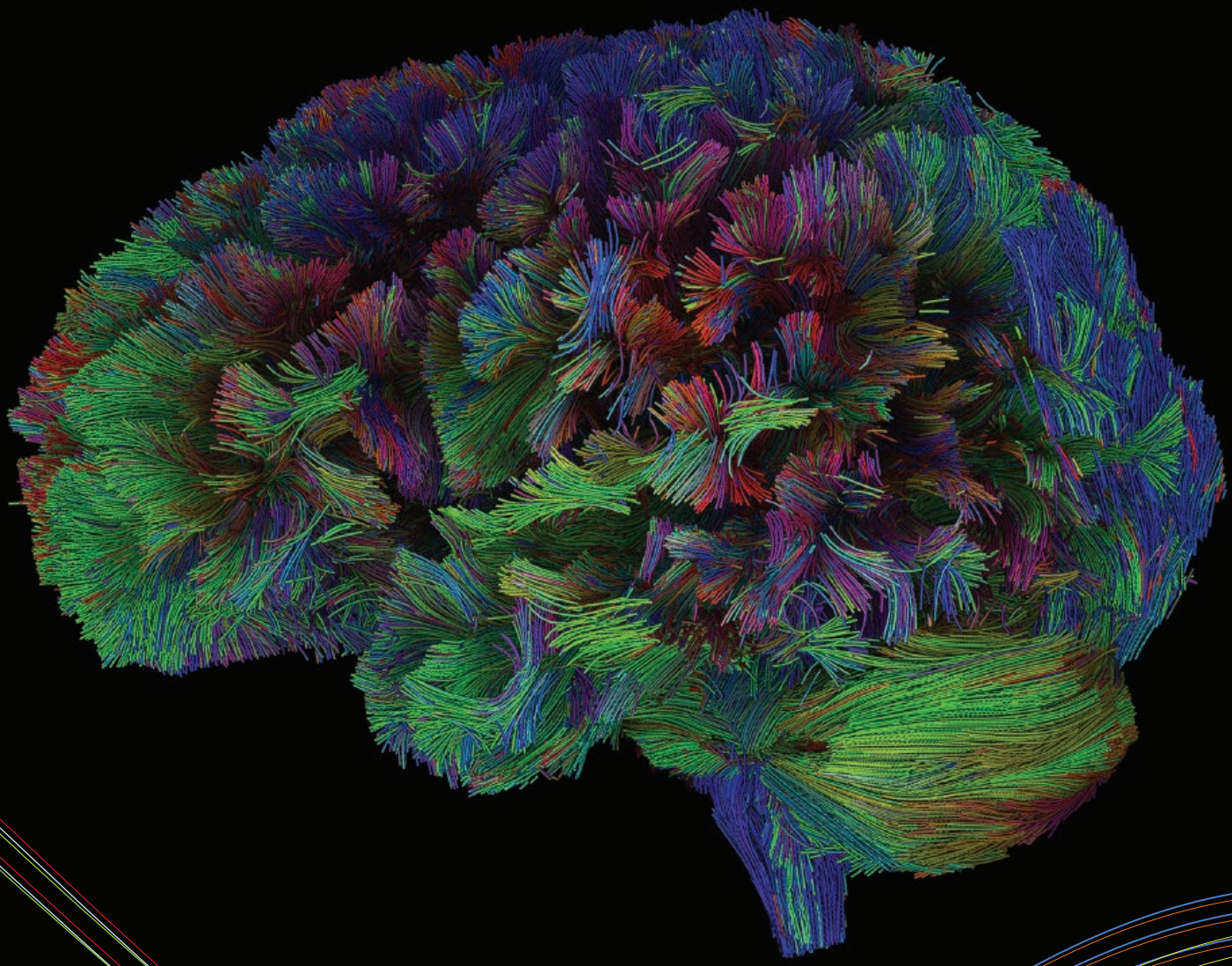
Photographs by David Ahntholz

An imaging technology that tracks the movement of water is helping surgeons navigate more precisely – and more safely – through the brain.

IN THE 23RD-CENTURY UNIVERSE OF *STAR TREK*, LEONARD "BONES" MCCOY, MD, could use his tricorder to image the brain and destroy a tumor without harming healthy tissue. While today's surgeons lack such nifty devices, some do have access to tractography – a way to map the brain that seems futuristic, but is a lifesaving reality for patients.

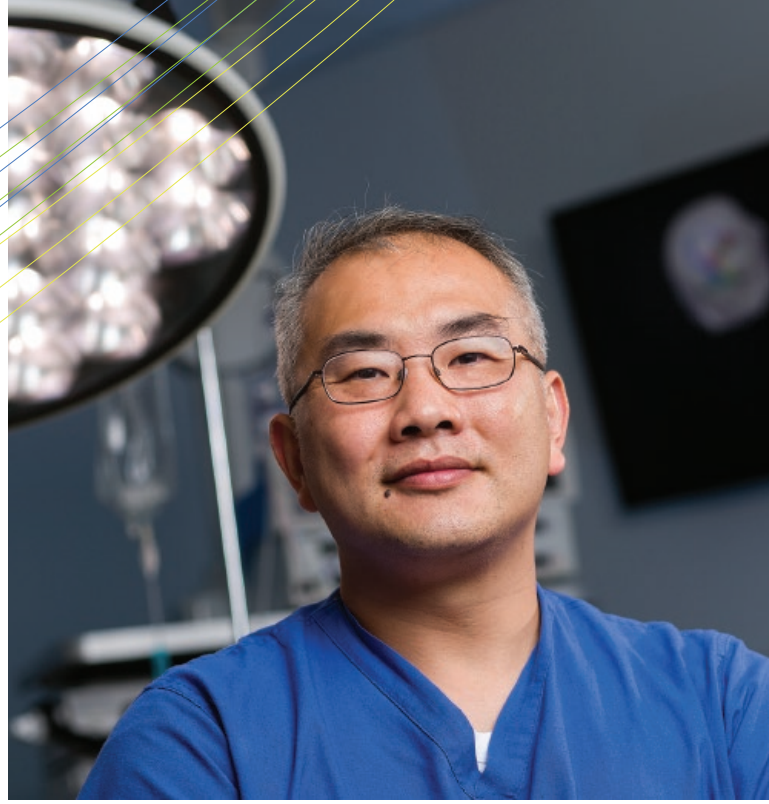
"Tractography allows us to identify tiny anatomical connections in the living human brain," said Anders Dale, PhD, vice-chair of radiology and director of the new Center for Translational Imaging and Personalized Medicine at the UC San Diego School of Medicine. "These specialized scans can be done in the same or less time as traditional MRI without sedation or injection."

Tractography reveals the myriad anatomical connections that visually capture the complexity of a living human brain. Image courtesy of Hauke Bartsch, Multimodal Imaging Laboratory, Department of Radiology, UC San Diego.



"There are no margins for error in the brain. Every centimeter of brain tissue contains millions of neural connections."

Clark Chen, MD, PhD,
Vice-chair of research, Division of Neurosurgery,
UC San Diego Health System



Anders Dale, PhD

Tractography maps the brain in vibrant colors by marking the movement of water within the organ. Water molecules inside connected neurons move in an oriented manner, whereas outside they wander randomly. Unlike other visual aids, tractography scans can reveal the orientation and density of individual nerve fibers and offer the ability to directly image cancer cells.

"What's remarkable about this newer scan is the incredible quality and accuracy of the image," said Dale. "Ultimately, what the scan helps the specialist to deliver is a better diagnosis or treatment, especially in the brain where visualization is particularly difficult."

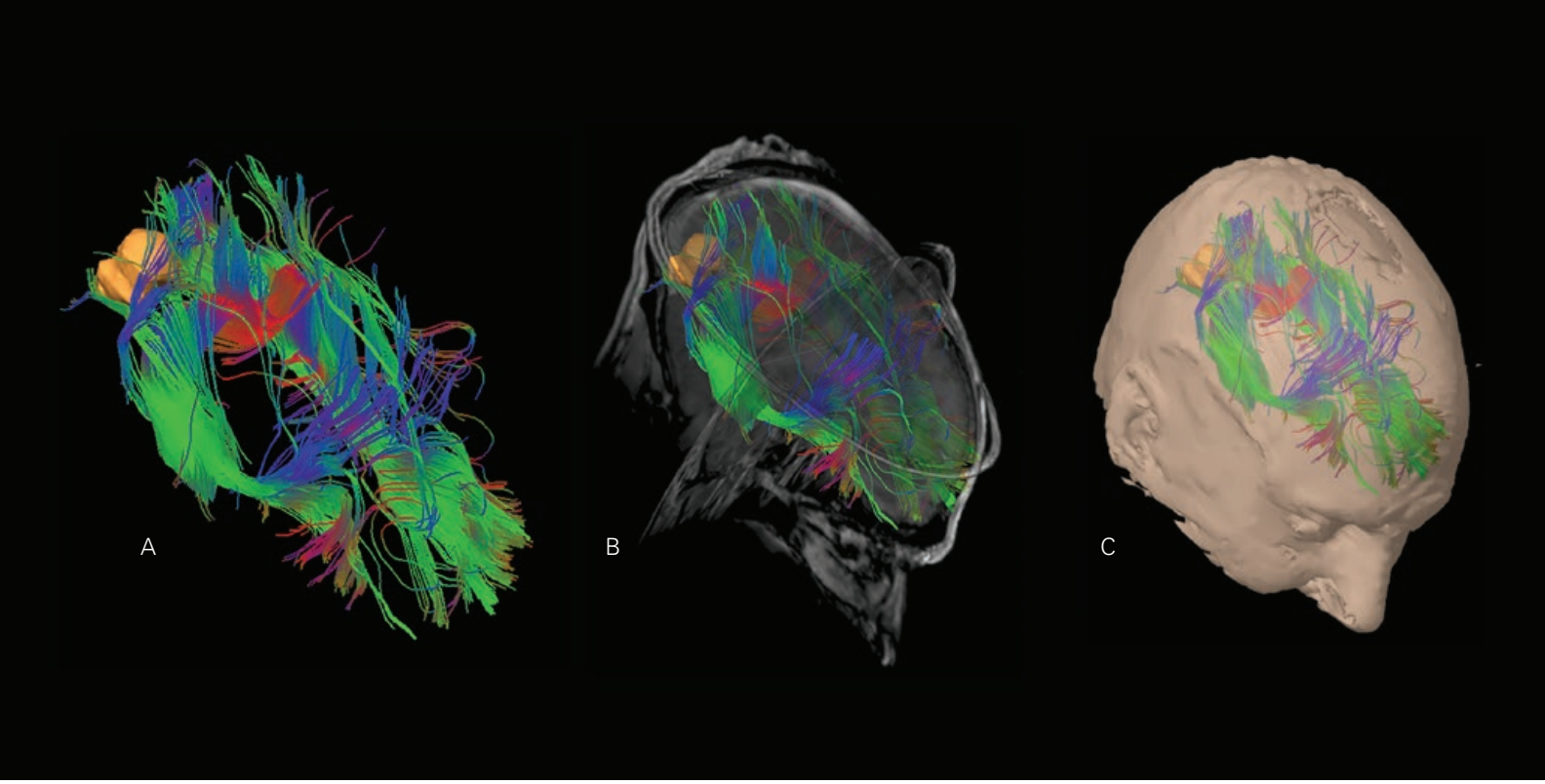
Due to the presence of air pockets, the brain often generates images with artifacts and distortions that radiologists must learn to ignore or work around. Air in sinuses, ear canals and bone, for example, create changes in the magnetic field, which in turn cause spatial shifts. With tractography, this vexing issue can be corrected to produce anatomically true pictures.

"Since a tumor and swelling distort the brain, we cannot use our standard neuroanatomical knowledge to know where the critical brain tracks are present," said Santosh Kesari, MD, PhD, director of neuro-oncology at UC San Diego Moores Cancer Center. "We use tractography to identify the eloquent, critical areas of the brain, such as motor, visual and speech fibers, to help plan surgery as well as radiation treatment."

NO MARGIN FOR ERROR

Clark Chen, MD, PhD, neurosurgeon and vice-chair of research for the Division of Neurosurgery in the UC San Diego Health System, has incorporated tractography into his clinical practice to treat patients with glioblastoma, one of the deadliest forms of brain cancer.

"There are no margins for error in the brain. Every centimeter of brain tissue contains millions of neural connections. What this means is that every centimeter of brain that a neurosurgeon injures in a surgery equates to the destruction of an average of 100 billion neural connections," Chen said. "With tractography, we can visualize the most important connections to avoid injury and in doing so, help preserve the quality of life for our patients."



Anthony Chetti was a beneficiary of tractography-guided brain surgery. Chetti had developed a tumor in the region of the brain called the occipital lobe, where visual information is processed.

"Anytime you're told that you can potentially lose your vision, you are scared," said Chetti, a San Diego schoolteacher. "But when Dr. Chen shared the tractography images with me and showed me how he was going to avoid injury to the connection between my eye and the occipital lobe, I was reassured."

Chetti underwent a complete excision of the brain tumor without any damage to his vision. "When I woke up from surgery, I asked for my glasses immediately and began running systems checks. I could see the clock. I could read the words on a sign. It was immediately evident that there were no problems," he said.

"What we are trying to develop is precision medicine," explained Dale. "Precision medicine is the idea that we can integrate multiple forms of data into medicine to make radiology scans as objective as possible. What we are trying to do is to build quantitative, calibrated images to reflect actual connections within a millimeter of accuracy so that what we are reporting is real, not post-processing, methods."

Dale is also studying the child's brain to determine its normal size range and stages of development. The goal is to understand the genetic basis of individual differences in brain structure and connectivity, cognition and personality.

"Peer-reviewed papers are great, but to change health care, we need to bring state-of-the art technology to the clinical routine," Dale said. "The plan is to share the protocols and procedures with referring physicians to help with the care of their own patients. High-powered research technologies need to be available in everyday practice to everyone. This is what we are working on."

Above left to right:
A series of tractographs depicting a patient with a glioblastoma tumor, indicated in gold. Images courtesy of Clark Chen, MD, PhD.

(A) Tractograph of neural connections in context with tumor.

(B) MRI scans provide three-dimensional planes.

(C) Computer-generated surface features of patient give spatial context.

Improving surgical techniques and outcomes is a key priority at UC San Diego. Read about Jacobs Medical Center's Hospital for Advanced Surgery, opening 2016, at futureofcare.com.

Cell-Help Program

Illustration by Mona Daly

"Mobile health technology applications like VDOT can be game-changers when it comes to accelerating the pace of TB control and eradication."

Richard Garfein, PhD, MPH,
Division of Global Public Health,
UC San Diego School of Medicine

TB or not TB isn't the question. Rather, it's ensuring that patients follow their drug regimen. A UC San Diego pilot program uses mobile phones to literally show one way to get things done.

IN HIS 24 YEARS AS AN ENLISTED OFFICER WITH THE U.S. MARINE CORPS, Thomas Mitchell traveled to 56 foreign locations, including the Caribbean, Central America and Vietnam. While in one of them, he unknowingly contracted tuberculosis.

Tuberculosis (TB) is an infectious global health threat affecting more than 2 billion people – one-third of the world's population – according to the World Health Organization. It is one of the three leading causes of death due to infectious disease worldwide. Globally, there are 8.8 million new TB cases per year, resulting in 1.4 million deaths.

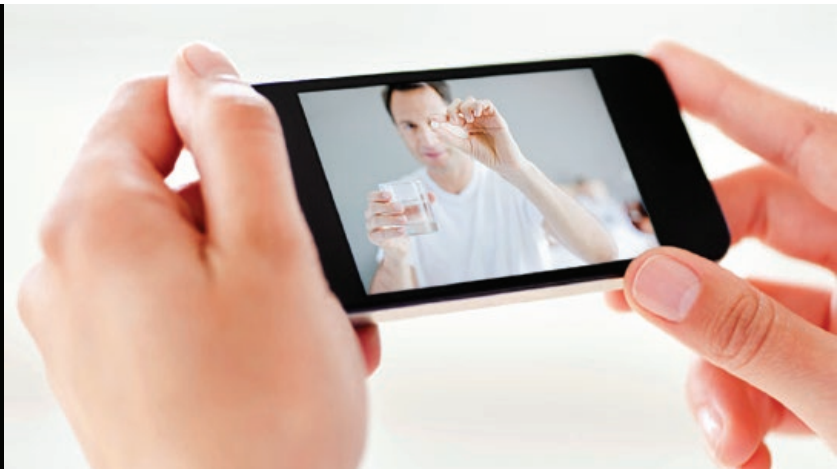
Despite the discovery of effective medications in the 1940s, TB remains a leading cause of death in low- and middle-income countries. It is also frequently seen among patients with HIV. But as Mitchell's case attests, TB is not a disease restricted by nationality or income level. It recognizes no borders or boundaries.

"Though my skin tests were 'positive' for TB every year, I was never put into a treatment program," Mitchell said. "It wasn't until many years after I'd left the military and was about to undergo surgery that the doctors did a chest X-ray and discovered a spot on my lung." The spot was active TB.

Poor compliance with TB treatment leads to a host of greater problems. Health departments in the United States routinely spend millions of dollars each year to send health care workers to patients' homes daily to monitor medication compliance. It is well documented that when patients do not closely adhere to treatment regimens, which typically last more than six months, the disease progresses, the bacteria becomes resistant to antibiotics and these drug-resistant strains spread. Complicating the situation is the fact that drug-resistant TB requires even longer treatments with costlier, more toxic and less effective drugs, often resulting in higher patient mortality.

As a way to ensure treatment compliance, health officials traditionally employ a process called Directly Observed Therapy (DOT). Health care providers or associates personally watch patients swallow every dose of medication for the duration of their treatment. While proven effective, DOT is expensive, time-consuming, inconvenient and stigmatizing to patients, as well as impractical for those living far from health centers.

For Mitchell, doctors prescribed an aggressive antibiotic regimen. Representatives of the San Diego County Health Department visited his home every day to watch him take his medication. "It was very chaotic," said Mitchell. "One day, they would show up at 8 a.m., the next 1 p.m., depending on the health care worker's availability rather than my schedule."



Left to right: Scanning electron micrograph of *Mycobacterium tuberculosis*; documenting daily TB drug treatment by cell phone.

VDOT PROCESS

"Waiting for someone to come and watch me take my many pills took 30 to 45 minutes each day. With VDOT, I was able to use my cell phone and record myself taking the medication – all in about a minute."

Thomas Mitchell, TB patient

VISUAL PROOF

In 2011, researchers at UC San Diego School of Medicine began a pilot study funded by the U.S. National Institutes of Health to evaluate the feasibility and acceptability of a mobile phone-based form of DOT called "Video Directly Observed Therapy" or VDOT, which was designed to overcome many of the barriers to traditional in-person monitoring.

With VDOT, patients use mobile phones to record videos of themselves taking their medication, after which the encrypted videos are wirelessly uploaded to a secure server where health care workers observe them through a password-protected website and document each dose taken.

"It's a simple technological solution to what has been an intrusive, time-consuming and costly process," said Richard Garfein, PhD, MPH, of UC San Diego's Division of Global Public Health, who is one of the VDOT developers and principal investigator of the pilot study conducted in San Diego and Tijuana, Mexico.

"Our study showed that VDOT was highly feasible and acceptable to patients and providers in both cities, with more than 95 percent of expected medication doses successfully observed using VDOT."

Mitchell was a study participant. "Waiting for someone to come and watch me take my many pills took 30 to 45 minutes each day. With VDOT, by the time I got to the end of the program, I was able to use my cell phone and record myself taking the medication – all in about a minute."

An economic analysis showed that the cost of VDOT for the pilot study was about one-third of the cost of in-person DOT in both San Diego and Tijuana. One hundred percent of participants said they would recommend VDOT to others.

"Given these results, we've received a second grant to upgrade the VDOT application by making it cloud-based and more user-friendly," said Garfein, adding that the improved VDOT is now being evaluated by health departments in San Diego, San Francisco and New York City.

Eventually, the researchers hope to introduce VDOT to countries like India, where drug-resistant TB is highly prevalent and medication adherence is even more difficult to track because patients often live in remote villages.

"Mobile health technology applications like VDOT can be game-changers when it comes to accelerating the pace of TB control and eradication," Garfein said. "By significantly reducing the cost and personnel burden of monitoring patient-treatment adherence, we can allow health care providers to concentrate their limited resources on the patients with the greatest need."

For their work, Garfein and School of Medicine colleague Kevin Patrick, MD, MS, have been named among the top ten Mobile-to-Mobile (M2M) Pioneers by *Connected World* magazine, which recognizes those who apply solid wireless and M2M principles to unique innovations that positively impact the lives of individuals on a daily basis.

Foster Cares

Pauline Foster

Cancer killed her husband and brother. Pauline Foster's gift to help build the new Hospital for Cancer Care at Jacobs Medical Center is meant to save others.

Join Pauline Foster and other generous donors in advancing the Future of Care through the Challenge for Jacobs Medical Center – a dollar-for-dollar match. Call 858-822-4562 or visit jacobschallenge.org.

ONE DAY DURING A 2001 TRIP TO CHINA, San Diego businessman Stanley Foster turned to his wife, Pauline, with a look of concern and puzzlement: "I don't understand what's wrong," he said. "My pants are too tight, and I haven't gained weight."

Back home, Foster consulted physicians. Their diagnosis: multiple myeloma, a blood cancer. He immediately began treatments, with Pauline invariably by his side, often sleeping on the floor next to his hospital bed. After a six-week fight, Foster succumbed on Nov. 14, 2001. He was 74. The experience left Pauline devastated and frustrated, with a sense that cancer patients had too few choices for care.

Thirteen years later, Pauline, a community philanthropist and longtime supporter of UC San Diego, says her husband's experience with cancer was one reason she gave $75 million this year to support construction of UC San Diego Jacobs Medical Center, which will feature three floors dedicated to cancer care.

"More recently, I also lost my brother to cancer. At the time, he needed to be in a hospital, but space was an issue," said Pauline. "After witnessing that, I felt the best thing I could do would be to help make sure that other people have beds and the opportunity to get the kind of care that will hopefully cure them."

The 10-story Jacobs Medical Center is slated to open in La Jolla in 2016, with three clinical care units under one roof: the Hospital for Advanced Surgery, the Hospital for Women and Infants, and the newly named Pauline and Stanley Foster Hospital for Cancer Care.

"Cancer patients in San Diego will no longer have to travel to get the kind of care they deserve and need," Pauline said. "They'll have it right at their fingertips, which is important because when you are undergoing chemotherapy or radiation, you don't want to have to travel far."

The new Foster Hospital for Cancer Care will be the only inpatient facility of its kind in San Diego County, the fifth most populous county in the United States, where cancer is the number one cause of death. With 108 dedicated beds, the new facility will double UC San Diego Health System's capacity to treat patients with every form of malignancy. It will also be the critical inpatient venue for delivering scientific discoveries and leading-edge treatments by university researchers and physicians.

For example, patients will have access to targeted, personalized therapies, such as stem cell-based treatments and immunotherapies, both requiring inpatient care by highly specialized staff. It will provide expanded state-of-the-art tools for treating some of the most fragile patients, including those in the Blood and Bone Marrow Transplant Program, jointly sponsored by UC San Diego Health System and Sharp Healthcare.

The proximity between the Foster Hospital for Cancer Care and UC San Diego Moores Cancer Center seamlessly connects and aligns patient care, said Scott M. Lippman, MD, director of the Moores Cancer Center and associate vice chancellor for cancer research and care.

"We will provide a familiar and healing environment, expert physicians and staff, and personalized cancer care with a continuum of services tailored to the needs of patients and their families, including treatment, clinical trials, nutrition, family support and other outpatient programs at Moores Cancer Center," he said.

With Pauline's help. In Stanley's memory.

EPI-CENTERED

UC San Diego Health Sciences is a center for epigenomics, which helps explain human development and may ultimately improve the human condition itself.

The sequencing of the human genome more than a decade ago was indisputably momentous. In announcing the accomplishment, President Bill Clinton declared "We are learning the language in which God created life."

AS STUNNING AS THE GENOME IS – WITH 20,000 OR SO GENES CONTAINING ALL OF THE essential instructions for building a human being – it is arguably more alphabet than language, which must necessarily include all of the molecules, compounds and chemicals that surround genes. These elements represent life's punctuation and syntax. They guide and influence genes and make it possible for a finite number of genes to do a seemingly infinite number of different jobs.

All of this is known as the "epigenome," and it represents the next stage in the study and understanding of the human genome, said Bing Ren, PhD, head of the Laboratory of Gene Regulation at Ludwig Cancer Research at UC San Diego.

In multicellular organisms, DNA is packaged within the nucleus in a complex, dynamic structure called chromatin, which plays a central role in regulating how and when DNA is copied, transcribed and put to work making the stuff of life. Chromatin varies by cell type. In multicellular organisms like human beings, there is just one genome, but as many epigenomes as cell types.

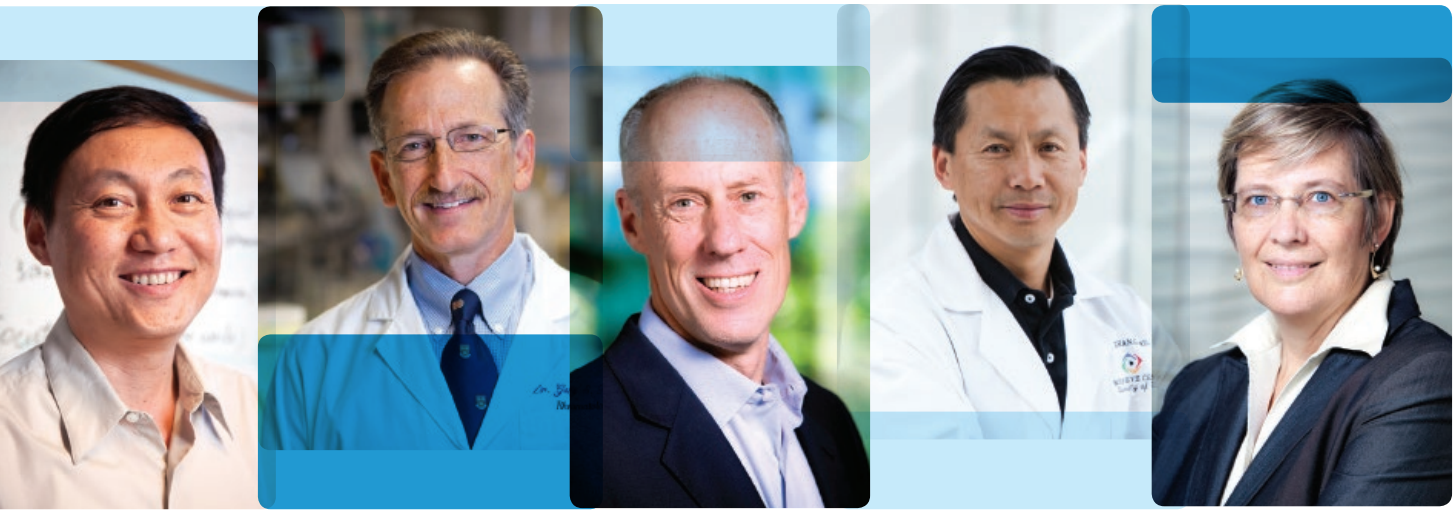
"Understanding the epigenome is the key to understanding how the same DNA produces distinct sets of genes and how it functions in more than 200 different cell types in the human body," said Ren. "It is essential not only to understanding the mechanisms of human development, but also how diseases occur and how individual responses may vary. It's a path to not just curing diseases like cancer and diabetes, but perhaps eventually preventing them altogether."

Ren is one of many UC San Diego faculty members hoping to help make that happen through work in their labs, in local collaborative endeavors like the Institute for Genomic Medicine based at UC San Diego, and in national efforts like the Roadmap Epigenomics Project and the ENCODE Project Consortium.

Much has happened in the 14 years since the Human Genome Project announcement, said Ren. "In the field of epigenomics, we've seen unprecedented growth with no sign of deceleration."

20,000

or so genes contain all of the essential instructions for building a human being.



Left to right:
Bing Ren, PhD,
Gary S. Firestein, MD,
Christopher Glass, MD, PhD,
Kang Zhang, MD, PhD,
Kelly A. Frazer, PhD

AT UC SAN DIEGO, FOR EXAMPLE:

Bing Ren, PhD, and colleagues have peeled away some of the mystery of how zygotes (fertilized eggs) determine which copies of parental genes will be used or ignored, which has obvious implications for some inherited conditions and diseases. "This can help us develop better diagnostic tools for detecting genetic abnormalities and perhaps learn how to predict whether something bad will happen."

Gary S. Firestein, MD, professor of medicine and director of the Clinical and Translational Research Institute, led a team that has linked a primary epigenetic mechanism called DNA methylation, normally involved in fetal development, to inflammation and joint damage in rheumatoid arthritis, one of the most common and serious forms of the disabling disease.

Christopher K. Glass, MD, PhD, a professor in the departments of medicine and cellular and molecular medicine, and colleagues have found a new way to decipher how special proteins called "master regulators" read the genome and consequently turn genes on and off, making it quicker and easier to identify specific gene mutations associated with increased disease risk. It's an essential step toward developing future targeted treatments, preventions and cures.

Kang Zhang, MD, PhD, professor of ophthalmology and chief of ophthalmic genetics at UC San Diego Shiley Eye Center, and **Trey Ideker, PhD**, chief of the Division of Medical Genetics in UC San Diego School of Medicine, and others have described markers and a model that quantify how aging occurs at the level of genes and molecules, providing not just a more precise way to determine how old someone is, but also perhaps to anticipate or treat ailments and diseases associated with aging.

Kelly A. Frazer, PhD, professor of pediatrics and director of the Institute for Genomic Medicine, and colleagues have used genome-wide association studies, which compare common genetic variants among many individuals, to link an altered inflammatory signaling response and a "gene desert" on chromosome 9 with an elevated risk of coronary artery disease.

This kind of work at UC San Diego and elsewhere, said Ren, is providing crucial new information and ideas, insights and possibilities. But while scientists are on better speaking terms with the language of life, much remains unknown and unsaid.

"We anticipate even greater progress in the coming years," Ren said.

It should be a conversation worth hearing.

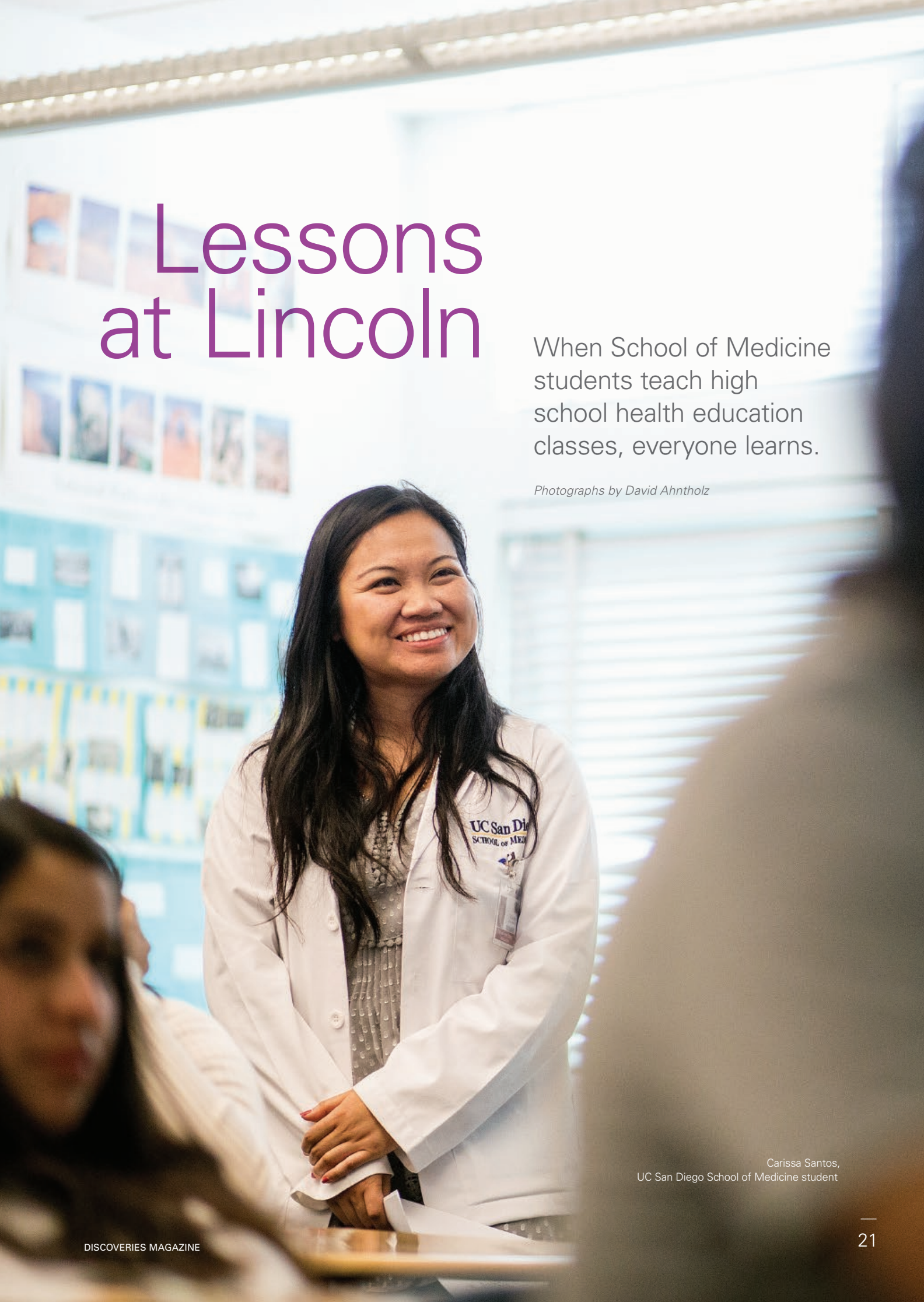
"In the field of epigenomics, we've seen unprecedented growth with no sign of deceleration."

Bing Ren, PhD,
Director, Laboratory of Gene Regulation, Ludwig Cancer Research at UC San Diego

Lessons at Lincoln

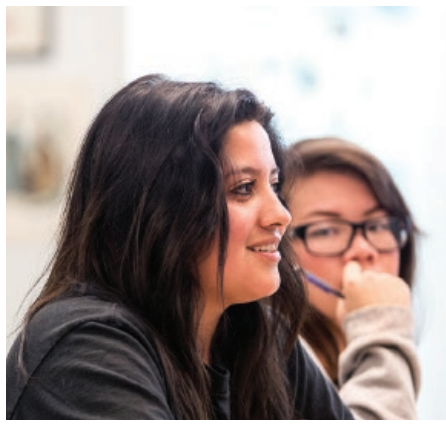
When School of Medicine students teach high school health education classes, everyone learns.

Photographs by David Ahntholz



Carissa Santos,
UC San Diego School of Medicine student

School nurse Kathy Ryan's patient load is made up of 1,400 buzzing Lincoln High School Hornets, whose minds are primarily occupied by exams, sports and date nights. When budget cuts forced the school to end its health education classes, Ryan, who runs the school's Wellness Center, required a remedy.



She knew the students' academic success depended as much upon their physical and emotional well-being as their GPA.

Lincoln High is located in a historically poor and diverse neighborhood of San Diego. Nearly 80 percent of students use the free or reduced-cost school meal program. The surrounding community is underserved in terms of health care.

AN UNMET NEED

Five years ago, Ryan caught the ear of Lindia Willies-Jacobo, MD, assistant dean for diversity and community partnerships at the UC San Diego School of Medicine and director of the Program in Medical Education – Health Equity (PRIME-HEq), an effort to prepare medical students to meet the needs of diverse populations who often don't have adequate access to health care.

"There are pockets in California with shortages of doctors," said Willies-Jacobo. "PRIME came about because of this recognized need to increase the number of doctors in underserved communities."

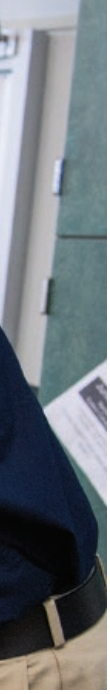
While Ryan lobbied high school officials, Willies-Jacobo, along with Jamie Peterson, a former PRIME-HEq participant, developed the Healthy Minds, Healthy Bodies curriculum and recruited PRIME-HEq students to teach health education at Lincoln High.

The narrow age difference between the high school and college students creates a peer-to-peer rapport that encourages greater communication and a deeper assimilation of the lessons.

Carissa Santos was one of 13 UC San Diego medical students who participated in PRIME-HEq this year. She and classmates spent 20 weeks training for and teaching health education classes at Lincoln on topics ranging from nutrition to substance abuse to sexual relations.

450

Lincoln High School students have participated in health education classes taught by UC San Diego medical school students.



"There are pockets in California with shortages of doctors. PRIME came about because of this recognized need to increase the number of doctors in underserved communities."

Lindia Willies-Jacobo, MD
Assistant Dean for Diversity and Community Partnerships, UC San Diego

CLASS DISCUSSION

It's the last class of the year, and Santos is reading a poem entitled "Maria Wears My Jacket" to spur classroom conversation about healthy relationships. In one stanza of the poem, the narrator proclaims love for Maria, but is infuriated by her actions:

"*Tonight I saw Maria without my jacket. And I screamed and called her a bitch.*"

One student exclaims: "What, he thinks he owns her?!" The class erupts in heated debate. Students opine on what constitutes a healthy relationship, how to create one and how to get out of unhealthy situations.

"It goes both ways," Santos says. "It's the person acting this way and the person receiving the abuse. From the outside, you can see problems in the relationship, but it isn't always easy when you're the person in it."

Another student recalls a friend whose boyfriend is "very controlling." She says she has spoken with her friend, but the other girl insists it's love. "He doesn't let her be who she really is," the teenager concludes, frowning.

Santos and her teaching companions, Ramsey Salem, MPH, and Lue Lao, spend 50 minutes encouraging the teens to evaluate their personal relationships with family and friends. They urge them to speak honestly and frankly.

"What if you can't get away from a bad situation?" a girl wonders aloud.

"The goal is prevention. Stop it before it happens," Salem suggests. "You have to look for the signs before it escalates."

When the bell rings, signaling the end of class, teacher Roberta Dobson says she wishes every student could benefit from these lessons. "It's been very enlightening, and the students appreciate it."

MUTUAL BENEFIT

So too do the UC San Diego students. "I feel I learned so much about adolescent medicine," says Diana Garcia, a first-year medical school student and PRIME-HEq group leader. "We're more equipped to meet the needs of the underserved. We're already serving some of the most marginalized groups. We can't just be good, we have to be great."

Garcia is one of 55 UC San Diego scholars who have participated in the Healthy Minds, Healthy Bodies program, which emphasizes real-life experience and a skill set not found in textbooks. So far, they have helped teach 450 Lincoln High teenagers.

Some PRIME-HEq participants also serve as role models. "Many of these high school kids have never had the thought of becoming a doctor on their radar," says Willies-Jacobo. "When they see that UC San Diego medical students are young, hip and from similar backgrounds, it seems attainable for the very first time."

PRIME programs are offered in all University of California medical schools. PRIME-HEq participants graduate from the five-year program with a medical degree and a master's degree of their choice.

Far Left to right:
UC San Diego student Ramsey Salem, MPH, explains a point while below a Lincoln High student listens. Diana Garcia (top center) says the high school students have taught her too. UC San Diego Assistant Dean Lindia Willies-Jacobo and high school nurse Kathy Ryan collaborated to create the PRIME-HEq program at Lincoln.

The important work of PRIME-HEq and the training of new generations of doctors depend upon the support of volunteers and donors. You can help by visiting meded.ucsd.edu.

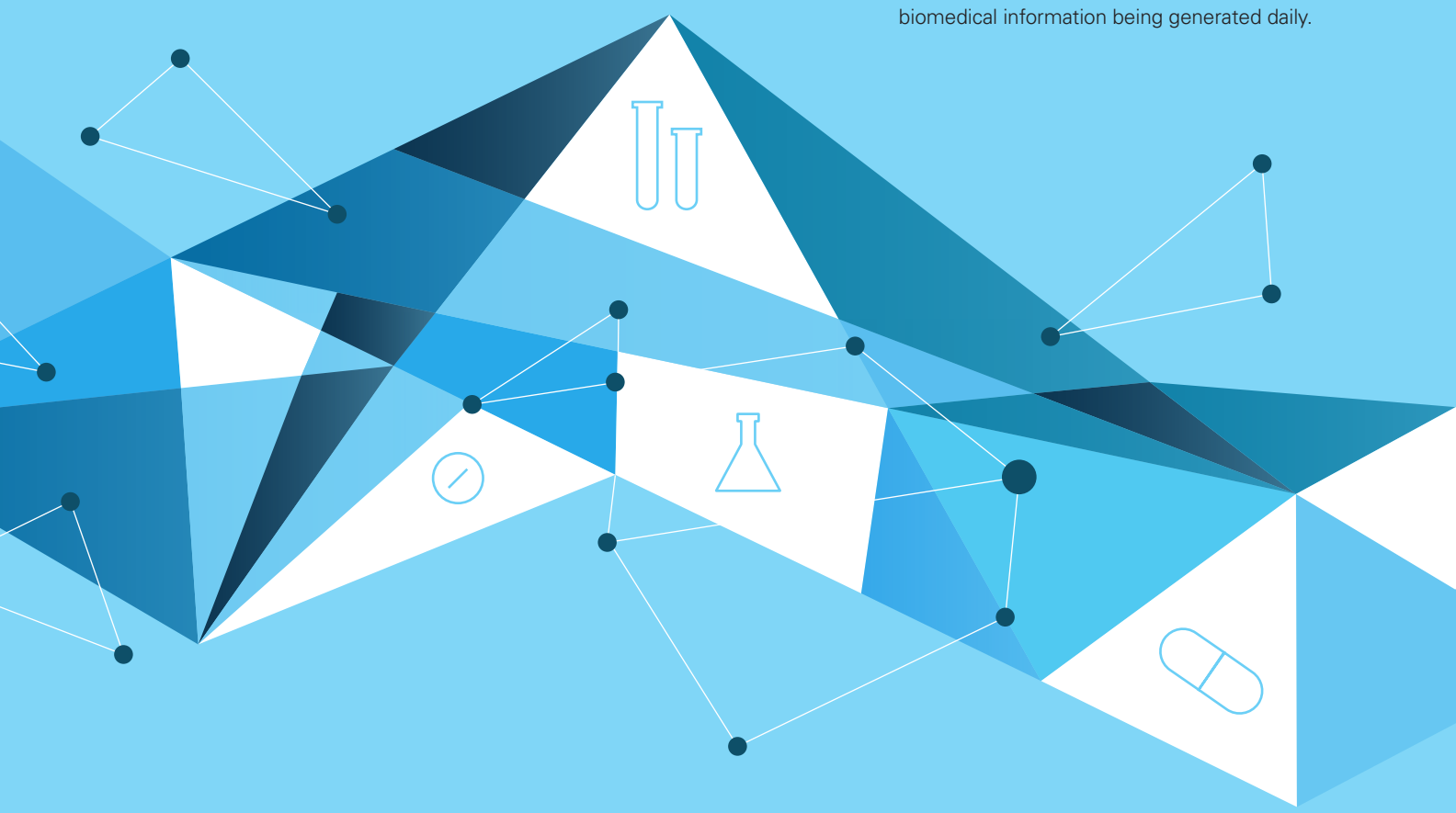
Counting on Big Data

Biomedical informatics is about more than just crunching numbers. It's about translating raw data into real improvements in medicine and health care.

AS MEDICAL SCIENCE MARCHES ONWARD, WITH DISCOVERIES MADE AT SEEMINGLY exponential rates, there comes a corollary conundrum: What do you do with all of that information? How do you collect, manage, maintain, manipulate, analyze and apply this *googolplexian* glob of "big data" in ways that actually translate into improved human health care and longer, better lives?

The answer lies partly in the relatively young, rapidly evolving discipline of biomedical informatics. "It's about converting data into knowledge that doctors can use," said Lucila Ohno-Machado, MD, PhD, professor of medicine and founding chief of the Division of Biomedical Informatics at UC San Diego School of Medicine. "With enough data, things start becoming clearer."

And clarity begins at home. In recent years, UC San Diego has established itself as a leading biomedical informatics center, regionally and beyond. It has received tens of millions of dollars in grants to develop new ways to gather, analyze, use and share the vast and ever-increasing amounts of biomedical information being generated daily.



iDASHing FORWARD

One effort is the ongoing iDASH program, which stands for Integrating Data for Analysis, Anonymization and SHaring. "This is a way to democratize science," said Ohno-Machado. "The idea is to create new systems and methods that give researchers everywhere access to information that can help push science forward by making optimal use of data and algorithms."

IDASH is fueled by "Driving Biological Projects (DBPs)," scientific endeavors in which the effective use of big data can truly impact real-world health issues. At UC San Diego, these DBPs include finding better ways to study Kawasaki disease among African-Americans while protecting their privacy and improving informed consent procedures and data-sharing for low-income, uninsured and under-insured women.

Complementing iDASH is the pSCANNER (patient-centered SCAlable National Network for Effectiveness Research), which makes it easier to integrate data from health care systems – and actual patients – without jeopardizing their privacy and personal rights. PSCANNER and similar efforts allow doctors and researchers to conduct studies that compare, for example, whether a new drug is more effective than an existing one or that measure the value added when a pharmacist participates in therapy management.

"Health care quality depends upon biomedical informatics," said David Chang, PhD, MPH, MBA, director of outcomes research in the Department of Surgery in the School of Medicine. "It's essential to assessing how and why things happen. If, for example, a patient has a bad outcome, was it due to individual factors – maybe the patient was very, very sick – or was it due to other factors related to the system? Quality – and improving quality – is best judged at a population level with big data, where similar patients can be compared and tracked over time and across hospitals."

All five UC medical centers are involved in a pair of collaborative programs, dubbed UC BRAID (Biomedical Research Acceleration, Integration and Development) and UC ReX (UC Research eXchange Data Explorer), that permit researchers to cull through data derived from more than 12 million UC patients served in San Diego, Los Angeles, Irvine, Davis and San Francisco. In the future, data from the Veterans Health Administration will also be connected for privacy-preserving analytics.

Such efforts have not come easily. The first attempts at creating digital health records date back to at least 1961 and a hospital using an IBM Ramac 305 computer, which required a 30-foot-by-50-foot room to house it and boasted data storage equivalent to 64,000 punch cards. Each card represented 125 bytes of information, or roughly 8 megabytes in total. That's maybe two MP3 songs nowadays.

A NUMBERS GAIN

While technology has clearly advanced – modern electronic health records are readily transmittable, for example, and can be read, assessed and addressed by many people in many places, often in real time – there are attendant questions and concerns, though Ohno-Machado said progress is being made here too. For example, she said, it's easier now to de-identify data to preserve patient privacy and to build cyber-secure networks.

That's spurred growth. Five years ago, just 17 percent of doctors nationwide used electronic health records. Last year, the U.S. Department of Health & Human Services reported that more than half of doctors use them, along with an estimated 80 percent of U.S. hospitals.

"Patients want the benefits of greater, better data collection," said Ohno-Machado. "Everybody understands what shared information can do, and so people have high expectations. We've achieved much, but systems are still evolving. Not all of the necessary technologies even exist yet. We're still tweaking and planning for integration of computable genomic data into the electronic health record."

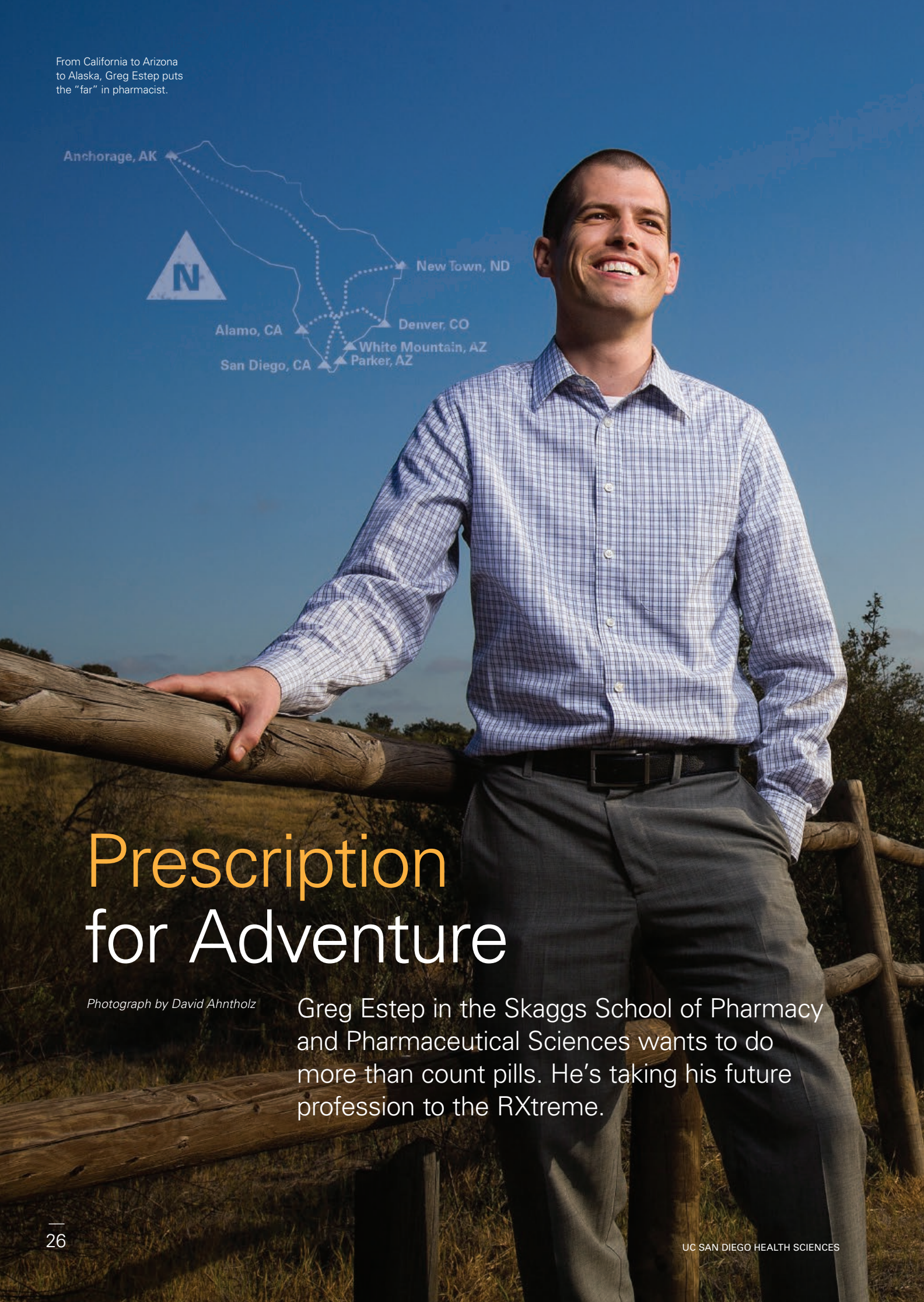
Much about modern medicine depends upon information, including acquiring new and vast amounts of it. Albert Einstein once reportedly said, "Information isn't knowledge." But he would likely agree that knowledge begins with information – and ever-improving ways of making sense of it.

"Patients want the benefits of greater, better data collection."

Lucila Ohno-Machado, MD, PhD, Founding Chief, Division of Biomedical Informatics, UC San Diego

googol

A googol is 10 to the 100th power (1 followed by 100 zeros). A googolplex is 10 to the power of googol: a 1 followed by 10 to the power of 100 zeros. It's estimated that the number of elementary particles in the observable universe is just 10 to the 80th power.



From California to Arizona to Alaska, Greg Estep puts the "far" in pharmacist.

Prescription for Adventure

Photograph by David Ahntholz

Greg Estep in the Skaggs School of Pharmacy and Pharmaceutical Sciences wants to do more than count pills. He's taking his future profession to the RXtreme.

For adventure, some people take trips to distant and exotic places. Others skydive, swim with sharks, hike jungle trails or join the Navy.

Greg Estep became a pharmacist.

GROWING UP IN ALAMO, A SMALL, UNINCORPORATED COMMUNITY BETWEEN the towns of Danville and Walnut Creek in San Francisco's East Bay region, Estep dreamed of seeing the world. After high school, he attended the University of Denver, in no small part for the grand glories of the greater outdoors.

He earned a bachelor's degree in psychology and became…a mortgage broker. "It just sort of happened. I wasn't sure what I really wanted to do, and this was a job. Of course, my timing wasn't great. It was 2006, and the real estate bubble was about to pop."

Estep was laid off, but found a job with a national firm that recruited pharmacists to work where there weren't enough of them. He concedes he didn't initially know much about what pharmacists do. "I thought they basically took pills from big bottles and put them into small bottles. I didn't realize how much patient care they actually did."

It got him thinking. And after listening to a recording by the late motivational speaker Earl Nightingale, it got him to act. "Nightingale said, 'You become what you think about.' That resonated. I slept on it for a weekend, then called my dad (who resides in San Diego) and said I was moving there in two weeks to become a pharmacist."

It wasn't that easy, of course. Estep lacked the academic credentials to enroll at the UC San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences, his first and only choice for pharmacy training. So he began with prerequisite math, biology and chemistry courses at Mesa Community College. In his spare time, he established the first Pre-Med/Pharmacy Club on campus.

Estep successfully entered Skaggs in 2010. He still wanted to see the world. After graduation, he said, "I had this naïve goal of living and working in five different states over five years. Obviously it wasn't practical. I'd need to get five different pharmacy licenses."

A visiting lecturer from the Indian Health Service (IHS), a division of the U.S. Department of Health and Human Services, offered a solution. "She said that if you worked for the federal government providing services to Native Americans on their lands, you just needed one license. Plus, you had a chance to go to lots of places."

There was another enticement as well. Estep is approximately one-quarter Native American, with ties to the Hidatsa people of the Great Plains, primarily in North Dakota. The call seemed to be in his blood.

ARIZONA TO ALASKA

Estep moved quickly to become part of the IHS. Now finishing his final year at Skaggs before residency, Estep has devoted the previous two summers to working as an extern for the IHS on Native American reservations in Arizona. His first summer was spent in Parker, a tiny town on the southwestern edge of the state, where he served the surrounding Colorado River Indian tribes, many in remote locations.

"People really have no idea of what it's like on some of these reservations," Estep said. "It's pretty damn bad, close to Third World. Some communities can only be reached by plane, boat or mule. Some homes have no running water, indoor plumbing or electricity. Dogs and donkeys roam the streets."

But there is medical care, he noted proudly, and most locals embrace it. As did Estep, who said he was able to work directly with residents, "doing lots of tests, counseling, helping with surgeries."

In his second summer externship, Estep served on the other side of Arizona in the White Mountain Apache Reservation. "It's a beautiful place. There's sort of a mini-Grand Canyon there, but things are even more spread out and people are even more self-determining."

The IHS clinic at White Mountain was larger, more like a hospital, and Estep was able to experience even more real-life medical situations, including helping staff the overnight emergency room. "You see a different sort of patient at 2 a.m.," he said wryly.

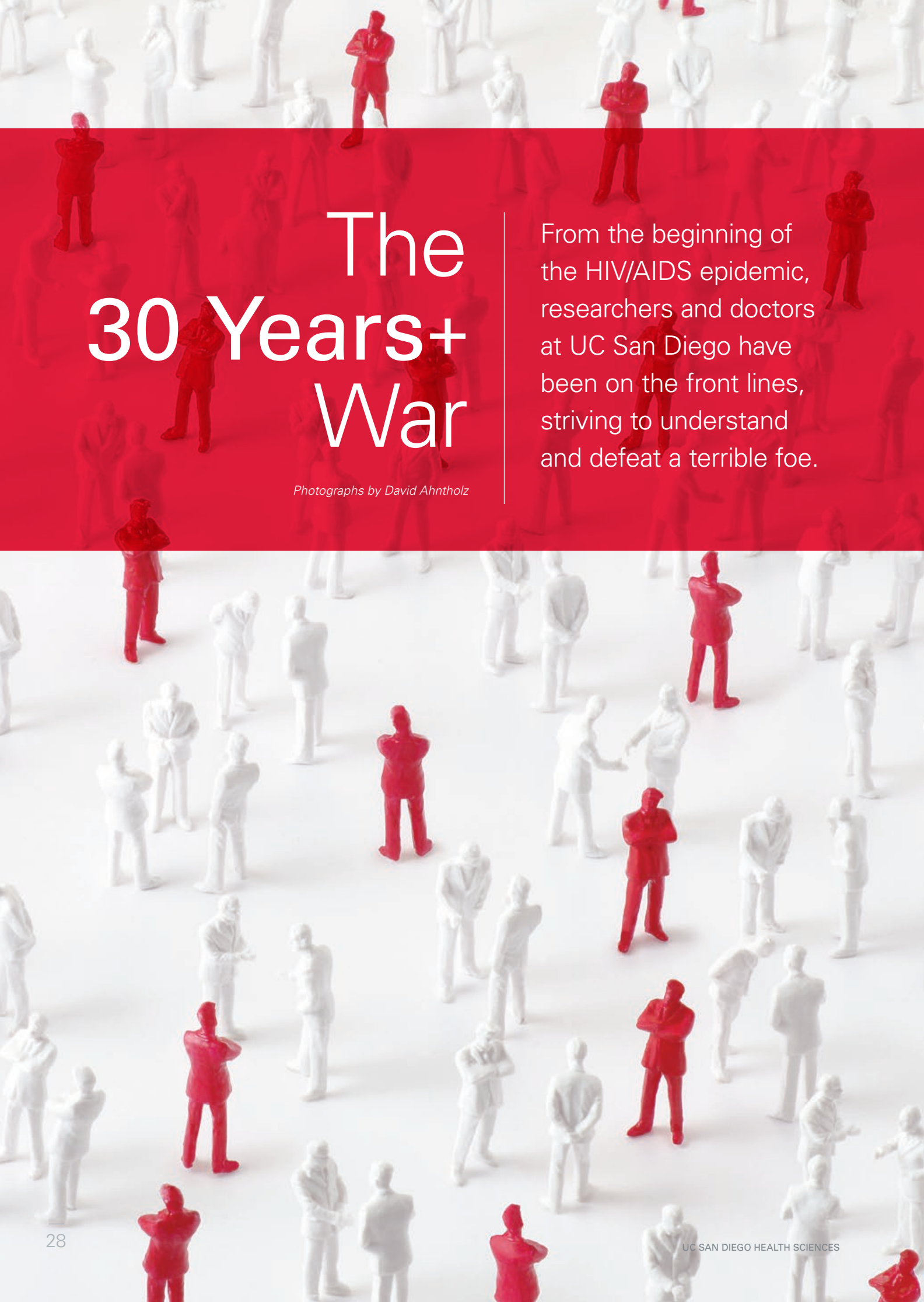
Estep's next stop is Anchorage, Alaska, where later this year he will begin a one-year residency at the local IHS hospital. "I'll also have a chance to conduct Arctic research with the U.S. Centers for Disease Control and Prevention. I'm not sure what that means, but it sounds extremely challenging."

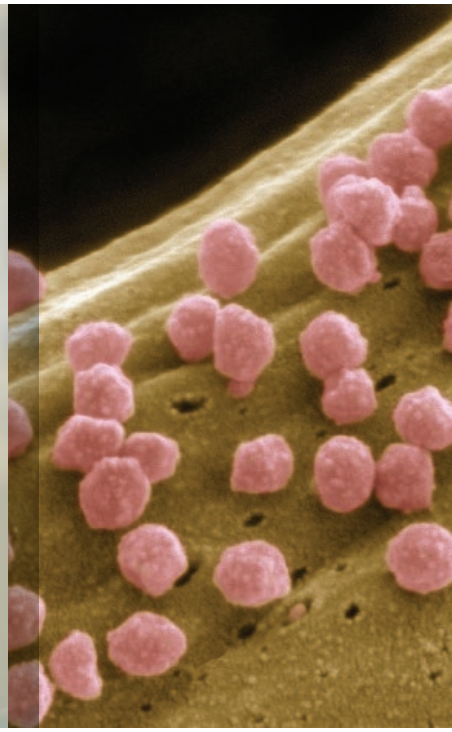
It sounds extremely perfect.

The 30 Years+ War

Photographs by David Ahntholz

From the beginning of the HIV/AIDS epidemic, researchers and doctors at UC San Diego have been on the front lines, striving to understand and defeat a terrible foe.





Left to right:
Douglas Richman, MD, has been studying the HIV virus for more than three decades. A scanning electron micrograph of HIV particles on the surface of a cell. Image courtesy of Thomas Deerinck and Mark Ellisman, National Center for Microscopy and Imaging Research, UC San Diego.

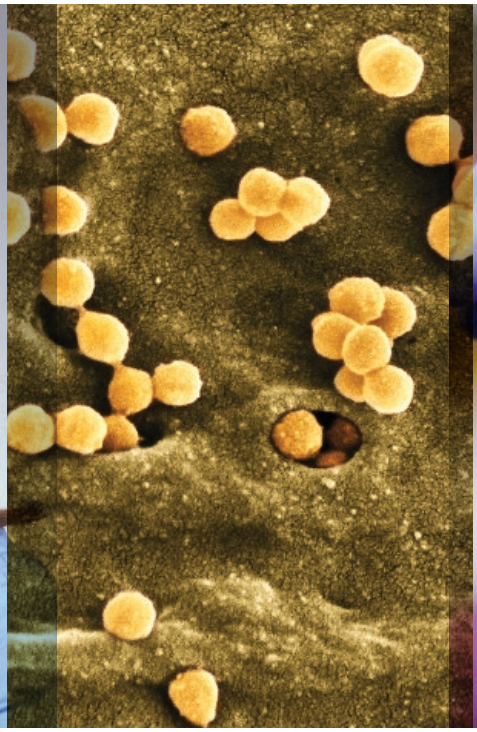
In 1981, Douglas Richman, MD, was an assistant professor operating a diagnostic virology laboratory at UC San Diego School of Medicine. His interests were primarily influenza and herpes, but that year, physicians in Los Angeles and elsewhere began reporting cases of healthy, young homosexual men dying from a type of pneumonia primarily limited to people with severely suppressed immune systems, such as cancer patients undergoing chemotherapy. Soon, similar men were discovered to be living – and dying – in San Diego.

It was the beginning of the AIDS epidemic.

"THE APPEARANCE OF THESE STRANGELY AFFLICTED PATIENTS WOULD CHANGE MY LIFE AND CAREER," RECALLED RICHMAN, now Distinguished Professor of Pathology and Medicine and the Florence Seeley Riford Chair in AIDS Research. "Those early years were hard. There were no treatments for HIV itself, and therapies for infections that complicated AIDS were difficult and often relatively ineffective."

In San Diego, HIV/AIDS patients were frequently referred to the renowned Owen Clinic at UC San Diego Medical Center in Hillcrest, founded and directed by Christopher Matthews, MD, or to the San Diego Veterans Affairs Medical Center Special Infectious Diseases Clinic in La Jolla.

"Within six months of becoming ill," said Richman, "my colleagues and I knew that at least half of these men with HIV would likely be dead. It was hugely disheartening. We felt like battlefield doctors with the sick and dying coming in faster than we could treat them, if we could treat them at all."



"HIV has no passport. Fighting it is about raising awareness, changing the social and environmental conditions that make some people more vulnerable to HIV, and getting lifesaving medicines to those who need them."

Steffanie Strathdee, PhD
Director, UC San Diego
Global Health Initiative

Please support current and future HIV/AIDS research and clinical services by contacting UC San Diego Health Sciences Development at 858-822-4562 or emailing giving@futureofcare.com.

It's a different and better story now. While HIV/AIDS remains a great threat to human health, it's not quite the dreaded killer it once was. With early detection and appropriate therapies, HIV/AIDS can be reduced to the status of a chronic disease, or a treatable condition like diabetes or arthritis.

How this happened is a credit to thousands of doctors and scientists around the world. Many live in San Diego, and most work at UC San Diego. Their scientific and medical contributions have often proved crucial to both better understanding the nature of HIV/AIDS and to finding effective ways to fight it.

For example, it was basic research at UC San Diego that helped overcome the problem of drug resistance, said Robert Schooley, MD, chief of the Division of Infectious Diseases in the School of Medicine.

"It became clear that if three drugs of different types were used simultaneously, the virus could be suppressed indefinitely in the majority of patients," Schooley said. "This radically changed the prognosis for those with an HIV infection. Many people who would have died in a matter of months returned to near full health, rejoining their families, the workforce and society."

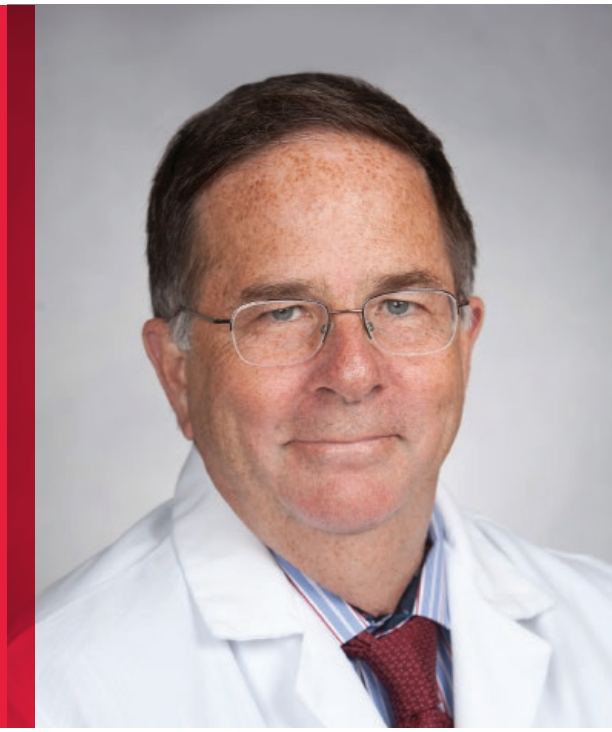
FIGHTING ON MULTIPLE FRONTS

Collaboration has been a hallmark of local HIV/AIDS research, and UC San Diego has provided multiple homes and programs for scientists and doctors to do their good work. For example, Constance Benson, MD, is director of the AntiViral Research Center at UC San Diego and a veteran leader in the National Institutes of Health's largest clinical trials consortium, which includes HIV/AIDS research sites in 22 countries.

The Center for AIDS Research, directed by Richman, is celebrating its 20th anniversary. It conducts basic research and development of vaccines and therapies for HIV infections and associated diseases. The HIV Neurobehavioral Research Program, directed by Igor Grant, MD, pursues the causes and treatments of neurologic complications of HIV infection. And the AIDS Research Institute, established by University of California Regents in 1996, coordinates diverse research, treatment and education activities at UC San Diego and in the community at large.

"We must remain fully committed to efforts to consolidate the gains we have made….If treatment programs are neglected, HIV-related morbidity and mortality will inevitably increase. Drug-resistant viruses will emerge, and it will be early days once again."

Robert Schooley, MD
Chief, Division of Infectious Diseases, UC San Diego School of Medicine



Left to right:
Steffanie Strathdee, PhD; HIV particles; testing lab samples; Robert Schooley, MD.

48%

Since the AIDS epidemic began, the World Health Organization says almost 75 million people worldwide have been infected with the HIV virus, and nearly 36 million – just under half – have died of HIV-related causes.

With progress have come new challenges. Among the largest is delivering effective therapies to infected patients, particularly in parts of the world where vital resources remain insufficient, said John Guatelli, MD, a professor of medicine in the Division of Infectious Diseases and an HIV/AIDS research veteran.

A GLOBAL EFFORT

UC San Diego faculty in the Division of Global Public Health, headed by Steffanie Strathdee, PhD, are helping remedy that situation by developing prevention and treatment programs in countries as diverse as Mexico, India and Guatemala. "HIV has no passport," Strathdee said. "Fighting it is about raising awareness, changing the social and environmental conditions that make some people more vulnerable to HIV and getting lifesaving medicines to those who need them."

In terms of basic research, Schooley said, some focus has shifted from developing new drugs that suppress patient viral loads "to learning how to eliminate all virus-infected cells from the body."

That's a task more daunting than just stopping the virus from killing, and Schooley cautions that an HIV vaccine breakthrough isn't likely for years. But Guatelli notes that HIV/AIDS science has significantly matured. Scientists know a lot about the virus now, and they have more weapons to fight it. Recently, for example, they uncovered previously unknown defenses used by the body, which Guatelli said could provide new ways to think about prevention and cure.

But perhaps the largest challenge is simply fighting the fight, observed Schooley.

"It's complacency. We must remain fully committed to efforts to consolidate the gains we have made. Major reductions in morbidity and mortality have led to a sense of complacency about HIV prevention and to a loss of interest in continuing to improve the quality and expansion of treatment efforts. If treatment programs are neglected, HIV-related morbidity and mortality will inevitably increase. Drug-resistant viruses will emerge, and it will be early days once again."

Scientists and doctors at UC San Diego are determined not to let that happen. For them, the fight continues. The band will play on until, perhaps, the scourge of HIV/AIDS no longer exists.

Highlights

2014

1. NEW SKAGGS SCHOOL DEAN

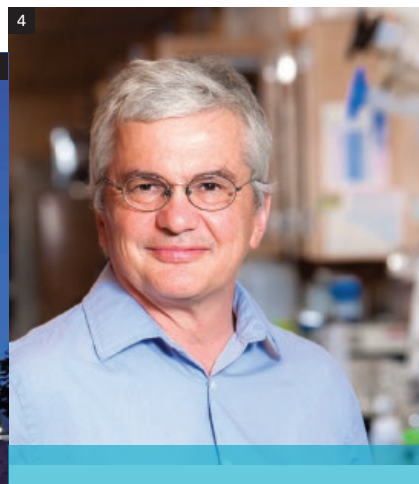
James H. McKerrow, MD, PhD, became the second dean of the UC San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences on July 1, succeeding Palmer Taylor, PhD. McKerrow, who earned his MD at SUNY, Stony Brook and his doctorate in biology at UC San Diego, is a noted expert in tropical diseases. Previously, he was professor of pathology and director of the Center for Discovery and Innovation in Parasitic Diseases at UC San Francisco.

3. TAYLOR HONORED BY FRANCE

Palmer Taylor, PhD, founding dean of the Skaggs School of Pharmacy and Pharmaceutical Sciences, was officially awarded the rank of "Chevalier dans l'Ordre National de la Légion d'Honneur" (Knight in the National Order of the Legion of Honor) for his commitment to international research. The Legion of Honor is France's highest national decoration, recognizing individuals who have contributed significantly to the development of relationships with France.


1


8


4

2. MCC/ VENTER GENOME SEQUENCING DEAL

A novel collaborative research agreement was announced between UC San Diego and Human Longevity, Inc., a company co-founded by genome sequencing pioneer and UC San Diego alumnus J. Craig Venter, PhD. The agreement will initially focus on cancer, with faculty at UC San Diego Moores Cancer Center developing protocols and procedures to conduct comprehensive genomic sequencing of consenting Moores Cancer Center patients. The resulting data would be used to develop and accelerate genome-based research and treatments.

4. FERRARA RECEIVES GAIRDNER AWARD

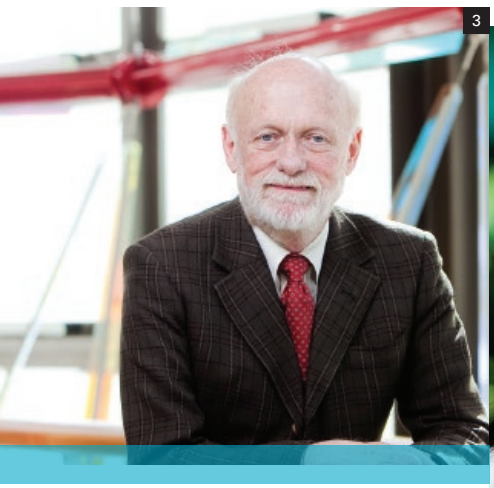
Napoleone Ferrara, MD, Distinguished Professor of Pathology and senior deputy director for basic sciences at UC San Diego Moores Cancer Center, received a Canada Gairdner Award, the nation's most esteemed honor in medical and life sciences. Ferrara was recognized for his work identifying the role of the human VEGF gene in promoting angiogenesis and development of two major drugs for treating cancer and wet age-related macular degeneration.

5. $6.5 MILLION GIFT FOR SHILEY EYE CENTER

A $6.5 million grant from a grateful patient will create the Richard C. Atkinson Laboratory for Regenerative Ophthalmology at UC San Diego Shiley Eye Center, headed by Robert N. Weinreb, MD. The new lab will investigate stem cell replacement therapies, tissue engineering and other biomedical advances to reverse vision loss and blindness.

8. BIOMEDICAL RESEARCH FACILITY OPENING

The Biomedical Research Facility 2 building, a seven-story, 196,000-square-foot edifice, opened its doors. The $113 million building is designed to encourage collaboration among scientists working in multiple, diverse departments and programs. It features distinctive open spaces, numerous laboratories and conference rooms, and LEED Platinum certification.


3


10


9

6. HEALTHGRADES' TOP HOSPITALS

UC San Diego Health System received Healthgrades' "Distinguished Hospital Award for Clinical Excellence," an honor bestowed only upon the top 5 percent of hospitals in the United States. The award is based on clinical excellence across a broad spectrum of care in specialty areas, such as cardiac surgery, gastrointestinal, neurosurgery, pulmonary and critical care.

7. BECKER'S REVIEW GREATEST HOSPITALS

Becker's Hospital Review named the UC San Diego Medical Center in Hillcrest one of "100 Great Hospitals in America," based on original research, nominations and evaluations by other hospital ranking sources.

9. JESTE APPOINTMENT

Dilip V. Jeste, MD, Distinguished Professor of Psychiatry and Neurosciences, was named the first associate dean for healthy aging and senior care at UC San Diego and will direct the new Center on Healthy Aging and Senior Care, which will study a broad range of issues related to aging – and doing it well.

10. PRESIDENTIAL PRIZE FOR NGUYEN

Quyen T. Nguyen, MD, PhD, associate professor of head and neck surgery and director of the Facial Nerve Clinic, received a Presidential Early Career Award, the highest honor bestowed by U.S. government on science and engineering professionals in the early stages of their independent research careers.

David A. Brenner, MD
Vice Chancellor,
Health Sciences and
Dean, School of Medicine

Paul S. Viviano
CEO, UC San Diego
Health System

Kim Kennedy
Executive Director,
Marketing and Communications

Executive Editor
Scott LaFee

Senior Writer
Jacqueline Carr

Contributors
Michelle Brubaker
Yadira Galindo
Debra Kain

Cover Image
Sebastian Eichelbaum
Mario Hlawitschka
Gerik Scheuermann

Publication Design
Traina Design

UC San Diego Health Sciences comprises one of the nation's top research-intensive schools of medicine; the Skaggs School of Pharmacy and Pharmaceutical Sciences; and UC San Diego Health System, the region's only academic health system.

discoveries.ucsd.edu

UC San Diego
HEALTH SCIENCES